640. *Steroids and Walden Inversion. Part XLVIII.* The Solvolysis of Some 3-Epimeric 4,4-Dimethyl-steroid Toluene-p-sulphonates.*

By C. W. Shoppee and G. A. R. Johnston.

Solvolysis of the 3-epimeric 4,4,14α-trimethyl-5α-cholest-8-en-3-yl and 4,4-dimethyl-5α-cholestan-3-yl toluene-*p*-sulphonates gives the expected rearranged tertiary alcohols and hydrocarbons, accompanied in each case by the unrearranged alcohol (or acetate) with retained configuration. No unrearranged alcohol (or acetate) with inverted configuration was found.

The solvolyses proceed by unimolecular heterolysis, at rates only slightly greater than that, under comparable conditions, of cyclohexyl toluene-*p*-sulphonate, so that synartetic acceleration is absent.

The structural and kinetic features of the solvolyses are discussed, and a mechanism to accommodate them is suggested.

The occurrence of nucleophilic molecular rearrangement in saturated systems requires fulfilment of two conditions: (1) an initial bond fission to give an electron-deficient centre, and (2) a decrease in free energy. In rigid cyclohexane systems, the rate and the product(s) of rearrangement depend also on the geometry of the original system. Thus solvolysis of isobornyl chloride (Cl equatorial) to yield products of the camphene series is faster by a factor of 10^5 than that of bornyl chloride (Cl axial) to give the same products,[1,2] whilst the acid-catalysed dehydration with acetic anhydride of *exo*-methylnopinol (OH equatorial) furnishes isobornyl acetate, whereas *endo*-methylnopinol (OH axial) affords α-fenchyl acetate.[3]

Solvolytic reactions of suitable steroid derivatives do not normally lead to ring contraction: † $^+CHR{-}CH_2R \longrightarrow CHR_2{-}CH_2^+$, because the free-energy change is in the wrong direction. Only 1β- and 12β-substituted steroids, where the substituent is equatorial and adjacent to a bridgehead, can comply with the thermodynamic condition (2): $^+CHR{-}CMeR_2 \longrightarrow CHR_2{-}{}^+CMeR$; in 4α-, 6α-, 7β-, and 11α-substituted steroids, although the substituent is equatorial and adjacent to a bridgehead, the thermodynamic situation is one of approximate balance: $^+CHR{-}CHR_2 \rightleftharpoons R_2CH{-}{}^+CHR$. Accordingly, alcoholysis of the 12β-toluene-*p*-sulphonate or 12β-methanesulphonate of rockogenin (3β,12β-dihydroxy-5α,20α,22β,25β-isospirostane) yields a C-nor-D-homo-steroid,[6] and we expect to realise the transformation of an appropriate steroid 1β-alcohol into an A-nor-B-homo-steroid.

4,4-Dimethyl-5α-steroids can fulfil the thermodynamic condition (2), and appropriate 3β-substituted derivatives should undergo solvolysis to give A-nor-steroids, whilst the epimeric 3α-substituted derivatives should undergo solvolysis, without contraction of ring A but with migration of the 4β-methyl group. We have observed such changes in solvolyses of the 3-epimeric 4,4,14α-trimethyl-5α-cholest-8-en-3-yl (lanost-8-en-3-yl) and 4,4-dimethyl-5α-cholestan-3-yl toluene-*p*-sulphonates.

4,4,14α-Trimethyl-5α-cholest-8-en-3β-yl toluene-*p*-sulphonate (as I) in refluxing aqueous acetone in the presence of sodium acetate gave the 3β-alcohol (as II; R = H) (5%) (unaccompanied by the epimeric 3α-alcohol), the tertiary A-nor-alcohol (as III; R = H) (22%), and the derived A-nor-5α-cholest-8-ene (as IV) (72%) (which appeared to be

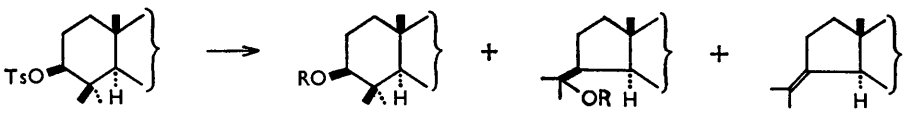
* Part XLVII, *J.*, 1961, 1583.

† The Favorski reaction applied to 5α- and 5β-cholestan-3-one leads to A-nor-5α- and A-nor-5β-cholestane derivatives,[4] but is considered to involve fission of an intermediate cyclopropanone.[5]

[1] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell and Sons Ltd., London, 1953, p. 515.
[2] Shoppee, *Chem. and Ind.*, 1952, 86.
[3] Burrows and Eastman, *J. Amer. Chem. Soc.*, 1959, **81**, 245.
[4] Evans, Paulet, Shoppee, and Winternitz, *J.*, 1957, 1451.
[5] Loftfield, *J. Amer. Chem. Soc.*, 1950, **72**, 632; 1951, **73**, 4707.
[6] Hirschmann, Snoddy, Hiskey, and Wendler, *J. Amer. Chem. Soc.*, 1954, **76**, 4013; cf. Wendler, Hirschmann, Slates, and Walker, *ibid.*, 1955, **77**, 1632.

homogeneous and free from the isopropenyl and endocyclic isomerides); dehydration of the tertiary A-nor-alcohol with phosphoryl chloride and pyridine gave the same hydrocarbon. Heating the same ester with acetic acid in the presence or absence of anhydrous sodium acetate at 95° gave the 3β-acetate (as II; R = Ac) (8%) [unaccompanied by the epimeric 3α-acetate or the tertiary acetate (as III; R = Ac)] and the A-nor-5α-cholest-8-ene (as IV) (90%); possibly the poor nucleophilic power of the acetate ion is responsible for the absence of the tertiary acetate (as III; R = Ac), the cationic precursor of which co-ordinates with an acetate ion less rapidly than it eliminates a proton to afford the hydrocarbon (as IV).

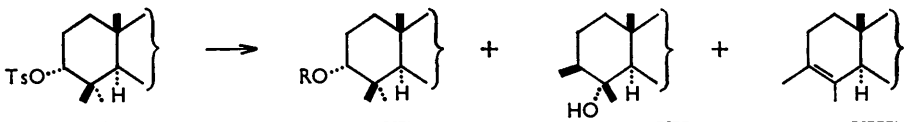
4,4-Dimethyl-5α-cholestan-3β-yl toluene-*p*-sulphonate (I) in refluxing aqueous acetone in the presence of sodium acetate afforded the 3β-alcohol (II; R = H) (5%), the tertiary



(I) (II) (III) (IV)

alcohol (III; R = H) (24%), and an apparently homogeneous A-nor-5α-cholestane (IV) (70%). The hydrocarbon (IV) was also obtained from 4,4-dimethyl-5α-cholestan-3β-ol (II; R = H) by dehydration with phosphorus pentachloride, and from the tertiary alcohol (III; R = H) by dehydration with phosphoryl chloride in pyridine. Use of acetic acid in the presence of anhydrous sodium acetate gave the 3β-acetate (II; R = Ac) (10%) and the A-nor-5α-cholestane (IV) (88%).

Since our work began, experimental analogies have become available. Moriarty and Wallis [7] established that in aqueous acetone 4,4-dimethylcholest-5-en-3β-yl toluene-*p*-sulphonate (cf. I) afforded the Δ^5-analogues of compounds (II; R = H), (III; R = H), and (IV with double-bond isomerides) in yields of 7·5%, 22·5%, and 70%, respectively. Haddad and Summers,[8] by the same reaction, obtained the Δ^5-analogue of (II; R = H) (16%), an isomeric alcohol, m. p. 126°, $[\alpha]_D$ −25° (24%) {which they regarded as 4,4-dimethyl-3,5-cyclocholestan-6β-ol though it is identical with the Δ^5-analogue of (III; R = H), m. p. 125—126°, $[\alpha]_D$ −22°, of Moriarty and Wallis}, and the Δ^5-analogue of (IV) (60%). Haddad and Summers also examined the acetolysis of 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3β-yl toluene-*p*-sulphonate (cf. I), which gave the $\Delta^{8,24}$-analogues of



(V) (VI) (VII) (VIII)

Ts = *p*-C_6H_4Me·SO_2.

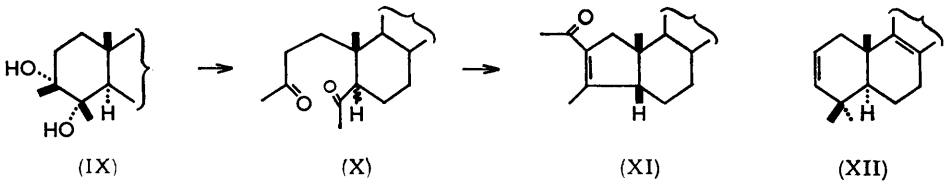
(II; R = Ac) and (IV) in 19% and 82% yield, respectively. Biellmann and Ourisson,[9] heating 4,4-dimethyl-5α-cholestan-3β-yl toluene-*p*-sulphonate (I) in aqueous acetone in the presence of calcium carbonate, obtained the A-nor-alcohol (III; R = H) (whose structure and configuration at positions 3 and 5 they proved by an unambiguous partial synthesis), and the A-nor-5α-cholestane (IV). Lastly, Atwater,[10] by methanolysis of 17β-acetoxy-4,4-dimethylandrost-5-en-3β-yl toluene-*p*-sulphonate (cf. I) in the presence of potassium acetate, obtained the corresponding 3β-alcohol (as II) (11%), the tertiary methyl ether (as III; R = Me) (29%), and the A-nor-5α-androstane (as IV), together with (probably) the isopropenyl and endocyclic isomerides (38%).

[7] Moriarty and Wallis, *J. Org. Chem.*, 1959, **24**, 1274, 1987.
[8] Haddad and Summers, *J.*, 1959, 769.
[9] Biellmann and Ourisson, *Bull. Soc. chim. France*, 1960, 348.
[10] Atwater, *J. Amer. Chem. Soc.*, 1960, **82**, 2847.

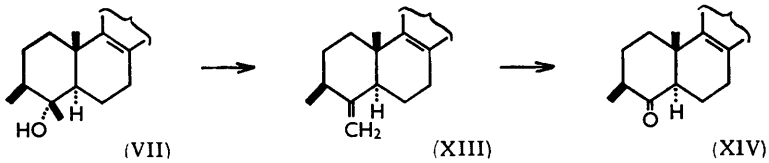
4,4,14α-Trimethyl-5α-cholest-8-en-3α-yl toluene-*p*-sulphonate (as V) in refluxing aqueous acetone in the presence of sodium acetate gave the 3α-alcohol (as VI; R = H) (7%), the tertiary alcohol (VII) (15%), and 3,4,14α-trimethyl-5α-cholesta-3,8-diene (as VIII) (75%). Acetolysis in the presence or absence of anhydrous sodium acetate in acetic acid at 95° gave the 3α-acetate (as VI; R = Ac) (17%) and the same diene (81%).

The structure of 3,4,14α-trimethyl-5α-cholesta-3,8-diene (as VIII) was proved by conversion with osmium tetroxide into the 3α,4α-glycol (as IX), which was oxidised with periodic acid to the 3,4-seco-3,4-diketone (as X), this being cyclized by aluminium oxide [11] to 2-acetyl-3,14α-dimethyl-A-nor-5β-cholesta-2,8-diene (as XI). The spectral characteristics of this compound, $\lambda_{max.}$ 1665 cm.$^{-1}$, $\nu_{max.}$ 260 mμ, and analogy with 1-acetyl-2-methylcyclopent-1-ene,[12] $\nu_{max.}$ 260 mμ, strongly support the αβ-unsaturated ketonic structure assigned (XI). Configuration at position 5 is indeterminate in the diketone (X) and regarded as β in the final product (XI).

Surprisingly, ionic dehydration of 4,4,14α-trimethyl-5α-cholest-8-en-3α-ol (as VI; R = H) with a wide variety of reagents failed to give the 3,8-diene (as VIII), and furnished



(IX) (X) (XI) (XII)



(VII) (XIII) (XIV)

in each case the isomeric 4,4,14α-trimethyl-5α-cholesta-2,8-diene [13] (XII). The 3β,4β-dimethyl-4α-hydroxy-structure (as VII) given to the tertiary alcoholic product of the solvolysis is that predicted on mechanistic grounds (see below); the equatorial 4α-hydroxyl group is supported by non-acetylation with acetic anhydride–pyridine (one week) and dehydration with phosphoryl chloride–pyridine to the 4-methylene compound (XIII), $\nu_{max.}$ (in CS_2) 885 cm.$^{-1}$, which on ozonolysis gives formaldehyde and a carbonyl compound (XIV), which could not be characterised satisfactorily. E. R. H. Jones and his colleagues [11] reported the formation of a 3-methylene compound from a 3α,4α-dimethyl-3β-hydroxy-steroid, with a tertiary equatorial hydroxyl group, by dehydration with phosphoryl chloride and pyridine.

4,4-Dimethyl-5α-cholestan-3α-yl toluene-*p*-sulphonate (as V), on solvolysis in buffered aqueous acetone, gave the 3α-alcohol (as VI; R = H) (10%), the tertiary alcohol 4α-alcohol (as VII) (15%), and 3,4-dimethyl-5α-cholest-3-ene [11] (as VIII) (72%). Acetolysis in the presence of anhydrous sodium acetate in acetic acid at 95° gave the corresponding 3α-acetate (as VI; as R = Ac) (19%) and the same hydrocarbon (VIII) (80%).

The most striking structural feature of the foregoing solvolyses is the absence of inverted unrearranged products, in contrast to the usual course of nucleophilic substitution at position 3 in saturated steroids.[14]

A kinetic study of the acetolyses of the 3-epimeric 4,4,14α-trimethyl-5α-cholest-8-en-3-yl and 4,4-dimethyl-5α-cholestan-3-yl toluene-*p*-sulphonates has been made. Selected results are given in Tables 1 and 2.

[11] Beton, Halsall, Jones, and Phillips, *J.*, 1957, 753.
[12] Schubert and Sweeney, *J. Amer. Chem. Soc.*, 1955, **77**, 2297.
[13] McGhie, Palmer, and Rosenberger, *Chem. and Ind.*, 1959, 1221.
[14] Shoppee, *J.*, 1946, 1138; Shoppee and Westcott, *J.*, 1955, 1891.

TABLE 1. *Acetolysis of* 3-*epimeric* 4,4,14α-*trimethyl*-5α-*cholest*-8-*en*-3-*yl toluene*-p-*sulphonates in anhydrous acetic acid at* 50°.

3β (a = 8·89 × 10^{-5} mole l.$^{-1}$)				3α (a = 4·37 × 10^{-5} mole l.$^{-1}$)			
Time (min.)	10^5x	log $a/(a-x)$	10^4k (min.$^{-1}$)	Time (min.)	10^5x	log $a/(a-x)$	10^4k (min.$^{-1}$)
360	0·60	0·0303	1·93	383	0·70	0·0758	4·56
1200	1·87	0·1026	1·96	845	1·41	0·1692	4·56
1290	1·99	0·1101	1·96	1035	1·65	0·2059	4·58
1930	2·84	0·1671	1·99	1320	1·95	0·2569	4·49
2850	3·86	0·2473	1·99	1455	2·10	0·2845	4·50
3500	4·45	0·3015	1·98	1895	2·50	0·3687	4·48
4000	4·90	0·3479	2·00	2230	2·78	0·4381	4·53
5000	5·60	0·4317	1·99	2380	2·86	0·4615	4·44
6000	6·21	0·5208	2·00	2744	3·08	0·5299	4·45

TABLE 2. *Acetolysis of* 3-*epimeric* 4,4-*dimethyl*-5α-*cholestan*-3-*yl toluene*-p-*sulphonates in anhydrous acetic acid at* 50°.

3β (a = 4·79 × 10^{-5} mole l.$^{-1}$)				3α (a = 2·53 × 10^{-5} mole l.$^{-1}$)			
Time (min.)	10^5x	log $a/(a-x)$	10^4k (min.$^{-1}$)	Time (min.)	10^5x	log $a/(a-x)$	10^4k (min.$^{-1}$)
407	0·89	0·0859	4·86	160	0·37	0·0686	9·87
644	1·32	0·1344	4·81	239	0·53	0·1021	9·85
933	1·78	0·1931	4·78	304	0·65	0·1289	9·78
1225	2·19	0·2530	4·75	379	0·78	0·1601	9·73
1510	2·53	0·3099	4·72	460	0·91	0·1946	9·75
1750	2·81	0·3631	4·78	543	1·04	0·2299	9·76
1970	3·03	0·4099	4·81	754	1·32	0·3203	9·78
2240	3·26	0·4651	4·79	805	1·59	0·4300	9·77
2575	3·43	0·5108	4·78	1255	1·75	0·5210	9·78

Each run was found to be kinetically of the first order, giving by use of the integrated first-order rate expression $k_1 = (1/t) \ln [a/(a-x)]$ the average specific rate constants summarised in Table 3. The increased rate in the presence of added acetate ions is of the order of magnitude expected from solvent and ionic-strength effects in acetic acid; moreover, the small increase in rate found in the presence of added lithium perchlorate

TABLE 3. *Acetolysis of* 3-*epimeric* 4,4,14α-*trimethyl*-5α-*cholest*-8-*en*-3-*yl toluene*-p-*sulphonates in acetic acid in the presence of added solutes at* 60°.

Added solute: nature		None	NaOAc		$LiClO_4$		H_2O
	concn. (M)	—	0·019	0·038	0·020	0·039	0·020
10^4k_1 (min.$^{-1}$):	3β (0·019M)	7·4	12·2	12·7	13·5	14·2	12·8
	3α (0·008M)	16·1	26·3	27·4	28·5	29·6	25·2

TABLE 4. *Acetolysis of* 4,4,14α-*trimethyl*-5α-*cholest*-8-*en*-3-*yl* (A) *and* 4,4-*dimethyl*-5α-*cholestan*-3-*yl toluene*-p-*sulphonates* (B) *in acetic acid at* 50° *and* 60°.

	3β-A	3α-A	3β-B	3α-B
10^4k_1 (min.$^{-1}$) at 50°	2·0	4·5	4·8	9·8
10^4k_1 (min.$^{-1}$) at 60°	7·4	16·1	17·1	34·2
E_A (kcal. mole^{-1})	27·4	27·2	27·2	26·7
$\Delta H^{\ddagger}$ (kcal. mole^{-1})	26·6	26·1	26·1	25·6
$\Delta S^{\ddagger}$ (kcal. mole^{-1} deg.$^{-1}$)	−1·1	−1·0	−1·0	−1·1

TABLE 5. *Acetolysis of toluene*-p-*sulphonates in acetic acid at* 50°.

	Cyclohexyl [15,16]	Cholest-5-en-3β-yl *	Cholest-5-en-3α-yl [17]	4,4-Dimethylcholest-5-en-3β-yl [8]
10^4k_1 (min.$^{-1}$) at 50°	1·1	75·79	15·3	960
E_A (kcal. mole^{-1})	27·9	25·0	25·2	—
$\Delta H^{\ddagger}$ (kcal. mole^{-1})	27·0	24·4	24·6	—
$\Delta S^{\ddagger}$ (kcal. mole^{-1} deg.$^{-1}$)	−1·1	−1·0	−3·7	—

* Davies, Meecham, and Shoppee, *J.*, 1955, 679.

is consistent with the greater degree of dissociation of this solute. Clearly, the acetolyses of the 3-epimeric 4,4,14α-trimethyl-5α-cholest-8-en-3-yl toluene-*p*-sulphonates are unimolecular reactions (S_N1) involving a rate-controlling heterolysis, and this has been found

likewise to be true for the acetolyses of the epimeric 4,4-dimethyl-5α-cholestan-3-yl toluene-*p*-sulphonates. The sensitivity of the acetolyses of the 4,4,14α-trimethyl-5α-cholest-8-en-3-yl toluene-*p*-sulphonates towards addition of water and salts is similar to that observed with cyclohexyl [15,16] and cholest-5-en-3α-yl toluene-*p*-sulphonate.[17] The acetolysis of cholest-5-en-3β-yl toluene-*p*-sulphonate is, however, much more sensitive to addition of water and salts than that of cyclohexyl toluene-*p*-sulphonate, and it has been suggested that this is due to the greater charge separation in the transition state of the former reaction.[16]

The specific rate constants and thermodynamic functions for acetolysis of 4,4,14α-trimethyl-5α-cholest-8-en-3-yl and 4,4-dimethyl-5α-cholestan-3-yl toluene-*p*-sulphonates are given in Table 4. These rate constants are only slightly greater than that $10^4k_1 = 1{\cdot}1$ min.$^{-1}$ for cyclohexyl toluene-*p*-sulphonate in acetic acid at 50° (cf. Table 5),[15,16] and are not very different from those, $10^4k_1 = 0{\cdot}65$ min.$^{-1}$ for 5α-cholestan-3β-yl toluene-*p*-sulphonate and $10^4k_1 = 4{\cdot}4$ min.$^{-1}$ for 5α-cholestan-3α-yl toluene-*p*-sulphonate in acetic acid at 50° (Winstein, personal communication). Apart from any effect possibly due to the 14α-methyl group, comparison of the specific rate constants for the respective Δ^8-4,4-14α-trimethyl and saturated 4,4-dimethyl epimers shows that the 8,9-ethylenic linkage exerts a long-range effect, causing an approximately 50% depression in rate.[18]

The specific rate constants for the acetolyses of the 3-epimeric 4,4,14α-trimethyl and 4,4-dimethyl toluene-*p*-sulphonates are only slightly greater than that for cyclohexyl toluene-*p*-sulphonate, whilst the activation parameters are remarkably similar in all five cases. Although quite small rate increases (ten-fold or less) have been attributed to neighbouring-group participation,[19] it appears that the slight increases now found are not due to such participation by the electrons of the 4,5-bond in the 3β-compounds, or of the 4β-methyl group in the 3α-derivatives.

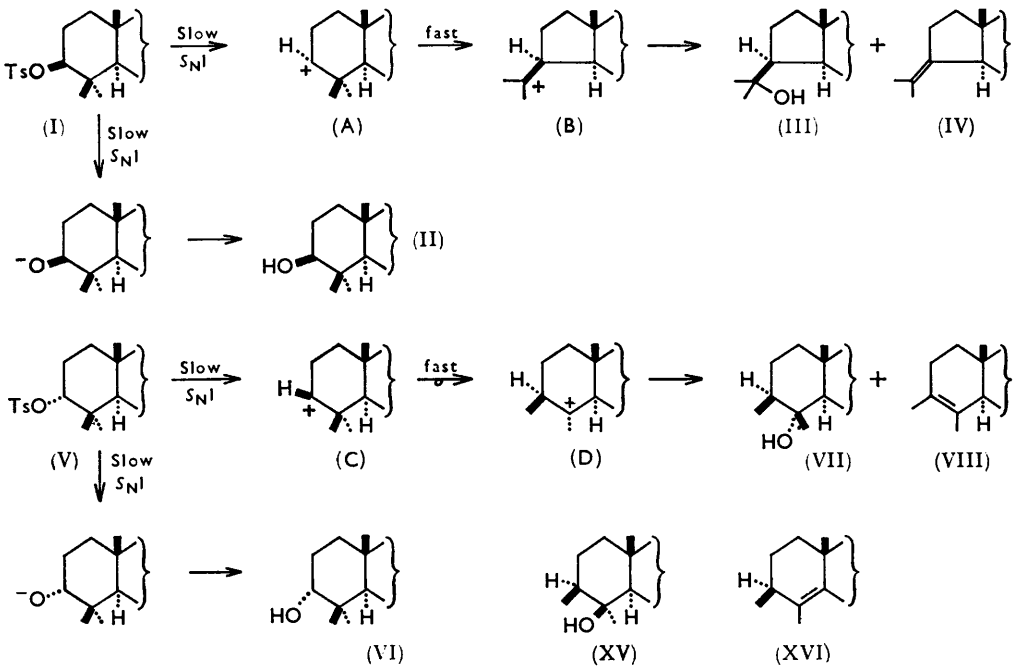
It may be noted that the enhanced rates of acetolysis of cholest-5-en-3β-yl and 4,4-dimethylcholest-5-en-3β-yl toluene-*p*-sulphonates (Table 5) are due to differences in the heats of activation ($\Delta H^{\ddagger}$), since the entropies of activation ($\Delta S^{\ddagger}$) have a nearly constant value of $-\sim$1 kcal. mole^{-1} deg.$^{-1}$.

The mechanism of solvolysis of the 3-epimeric 4,4,14α-trimethyl-5α-cholest-8-en-3-yl and 4,4-dimethyl-5α-cholestan-3-yl toluene-*p*-sulphonates (as I, V) must account (*a*) for the absence of inversion without rearrangement and the presence of some retention, and (*b*) for the absence of synartetic acceleration and the presence of some steric acceleration, in all four cases. Solvolysis may proceed by a slow unimolecular heterolysis (S_N1) to give the classical carbonium ions (A, C); since individuality is maintained, these probably exist as intimate ion-pairs with the departing toluene-*p*-sulphonate anions; they are short-lived and rapidly rearrange, before co-ordination with an external anion or depolarisation can occur, to the more thermodynamically stable carbonium ions (B, D), yielding rearranged tertiary alcohols (as III, VII) and unsaturated hydrocarbons (as IV, VIII). The occurrence of substitution with retention to afford the alcohols (as II, VI) would then be due to fission of the oxygen–sulphur bond R·O|–SO_2Ar as opposed to the usual carbon–oxygen cleavage R–O·SO_2Ar. In fact such oxygen–sulphur fission can arise if the carbon–oxygen heterolysis becomes sufficiently difficult; thus Bunton and Frei [20] showed by use of isotopic oxygen that hydrolysis of phenyl toluene-*p*-sulphonate in alkaline aqueous dioxan with water enriched in ^{18}O occurred by oxygen–sulphur fission: *p*-Tol·SO_2|–OPh + $^{18}OH^-$ ⟶ *p*-Tol·SO_2·^{18}OH + Ph·OH. However, the products isolated from the acetolyses are the acetates (II, VI; R = Ac), corresponding to the original toluene-*p*-sulphonates, and not the alcohols (II, VI) predicted by this mechanism. Further, it is difficult to explain the absence of the 4-epimeric alcohols (as XV) and the double-bond isomers (as XVI) from the products

[15] Winstein, Grunwald, and Ingraham, *J. Amer. Chem. Soc.*, 1948, **70**, 821.
[16] Winstein and Adams, *J. Amer. Chem. Soc.*, 1948, **70**, 838.
[17] Shoppee and Williams, *J.*, 1955, 686.
[18] Cf. Barton, McCapra, May, and Thudium, *J.*, 1960, 1297.
[19] Cf. Bethell and Gold, *Quart. Rev.*, 1958, **12**, 173.
[20] Bunton and Frei, *J.*, 1951, 1872.

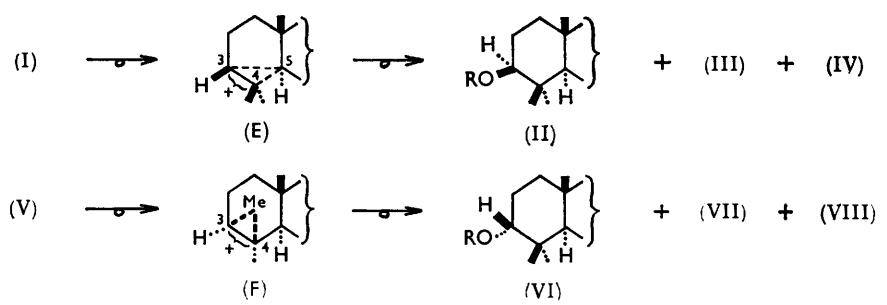
of solvolysis of the 3α-yl toluene-*p*-sulphonates (as V) if the carbonium ion (D) exists as a single classical entity.

Both these difficulties disappear if non-classical carbonium ions (E, F) (or intimate ion pairs) are postulated, and the following reaction mechanism involving them is in agreement with all the structural evidence. Thus the carbonium ions (E, F) are formed with



inversion at position 3,* and attack by a hydroxyl ion or an acetate ion at position 3 leads by a second inversion to the alcohols or acetates (as II, VI; R = H or Ac) with preservation of configuration.

The kinetic evidence requires one further assumption. Generation of the non-classical



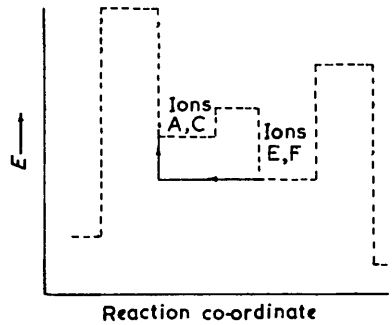
ions (E, F) in preference to the classical ions (A, C) is intelligible if the former are thermodynamically more stable; this would involve stabilised transition states of ionisation, and therefore accelerated unimolecular heterolyses. The solvolysis rates are effectively not accelerated, and the above mechanism must be modified by postulating that the rate-controlling ionisation produces classical carbonium ions (A, C) (as intimate ion-pairs) of short life, rearranging to the more stable non-classical carbonium ions (E, F), the timing of the covalency changes being such that formation of the latter does not kinetically affect

* There is a mechanistic inversion, but no formal inversion, in the process (I ⟶ III) because the 3-hydrogen atom does not cross the plane of the five-membered ring.

the initial ionisation. On this interpretation, the situation is illustrated by the broken-line portion of the symbolic energy diagram given by Ingold [21] and reproduced in the annexed Figure, subject only to the qualification that the difference in height between the left-hand and the right-hand energy barrier is insufficient to prevent return over the left-hand barrier by the combined full-line and broken-line route.

Reaction co-ordinates.

Representative points entering from the left and leaving by the right describe by the broken-line route the non-accelerated unimolecular rearrangements I ⟶ III + IV *and* V ⟶ VII + VIII. *Points entering from the left by the broken-line route, and leaving by the left by the combined full-line and broken-line route describe the non-accelerated, non-rearranging unimolecular reactions* I ⟶ II *and* V ⟶ VI.



Experimental

For general experimental directions see *J.*, 1959, 345. $[\alpha]_D$ refer to chloroform solutions at room temperature. Ultraviolet absorption spectra were determined for ethanol solutions in a Hilger Uvispec spectrophotometer. Infrared absorption spectra were measured by use of a Perkin–Elmer model 137 Infracord double-beam spectrometer. Unless otherwise stated, aluminium oxide used was Spence's type H (activity II). M. p.s were determined on a Kofler block and are corrected.

4,4,14α-*Trimethyl*-5α-*cholest*-8-*en*-3β-*yl Toluene*-p-*sulphonate*.—To a solution of 4,4,14α-trimethyl-5α-cholest-8-en-3β-ol [22] (1·02 g.) in dry pyridine (50 c.c.), toluene-*p*-sulphonyl chloride (2·60 g.) was added gradually at 0°. After 3 days at 25°, ice was added and the mixture set aside for 1·5 hr. The product was extracted with ether, and the extract washed with cold 2N-hydrochloric acid, water, 2N-sodium hydrogen carbonate, and to neutrality with water, dried, and evaporated. The solid residue (1·19 g.) gave, after several recrystallisations from acetone, 4,4,14α-*trimethyl*-5α-*cholest*-8-*en*-3β-*yl toluene*-p-*sulphonate*, m. p. 125—126°, $[\alpha]_D$ +54° (*c* 0·9) [Found (after drying at 60°/0·2 mm. for 3 hr.): C, 76·2; H, 10·0. $C_{37}H_{58}O_3S$ requires C, 76·2; H, 10·0%]. The ester (50 mg.) was eluted unchanged (m. p. 124—126°; 45 mg.) from neutralised aluminium oxide (1·5 g.; Woelm) by benzene–pentane (1 : 2).

Solvolysis of 4,4,14α-*Trimethyl*-5α-*cholest*-8-*en*-3β-*yl Toluene*-p-*sulphonate*.—A solution of 4,4,14α-trimethyl-5α-cholest-8-en-3β-yl toluene-*p*-sulphonate (1·285 g.) in acetone (25 c.c.) was treated with water (7 c.c.) and anhydrous sodium acetate (1·0 g.) and refluxed for 60 hr. Most of the acetone was removed under reduced pressure, and the residue extracted with ether, and worked up in the usual way to give a solid (930 mg.). Chromatography on aluminium oxide (30 g.) prepared in pentane and elution with pentane (4 × 80 c.c.) gave 3-isopropylidene-14α-methyl-A-nor-5α-cholest-8-ene [23] (652 mg., 72%), m. p. 145—146°, $[\alpha]_D$ +67° (*c* 0·7), after crystallisation from chloroform–methanol. Elution with ether–pentane (1 : 19; 10 × 80 c.c.) afforded 3β-(1-*hydroxy*-1-*methylethyl*)-14α-*methyl*-A-*nor*-5α-*cholest*-8-*ene* (214 mg., 22%), m. p. 137—138° (from methanol), $[\alpha]_D$ +52° (*c* 0·9) [Found (after drying at 80°/0·2 mm. for 16 hr.): C, 83·8; H, 12·3. $C_{30}H_{52}O$ requires C, 84·0; H, 12·3%]; treatment with acetic anhydride and pyridine at 25° for 1 week failed to bring about acetylation. Further elution with ether–pentane (1 : 4; 10 × 80 c.c.) gave 4,4,14α-trimethyl-5α-cholest-8-en-3β-ol (48 mg., 5%), m. p. 145—146°, $[\alpha]_D$ +62° (*c* 0·6), after crystallisation from benzene–methanol, unaccompanied by the epimeric 3α-alcohol.

Dehydration of 3β-(1-*Hydroxy*-1-*methylethyl*)-14α-*methyl*-A-*nor*-5α-*cholest*-8-*ene*.—The foregoing alcohol (78 mg.) in pyridine (8 c.c.) was heated at 95° for 1 hr. with freshly distilled phosphoryl chloride (1·5 c.c.). Dilution with water and extraction with ether gave a product,

[21] Ingold, cf. ref. 1, Fig. 36.2, p. 520.
[22] Ruzicka, Denss, and Jeger, *Helv. Chim. Acta*, 1945, **28**, 759.
[23] Dorée, McGhie, and Kurzer, *J.*, in the press.

which was chromatographed on aluminium oxide (3 g.) prepared in pentane. Elution with pentane (50 c.c.) and two crystallisations of the product from chloroform–methanol gave 3-isopropylidene-14α-methyl-A-nor-5α-cholest-8-ene (43 mg.), m. p. 145—146°, $[\alpha]_D$ +66° (*c* 0·9).

Acetolysis of 4,4,14α-*Trimethyl*-5α-*cholest*-8-*en*-3β-*yl Toluene*-p-*sulphonate*.—This ester (504 mg.) in acetic acid (70 c.c.) containing anhydrous sodium acetate (287 mg.) was heated at 95° for 3 hr. Removal of the solvent *in vacuo*, extraction with ether, and working up in the usual way gave an oil which showed $\nu_{max.}$ 1240 cm.$^{-1}$ in carbon disulphide but no band in the 3500 cm.$^{-1}$ region and so was devoid of 4,4,14α-trimethyl-5α-cholest-8-en-3β-ol,[24] this was hydrolysed with refluxing 5% ethanolic potassium hydroxide (20 c.c.) for 1 hr. The resulting solid (355 mg.) in pentane was chromatographed on aluminium oxide (11 g.) prepared in the same solvent. Elution with pentane (2 × 80 c.c.) gave 3-isopropylidene-14α-methyl-A-nor-5α-cholest-8-ene (318 mg., 90%), m. p. 145—146°, $[\alpha]_D$ +67° (*c* 0·7), after crystallisation from chloroform–methanol. Further elution with pentane and later benzene yielded only traces of material, whilst use of ether–benzene (1 : 99; 2 × 80 c.c.) afforded 4,4,14α-trimethyl-5α-cholest-8-en-3β-ol (32 mg., 8%), m. p. 145—146°, $[\alpha]_D$ +63° (*c* 1·0), after crystallisation from benzene–methanol, unaccompanied by the epimeric 3α-alcohol. Similar results were obtained in a second experiment without the sodium acetate buffer.

4,4-*Dimethyl*-5α-*cholestan*-3β-*yl Toluene*-p-*sulphonate*.—4,4-Dimethyl-5α-cholestan-3β-ol [25] (200 mg.) in dry pyridine (5 c.c.) was treated at 0° with toluene-*p*-sulphonyl chloride (470 mg.) and left at 25° for 3 days. The solid product (310 mg.), after several recrystallisations from acetone, yielded the *toluene*-p-*sulphonate*, m. p. 125—126°, $[\alpha]_D$ +7° (*c* 1·3) [Found (after drying at 60°/0·2 mm. for 3 hr.): C, 75·8; H, 10·2. $C_{36}H_{58}O_3S$ requires C, 75·7; H, 10·2%]. The ester (50 mg.) was eluted unchanged (m. p. 124—125°; 43 mg.) from neutralised aluminium oxide (1·5 g., Woelm) by benzene–pentane (1 : 2).

Solvolysis of 4,4-*Dimethyl*-5α-*cholestan*-3β-*yl Toluene*-p-*sulphonate*.—4,4-Dimethyl-5α-cholestan-3β-yl toluene-*p*-sulphonate (252 mg.) in acetone (10 c.c.) was refluxed with water (1 c.c.) and anhydrous sodium acetate (200 mg.) for 60 hr. Working up in the usual way gave an oil (180 mg.). Chromatography on aluminium oxide (6 g.) prepared in pentane, and elution with pentane (6 × 15 c.c.), gave an oil (123 mg., 70%) which yielded, by crystallisation from chloroform–methanol, 3-*isopropylidene*-A-*nor*-5α-*cholestane*, m. p. 87—89°, $[\alpha]_D$ +18° (*c* 1·0) [Found (after drying at 35°/0·2 mm. for 8 hr.): C, 87·25; H, 12·8. $C_{29}H_{50}$ requires C, 87·4; H, 12·6%]. The isopropenyl and endocyclic isomerides may have been present in this material. Elution with ether–pentane (1 : 19; 10 × 15 c.c.) gave 3β-(1-hydroxy-1-methylethyl)-A-nor-5α-cholestane (44 mg., 24%), m. p. 100—101° (from methanol), $[\alpha]_D$ +31° (*c* 1·0). Biellmann and Ourisson [10] give m. p. 102°, $[\alpha]_{600}$ +27°, $[\alpha]_{400}$ +69°. Elution with ether–pentane (1 : 4; 7 × 15 c.c.) gave 4,4-dimethyl-5α-cholestan-3β-ol (9 mg., 5%), m. p. 156—157°, $[\alpha]_D$ +13° (*c* 0·6), after crystallisation from methanol, unaccompanied by the epimeric 3α-alcohol.

Acetolysis of 4,4-*Dimethyl*-5α-*cholestan*-3β-*yl Toluene*-p-*sulphonate*.—The toluene-*p*-sulphonate (260 mg.) in acetic acid (35 c.c.) containing anhydrous sodium acetate (150 mg.) was heated at 95° for 3 hr. The product which had $\nu_{max.}$ (in CS_2) at 1240 cm.$^{-1}$ but no band in the 3500 cm.$^{-1}$ region and was devoid of 4,4-dimethyl-5α-cholestan-3β-ol, was hydrolysed with 5% ethanolic potassium hydroxide (10 c.c.), and the resulting oil was chromatographed on aluminium oxide (6 g.) prepared in pentane. Elution with pentane (3 × 50 c.c.) gave 3-isopropylidene-A-nor-5α-cholestane (167 mg., 88%) which, crystallised from chloroform–methanol, had m. p. 87—89°, $[\alpha]_D$ +19° (*c* 1·0). Elution with ether–pentane (1 : 4; 4 × 50 c.c.) gave 4,4-dimethyl-5α-cholestan-3β-ol (19 mg., 10%), m. p. 156—157°, $[\alpha]_D$ +11° (*c* 0·93) after crystallisation from methanol, unaccompanied by the epimeric 3α-alcohol.

3-*Isopropylidene*-A-*nor*-5α-*cholestane*.—(*a*) 4,4-Dimethyl-5α-cholestan-3β-ol (125 mg.) in hexane (10 c.c.) was heated under reflux with phosphorus pentachloride (125 mg.) for 10 min. Dilution with ice-water, extraction with ether, and working up in the usual way gave a yellow oil. Filtration through aluminium oxide (0·5 g. in pentane, 20 c.c.) and removal of the solvent *in vacuo* afforded an oil, which by repeated crystallisation from chloroform–methanol gave 3-isopropylidene-A-nor-5α-cholestane as needles, m. p. 88—90°, $[\alpha]_D$ +19° (*c* 0·8).

(*b*) To a solution of 3β-(1-hydroxy-1-methylethyl)-A-nor-5α-cholestane, 35 mg.) in pyridine

[24] Marker and Wittle, *J. Amer. Chem. Soc.*, 1937, **59**, 2289; Allsop, Cole, White, and Willix, *J.*, 1956, 4868.

[25] Mazur and Sondheimer, *J. Amer. Chem. Soc.*, 1958, **80**, 5220.

(2 c.c.), freshly distilled phosphoryl chloride (0·5 c.c.) was added. After 1 hr. at 95°, the mixture was cooled and ice-water cautiously added. Extraction with ether and working up in the usual way gave 3-isopropylidene-A-nor-5α-cholestane, m. p. 88—90°, $[\alpha]_D$ +19° (*c* 1·1), after repeated crystallisation from chloroform–methanol.

4,4,14α-Trimethyl-5α-cholest-8-en-3α-yl Toluene-p-sulphonate.—4,4,14α-Trimethyl-5α-cholest-8-en-3α-ol [24] (104 mg.) in dry pyridine (5 c.c.) was treated at 0° with toluene-*p*-sulphonyl chloride (264 mg.) and left at 25° for 3 days. The solid product (118 mg.) afforded, after several recrystallisations from acetone, *4,4,14α-trimethyl-5α-cholest-8-en-3α-yl toluene-p-sulphonate*, m. p. 139—140° (decomp.), $[\alpha]_D$ −5° (*c* 1·0) [Found (after drying at 60°/0·2 mm. for 1 hr.): C, 76·2; H, 10·3. $C_{37}H_{58}O_3S$ requires C, 76·2; H, 10·0%].

Solvolysis of 4,4,14α-Trimethyl-5α-cholest-8-en-3α-yl Toluene-p-sulphonate.—A solution of 4,4,14α-trimethyl-5α-cholest-8-en-3α-yl toluene-*p*-sulphonate (1·247 g.) in acetone (25 c.c.) was treated with water (7 c.c.) and anhydrous sodium acetate (1·0 g.), and refluxed for 60 hr. Working up in the usual way gave a solid (871 mg.), which by chromatography on a column of aluminium oxide (30 g.) prepared in pentane and elution with pentane (4 × 80 c.c.) gave *3,4,14α-trimethyl-5α-cholesta-3,8-diene* (661 mg., 75%), m. p. 94—95°, $[\alpha]_D$ +76·5° (*c* 0·8) after crystallisation from chloroform–methanol [Found (after drying at 40°/0·2 mm. for 6 hr.): C, 87·45; H, 12·3. $C_{30}H_{50}$ requires C, 87·7; H, 12·3%]. Elution with ether–pentane (1 : 9; 6 × 80 c.c.) gave *3β,4β,14α-trimethyl-5α-cholest-8-en-4α-ol* (135 mg., 15%), m. p. 138—139°, $[\alpha]_D$ +95° (*c* 0·8), after crystallisation from aqueous ethanol [Found (after drying at 90°/0·2 mm. for 12 hr.): C, 83·8; H, 12·4. $C_{30}H_{52}O$ requires C, 84·1; H, 12·2%]. Treating 3β,4β,14α-trimethyl-5α-cholest-8-en-4α-ol with acetic anhydride–pyridine at 25° for 1 week failed to bring about acetylation. Elution with ether–pentane (1 : 4; 3 × 80 c.c.) yielded 4,4,14α-trimethyl-5α-cholest-8-en-3α-ol (65 mg., 7%) which, crystallised from acetone–methanol, had m. p. 138—139°, $[\alpha]_D$ +48° (*c* 1·1); it was not accompanied by the epimeric 3β-alcohol.

Acetolysis of 4,4,14α-Trimethyl-5α-cholest-8-en-3α-yl Toluene-p-sulphonate.—4,4,14α-Trimethyl-5α-cholest-8-en-3α-yl toluene-*p*-sulphonate (610 mg.) in acetic acid (80 c.c.) containing anhydrous sodium acetate (328 mg.) was heated at 95° for 3 hr. Removal of the solvent *in vacuo*, extraction with ether, and working up in the usual way gave a yellow oil, which had $\nu_{max.}$ (in CS_2) 1240 and 1180 cm.$^{-1}$ but no band in the 3500 cm.$^{-1}$ region and was devoid of 4,4,14α-trimethyl-5α-cholest-8-en-3α-ol; [24] it was hydrolysed with refluxing 5% ethanolic potassium hydroxide (20 c.c.) for 30 min. The resulting crystals (432 mg.) were chromatographed on aluminium oxide (12 g.) prepared in pentane. Elution with pentane (2 × 80 c.c.) gave 3,4,14α-trimethyl-5α-cholesta-3,8-diene (348 mg., 81%), m. p. 94—95°, $[\alpha]_D$ +76·5° (*c* 0·8), after crystallisation from chloroform–methanol. Elution with ether–benzene (1 : 99; 10 × 80 c.c.) yielded 4,4,14α-trimethyl-5α-cholest-8-en-3α-ol (78 mg., 17%), m. p. 138—139°, $[\alpha]_D$ +48° (*c* 1·1), after crystallisation from acetone–methanol, unaccompanied by the epimeric 3β-alcohol. Similar results were obtained in a second experiment without the sodium acetate buffer.

Dehydration of 3β,4β,14α-Trimethyl-5α-cholest-8-en-4α-ol.—3β,4β,14α-Trimethyl-5α-cholest-8-en-4α-ol (75 mg.) in pyridine (8 c.c.) was heated at 95° for 1 hr. with freshly distilled phosphoryl chloride (1·5 c.c.). Dilution with water and extraction with ether gave a product which was chromatographed on aluminium oxide (3 g.) prepared in pentane. Elution with pentane (50 c.c.) afforded *3β,14α-dimethyl-4-methylene-5α-cholest-8-ene* (35 mg.), m. p. 81—82°, $[\alpha]_D$ +83° (*c* 1·0), $\nu_{max.}$ (in CS_2) 885 cm.$^{-1}$, after crystallisation from acetone [Found (after drying at 45°/0·2 mm. for 17 hr.): C, 88·05; H, 12·25. $C_{30}H_{50}$ requires C, 87·7; H, 12·3%].

Ozonolysis of 3β,14α-Dimethyl-4-methylene-5α-cholest-8-ene.—3β,14α-Dimethyl-4-methylene-5α-cholest-8-ene (28 mg.) in carbon tetrachloride (10 c.c.) was treated with excess of ozonised oxygen at −15° for 30 min. The solvent was removed under reduced pressure at 0° and water (10 c.c.) added to the residue. Most of this solution was distilled into a solution of 2,4-dinitrophenylhydrazine (300 mg.) in methanol (15 c.c.) containing hydrochloric acid (0·5 c.c.). Addition of water and extraction with benzene gave a product which was chromatographed on neutralised aluminium oxide (0·5 g.; Woelm) prepared in benzene. Elution with ether gave formaldehyde 2,4-dinitrophenylhydrazone (7 mg.), m. p. and mixed m. p. 166°. Paper chromatography [26] (cyclohexane and No. 1 paper impregnated with dimethylformamide) showed the product to be free from other 2,4-dinitrophenylhydrazones.

3,4,14α-Trimethyl-5α-cholesta-3,8-diene.—In a series of experiments 4,4,14α-trimethyl-5α-cholest-8-en-3α-ol was treated with the following reagents: PCl_5–hexane, PCl_5–pyridine,

[26] Gasparic and Vecera, *Coll. Czech. Chem. Comm.*, 1957, **22**, 1426.

PCl_5–$POCl_3$, $POCl_3$–pyridine, $SOCl_2$, $SOCl_2$–benzene, $SOCl_2$–pyridine, but failed to give 3,4,14α-trimethyl-5α-cholesta-3,8-diene. Chromatography of the products gave, by elution with pentane, variable quantities of oil which on crystallisation from chloroform–methanol furnished 4,4,14α-trimethyl-5α-cholesta-2,8-diene,[13] m. p. 80—82°, $[\alpha]_D$ +120° (*c* 1·0).

Oxidation of 3,4,14α-*Trimethyl*-5α-*cholesta*-3,8-*diene with Osmium Tetroxide.*—3,4,14α-Trimethyl-5α-cholesta-3,8-diene (319 mg.) in benzene (6 c.c.) was treated with a solution of osmium tetroxide (228 mg., 1·1 mol.) in pyridine (6 c.c.), and the mixture kept in the dark for 18 days at 25°. After removal of the solvents under reduced pressure, the residue was heated under reflux with benzene (9 c.c.), methanol (9 c.c.), ethanol (9 c.c.), water (5 c.c.), mannitol (1·85 g.), and potassium hydroxide (1·85 g.). After 3½ hr. sodium sulphite (320 mg.) was added and the heating continued for a further 2 hr. Removal of the solvents under reduced pressure and extraction with ether afforded a solid which was chromatographed on aluminium oxide (10 g.) prepared in pentane. Elution with pentane (2 × 80 c.c.) afforded starting material (58 mg.). Elution with ether–pentane (1 : 9; 15 × 80 c.c.) gave 3β,4β,14α-*trimethyl*-5α-*cholest*-8-*ene*-3α,4α-*diol* (185 mg.), having m. p. 158—159°, $[\alpha]_D$ +70° (*c* 0·5), after crystallisation from methanol [Found (after drying at 50°/0·2 mm. for 36 hr.): C, 81·3; H, 11·6. $C_{30}H_{52}O_2$ requires C, 81·0; H, 11·8%]. Further elution with ether–pentane (1 : 9; 4 × 80 c.c.) gave material (15 mg.), m. p. 161—168° (from chloroform–methanol), probably impure 3β,4β-diol.

Oxidation of 3β,4β,14α-*Trimethyl*-5α-*cholest*-8-*ene*-3α,4α-*diol with Periodic Acid.*—The presumed diol (103 mg.) in dioxan (10 c.c.) was treated with periodic acid (125 mg.) in water (1 c.c.) for 25 hr. in the dark at 20°. Dilution with water, extraction with ether, and working up in the usual way gave a yellow oil (98 mg.). Chromatography on silica gel (10 g.) prepared in pentane, and elution with ether–pentane (1 : 19; 8 × 40 c.c.), gave 3,4,14α-*trimethyl*-3,4-*seco*-5α-*cholest*-8-*ene*-3,4-*dione* (83 mg.), m. p. 149—150°, $[\alpha]_D$ +83° (*c* 1·25), $\nu_{max.}$ (in CCl_4) 1710 cm.$^{-1}$, after crystallisation from methanol [Found (after drying at 60°/0·2 mm. for 3 hr.): C, 81·6; H, 11·5. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%].

2-*Acetyl*-3,14α-*dimethyl*-A-*nor*-5α-*cholesta*-2,8-*diene.*—The preceding diketone (40 mg.) in pentane (3 c.c.) was adsorbed on aluminium oxide (10 g.) (cf. ref. 11). Elution after 2 hr. with benzene gave 2-*acetyl*-3,14α-*dimethyl*-A-*nor*-5α-*cholesta*-2,8-*diene*, m. p. 124—125°, $\lambda_{max.}$ 260 mμ, $\nu_{max.}$ (in CCl_4) 1665 cm.$^{-1}$ (after crystallisation from aqueous methanol) [Found (after drying at 60°/0·2 mm. for 3 hr.): C, 84·35; H, 11·6. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%].

4,4-*Dimethyl*-5α-*cholestan*-3α-*ol.*—4,4-Dimethyl-5α-cholestan-3-one [11] (1·003 g.) in dry propan-2-ol (100 c.c.) was refluxed for 6 hr. in the presence of aluminium isopropoxide (1·0 g.). The mixture was then slowly distilled until the distillate was free from acetone (3 hr.). The mixture was next poured into water (100 c.c.) and ether (100 c.c.), shaken, and acidified with dilute hydrochloric acid. Working up in the usual way gave crystals (998 mg.) which were chromatographed on aluminium oxide (30 g.) prepared in pentane. Elution with ether–pentane (1 : 19; 16 × 80 c.c.) gave 4,4-*dimethyl*-5α-*cholestan*-3α-*ol* (348 mg.), m. p. 152—153°, $[\alpha]_D$ +5° (*c* 1·0), $\nu_{max.}$ (in CS_2) 3640, 1060, 975 cm.$^{-1}$, after crystallisation from methanol [Found (after drying at 60°/0·2 mm. for 24 hr.): C, 83·4; H, 12·65. $C_{29}H_{52}O$ requires C, 83·6; H, 12·6%]. Treatment with acetic anhydride–pyridine overnight at 25° afforded 4,4-*dimethyl*-5α-*cholestan*-3α-*yl acetate*, m. p. 146—147°, $[\alpha]_D$ −8° (*c* 1·1), $\nu_{max.}$ (in CS_2) 1240, 1180, 1035, 1010, 965 cm.$^{-1}$, after crystallisation from methanol [Found (after drying at 60°/0·2 mm. for 4 hr.): C, 81·3; H, 11·8. $C_{31}H_{54}O_2$ requires C, 81·2; H, 11·9%]. Further elution with ether–pentane (1 : 19; 6 × 80 c.c.; and 1 : 9, 23 × 80 c.c.) yielded 4,4-dimethyl-5α-cholestan-3β-ol (638 mg.), m. p. 157—158°, $[\alpha]_D$ +12° (*c* 1·8), $\nu_{max.}$ (in CS_2) 3640, 1025 cm.$^{-1}$, after crystallisation from methanol.

4,4-*Dimethyl*-5α-*cholestan*-3α-*yl Toluene*-p-*sulphonate.*—4,4-Dimethyl-5α-cholestan-3α-ol (200 mg.) in dry pyridine (5 c.c.) was treated at 0° with toluene-*p*-sulphonyl chloride (470 mg.) and left at 25° for 3 days. The product (298 mg.), on recrystallisation from acetone, gave 4,4-*dimethyl*-5α-*cholestan*-3α-*yl toluene*-p-*sulphonate*, m. p. 158—159° (decomp.), $[\alpha]_D$ −10° (*c* 1·0) [Found (after drying at 60°/0·2 mm. for 3 hr.): C, 75·8; H, 10·3. $C_{36}H_{58}O_3S$ requires C, 75·7; H, 10·2%].

Solvolysis of 4,4-*Dimethyl*-5α-*cholestan*-3α-*yl Toluene*-p-*sulphonate.*—A solution of 4,4-dimethyl-5α-cholestan-3α-yl toluene-*p*-sulphonate (128 mg.) in acetone (5 c.c.) was treated with water (0·7 c.c.) and anhydrous sodium acetate (0·1 g.), and refluxed for 60 hr. The product was chromatographed on aluminium oxide (3 g.) prepared in pentane. Elution with pentane (4 × 10 c.c.) gave 3,4-dimethyl-5α-cholest-3-ene (65 mg., 72%), m. p. 105—106°,

$[\alpha]_D$ +8° (*c* 1·1), after crystallisation from acetone. Beton *et al.*[11] report m. p. 106·5—108°, $[\alpha]_D$ +5° (*c* 0·57). Elution with ether–pentane (1 : 9; 5 × 10 c.c.) gave 3β,4β-*dimethyl-5α-cholestan-4α-ol* (14 mg., 15%), m. p. 145—147°, after crystallisation from methanol [Found (after drying at 60°/0·2 mm. for 18 hr.): C, 83·75; H, 12·5. $C_{29}H_{52}O$ requires C, 83·6; H, 12·6%]. Further elution with ether–pentane (1 : 4; 6 × 10 c.c.) afforded 4,4-dimethyl-5α-cholestan-3α-ol (8 mg., 10%), m. p. 152—153°.

*Acetolysis of 4,4-Dimethyl-5α-cholestan-3α-yl Toluene-*p*-sulphonate.*—4,4-Dimethyl-5α-cholestan-3α-yl toluene-*p*-sulphonate (58 mg.) in acetic acid (8 c.c.) containing anhydrous sodium acetate (30 mg.) was heated at 95° for 3 hr. Removal of the solvent *in vacuo*, extraction with ether, and working up in the usual way gave an oil, which had $\nu_{max.}$ (in CS_2) 1240 and 1180 cm.$^{-1}$ but no band in the 3500 cm.$^{-1}$ region and was devoid of 4,4-dimethyl-5α-cholestan-3α-ol; it was hydrolysed with refluxing 5% ethanolic potassium hydroxide (20 c.c.) for 30 min. The product was chromatographed on aluminium oxide (1 g.) prepared in pentane. Elution with pentane (4 × 10 c.c.) gave 3,4-dimethyl-5α-cholest-3-ene (32 mg., 80%), m. p. 104—106°, $[\alpha]_D$ +9° (*c* 0·9), after crystallisation from acetone. Elution with ether–pentane (1 : 9; 5 × 10 c.c.) yielded 4,4-dimethyl-5α-cholestan-3α-ol (8 mg., 19%), m. p. 151—152°.

Kinetic Measurements.—The rates of acetolysis were studied at 50·00° ± 0·01° and at 60·00° ± 0·01°. For each run, about 50 c.c. of a solution of the toluene-*p*-sulphonate (0·005M to 0·02M, depending on solubility and rate of solution) were made up by weight in a glass-stoppered flask. Analyses were performed on 5 c.c. portions with approximately 0·02M-perchloric acid and/or sodium acetate in anhydrous acetic acid. Titrations were carried out with 5 c.c. microburettes and were conducted at a uniform room temperature. A saturated acetic acid solution of Bromophenyl Blue was used as indicator.[15]

Darkening of the solution towards the end of a run made it impossible to obtain an infinity titre. Rates were followed to approximately 70% completion, the mean deviation of the individual first-order constants in one run being within 3%.

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