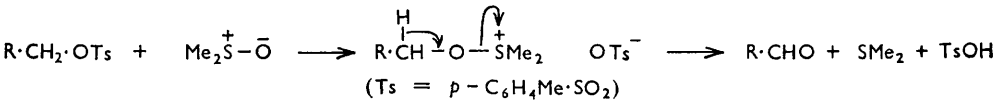
891. *The Reaction between Steroid Sulphonate Esters and Dimethyl Sulphoxide.*

By D. Neville Jones and M. A. Saeed.

Reaction of some sulphonic esters of steroidal alcohols with dimethyl sulphoxide gives mainly olefins, with ketones and alcohols as minor products. Presence of collidine in the reaction mixture increases the amount of ketone produced. The relation between the steric environment of the ester group and the yield of ketone suggests that the latter is formed in an S_N2 reaction, with dimethyl sulphoxide as nucleophile.

Dimethyl sulphoxide is a favourable medium for nucleophilic substitutions,[1,2] but solvolyses in this medium are also known. For example, primary alkyl toluene-*p*-sulphonates and halides are readily converted into aldehydes by hot dimethyl sulphoxide,[3-7] especially if solid sodium hydrogen carbonate is added to remove the acid formed. In the sequel we call this type of reaction "solvolytic oxidation." The mechanism suggested for it involves initial nucleophilic attack by dimethyl sulphoxide followed by collapse of the intermediate to aldehyde and dimethyl sulphoxide:[5,7]



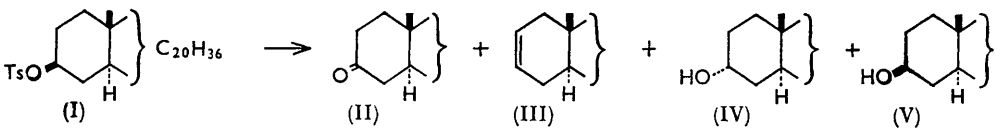
In accordance with this, activated alkyl halides such as phenacyl halides [3,4] and α-halogeno-acids [5] which are known readily to undergo nucleophilic substitution are oxidised by dimethyl sulphoxide with remarkable ease. With primary alkyl halides [6] and sulphonic esters,[6,7] this substitution is accompanied by little olefin-forming elimination.

Solvolytic oxidation of sulphonic esters of secondary alcohols can occur in favourable cases such as with diphenylmethyl chloride [7] and toluene-*p*-sulphonate,[8] both of which are oxidised to benzophenone. However, with the sulphonic esters of secondary cyclic alcohols it has been reported that elimination preponderates.[9] For instance, Nace [9] found that sulphonic esters of 5α-cholestan-3β-ol in hot dimethyl sulphoxide gave a mixture of 5α-cholest-2-ene and -3-ene, but there was no indication that 5α-cholestan-3-one was, or might have been, formed. No other steroid examples were given.

We found that solvolytic oxidation frequently occurred as a side reaction when dimethyl

[1] Schlafer and Schaffernicht, *Angew. Chem.*, 1960, **72**, 618.
[2] Miller and Parker, *J. Amer. Chem. Soc.*, 1961, **83**, 117; Cava, Little, and Napier, *ibid.*, 1958, **80**, 2257; Smiley and Arnold, *J. Org. Chem.*, 1960, **25**, 257; Friedman and Shechter, *ibid.*, p. 877.
[3] Kornblum, Power, Anderson, Jones, Larsen, and Weaver, *J. Amer. Chem. Soc.*, 1957, **79**, 6562.
[4] Major and Hess, *J. Org. Chem.*, 1958, **23**, 1563.
[5] Hunsberger and Tien, *Chem. and Ind.*, 1959, 88.
[6] Kornblum, Jones, and Anderson, *J. Amer. Chem. Soc.*, 1959, **81**, 4113.
[7] Nace and Monagle, *J. Org. Chem.*, 1959, **24**, 1792.
[8] Baizer, *J. Org. Chem.*, 1960, **25**, 670.
[9] Nace, *J. Amer. Chem. Soc.*, 1959, **81**, 5428.

sulphoxide was used as solvent for nucleophilic reactions of steroid toluene-*p*-sulphonates; for example, cholesteryl toluene-*p*-sulphonate is converted by treatment with azide ion in dimethyl sulphoxide into cholest-4-en-3-one as well as the expected cholesteryl azides.[10] We have examined the reactions of the sulphonic esters of steroidal alcohols with dimethyl sulphoxide in order to gain some insight into the possible complications due to solvolysis when dimethyl sulphoxide is used as a solvent for nucleophilic reactions, and to explore the preparative use of solvolytic oxidation in this field.



A re-examination of the reaction between 5α-cholestan-3β-yl toluene-*p*-sulphonate (I) and dimethyl sulphoxide, with chromatographic separation of the products, revealed that 11% of 5α-cholestan-3-one (II) was formed, together with 5α-cholest-2-ene (III) (81%) and 5α-cholestan-3α-ol (IV) (4%) and -3β-ol (V) (trace). (All the reactions with dimethyl sulphoxide referred to in this paper were performed at 100° for 3 hours unless otherwise stated.) Nace's isolation procedure [9] involved precipitation of the olefins from the reaction mixture by dilution with water and did not permit the detection of 5α-cholestan-3-one (II); it also provided a substantially lower yield (59%) of olefin. Addition of sodium hydrogen carbonate to the reaction mixture resulted in a much lower yield (16%) of olefin (III) and a higher yield (46%) of ketone (II). It had previously been suggested [9] that the addition of sodium hydrogen carbonate prevented the isomerisation of sensitive olefins prepared by this method; it is now evident that lower yields of olefin might also be expected. Infrared absorption measurements revealed that the once crystallised olefinic product formed in either the presence or the absence of base was essentially 5α-cholest-2-ene, in contrast to the previous report [9] that a mixture of 5α-cholest-2-ene and -3-ene was obtained. The best yield (64%) of 5α-cholestan-3-one (II) was obtained when one mol. of collidine was added; the olefin (III) was then produced in 26% yield, together with 5α-cholestan-3α-ol (IV) (10%). Under the same conditions 5α-cholestan-3β-yl methanesulphonate was somewhat less reactive, but gave the same products (see Table), whilst 3β-bromo-5α-cholestane gave 5α-cholestan-3-one (55%) and 5α-cholest-2-ene (27%) after reaction at 125° for 24 hours.

5α-Cholest-7-ene was the sole product (79%) when 5α-cholestan-7β-yl toluene-*p*-sulphonate was heated with dimethyl sulphoxide alone, but in the presence of collidine the yield of olefin was reduced to 23%, and 5α-cholestan-7-one was obtained in 76% yield. Similarly, the 2α-toluene-*p*-sulphonate gave a quantitative yield of 5α-cholest-2-ene with pure dimethyl sulphoxide, but when collidine was added the yield of olefin was reduced (74%) and some 5α-cholestan-2-one (19%) was formed. Further study is in progress to determine whether the function of the base is to retard the formation of olefin or to catalyse that of ketone.

Solvolytic oxidation of other sulphonic esters of steroid alcohols was then performed (under the usual conditions in the presence of 1 mol. of collidine) on the sulphonic esters of the simple 5α-cholestanyl alcohols, except for the 11α- and 17β-esters where 3β-methoxy-5α,22α-spirostan-11α-yl toluene-*p*-sulphonate and 3β-methoxyandrost-5-en-17β-yl toluene-*p*-sulphonate were used. We were unable to prepare the toluene-*p*-sulphonic esters of the axial alcohols, 5α-cholestan-6β-ol and 5α-cholestan-7α-ol; [11] under a variety of conditions either the alcohol was recovered or pure olefin (cholest-5-ene and 5α-cholest-7-ene) was obtained, presumably by rapid elimination from the sulphonic ester. The methanesulphonic esters of 5α-cholestan-6β-ol and -7α-ol, which were unstable but could be obtained pure, were used in this investigation. The results are included in the Table.

[10] Jones, *Chem. and Ind.*, 1962, 179.
[11] Cremlyn and Shoppee, *J.*, 1954, 3515.

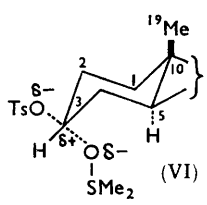
Ester *		Ketone (%)	Olefin (%)	Alcohol (%) α	Alcohol (%) β	Unchanged (%)
2α-OTs	Equat.	19	74	0	0	0
2β-OTs	Axial †	13	68	4	4	0
3β-OMs	Equat.	42	13	11	0·5	20
3β-OTs	Equat.	64	26	10	Trace	0
3α-OTs	Axial	34	57	0	7	0
6α-OTs	Equat.	6	26	0	0	29
6α-OMs	Equat.	0	Trace	0	0	96
6β-OMs	Axial	0	90	0	0	0
7α-OMs	Axial	8	88	0	0	0
7β-OMs	Equat.	64	10	4	2	0
7β-OTs	Equat.	76	23	0	0	0
11α-OTs	Equat.	0	54	10	10	0
17β-OTs	ψ-Equat.	0	0	0	0	95

* Ts = p-Me·C_6H_4·SO_2. Ms = Me·SO_2. † Chair conformation assumed for ring A.

Ketones were obtained in yields of preparative significance only with 3β- and 7β-sulphonic esters. Since double bonds remain unaffected this prodecure may be useful for selective oxidation of unsaturated 3β- and 7β-steroidal alcohols. Alcohols remain unaffected (much more drastic conditions are required to dehydrate even tertiary aliphatic alcohols by hot dimethyl sulphoxide [12]) and, since selective acylation of polyhydric steroid alcohols is possible, selective oxidation of these compounds is also feasible.

An axial sulphonic ester gave more olefin and (with one exception) less ketone than its equatorial epimer. This has analogy in the reactions of 5α-cholestan-3α- and -3β-yl toluene-p-sulphonate with other nucleophiles,[13] where the axial 3α-ester gives more elimination product and less substitution product than its equatorial 3β-epimer. It is also consistent with predictions of the relative ease of elimination from the two epimeric esters made from a consideration of stereoelectronic factors.[14]

With the equatorial esters the yield of ketone decreases approximately in the order expected ($3\beta < 7\beta < 2\alpha < 6\alpha < 11\alpha$) for progressively increasing steric hindrance to the development of a linear transition state which would follow S_N2 attack by a nucleophile (*e.g.*, dimethyl sulphoxide). With the 3β- and 7β-esters the steric compression in the transition state would not be marked (VI and VII), but it would be more severe in the



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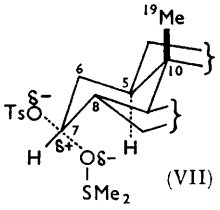

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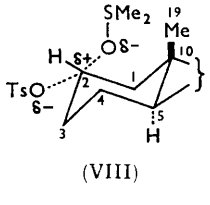

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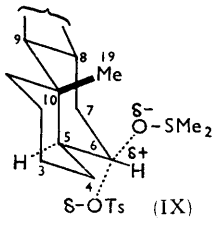

(IX)

transition state for the 2α-ester (VIII), mainly owing to interaction of the 19-methyl group and the dimethyl sulphoxide. The interaction would be minimised by distortion of the flexible ring A analogous to that occurring in 2α-bromo-2β-methyl-5α-cholestan-3-one,[15] but in the rigid ring B distortion is impossible and the transition state for S_N2 attack on the 6α-ester (IX) would be severely compressed by interaction with the 19-methyl group. In fact 5α-cholestan-6α-yl toluene-p-sulphonate gave very little ketone and the methanesulphonate did not react under the conditions used. Similarly, interaction with

[12] Traynelis, Hergenrother, Livingston, and Valicenti, *J. Org. Chem.*, 1962, **27**, 2377.
[13] (*a*) Nace, *J. Amer. Chem. Soc.*, 1952, **74**, 5937; (*b*) Henbest and Jackson, *J.*, 1962, 954.
[14] Barton and Cookson, *Quart. Rev.*, 1956, **10**, 61.
[15] Barton, Lewis, and McGhie, *J.*, 1957, 2907; Djerassi, Finch, Cookson, and Bird, *J. Amer. Chem. Soc.*, 1960, **82**, 5488.

the 18- and 19-methyl groups would cause hindrance in the transition state for an 11α-ester, and no ketone was obtained in this case (however, in the latter case no starting material was recovered). Thus the results are rational on the basis of an S_N2 mechanism, but an S_N1 mechanism does not provide an explanation for them.

3β-Methoxyandrost-5-en-17β-yl toluene-*p*-sulphonate failed to react with dimethyl sulphoxide under the usual conditions. Under more vigorous conditions (3 hours at 140°) 18% of 3β-methoxyandrost-5-en-17-one was obtained, but starting material (37%) was recovered. Similar reluctance of testosterone toluene-*p*-sulphonate to undergo S_N2 reaction with halide ion was recently [13b] ascribed to steric hindrance to development of the linear transition state by the neighbouring 18β-methyl and 12-methylene groups.

Alcohols occurred among the products from many of the reactions. They were obtained from apparently anhydrous reaction mixtures and so may arise by hydrolysis of some intermediate species during working up. It is significant that Smith and Winstein [16] showed dimethyl sulphoxide to react with alkyl halides, giving both *O*-alkyl and *S*-alkyl sulphonium salts, the former being very rapidly hydrolysed. We could not detect sulphonium salts in our reaction mixtures even under a variety of conditions, and so we could not investigate the reason why the hydrolysis proceeded largely by inversion.

Cholesteryl toluene-*p*-sulphonate and dimethyl sulphoxide in the presence of collidine gave cholest-4-en-3-one (55%), cholestadiene (17%), and cholesterol (19%). When this investigation was complete Goutarel and his co-workers [17] reported similar results (with potassium hydrogen carbonate instead of collidine) but showed that in the presence of sodium acetate 3,5-cyclocholestan-6-one was a major product. Hence solvolysis in this case is anchimerically assisted by the 5,6-double bond. The same workers also reported the conversion of 5α-cholestan-3β-yl toluene-*p*-sulphonate into 5α-cholestan-3-one in 20% yield by hot dimethyl sulphoxide in the presence of potassium hydrogen carbonate.

Experimental

Dimethyl sulphoxide was distilled from calcium hydride, and redistilled, the fraction of b. p. 83°/17 mm. being collected. Collidine was dried (KOH) and redistilled before use. Alumina (Spence's grade H) was used for column chromatography, and Merck's silica gel G for thin-layer chromatography on glass (chromatoplate technique). Thin-layer chromatography on a preparative scale was performed on glass plates 25 cm. square, with a layer of adsorbent ~1 mm. thick (loading 60—100 mg. of substance per plate). Light petroleum refers to the fraction of b. p. 40—60°. Rotations are for chloroform solutions, and m. p.s were determined on a Kofler hot stage. The identity of the products was usually confirmed by mixed m. p. determinations, by comparison of their infrared spectra (determined with a Perkin-Elmer Infracord spectrophotometer) with that of authentic samples, and by thin-layer chromatography.

3β-*Methoxy*-5α,22α-*spirostan*-11-*one*.—3β-Hydroxy-5α,22α-spirostan-11-one (1·0 g.) was treated with a boiling suspension of freshly prepared silver oxide (1·0 g.) in methyl iodide for 12 hr. The residue after filtration and evaporation was dissolved in ether and washed with saturated sodium hydrogen sulphite solution, then with water. Evaporation and crystallisation from acetone–methanol gave 3β-*methoxy*-5α,22α-*spirostan*-11-*one* (815 mg.), m. p. 194—197°, $[\alpha]_D$ −31° (*c* 1·7) (Found: C, 75·5; H, 10·3. $C_{28}H_{44}O_4$ requires C, 75·7; H, 10·0%).

3β-*Methoxy*-5α,22α-*spirostan*-11α-*ol*.—3β-Methoxy-5α,22α-spirostan-11-one (815 mg.) in boiling propan-1-ol (200 ml.) was treated with sodium (10 g.) in small pieces during 1 hr. After a further 2 hr. the mixture was poured into water and worked up in ether, to give 3β-*methoxy*-5α,22α-*spirostan*-11α-*ol* (710 mg.) as needles, m. p. 209—210°, $[\alpha]_D$ −75° (*c* 1·2) (Found: C, 74·9; H, 10·4. $C_{28}H_{46}O_4$ requires C, 75·3; H, 10·4%), after crystallisation from ethanol.

Steroid Sulphonic Esters.—The preparation of 5α-cholestan-2α-yl toluene-*p*-sulphonate described below is typical. 5α-Cholestan-2α-ol (400 mg.) and toluene-*p*-sulphonyl chloride (400 mg.) in dry pyridine (5 ml.) were set aside overnight, then poured into water and extracted

[16] Smith and Winstein, *Tetrahedron*, 1958, **3**, 317.
[17] Jarreau, Tchoubar, and Goutarel, *Bull. Soc. chim. France*, 1962, 887.

with ether. The extract was washed with ice-cold dilute hydrochloric acid (three times), water (once), and saturated sodium hydrogen carbonate solution (twice). After drying (Na_2SO_4), the ether was evaporated and the residue crystallised from acetone, to give the toluene-*p*-sulphonate (390 mg.) as needles, double m. p. 129—130°/140—142°, $[\alpha]_D$ −17° (*c* 0·9) (Found: C, 75·7; H, 10·2. Calc. for $C_{34}H_{54}O_3S$: C, 75·2; H, 10·0%). The m. p. (141—143°) of an authentic sample [18] supplied by Dr. Nishida was not depressed on admixture with our specimen.

3β-*Methoxy*-5α,22α-*spirostan*-11α-*yl toluene*-p-*sulphonate*, m. p. 125—127° (from acetone), $[\alpha]_D$ −48° (*c* 0·6) (Found: C, 69·5; H, 8·5. $C_{35}H_{52}O_6S$ requires C, 69·95; H, 8·7%), was prepared in the above manner, as were all the known toluene-*p*-sulphonates used in this investigation. The m. p. and $[\alpha]_D$ agreed with published values and the compounds were shown to be homogeneous by thin-layer chromatography.

5α-Cholestan-2β-yl toluene-*p*-sulphonate, m. p. 112—114° (decomp.), $[\alpha]_D$ +22° (*c* 1·3) (Found: C, 75·1; H, 10·3%) [Nishida [18] gave m. p. 114—115° (decomp.)], rapidly decomposed in warm solvents, so its ethereal solution was evaporated under reduced pressure at room temperature, and the compound was crystallised from ice-cold acetone.

Methanesulphonates were prepared as for toluene-*p*-sulphonates except that the ethereal solutions were evaporated at room temperature and cold solvents were used for crystallisation. In this manner *methanesulphonates* of the following were prepared: 5α-cholestan-6α-ol, m. p. 104—106° (from acetone), $[\alpha]_D$ −55° (*c* 0·9) (Found: C, 72·4; H, 11·0. $C_{28}H_{50}O_3S$ requires C, 72·1; H, 10·7%), -6β-ol, m. p. 90—91° (from acetone), $[\alpha]_D$ −2° (*c* 1·0) (Found: C, 72·1; H, 10·9%), -7α-ol, m. p. 89—90° (prisms from acetone), $[\alpha]_D$ −24° (*c* 1·1) (Found: C, 72·1; H, 10·9%), and -7β-ol, m. p. 106—108° (from acetone), $[\alpha]_D$ +53° (*c* 1·2) (Found: C, 72·15; H, 10·8%).

Reaction between Dimethyl Sulphoxide and Steroid Sulphonic Esters.—(*a*) *With* 5α-*cholestan*-3β-*yl toluene*-p-*sulphonate*. (i) The toluene-*p*-sulphonate [13a] (2·8 g.) in dimethyl sulphoxide (25 ml.) containing collidine (0·75 ml.) was heated at 100° for 3 hr. The mixture was poured into water and extracted with ether. The extract was washed four times with water, twice with 2N-hydrochloric acid, once with water and with saturated sodium hydrogen carbonate solution. The oily product (2·1 g.) obtained on evaporation of the ether and drying at 60° in a high vacuum for 2 hr. was chromatographed on alumina (60 g.). Elution with light petroleum gave 5α-cholest-2-ene (495 mg., 26%), m. p. and mixed m. p. 68—70° (from acetone); elution with light petroleum–benzene furnished 5α-cholestan-3-one (1·25 g., 64%), m. p. and mixed m. p. 127—128° (from acetone–methanol); elution with ether–benzene gave 5α-cholestan-3α-ol (196 mg., 10%), m. p. and mixed m. p. 182—184° (from acetone–methanol). Thin-layer chromatography of the crude product revealed also a trace of 5α-cholestan-3β-ol.

(ii) Treatment of the toluene-*p*-sulphonate (754 mg.) with dimethyl sulphoxide (25 ml.) in the above manner but with sodium hydrogen carbonate (5·03 g.) in stirred suspension gave, after chromatography on alumina (15 g.), 5α-cholest-2-ene (83 mg., 16%), 5α-cholestan-3-one 243 smg., 46%), 5α-cholestan-3α-ol (64 mg., 12%), and a gum (60 mg.) which was mainly 5α-(choletan-3β-ol according to thin-layer chromatography.

(iii) Treatment of the toluene-*p*-sulphonate (1·46 g.) with dimethyl sulphoxide (15 ml.) in the above manner but without collidine or sodium hydrogen carbonate gave, after chromatography on alumina, 5α-cholest-2-ene (800 mg., 81%) 5α-cholestan-3-one (104 mg., 11%), and 5α-cholestan-3α-ol (46 mg., 4%) and -3β-ol (15 mg., 1%), m. p. and mixed m. p. 140—142° (from ethanol).

(*b*) *With* 5α-*cholestan*-3β-*yl methanesulphonate*. The ester (580 mg.) was treated with dimethyl sulphoxide (10 ml.) containing collidine (0·2 ml.) in the above manner, and the oily product (448 mg.) chromatographed on four silica-gel chromatoplates. Elution with benzene gave five bands which were severally extracted with ether, to give (in order of decreasing rate of flow) 5α-cholest-2-ene (55 mg., 13%), unchanged ester (113 mg., 19%), 5α-cholestan-3-one (197 mg., 42%), and 5α-cholestan-3α-ol (53 mg., 11%) and -3β-ol (3 mg., 0·5%).

(*c*) *With* 5α-*cholestan*-3α-*yl toluene*-p-*sulphonate*. Treatment of the toluene-*p*-sulphonate [13a] (1·05 g.) with dimethyl sulphoxide (10 ml.) and collidine (0·35 ml.) as above gave 5α-cholest-2-ene (387 mg., 57%), 5α-cholestan-3-one (251 mg., 34%), and 5α-cholestan-3β-ol (53 mg., 7%).

(*d*) *With* 5α-*cholestan*-7β-*yl toluene*-p-*sulphonate*. (i) Treatment of the toluene-*p*-sulphonate [19] (508 mg.) with dimethyl sulphoxide (5 ml.) containing collidine (0·17 ml.) as above

[18] Nishida, *J. Amer. Chem. Soc.*, 1960, **82**, 4290.
[19] Karrer, Asmis, Sareen, and Schwyzer, *Helv. Chim. Acta*, 1951, **34**, 1022.

and chromatography on alumina gave 5α-cholest-7-ene (80 mg., 23%), m. p. 85° (from acetone), $[\alpha]_D$ +6° (lit.,[20] m. p. 87°, $[\alpha]_D$ +12°; lit.,[21] for 5α-cholest-6-ene, m. p. 87°, $[\alpha]_D$ −88°), and 5α-cholestan-7-one (273 mg., 76%), m. p. and mixed m. p. 113—115°, $[\alpha]_D$ −45°, after crystallisation from acetone–methanol.

(ii) Treatment of the toluene-*p*-sulphonate (238 mg.) with dimethyl sulphoxide (5 ml.) as above, but in the absence of collidine, gave a product (173 mg.) which was homogeneous (chromatoplate) and crystallised from acetone to give 5α-cholest-7-ene, m. p. and mixed m. p. 82—84°.

(*e*) *With 5α-cholestan-7β-yl methanesulphonate.* Treatment of the methanesulphonate (141 mg.) with dimethyl sulphoxide (7 ml.) and collidine (0·07 ml.) as above gave an oil (120 mg.), a portion (98 mg.) of which was chromatographed on two silica-gel chromatoplates. Development with benzene gave four bands which were severally extracted with ether, to give 5α-cholest-7-ene (9 mg., 10%), 5α-cholestan-7-one (61 mg., 64%), and 5α-cholestan-7α-ol (4 mg., 4%) and -7β-ol (2 mg., 2%).

(*f*) *With 5α-cholestan-7α-yl methanesulphonate.* Treatment of the methanesulphonate (201 mg.) with dimethyl sulphoxide (15 ml.) and collidine (0·2 ml.) as above gave a solid (168 mg.) which contained only 5α-cholest-7-ene and 5α-cholestan-7-one (chromatoplate). Chromatography on alumina (6 g.) and elution with light petroleum gave the cholestene (140 mg., 88%), m. p. and mixed m. p. 80—81° (from acetone); elution with benzene–ether gave a solid (19 mg.), m. p. 110—112°, crystallising from acetone to give 5α-cholestan-7-one (14 mg., 8%), m. p. and mixed m. p. 113—115°.

(*g*) *With 5α-cholestan-2α-yl toluene-*p*-sulphonate.* (i) The toluene-*p*-sulphonate (350 mg.) in dimethyl sulphoxide (10 ml.) containing collidine (0·1 ml.) was heated at 100° for 3 hr. The usual isolation procedure gave a product (219 mg.) which was subjected to thin-layer chromatography. Development with benzene produced two distinct bands which were severally extracted with ether, to give 5α-cholest-2-ene (176 mg., 74%), m. p. and mixed m. p. 68—70° (from acetone), and 5α-cholestan-2-one (47 mg., 19%), m. p. and mixed m. p. 128—129° (from acetone–methanol).

(ii) The ester (143 mg.) was treated with dimethyl sulphoxide (4 ml.) for 5 hr. at 100°. The usual procedure gave a homogeneous (chromatoplate) solid (97 mg.) which crystallised from acetone to give 5α-cholest-2-ene, m. p. and mixed m. p. 69—71°.

(*h*) *With 5α-cholestan-2β-yl toluene-*p*-sulphonate.* Treatment of the ester (70 mg.) with dimethyl sulphoxide (95 ml.) and collidine (0·25 ml.) as above gave a product (54 mg.) which was chromatographed on a thin layer of silica gel. Elution with benzene gave four bands, which were severally extracted with cold ether. Band 1 gave 5α-cholest-2-ene (32 mg., 68%), m. p. and mixed m. p. 68—70° (from acetone–methanol). Band 2 gave 5α-cholestan-2-one (6·5 mg., 13%), m. p. and mixed m. p. 127—129° (from acetone–methanol). Bands 3 and 4 gave 5α-cholestan-2α-ol (2 mg.) and -2β-ol (2 mg.), respectively, which were identified chromatographically (thin-layer technique) and by means of their infrared spectra.

(*i*) *With 5α-cholestan-6α-yl toluene-*p*-sulphonate.* Treatment of the toluene-*p*-sulphonate[22] (166 mg.) with dimethyl sulphoxide (5 ml.) and collidine (0·09 ml.) as above gave a product (116 mg.) which was subjected to thin-layer chromatography. Elution with benzene gave three bands (1, 2, and 3 in order of decreasing rate of elution), which were extracted with cold ether. Band 1 gave cholest-5-ene (31·5 mg., 26%), m. p. and mixed m. p. 88—90° (from acetone), $[\alpha]_D$ −54°; band 2 gave starting material (49 mg., 29%), m. p. and mixed m. p. 106—108° (from acetone); band 3 furnished 5α-cholestan-6-one (7·5 mg., 6%), m. p. and mixed m. p. 87—89° (from acetone–methanol).

(*j*) *With 5α-cholestan-6α-yl methanesulphonate.* Treatment of the methanesulphonate (600 mg.) with dimethyl sulphoxide (10 ml.) and collidine (0·2 ml.) as above gave a solid (580 mg., 96%), m. p. 101—103°, which contained only starting material and a trace of cholest-5-ene (chromatoplate). Crystallisation from acetone gave starting material, m. p. and mixed m. p. 103—105°.

(*k*) *With 5α-cholestan-6β-yl methanesulphonate.* Treatment of the methanesulphonate (409 mg.) with dimethyl sulphoxide (7 ml.) and collidine (0·14 ml.) as above gave an oil (320 mg.) which on thin-layer chromatography gave only one spot corresponding to cholest-5-ene.

[20] Eck and Hollingsworth, *J. Amer. Chem. Soc.*, 1941, **63**, 2986; Barton, *J.*, 1945, 813.
[21] Fischer, Lardelli, and Jeger, *Helv. Chim. Acta*, 1951, **34**, 1577.
[22] Shoppee and Summers, *J.*, 1952, 3361.

Crystallisation from acetone gave cholest-5-ene (291 mg., 80%) as needles, m. p. and mixed m. p. 89—92°.

(*l*) *With* 3β-*methoxy*-5α,22α-*spirostan*-11α-*yl toluene*-p-*sulphonate*. The ester (456 mg.) was treated with dimethyl sulphoxide (10 ml.) containing collidine (0·2 ml.) for 3 hr. at 100°. The product (283 mg.) which contained neither a ketone nor a toluene-*p*-sulphonate (infrared spectrum) was chromatographed on alumina (15 g.). Elution with light petroleum–benzene and crystallisation from acetone gave 3β-*methoxy*-5α,22α-*spirost*-9(11)-*ene* (177 mg., 54%), m. p. 151—153°, $[\alpha]_D$ −40° (*c* 0·8) (Found: C, 78·7; H, 10·6. $C_{28}H_{44}O_3$ requires C, 78·5; H, 10·3%) (ΔM_D +134°. Calc. for 9(11)-double bond + 109°; for 11,12-double bond + 33°). Elution with benzene gave a mixture of 3β-methoxy-5α,22α-spirostan-11α- and -11β-ol (69 mg., 21%), m. p. 196—200°, which could not be separated either by crystallisation or chromatography on alumina or silica gel. Thin-layer chromatography revealed approximately equal amounts of two substances of slightly unequal R_F, the slower of which had identical R_F (by direct comparison) with that of 3α-methoxy-5α,22α-spirostan-11α-ol.

(*m*) *With cholesteryl toluene*-p-*sulphonate*. The ester [23] (1·03 g.) in dimethyl sulphoxide (15 ml.) containing collidine (0·38 ml.) was kept at 100° for 3 hr. The residue (675 mg.) obtained by the usual procedure was chromatographed on alumina (20 g.). Elution with light petroleum gave a mixture of cholestadienes, m. p. 60—68°, $[\alpha]_D$ −80° (*c* 1·0), $\lambda_{max.}$ 234 (ε 15,400) and 267 mμ (ε 2900), {lit.,[24] for cholesta-3,5-diene, m. p. 80—81°, $[\alpha]_D$ −129°, $\lambda_{max.}$ 235 mμ (ε 21,300); lit.,[25] for cholesta-2,4-diene, m. p. 69°, $[\alpha]_D$ +169°, $\lambda_{max.}$ 267 mμ (ε 6300); the mixture therefore contains ~80% of cholesta-3,5-diene}. Elution with light petroleum–benzene gave cholest-4-en-3-one (401 mg., 55%), m. p. and mixed m. p. 81—82° (from ether–methanol). Elution with ether–chloroform gave cholesterol (137 mg., 19%), m. p. and mixed m. p. 148—149° (from acetone–methanol).

Reaction of 3β-*Bromo*-5α-*cholestane with Dimethyl Sulphoxide*.—3β-Bromo-5α-cholestane (119 mg.) was treated with dimethyl sulphoxide (5 ml.) containing collidine (0·1 ml.) at 125° for 24 hr. The mixture was worked up in the usual manner to furnish an oil (110 mg.) which was chromatographed on alumina (3 g.). Elution with light petroleum gave an oil (26 mg., 27%) which crystallised from methanol to give 5α-cholest-2-ene, m. p. and mixed m. p. 69—72°. Elution with light petroleum–benzene gave an oil (56 mg., 55%) which crystallised from methanol to give 5α-cholestan-3-one, m. p. and mixed m. p. 128—129°.

We thank Dr. J. McKenna for gifts of chemicals, and Dr. G. H. R. Summers and Dr. S. Nishida for samples. One of us (M. A. S.) thanks the Pakistan Council of Scientific and Industrial Research for paid study leave.

THE UNIVERSITY, SHEFFIELD 10. [*Received, February 28th,* 1963.]

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