SPLITTING OFF OF WATER FROM THE MOLECULAR IONS OF STEROIDAL CYCLOPROPYL KETONES*

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Mass spectra of 14 steroids containing a cyclopropane ring in the vicinity of a keto group were measured and the signals of the ions $[M-H_2O]^+$, $[M-CH_3]^+$ and $[M-CO]^+$ were sought. Using models labelled selectively with deuterium it was shown that the water molecule, split off from the molecular ion of 3α,5-cyclo-5α-cholestan-6-one (*I*) is formed from the hydrogen atoms located in the positions 2β and 9α.

The splitting off of a water molecule from the molecular ion of ketones represents a fragmentation which often takes place to a small extent only and the mechanism of which is never quite simple. While, for example, the molecular ion of cyclohexanone loses water to the detriment of the α- and β-hydrogen atoms (proved by experiments with labelled compounds[1]), the water molecule lost in this manner from the molecular ion of *trans*-decalone is formed from hydrogen atoms coming from any position of the molecule[2]. The loss of a methyl group and of a water molecule represents a typical fragmentation of majority[3] of steroidal ketones, in which the hydrogen atoms from the positions γ and δ mostly contribute to the formation of the molecule of water. Recently we observed that the molecular ion of 3α,5-cyclo-5α-cholestan-6-one (*I*) loses a molecule of water to a much higher extent than 5α-cholestan-6-one (*II*). The introduction of a double bond into the molecule of compound *II* (for example under formation of unsaturated ketones *III* and *IV*) results in an increase in abundance of the ions $[M-H_2O]^+$.

When a double bond or its equivalent was shown to be indispensable for an easier elimination of water from a molecular ion, we measured the mass spectra of a number of steroidal cyclopropyl ketones with the aim of finding the dependence of this type of fragmentation on the structure of the compounds. Table I shows that with a single exception (4α,5-cyclo-A-homo-5α-cholestan-3-one) the loss of water from the molecular ion becomes significant only when the substrate molecule contains at least one hydrogen atom in the position γ with respect to the corresponding keto group. Further it was noticed, that water is lost only when no other, more favourable

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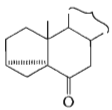
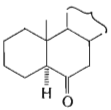
mechanism of stabilisation exists for the given molecular ion (for example the loss of a methyl radical or of a molecule of carbon monoxide). These observations indicated that the most probable candidates for the loss of water from the molecular ion of compound *I* are the hydrogen atoms in positions 1 and 2: we considered that in the first step a severing of the bond between the carbons 5 and 6 takes place under formation of the radical-ion *V* in which free rotation along the bond between the carbons $C_{(9)}$—$C_{(10)}$ permits the assuming of a conformation suitable for the elimination of water (the structure of ion *V* was proposed in analogy with the structure of the hypothetic[4] intermediate *VI*, by which the loss of a water molecule from the molecular ion of 5α-androstan-17-one has been explained).

Selective labelling of compound *I* in the positions 1 and 2 was carried out in the following manner: 1,4-cholestadien-3-one was reduced with deuterium under catalysis with tris(triphenylphosphine)chlororhodium[14,15] to [1α,2α-$^2H_2$]-4-cholest--en-3-one (*VIII*), which we converted to the corresponding enolacetate and further submitted to sodium borohydride reduction. The mass spectrum of [1α,2α-$^2H_2$]-cholesterol (*IX*) formed in this manner confirmed that no deuterium was lost during this process. Compound *IX* was converted to its tosylate, 3α,5-cyclo-5α-cholestan--6β-ol and 3α,5-cyclo-5α-cholestan-6-one (*X*), in the mass spectrum of which signals were found that indicated the loss of water only. Similarly [1β-^2H]-cholesterol[16] was converted to ketone *XII*, the molecular ion of which loses H_2O only. The remaining 2β-hydrogen atom was shown, however, to participate in the water elimination, as evidenced by the spectral properties of compound *XIV*, prepared in the following way: Huang–Minlon reduction of 6α-hydroxy-3α,5-cyclo-5α-cholestan-2-one (*XIII*) was carried out in [$^2H_2$]-ethylene glycol in the presence of potassium deuteroxide The mass spectrum showed that in this modification an exchange of both $C_{(1)}$-hydrogen atoms and a substitution of the oxygen atom for two deuterium atoms took place. The oxidation of this product afforded ketone *XIV* the molecular ion of which *l* oses water as $^1H^2HO$.

This finding confirmed the hypothesis that one hydrogen atom, necessary for the formation of a molecule of water must be "activated" by the neighbourhood of a cyclopropane ring, and that the second hydrogen atom necessary in the fragmentation studied is to be found elsewhere; in view of the general trend derived from the inspection of Table I we assumed that this atom is localized in the position γ with respect to the 6-keto group, *i.e.* in the position 9α. Therefore the synthesis of the 9α-deuterio substrate seemed desirable. The simplest way to such substance was the reduction of 3α,5-cyclo-7,9(11),22-ergostatrien-6-one (*XV*). It is known[17] that the hydrogenation of the $\Delta^{7,9,11}$-dien-6-one system can be conducted in such a way that absorption of a single equivalent of hydrogen may be absorbed. Reduction of compound *XV* with deuterium afforded unsaturated ketone *XVI* from which the required 3α,5-cyclo-5α-ergostan-6-one, labelled in the positions 9α, 11α, 22ξ, 23ξ (*XVII*) was prepared on reduction with lithium in liquid ammonia. The fact that



I



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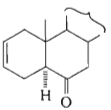

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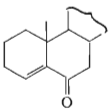

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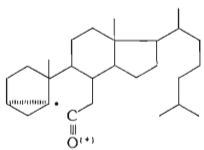

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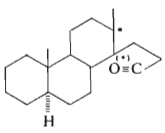

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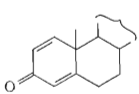

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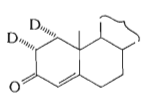

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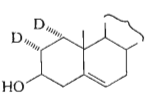

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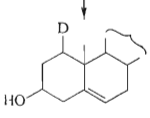

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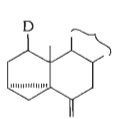

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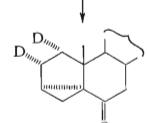
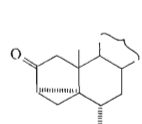


X



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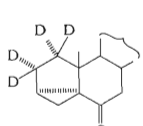
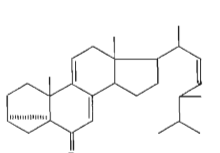
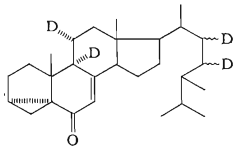


XIV

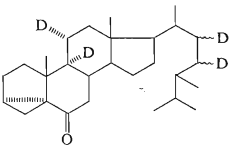


XV

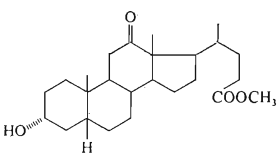
the molecular ion of compound *XVII* splits off a molecule of $^1H^2HO$ agrees with the hypothesis that 2β- and 9-αhydrogen atoms participate in the formation of water from the molecular ion of compounds of type *I*. This hypothesis had to be confirmed by an analysis of the mass spectra of further compounds of type *I*, containing deuterium in close positions. These substrates were prepared in the following manner: 11,11-deuteration was carried out by alkali-catalyzed exchange of enolizable hydrogen atoms in the 12-ketone *XVIII*, while the reduction of the 12-keto group took place best *via* the corresponding dithiolane derivative which was reduced with Raney



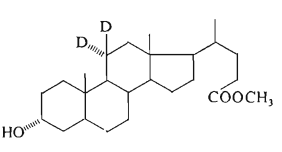
XVI



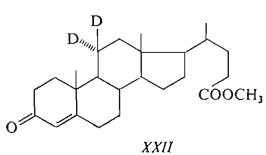
XVII



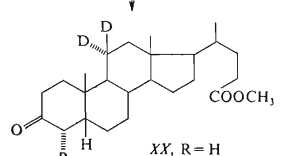
XVIII



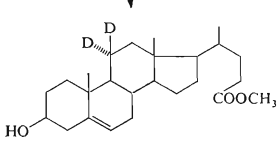
XIX



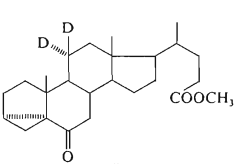
XXII



XX, R = H
XXI, R = Br



XXIII



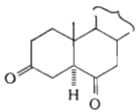
XXIV

nickel. The conversion of compound *XIX* to the required 3α,5-cyclo derivative *XXIV* is shown in the scheme. Similarly, 5α-cholestane-3,6-dione was exposed to heavy water and potassium deuteroxide, leading to an exchange of 7 hydrogen atoms for deuterium. The crude product was partially reduced with tri-tert-butoxylithium aluminum hydride to [2,2,4,4,5,7,7-$^2H_7$]-hydroxy ketone *XXVI* which was then converted to tetradeuterio ketone *XXVII via* the corresponding tosylate (solvolysis in methanolic potassium hydroxide). 8β-Deuterioketone *XXX* was prepared from 3α,5-cyclo-5α-cholest-7-en-6-one (*XXIX*) on reduction with lithium in liquid ammonia. [3-^2H]-Cholesterol (L, ref.[18]) and [19,19-$^2H_2$]-cholesterol (*XXXV*) were isomerized to corresponding i-steroids *via* tosylates, and oxidized to ketones *LI* and *XXXVI*. The mass spectra of ketones *LI*, *XXVII*, *XXX*, *XXIV*, and *XXXVI* confirmed that the water molecule split off from molecular ions does not contain hydrogen atoms from positions 3,4,7,8,11 and 19 and hence, that the only deuterium atoms which contributed to the elimination of $^1H^2HO$, come from the positions 2β and 9α. The mass spectrum of [19,19-$^2H_2$]3α,5-cyclo-5α-cholestan-6-one (*XXXVI*) showed that the methyl radical elimination from the molecular ions of these compounds is mostly due to the loss of the methyl group in the position 10.

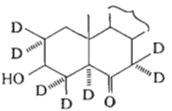
TABLE I
Mass Spectra of Some Cyclopropyl Ketones

Compound	Relative abundances[a] of $[M—X]^+$ ions			Reference
	X = H_2O	X = CH_3	X = CO	
I	15	19	—	
XXXVII	6	24	8	4
XXXVIII	4·5	24·5	36·4	4
XXXIX	1·7	6	0·9	5
XL	10·5	47·5	10·5	6
XLI	14·5	55	5	7
XLII	16·7	14·7	1·3	8
XLIII	9·6	48	10	8
XLIV	5·7	20·1	1·9	9
XLV	83	64	15	9
XLVI	1·8	44	48	10
XLVII	1·5	45	40	11
XLVIII	12·3	12·3	11·4	12
IL	2·1	41·4	2·1	13

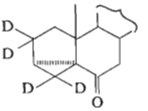
[a] The abundances are based on molecular peaks, not on base peak.



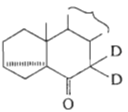
XXV



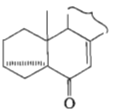
XXVI



XXVII



XXVIII



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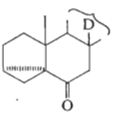
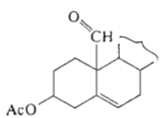
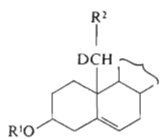


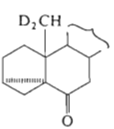
XXX



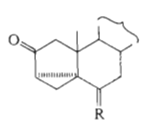
XXXI



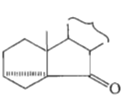
XXXII, $R^1 = Ac$, $R^2 = OH$
XXXIII, $R^1 = Ac$, $R^2 = OMes$
XXXIV, $R^1 = Ac$, $R^2 = D$
XXXV, $R^1 = H$, $R^2 = D$



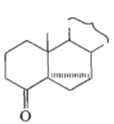
XXXVI



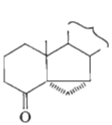
XXXVII, R = H_2
XXXVIII, R = O



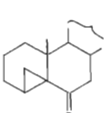
XXXIX



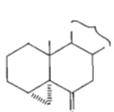
XL



XLI

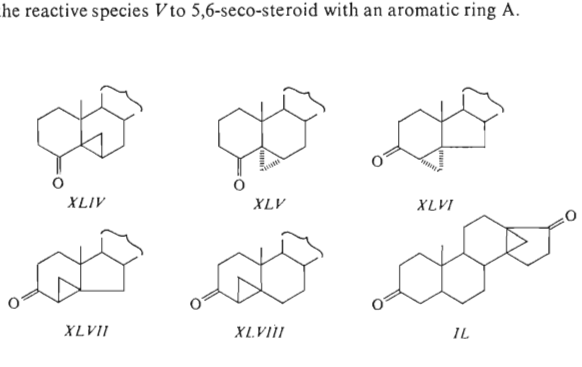


XLII



XLIII

The mechanism of formation of water could be formulated only tentatively. An inspection of the model showed that in the intermediate *V* all 3 atoms that should be combined to a water molecule are rather apart from one another and the probability of their interaction is very low. In addition to this the approach of the oxonium group to the hydrogen atom in the position 2β is hindered by the large methyl group in the position 10. It is also improbable that the cyclopropyl radical formed would be-main unrearranged. Therefore we assume that previous to the water molecule formation a rearrangement of the methyl group to the position 5 and of the 2β-hydrogen atom to the carbon atom $C_{(10)}$ take place in the radical-ion *V*. Thus all three atoms under consideration come close to each other. The driving force for the splitting off of a molecule of water and of the methyl radical is probably the partial stabilization of the reactive species *V* to 5,6-seco-steroid with an aromatic ring A.



Partial formulae represent cholestane derivatives.

EXPERIMENTAL

The melting points were determined on a Kofler block and they are not corrected. Samples for analysis were dried at room temperature and 53·3 Pa over phosphorus pentoxide. Optical rotation and the IR spectra were measured in chloroform, unless stated otherwise, the ^{1}H-NMR spectra in deuteriochloroform on a Tesla 60 instrument. Chemical shifts are given in δ-scale (ppm, tetramethylsilane). The mass spectra were measured on an AEI MS 902 instrument.

[1α,2α-$^2H_2$]-3β-Hydroxy-5-cholestene (*IX*)

[1α,2α-$^2H_2$]-4-cholesten-3-one (90 mg), prepared from 1,4-cholestadien-3-one (*VII*) according to ref.[15], was dissolved in ethyl acetate (4 ml) and acetic anhydride (0·8 ml) and a drop of a catalyst containing 2·5 mg of perchloric acid was added. After 15 min the reagent was decomposed by stirring with 2 g of sodium hydrogen carbonate in 4 ml of water. The organic layer was washed with aqueous saturated sodium chloride solution and dried over sodium sulfate. After evaporation of the solvents *in vacuo* the residue was dissolved in ethanol (10 ml) and reduced with sodium borohydride (60 mg) at room temperature. After 20 h the solution was concentrated in a vacuum, diluted with aqueous sodium chloride solution and the precipitated product *IX* was extracted with ether. The product was purified by thin-layer chromatography on silica gel (benzene), m.p. 146—147°C (62 mg), lit.[19] gives 146—147°C.

[1α,2α-$^2H_2$]-3α,5-Cyclo-5α-cholestan-6-one (*X*)

p-Toluenesulfonyl chloride (90 mg) was added to a solution of compound *IX* (50 mg) in 0·2 ml of pyridine. The mixture was allowed to stand at 25°C for 20 h, then poured into water and the product extracted with ether. The extract was washed with dilute hydrochloric acid, saturated sodium chloride solution and potassium hydrogen carbonate solution, filtered and the filtrate evaporated. The product was refluxed with potassium carbonate solution (100 mg) in 1 ml of water and 5 ml of dioxane. After 6 h the mixture was concentrated in a vacuum and the product dissolved in ether. After washing with water and drying by filtration through a column of sodium sulfate the filtrate was concentrated and the residue dissolved in acetone (4 ml) and oxidized according to Jones at 0°C. The product was precipitated with aqueous potassium hydrogen carbonate, extracted with ether, the extract washed with sodium chloride solution, dried over sodium sulfate and evaporated. The residue was purified by thin-layer chromatograpny on silica gel in benzene; the zone corresponding to compound *I* was eluted with ether, the product (35 mg) was crystallized from methanol giving crystals melting at 92—97°C (ref.[19] gives m.p. 96—98°C). Mass spectrum: $M^+ = 388$.

[1β-^2H]-3α,5-Cyclo-5α-cholestan-6-one (*XII*)

Analogously [1β-^2H]-cholesterol (*XI*, 40 mg) was tosylated, solvolysed and then oxidized to compound *XII*(17 mg), m.p. 90—95°C, mass spectrum: $M^+ = 385$.

[1,1,2,2-$^2H_4$]-3α,5-Cyclo-5α-cholestan-6-one (*XIV*)

A mixture of 6α-hydroxy-3α,5-cyclo-5α-cholestan-2-one (*XIII*), ref.[4], 8 mg) and hydrazine hydrate (99%, 0·2 ml) were heated at 100°C for 20 h, the mixture was concentrated in a vacuum and dried. Chromatography on a thin layer of silica gel (5% ether in benzene) demonstrated the absence of the starting compound (R_F 0·40) in the product (R_F 0·1). The residue was heated at 200°C with 4% potassium deuteroxide in [$^2H_2$]-ethylene glycol (2 ml). After 3 h heating the mixture was poured into an aqueous solution of sodium chloride and the product was extracted with ether. After washing of the extract and evaporation the residue was oxidized according to Jones in acetone; the mixture was worked up as in the preceding cases, yielding 2 mg of [1,1,2,2-$^2H_4$]-3α,5-cyclo-5α-cholestan-6-one (*XIV*), m.p. 87—93°C.

[9α,11α,22ξ,23ξ-$^2H_4$]-3α,5-Cyclo-5α-ergostan-6-one (*XVII*)

A solution of 3α,5-cyclo-5α-ergosta-7,9(11),22-trien-6-one[20] (*XV*, 85 mg) in cyclohexane (5 ml) was shaken with platinum dioxide (40 mg) under deuterium. After 1 h the catalyst was filtered

off and the solution concentrated in a vacuum. The UV spectrum of the residue showed the presence of an α,β-unsaturated ketone (*XVI*, λ_{max} = 238 nm) accompanied by a dienone (λ_{max} = = 287 nm). The ^{1}H-NMR spectrum confirmed the disappearance of the Δ^{22} double bond (5·22 ppm, mt) and a substantial decrease in the intensity of the signal of the $C_{(11)}$-vinyl proton (6·08 ppm, mt). The product, in which compound *XVI* prevailed, was reduced with lithium (100 mg) in liquid ammonia (30 ml) and tetrahydrofuran (6 ml). After 10 min reaction the mixture was decomposed with solid ammonium chloride (2 g) and the product was partitioned between water and ether. The ethereal layer was washed with water, dried over sodium sulfate and dried. After evaporation of the solvent the product was applied onto a thin layer of silica gel (benzene). The main component of the mixture (22 mg) was oxidized with *m*-chloroperbenzoic acid (40 mg in 1 ml of ether, —5°C, 3 h). The unchanged part was isolated by means of preparative thin-layer chromatography, m.p. 104—108°C (ref.[21] gives m.p. 108—110°C); mass spectrum: M^+ = 402.

Methyl [11,11-$^2H_2$]-3α-hydroxy-12-oxo-5β-cholanoate (*XIX*)

Ketone *XVIII* (300 mg) was reacted with potassium deuteroxide (1 ml), 10% in D_2O in dioxane (5 ml). The mixture was heated at 100°C for 20 h, concentrated to 1 ml and acidified with a mixture prepared from thionyl chloride (0·5 ml) and deuterium oxide (2 ml). The precipitate was extracted with chloroform and the extract evaporated. The crude product was dissolved in tetrahydrofuran and mixed with an ethereal diazomethane solution. The solution of the ester formed was concentrated *in vacuo*, the residue dissolved in ethanedithiol (1 ml) and boron trifluoride etherate (1 ml). After 30 min it was shown by thin-layer chromatography that the starting compound had disappeared. The solution was diluted with benzene and washed with 10% potassium hydroxide in water and water. The mixture was evaporated in a vacuum and the residue stirred with Raney nickel (8 ml) in boiling methanol (70 ml) for 18 h. Inorganic components were filtered off, the filtrate concentrated and chromatographed on silica gel. Ether (20%) in benzene eluted 200 mg of labelled product which crystallized from methanol, m.p. 112—113°C (ref.[22] gives m.p. 111 to 112°C).

Methyl [11,11-$^2H_2$]-3-oxo-5β-cholanoate (*XX*)

Hydroxy derivative *XIX* (190 mg) was oxidized in acetone (10 ml, 20°C) according to Jones until thin-layer chromatography on silica gel in 25% ether in benzene showed that the starting compound had disappeared. After working up the yield was 180 mg of compound *XX*, m.p. 114—116°C (an authentic sample of methyl 3-oxo-5β-cholanoate[23], melted at 116—118°C). Mass spectrum: M^+ = 390.

Methyl [11,11-$^2H_2$]-3-oxo-4-cholenoate (*XXII*)

Ketone *XX* (174 mg) was dissolved in acetic acid (9 ml) at 40°C and pyridinium bromide perbromide[24] (87%, 158 mg) was added to it. After one minute the solution lost its original red colour and the temperature was decreased to 20°C. After another 10 min, chromatography indicated that the mixture no longer contained the starting compound *XX*. The mixture was decomposed with aqueous sodium chloride solution (100 ml) and the precipitate of compound *XXI* was filtered off. The product was treated with calcium carbonate (0·4 g) in boiling dimethylacetamide (5 ml) for 1 h. The majority of the solvent was evaporated *in vacuo* and the product was dissolved in chloroform, applied on a thin layer of silica gel (4 plates of 20 × 20 × 0·1 dimensions) and developed with 10% of ether in benzene. The main product (85 mg) had equal

chromatographic properties as methyl 3-oxo-4-cholenoate. M.p. 124—126°C (ref.[25] gives m.p. 126—127°C). Mass spectrum: $M^+ = 388$.

Methyl [11,11-$^2H_2$]-3β-hydroxy-5-cholenoate (*XXIII*)

Ketone *XXII* (83 mg) was dissolved in a mixture of ethyl acetate (7 ml) and acetic anhydride (0·88 ml) and 1·7 ml of dilute perchloric acid (0·05 ml in 25 ml of ethyl acetate) were added to it. After 15 min standing the mixture was decomposed with aqueous sodium hydrogen carbonate. The product was dissolved in methanol and reduced with an aqueous solution of sodium borohydride (100 mg, 10 ml). After 20 h standing the mixture was worked up and a substance isolated the polarity of which was equal to that of methyl-3β-hydroxy-5-cholenoate[26]; mass spectrum $M^+ = 390$.

Methyl [11,11-$^2H_2$]-6-oxo-3α,5-cyclo-5α-cholanoate (*XXIV*)

Hydroxy derivative *XXIII* (40 mg) was tosylated, solvolysed and oxidized in the same manner as in the preparation of compound *X*. The product was purified using thin-layer chromatography on silica gel (10% ether in benzene, 28 mg), m.p. 81—83°C (methanol), $[\alpha]_D^{20}$ +103 (*c* 0·9); mass spectrum: $M^+ = 388$.

[2,2,4,4-$^2H_4$]-3α,5-Cyclo-5α-cholestan-6-one (*XXVII*)

4α-Cholestane-3,6-dione[27] (*XXV*, 200 mg) was reacted with potassium deuteroxide under the conditions used in the preparation of compound *XVIII*. The crude product was dissolved in tetrahydrofuran (5 ml) and reduced at 0°C with tri-tert-butoxylithium aluminum hydride (200 mg). After 15 min the mixture was poured into dilute hydrochloric acid, the product was extracted with chloroform and purified chromatographically. Compound *XXVI* (83 mg) was tosylated with 200 mg of *p*-toluenesulfonyl chloride in 0·5 ml of pyridine at 20°C and the mixture was worked up. The product was solvolysed in a 5% potassium hydroxide solution in methanol (10 ml) for 90 min, the mixture was concentrated *in vacuo* to 2 ml volume and then diluted with water. The precipitated compound was filtered off and crystallized from aqueous methanol. M.p. 94—96°C, IR spectrum (CCl_4): 1 693, 2 208, 2 180, 2 212 cm^{-1}. Mass spectrum: $M^+ = 388$.

[3-^{2}H]-3α,5-Cyclo-5α-cholestan-6-one (*LI*)

Hydroxy compound *L* (50 mg, ref.[18] was converted in the same manner to compound *LI*, *i.e.* by tosylation, solvolysis and oxidation. M.p. 95—97°C; mass spectrum: $M^+ = 385$.

[7,7-$^2H_2$]-3α,5-Cyclo-5α-cholestan-6-one (*XXVIII*)

The exchange of enolisable hydrogen atoms of ketone *I* was carried out in the same manner as in the preparation of compound *XIX*. The product was measured without further purification. Mass spectrum: $M^+ = 386$.

[8β-^{2}H]-3α,5-Cyclo-5α-cholestan-6-one (*XXX*)

Lithium (40 mg) was dissolved in 5 ml of deuterioammonia, prepared from magnesium nitride and heavy water, and a solution of 50 mg of 3α,5-cyclo-5α-cholest-7-en-6-one[30] (*XXIX*) in 1 ml of toluene was added to the blue solution of lithium. The reaction mixture was stirred and re-

fluxed for 30 min, ammonia was distilled off and the mixture saturated with solid ammonium chloride. Organic material was extracted with ether, the extract washed with water, dried, evaporated, and the residue applied on a silica gel in layer. After chromatography in benzene the main product was eluted and isolated, M.p. 90—94°C; mass spectrum = 385.

[19-^{2}H]-3-Acetoxy-5-cholesten-19-ol (*XXXII*)

Aldehyde *XXXI* (ref.[31], 100 mg) was reduced with sodium borodeuteride (50 mg) in a mixture of tetrahydrofuran (4 ml) and ethyl acetate (0·8 ml) at 0°C. Heavy water (10 drops) was added dropwise over 50 min. After 2 h standing the solution was diluted with benzene, washed with a saturated sodium chloride solution in water, dried over sodium sulfate and evaporated in a vacuum. The residue crystallized from acetone, m.p. 119—121°C (m.p. of authentic non-labelled sample[28] is 120—121°C).

[19-^{2}H]-3β-Acetoxy-19-methanesulfonyloxy-5-cholestene (*XXXIII*)

Hydroxy derivative *XXXII* (50 mg) was allowed to stand in the presence of methanesulfonyl chloride (0·2 ml) in pyridine (0·5 ml) at 20°C for 18 h. After working up of the mixture the product was crystallized from a mixture of dichloromethane and heptane; m.p. 142—144°C (ref.[29] gives m.p. 144—146°C), mass spectrum: $[M-60]^+ = 463$, $[M-96]^+ = 427$; ^{1}H-NMR spectrum: 0·71 (s, 3 protons), 0·85 (d, $J = 6·5$ Hz, 6 protons), 2·02 (s, 3 protons), 2·99 (s, 3 protons), 4·50 (broad s, 0·8 protons), 4·18 (broad, s, 0·2 protons), 4·63 (broad mt, 1 proton), 5·69 (mt, $W_{1/2} = 10$ Hz, 1 proton) ppm; IR spectrum: 1 730, 1 255, 1 037, 1 340, 1 179, 3 040 cm^{-1}.

[19,19-$^2H_2$]-3β-Acetoxy-5-cholestane (*XXXIV*)

Mesylate *XXXIII* (45 mg) was dissolved in dimethoxyethane (4 ml) and heavy water (1 ml) and the solution stirred with sodium iodide (0·2 g) and zinc dust (1 g) under refluxing for 6 h. Inorganic material was then filtered off and washed with ether, the filtrate was washed with water, dried and purified by chromatography in 50% benzene in light petroleum. The main product was chromatographically identical with cholesteryl acetate, m.p. 115—116°C (18 mg methanol), undepressed on admixture of an authentic sample. Mass spectrum: $M^+ = 430$.

[19,19-$^2H_2$]-3α,5-Cyclo-5α-cholestan-6-one (*XXXVI*)

Acetate *XXXVI* (18 mg) was hydrolysed with 1% potassium hydroxide in methanol (60°C, 15 min) and the formed alcohol *XXXV* was tosylated, solvolysed and oxidized as in the preparation of compound *VIII*. M.p. 94—96°C, mass spectrum: $M^+ = 386$.

Partial Mass Spectra of Some Cyclopropyl Ketones

The abundances in % of molecular ion are given in brackets after the corresponding m/z values.

I: 351 (2·2); 355 (8·7); 356 (12·4); 357 (3·3); 366 (32·4); 367 (8·7); 368 (1·8); 369 (29·1); 360 (6·9); 384 (100·0); 385 (31·6); 386 (5·5).

II: 353 (2·0); 355 (1·3); 357 (5·4); 358 (1·8); 368 (2·9); 370 (7·0); 371 (28·0); 372 (16·9); 373 (4·0); 386 (100·0); 387 (31·5); 388 (5·4).

III: 351 (3·3); 355 (4·0); 356 (21·7); 357 (6·0); 366 (15·8); 367 (5·2); 368 (3·0); 369 (100·0); 370 (28·3); 371 (4·3); 384 (100·0); 385 (28·3); 386 (4·5).

IV: 341 (4·0); 342 (1·9); 351 (4·3); 352 (1·3); 355 (4·0); 356 (10·7); 357 (3·2); 366 (17·0); 367 (5·6); 369 (26·7); 370 (8·0); 371 (1·9); 384 (100·0); 385 (30·7); 386 (6·1);

IX: 355 (25·8); 356 (7·5); 366 (7·5); 367 (7·5); 368 (17·5); 369 (10·0); 370 (41·7); 371 (14·2); 372 (4·2); 373 (25·0); 374 (6·7); 386 (11·7); 387 (9·2); 388 (100·0); 389 (26·7).

X: 355 (5·3); 356 (7·5); 357 (4·2); 358 (6·1); 359 (1·7); 366 (1·7); 367 (8·6); 368 (14·7); 369 (5·3); 370 (2·8); 371 (17·0); 372 (5·3); 384 (8·0); 385 (8·9); 386 (100·0); 387 (31·9); 388 (5·0).

XII: 355 (7·1); 356 (13·0); 357 (9·5); 358 (2·4); 366 (8·9); 367 (18·6); 368 (6·8); 369 (9·5); 370 (17·7); 271 (6·4); 384 (44·3); 385 (100·0); 386 (36·7); 387 (7·3).

XIV: 355 (6·6); 356 (11·0); 357 (4·6); 358 (3·2); 359 (3·6); 360 (7·3); 361 (2·4;) 368 (4·9); 369 (20·0); 370 (13·4); 371 (5·1); 372 (7·6); 373 (20·2); 374 (7·6); 385 (2·4); 386 (5·6); 387 (31·7); 388 (100·0); 389 (37·8); 390 (8·0).

XVII: 346 (4·7); 347 (14·7); 348 (28·2); 349 (40·0); 350 (21·8); 351 (7·6); 352 (4·1); 353 (2·3); 371 (4·1); 372 (7·6); 373 (11·7); 374 (11·2); 375 (5·3); 376 (2·3); 381 (2·3); 382 (10·0); 383 (17·6); 384 (13·0); 385 (10·6); 386 (14·7); 387 (23·5); 388 (24·1); 389 (26·5); 390 (14·1); 391 (5·3); 392 (1·8); 398 (2·3); 399 (7·6); 400 (30·6); 401 (64·7); 402 (100·0); 403 (64·7); 404 (41·2); 405 (18·2); 406 (7·6); 407 (3·5); 408 (1·8).

XVIII: 373 (5·7); 374 (5·7); 375 (2·8); 386 (10·0); 387 (8·6); 388 (5·7); 389 (2·8); 404 (74·3); 405 (100·0); 406 (61·4); 407 (22·8); 408 (6·4).

XXIV: 353 (2·2); 354 (4·8); 355 (7·4); 356 (8·5); 357 (9·6); 358 (14·8); 359 (15·9); 360 (8·5); 361 (2·6); 367 (3·0); 368 (13·7); 369 (33·3); 370 (23·3); 371 (15·9); 372 (21·8); 373 (13·7); 374 (4·4); 385 (3·7); 386 (45·2); 387 (100·0); 388 (66·6); 389 (19·6); 390 (4·8);

XXVI: 371 (2·3); 372 (3·4); 373 (5·7); 374 (9·1); 375 (9·1); 376 (4·6); 388 (4·9); 389 (11); 390 (10·3); 391 (11·9); 392 (10·8); 393 (11·4); 394 (5·4); 404 (4·6); 405 (12·6); 406 (38·3); 407 (81·7); 408 (100·0); 409 (51·4); 410 (12·6).

XXVII: 355 (2·3); 356 (6·4); 357 (9·8); 358 (20·4); 359 (7·0); 360 (2·8); 367 (1·9); 368 (7·9); 369 (16·2); 370 (7·0); 371 (5·1); 372 (14·0); 373 (19·5); 374 (5·1); 384 (1·9); 385 (3·2); 386 (21·9); 387 (69·8); 388 (100·0); 389 (29·3); 390 (5·1).

XXVIII: 353 (2·6); 357 (7·4); 358 (11·1); 359 (3·0); 367 (2·2); 368 (24·0); 369 (7·8); 370 (3·0); 371 (18·9); 372 (5·9); 385 (8·1); 386 (100·0); 387 (23·7); 388 (5·2).

XXX: 356 (7·6); 357 (10·6); 358 (3·0); 366 (3·3); 367 (13·6); 368 (4·2); 369 (3·0); 370 (15·1); 371 (4·8); 384 (14·8); 385 (100·0); 386 (31·8); 387 (5·4).

XXXVI: 356 (4·9); 357 (10·1); 358 (7·0); 367 (5·2); 368 (30·1); 369 (24·9); 370 (7·8); 371 (7·0); 385 (17·2); 386 (100·0); 387 (32·3); 388 (5·2).

LI: 356 (7·3); 357 (10·7); 358 (4·0); 366 (7·7); 367 (20·0); 368 (6·7); 369 (2·0); 370 (16·0); 371 (5·3); 384 (4·7); 385 (100·0); 386 (26·0); 397 (4·7).

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