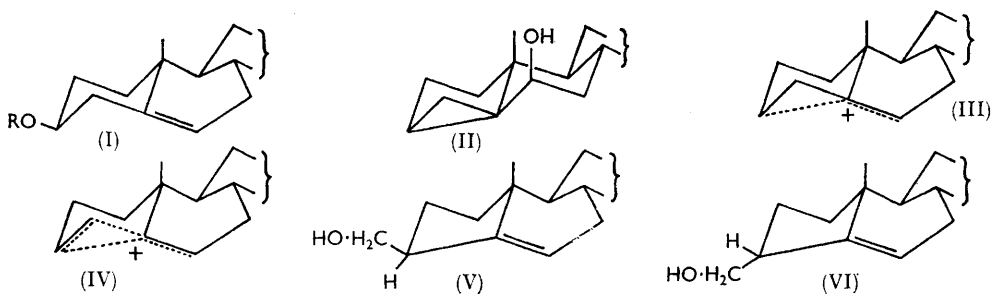
326. *Solvolysis of the Toluene*-p-*sulphonates of* 3β- *and* 3α-*Hydroxymethyl*-A-*norcholest*-5-*ene.*

By G. H. Whitham and (in part) J. A. F. Wickramasinghe.

Solvolysis of the toluene-*p*-sulphonate of 3β-hydroxymethyl-A-norcholest-5-ene gives the same alcohols, in the same proportions, as those obtained from cholesteryl toluene-*p*-sulphonate. In contrast, the toluene-*p*-sulphonate of 3α-hydroxymethyl-A-norcholest-5-ene affords 3β,5-cyclo-5β-cholestan-6β-ol, together with the parent alcohol. The two A-nor-systems can, therefore, have no cationic intermediates in common. The bearing of these results on the mechanism of the cyclo-sterol rearrangement is discussed.[1]

A considerable amount of work has been devoted towards an understanding of the processes involved in the conversion of derivatives of cholesterol (I; R = H),* *e.g.*, the toluene-*p*-sulphonate (I; R = *p*-Me·C_6H_4·SO_2), into 3α,5-cyclo-5α-cholestan-6β-ol (II) (the cyclo-sterol rearrangement [2]). Strong evidence that the double bond of cholesteryl toluene-*p*-sulphonate assists in the rate-determining ionisation is provided by the fact that, at 50°, it undergoes acetolysis 120 times faster than 5α-cholestan-3β-yl toluene-*p*-sulphonate. This has been explained in terms of the formation of an intermediate non-classical cation.† Thus, the transition state for formation of the intermediate is considered to be stabilised by overlap between the π-orbital of the double bond and the developing vacant orbital at C-3. Two possible non-classical cations have been envisaged, *viz.*, the " unsymmetrical ion " (III) involving only delocalisation of the π-electrons of the



double bond, and the " symmetrical ion " (IV) which implies additional delocalisation of the σ-electrons of the C-4–C-5 bond.[2] In an attempt to decide between these two possibilities, and to gain further information about related cationic intermediates, we investigated the solvolyses of the toluene-*p*-sulphonates of the epimeric A-nor-alcohols (V) and (VI).

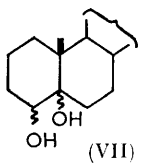
3β-Hydroxymethyl-A-norcholest-5-ene (V) is not described in the literature, and was synthesised as follows. Hydroxylation of cholest-4-ene with osmium tetroxide gave a mixture of two glycols (VII); the major isomer is presumably 5α-cholestane-4α-,5α-diol and the minor one 5β-cholestane-4β,5β-diol, though no attempt was made to verify these assignments. Cleavage of either glycol with lead tetra-acetate gave the keto-aldehyde (VIII), which was cyclised directly to the unsaturated aldehyde (IX) using hydrochloric

* Three-dimensional formulæ will be used where necessary, to avoid the designation of α-bonds with dotted lines. Dotted lines will be reserved to indicate partial bonds in non-classical intermediates and transition states.

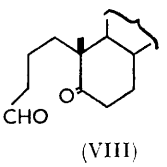
† There seem to be no steric ambiguities of the type discussed by H. C. Brown [3] in this system, so that replacement of the non-classical cation by an equilibrating set of classical ions would render it very difficult to understand the rate difference, particularly since the sp^3-hybridised C-5 would be expected inductively to destabilise a classical cholesteryl cation.

[1] Preliminary communications: Whitham, *Proc. Chem. Soc.*, 1961, 422; 1962, 330.
[2] Winstein and Kosower, *J. Amer. Chem. Soc.*, 1959, **81**, 4399, and references cited there.
[3] Brown, " The Transition State," *Chem. Soc. Special Publ.* No. 16, 1962, p. 140.

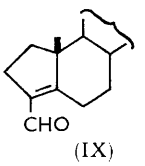
acid in acetic acid. Treatment of (IX) with isopropenyl acetate and mineral acid gave an enol acetate (X), which was reduced, using sodium borohydride in aqueous ethanol,[4] to the alcohol (V). This compound was a homoallylic alcohol, as indicated by its non-identity with the allylic alcohol (XI) derived by lithium aluminium hydride reduction of the aldehyde (IX). Further confirmation of the gross structure of (V) was given by its negative rotation, $[\alpha]_D$ −26°, in contrast to the positive rotation of (XI), $[\alpha]_D$ +57°, cf. cholesterol, $[\alpha]_D$ −39°,[5] and cholest-4-en-3β-ol, $[\alpha]_D$ +45°.[6] That the homoallylic alcohol has the stereochemistry shown, with a 3β-hydroxymethyl group, was strongly indicated



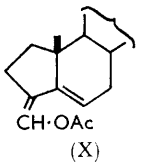
(VII)



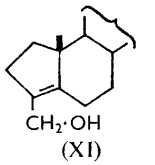
(VIII)



(IX)



(X)



(XI)

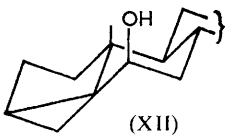
by its method of formation. It is probable that the reduction of the enol acetate (X) proceeds by initial generation of the enolate ion, kinetically controlled protonation of this at C-3, and immediate reduction of the resulting βγ-unsaturated aldehyde. In the protonation step, attack should occur from the less-hindered side α to the C-19 methyl group, to give a 3β-formyl group. Further confirmation of the stereochemistry of (V) comes from the solvolyses discussed below.

3α-Hydroxymethyl-A-norcholest-5-ene (VI) was obtained by the procedure of Dauben and Ross.[7] The solvolyses to be described here have a bearing on the method of formation of (VI), and this will, therefore, be discussed later.

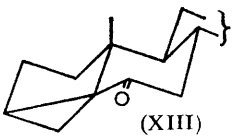
Results and Discussion

The toluene-*p*-sulphonate of 3β-hydroxymethyl-A-norcholest-5-ene was solvolysed in aqueous acetone, buffered with potassium acetate. The product comprised an alcohol fraction (85%), which was shown to consist of 3α,5-cyclo-5α-cholestan-6β-ol (II) (82%) and cholesterol (I; R = H) (18%), together with small amounts of acetates which were not investigated. No hydrocarbons were formed. The composition of the alcohol fraction was identical, within experimental error, with that derived from cholesteryl toluene-*p*-sulphonate under the same conditions. In the latter case, however, 1—2% of cholesta-3,5-diene was also produced, in addition to acetates.

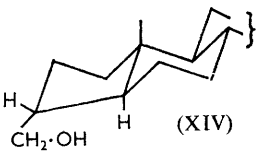
The toluene-*p*-sulphonate of 3α-hydroxymethyl-A-norcholest-5-ene (VI) was solvolysed under the same conditions. Again no hydrocarbon was obtained, and, besides small amounts of acetates, the alcohol fraction contained two components, *viz.*, the original homoallylic alcohol (IV) (11%) and a new isomeric alcohol (89%). The latter was a 3β,5-cyclo-5β-cholestan-6-ol (XII), as indicated by (i) reconversion into the parent alcohol (VI) on heating with aqueous mineral acid, and (ii) oxidation with pyridine–chromium



(XII)



(XIII)



(XIV)

trioxide to the saturated ketone (XIII), $\nu_{max.}$ 1710 cm.$^{-1}$. The 6β-orientation of the hydroxyl group in the cyclo-alcohol (XII) is assigned on the basis of later considerations.

First-order rate constants (10^6k at 50°) for acetolysis of the toluene-*p*-sulphonates of

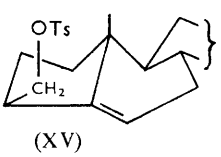
[4] Belleau and Gallagher, *J. Amer. Chem. Soc.*, 1951, **73**, 4458; Dauben and Eastham, *ibid.*, 4463.
[5] Fieser and Fieser, "Steroids," Reinhold, New York, 1959, p. 28.
[6] Ref. 5, p. 260.

the two homoallylic alcohols (V) and (VI) were determined in the usual way, and are 56 and 87 sec.$^{-1}$, respectively; that for the corresponding derivative of 3α-hydroxymethyl-A-nor-5α-cholestane (XIV) [7] is 1·3 (extrapolated). The rate of acetolysis of the toluene-*p*-sulphonate of (XIV) is rather high, being about twenty times that [8] of the toluene-*p*-sulphonate of cyclopentylmethanol at 80°. The reason for this is being investigated, but it appears to be mainly steric in origin. In any event, it seems clear that there should be no additional steric factors present in the toluene-*p*-sulphonates of (V) and (VI) which could lead to a further rate enhancement of the magnitude of that observed.

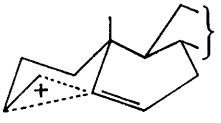
The A/B *trans*-geometry of the saturated alcohol (XIV) obtained by hydrogenation of the homoallylic alcohol (VI) is assigned tentatively on the basis of catalyst approach from the α-side of the molecule. It is recognised that this deduction is not necessarily valid, and experiments are in progress to define the stereochemistry of this compound.

The increased rate of acetolysis of the toluene-*p*-sulphonate (XV) compared with that for the toluene-*p*-sulphonate of alcohol (XIV) strongly indicates that π-electron participation occurs in the rate-determining ionisation. Thus, a simple Wagner–Meerwein migration of the 3,5-bond, *i.e.*, (XV) ⟶ (XVI) ⟶ (XVII), leading to a classical cholesteryl cation, may be discounted at the outset.

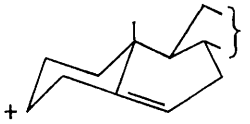
Two possible representations of the initial cationic species, resulting from π-electron participation in the ionisation of the toluene-*p*-sulphonate (XV), are the unsymmetrical ion (XVIII), in which the positive charge is shared between C-4 and C-6, and the symmetrical ion (IV), involving further delocalisation. However the nature of the solvolysis products from (XV) indicates that the product-determining intermediate ion cannot be (XVIII), but is more likely to be (III) or (IV). Two different pathways for the formation of products from the toluene-*p*-sulphonate (XV) should, therefore, be considered: (XV) ⟶ (XVIII) ⟶ (III) ⟶ products; and (XV) ⟶ (IV) ⟶ products. The former route requires the qualifying assumption that the rate of rearrangement of (XVIII) to (III) is much faster than the rate of reaction of (XVIII) with the solvent. The second



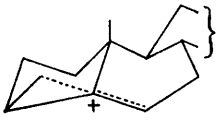
(XV)



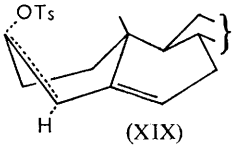
(XVI)



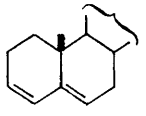
(XVII)



(XVIII)



(XIX)


(XX)

route, however, seems to be the more satisfactory interpretation, since it does not require any qualifying assumption of this sort. The symmetrical cation (IV) is unique in being readily derivable from the A-nor-system (XV), or the cholesteryl system (I), or the 3α,5-cyclo-5α-cholestan-6-yl system, with only little electronic reorganisation. Winstein and Kosower [9] demonstrated that 3α,5-cyclo-5α-cholestan-6β- and -6α-yl derivatives lead, on solvolysis, to essentially the same mixture of cholesterol and cyclocholestanol as obtained from cholesteryl toluene-*p*-sulphonate. In our opinion, the simplest explanation for the identity of the alcohol products from all three types of precursor is that (IV) is the common cationic intermediate. This view is strengthened by results on the solvolysis of the methanesulphonate of 4α-methylcholesterol,[10] where a rate enhancement of about twenty

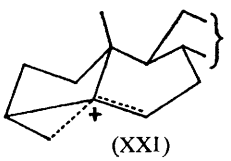
[7] Dauben and Ross, *J. Amer. Chem. Soc.*, 1959, **81**, 6521.
[8] Whitham and Wickramasinghe, unpublished work.
[9] Winstein and Kosower, *J. Amer. Chem. Soc.*, 1956, **78**, 4347.
[10] Pathak and Whitham, unpublished work.

times, with respect to the cholesteryl derivative, is observed even though the products are analogous to those in the cholesteryl case.

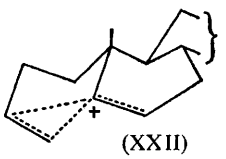
An additional point requiring comment is the origin of the cholesta-3,5-diene formed in the solvolysis of cholesteryl toluene-*p*-sulphonate. If the above hypothesis is correct, this cannot have originated from the cholesteryl cation (IV). Related work on 4-methylated derivatives of cholesterol [10] strongly suggests that the diene is derived by an alternative mode of reaction, probably involving a ring-A boat or twist conformation of cholesteryl toluene-*p*-sulphonate, *i.e.*, (XIX) ⟶ (XX). This interpretation is consistent with the absence of cholesta-3,5-diene in the solvolysis products from the toluene-*p*-sulphonate of the alcohol (V) or from derivatives of 3α,5-cyclocholestan-6-ol.[9]

In the solvolysis of the toluene-*p*-sulphonate of 3α-hydroxymethyl-A-norcholest-5-ene (VI), no products are formed in common with those from cholesteryl toluene-*p*-sulphonate. The cationic intermediate (or intermediates) involved in the two processes are, therefore, quite distinct. Again, the enhanced rate of acetolysis of the toluene-*p*-sulphonate of the homoallylic alcohol (VI), relative to that of the saturated alcohol (XIV), indicates π-electron participation in the rate-determining ionisation. This leads to the cations (XXI, unsymmetrical) and (XXII, symmetrical) as two possible intermediates, analogous to (XVIII) and (IV) in the cholesteryl system. In the present case, however, the unsymmetrical ion (XXI) appears to lead to the more satisfactory explanation for the formation of the alcohols (VI) and (XII) by co-ordination of water at C-4 and C-6, respectively. The symmetrical ion (XXII) would surely lead to the formation of some cholesterol by co-ordination at C-3, since this is an unhindered secondary position. This argument is not completely satisfactory, and it remains possible that the symmetrical cation may be involved but, owing to unforseen steric and electronic factors, reaction at C-3 occurs to a negligible extent only. Thus, the unsymmetrical structure is preferred since there is at present no evidence which appears to favour the symmetrical structure.

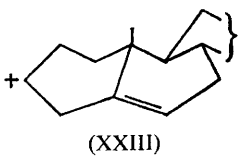
Structure (XXII) implies, in resonance terminology, a contribution from the canonical (XXIII) which is a cholesteryl cation with a boat A-ring. The higher energy of the latter, relative to the cholesteryl cation with a chair A-ring, which is implied as a contributor to the ion (IV), may be a reason for the apparent barrier to the formation of (XXII) from (XXI).



(XXI)

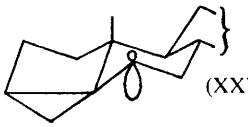


(XXII)



(XXIII)

(XXIV)

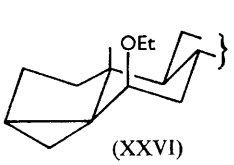


(XXV)

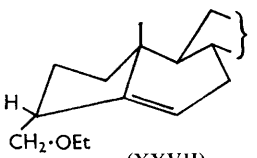
Accepting (XXI) as a satisfactory representation for the cationic intermediate in the solvolysis of the toluene-*p*-sulphonate of the 3α-alcohol (VI), it should be considered whether this leads to a prediction of the stereochemistry of the single cyclo-alcohol formed in the reaction. Formulæ (XXIV) and (XXV) for the two possible extreme forms, with the vacant orbital (sp^3-hybridisation) localised on C-6, show that only in (XXIV) is the orbital correctly placed, parallel to the plane of the cyclopropane ring, for favourable overlap with the pseudo-π-system of cyclopropane. In (XXV) the vacant orbital is almost at ring angles to the cyclopropane ring. (XXIV) is, therefore, the probable structure of the cation at the instant of reaction with a nucleophile at C-6, thus leading to a 6β-orientation of the entering group.

The aqueous acid-catalysed rearrangement of the 3β,5-cyclo-5β-cholestan-6β-ol to the parent homoallylic alcohol (VI) is a thermodynamically controlled process closely analogous to the rearrangement of 3α,5-cyclo-5α-cholestan-6β-ol to cholesterol. Generation of the cation (XXI) by fission of the protonated form of the cycloalcohol (XII) is followed by partition of the cation into the cycloalcohol (XII) and the homoallylic alcohol (VI), as before. Repeated formation of the cation (XXI) leads eventually to complete conversion into the thermodynamically more stable alcohol (VI). The conversion of the ether (XXVI) into the homoallylic alcohol [7] (VI) is interpreted similarly.

The above discussion has a bearing on the photochemical transformation of cholesta-3,5-diene (XX) into 3β,5-cyclo-5β-cholestan-6-yl ethyl ether (XXVI) on irradiation in ethanol.[7,11] The recent experiments of Dauben and Willey [11] provide strong evidence that the primary photoproduct is a highly strained hexacyclic hydrocarbon, which reacts with ethanol to give the ether (XXVI) together with small amounts of the A-nor-ether (XXVII). Structure (XXVIII) has been suggested for this hydrocarbon. Our solvolytic experiments indicate that the reaction of the hydrocarbon (XXVIII) with ethanol involves protonation at C-4 leading directly to the cation (XXI). Co-ordination of the latter with ethanol would give the two ethers. In agreement with this, we have shown than ethanolysis of the toluene-*p*-sulphonate of the alcohol (VII) under buffered conditions leads to a similar mixture of ethers.



(XXVI)



(XXVII)

(XXVIII)

(XXIX)

The formation of a carbonium ion by solvolysis of a strained hydrocarbon is paralleled by the reaction of " quadricyclene " (XXIX) with acetic acid.[12] In the latter case, however, the ratio of *exo*-norbornenyl and nortricyclenyl acetates formed is rather different from that formed by acetolysis of *exo*-norbornenyl or nortricyclenyl bromobenzenesulphonates.

Experimental

Thin-layer chromatograms were on silica gel " G " and were developed by spraying with a mixture of anisaldehyde (6 drops) and concentrated sulphuric acid (6 drops) in ethanol (10 ml.), then heating at 120° for 10 min. Optical rotations are for chloroform solutions. Light petroleum had b. p. 40—60°.

Hydroxylation of Cholest-4-ene.—Cholest-4-ene [13] (2·04 g.) in dry ether (40 ml.) containing dry pyridine (2·5 ml.) was treated with osmium tetroxide (1·4 g.) in dry ether (20 ml.). The solution was set aside at 25° for 3 days, and evaporated to dryness; the residue was dissolved in chloroform (100 ml.), and the solution was shaken with a solution of potassium hydroxide (20 g.) and mannitol (20 g.) in water (200 ml.) until the chloroform layer was nearly colourless (5 hr.). The chloroform layer was washed with water until free from alkali, dried, and evaporated. The residue (2·31 g.) was chromatographed on alumina (activity III), giving cholest-4-ene (100 mg.), cholestane-4β,5β-diol (?), eluted with benzene and benzene–ether (19 : 1), plates (0·33 g.) from methanol, m. p. 141—142°, $[\alpha]_D$ +16° (*c* 1·5), and cholestane-4α,5α-diol (?), eluted with benzene–ether (17 : 3), needles (1·57 g.) from methanol, m. p. 139—141°, $[\alpha]_D$ +23° (*c* 2·2). The mixed m. p. of the two glycols was 129—134° (lit.,[14] m. p. 135° for " cholestane-4α,5α-diol ").

[11] Dauben and Willey, *Tetrahedron Letters*, 1962, **20**, 893.
[12] Dauben and Cargill, *Tetrahedron*, 1961, **15**, 197.
[13] Ireland, Wrigley, and Young, *J. Amer. Chem. Soc.*, 1958, **80**, 4604.
[14] Jones, Lewis, Shoppee, and Summers, *J.*, 1955, 2876.

3β-*Hydroxymethyl*-A-*norcholest*-5-*ene*.—Cholestane-4α,5α-diol (1·45 g.) in dry benzene (50 ml.), was treated at 20° with lead tetra-acetate (2·8 g.) After 30 min., water was added, and the mixture was shaken to destroy the excess of lead tetra-acetate. The precipitated lead dioxide was filtered off, and the benzene layer was separated, dried, and evaporated. The residual oil (1·5 g.) exhibited infrared bands (in CS_2) at 2720 and 1707 (CHO), and 1725 $cm.^{-1}$ (C=O). Attempts at purification resulted in decomposition, and the crude keto-aldehyde was cyclised directly using hydrochloric acid in acetic acid (1%) at 100° for 30 min. After evaporation of most of the acetic acid under reduced pressure, water was added and the product was isolated with ether as an oil (1·39 g.) which showed one spot on thin-layer chromatography, R_F (in benzene) 0·40.

On one occasion the unsaturated aldehyde was purified by chromatography on alumina (activity III), and was obtained as needles, m. p. 70·5—72·5° (from ethanol). However, the recovery was low and the aldehyde was readily oxidised in air, so that the crude material was usually used directly for the next stage.

The crude aldehyde (1·39 g.), in isopropenyl acetate (75 ml.) and concentrated sulphuric acid (3 drops), was heated under reflux for 2 hr. After distillation of most of the isopropenyl acetate, water was added and the product was isolated with ether. The ether extract was washed with aqueous sodium hydrogen carbonate, dried, and evaporated, and the residue was azeotropically distilled with benzene to remove residual isopropenyl acetate. The brown residue, in benzene (50 ml.), was filtered through a short column of silica gel and the column was washed with benzene (50 ml.). Evaporation of the filtrate and washings left a pale yellow gum (1·31 g.) which showed one spot on thin-layer chromatography, R_F (in benzene) 0·82.

The enol acetate was dissolved in ethanol (50 ml.), a small amount of insoluble yellow gum was discarded, and the solution was added during 2 hr. to a stirred solution of sodium borohydride (2 g.) in aqueous ethanol (95%; 15 ml.) at 0°. After 16 hr. at 20° most of the ethanol was removed by distillation, water was added, and the product was isolated with ether as a yellow oil (1·2 g.), which was chromatographed on a column of alumina (50 g.; activity III). Elution with light petroleum–benzene (1 : 1) gave the *homoallylic alcohol* as plates (260 mg.), m. p. 99—101° (from methanol), $[\alpha]_D$ −26° (*c* 1·56), one spot on thin-layer chromatography, R_F (in benzene) 0·18 (Found: C, 83·4; H, 11·85. $C_{27}H_{46}O$ requires C, 83·85; H, 12·0%).

The toluene-*p*-sulphonate, prepared from the alcohol (200 mg.), toluene-*p*-sulphonyl chloride (360 mg.), and dry pyridine (3 ml.), was filtered, in benzene, through a column of alumina (activity I). Evaporation of the benzene and crystallisation of the residue from light petroleum gave feathery needles, m. p. 89—92°.

3-*Hydroxymethyl*-A-*norcholest*-3-*ene*.—Cholestane-4α,5α-diol (220 mg.) was converted as before into the crude αβ-unsaturated aldehyde (IX). The latter, in dry ether (30 ml.), was heated under reflux with lithium aluminium hydride (100 mg.) for 30 min. After addition of water and aqueous Rochelle salt, the ether layer was separated and dried. Evaporation gave an oil which was filtered, in benzene, through a short column of alumina (activity III). Crystallisation from methanol gave the *allylic alcohol* as stout needles, m. p. 116—118°, $[\alpha]_D$ +57°, one spot on thin-layer chromatography, R_F (in benzene) 0·17 (Found: C, 83·5; H, 11·6. $C_{27}H_{46}O$ requires C, 83·85; H, 12·0%).

3α-*Hydroxymethyl*-A-*norcholest*-5-*ene*.—This was prepared according to the method of Dauben and Ross,[7] and chromatographed on silica gel. It crystallised in felted needles from aqueous acetone, and had m. p. 100—101·5° with partial solidification and remelting at 104—105°, $[\alpha]_D$ −45° (*c* 1·4) (lit.,[7] m. p. 102—103°, $[\alpha]_D$ −45°). Mixed m. p. with 3β-hydroxymethyl-A-norcholest-5-ene was 95—99·5°; the two isomeric alcohols had identical mobilities on thin-layer chromatography.

The toluene-*p*-sulphonate, obtained as before, could not be crystallised; it separated from light petroleum as a gelatinous mass which gave an amorphous solid on drying in high vacuum at room temperature. The infinity titre on acetolysis showed it to be 98% pure.

*Preparative Solvolysis of the Toluene-*p*-sulphonate of* 3β-*Hydroxymethyl*-A-*norcholest*-5-*ene*.—The toluene-*p*-sulphonate (150 mg.), in acetone (8 ml.) and water (2 ml.) containing potassium acetate (200 mg.), was heated under reflux for 16 hr. After evaporation of the acetone, the product was isolated with ether as an oil. Thin-layer chromatography in benzene showed a medium spot at R_F 0·78 (acetates), a strong spot at R_F 0·28 (3α,5-cyclo-5α-cholestan-6β-ol), and a medium spot at R_F 0·08 (cholesterol). No trace of the parent alcohol was detected. The oil was dissolved in light petroleum (3 ml.) and adsorbed on to a column of alumina (activity I;

10 g.). Elution with light petroleum (100 ml.) gave no material, *i.e.*, hydrocarbons absent, elution with benzene (100 ml.) gave an oil (10·2 mg.), $\nu_{max.}$ (in CCl_4) 1740 and 1240 cm.$^{-1}$ (O·COMe). Elution with chloroform (200 ml.) gave an oil (90·6 mg.) shown by thin-layer chromatography to contain only two components (R_F in benzene 0·28 and 0·08) with the mobilities of cyclocholesterol and cholesterol, respectively. The latter oil had $[\alpha]_D$ +35·1°, indicating that it contained 83% of 3α,5-cyclo-5α-cholestan-6β-ol and 17% of cholesterol (cholesterol has $[\alpha]_D$ −39° and 3α,5-cyclo-5α-cholestan-6β-ol has $[\alpha]_D$ +50·4°).

A portion of the alcohol mixture was rechromatographed on alumina (activity I). Elution with ether gave an oil which crystallised on cooling an acetone solution and scratching with a glass rod. The product had m. p. 64—66°, undepressed on admixture with an authentic sample of 3α,5-cyclo-5α-cholestan-6β-ol. The infrared spectra of the two samples (in CS_2) were identical. Elution with chloroform, evaporation, and crystallisation of the residue from acetone gave cholesterol, identified by m. p., mixed m. p., and infrared spectrum.

Preparative Solvolysis of Cholesteryl Toluene-p-*sulphonate*.—A preparative solvolysis of cholesteryl toluene-*p*-sulphonate was carried out as above. In this case, the alcohol fraction had $[\alpha]_D$ +34·3°, indicating the composition, 3α,5-cyclo-5α-cholestan-6β-ol (82%) and cholesterol (18%).

Preparative Solvolysis of the Toluene-p-*sulphonate of* 3α-*Hydroxymethyl*-A-*norcholest*-5-*ene*.—(*a*) The toluene-*p*-sulphonate (300 mg.) was solvolysed, as above, in acetone (8 ml.), water (2 ml.), and potassium acetate (300 mg.). The oily product, on thin-layer chromatography, showed two spots R_F (in benzene) 0·38, 0·24 (identical with starting homoallylic alcohol), and a diffuse spot, R_F 0·7, attributed to acetates. No hydrocarbons were present. Chromatography on silica gel and elution with light petroleum–benzene (3 : 2) gave an oil (15 mg., infrared bands for O·COMe), and further elution with light petroleum–benzene (2 : 3) and (3 : 7) gave 3β,5-*cyclo*-5β-*cholestan*-6β-*ol* (110 mg.) as needles, m. p. 98—100·5° (from aqueous acetone), $[\alpha]_D$ +22·5°, which showed one spot on thin-layer chromatography, R_F 0·38 (in benzene) (Found: C, 83·55; H, 12·0. $C_{27}H_{46}O$ requires C, 83·85; H, 12·0%). Further elution afforded oily fractions, shown by thin-layer chromatography to be mixtures of the two alcohols.

(*b*) To determine the composition of the alcohol fraction a sample of the toluene-*p*-sulphonate (62 mg.) was solvolysed as above, and the total alcohol fraction (43 mg.), shown by thin-layer chromatography to contain only the cyclo-alcohol and the homoallylic alcohol, was isolated by chromatography. It had $[\alpha]_D$ +15·4° corresponding to 89% of cyclo-alcohol and 11% of homoallylic alcohol.

Rearrangement of 3β,5-*Cyclo*-5β-*cholestan*-6β-*ol with Acid*.—The alcohol (5 mg.), in acetone (5 ml.) containing aqueous sulphuric acid (1%; 5 drops), was heated under reflux for 30 min. After addition of water the precipitate was filtered off and dissolved in light petroleum. The solution was filtered through a short column of silica gel and the filtrate was discarded. Elution with ether, evaporation of the eluate, and crystallisation of the residue from aqueous acetone gave 3α-hydroxymethyl-A-norcholest-5-ene, identical with an authentic specimen (m. p., mixed m. p., and thin-layer chromatography).

3β,5-*Cyclo*-5β-*cholestan*-6-*one*.—The cyclo-alcohol, (XII) (60 mg.), in pyridine (5 ml.), was added to pyridine–chromium trioxide (500 mg.) and pyridine (5 ml.). After 16 hr. at 15°, water was added, and the oily product, isolated with ether, was dissolved in benzene and filtered through a short column of silica gel. Evaporation of the filtrate and crystallisation of the residue from methanol gave the *ketone* as plates, m. p. 109—110°, $[\alpha]_D$ +80° (*c* 1·5) (Found: C, 84·45; H, 11·0. $C_{27}H_{44}O$ requires C, 84·3; H, 11·5%).

Ethanolysis of the Toluene-p-*sulphonate of* 3α-*Hydroxymethyl*-A-*norcholest*-5-*ene*.—The toluene-*p*-sulphonate (31 mg.), potassium acetate (50 mg.), and dry ethanol (20 ml.) were heated under reflux for 30 hr. After removal of most of the ethanol, water was added and the product was isolated with ether. It showed two components on thin-layer chromatography in light petroleum; the major one, R_F 0·2, was identical with the ethyl ether (XXVI), and the minor one, R_F 0·1, was presumably the ethyl ether (XXVII). Adsorption on a column of silica gel and elution with light petroleum–benzene (17 : 3) gave crystalline material (23 mg.), m. p. 88—91° (from ethanol), showing only one spot on thin-layer chromatography, R_F (in light petroleum) 0·2, identical (mixed m. p. and infrared spectrum) with the ethyl ether (XXVI).

Rate Determinations.—Rates of acetolysis of the toluene-*p*-sulphonates in acetic acid containing a small amount of acetic anhydride were determined by titration against sodium acetate in acetic acid using Bromophenol Blue as indicator. Owing to the relatively small

quantities of the toluene-*p*-sulphonates available, only a few readings could be obtained. In each case the rate constant quoted is the average of three or four values taken at various times. No obvious trends were noted.

We thank Professor M. Stacey, F.R.S., for encouragement.

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM 15.

[*Received, September* 16*th*, 1963.]