Dienone–Phenol Type Rearrangements. Part IV.[1] 2-Hydroxy-3-oxo-Δ^4-steroids

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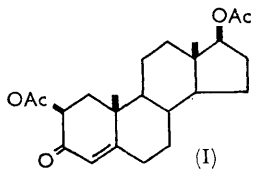
The rearrangement of some steroidal hydroxy-cyclohexenones under a variety of acidic conditions has been studied. 2α-Hydroxy-cholest-4-en-3-ones give, in general, products with functionality at C-6 while C-2 becomes saturated. Enol acetates are also formed, but only one case of aromatisation was observed.

THE rearrangement of cyclohexadienones to phenols is now a well documented reaction.[2] However, there are other compounds, at the same formal level of oxidation, whose reactivity has been less extensively studied. Among these are the hydroxycyclohexenones. Clarke has shown that 2β-hydroxytestosterone diacetate (I), on reaction with toluene-*p*-sulphonic acid in boiling methanol, gives the 3,6-diketone (II; R = OAc),[3]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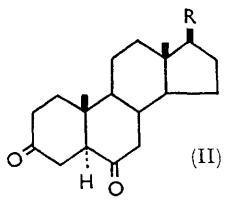
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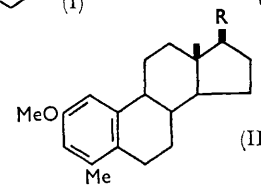
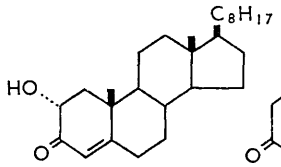

(III)

while the corresponding 2α-hydroxy-compound gave the 3,6-dione (II; R = OAc) together with a phenol ether identified as 2-methoxy-4-methyl-1,3,5(10)-estratrien-17β-ol (III; R = OH).[4] The rearrangement of two compounds containing γ-hydroxy-αβ-unsaturated ketone systems to phenols has been reported [5] while in a monocyclic system, Fort [6] has shown that the toluene-*p*-sulphonate of 6-hydroxy-3,5,5-trimethylcyclohex-2-enone rearranges to 3,4,5-trimethylphenol. It appears that under acid conditions, α′-hydroxy-αβ-unsaturated ketones show electrophilic character on the γ-carbon atom. In order to characterise this reaction further, we have investigated the acid-catalysed rearrangement of 2α-hydroxycholest-4-en-3-ones under a variety of conditions.

2α-Hydroxycholest-4-en-3-one (IV) was prepared from 4β,5-epoxy-5β-cholestan-3-one by reaction with sulphuric acid in acetone.[7] The epoxide was best prepared by treatment of cholest-4-en-3-one with alkaline hydrogen peroxide in methanol–ether. Use of methanol–acetone media led to an extended reaction of nucleophilic opening of the epoxide ring by the acetonyl anion to produce 5-acetonyl-4-hydroxycholestan-3-one (V) identified by its spectral properties and combustion analysis. The 4- and 6α-methyl homologues were prepared in a similar manner from the corresponding cholest-4-en-3-ones.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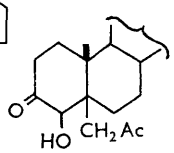
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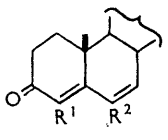
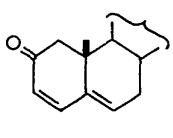

(VI)

The various hydroxycholestenones were rearranged using toluene-*p*-sulphonic acid in benzene, toluene-*p*-sulphonic acid in methanol, or perchloric acid in acetic anhydride–ethyl acetate.

With toluene-*p*-sulphonic acid in benzene, 2α-hydroxycholest-4-en-3-one (IV) gave cholesta-4,6-dien-3-one (VI; $R^1 = R^2 = H$) as the major product, together with 5α-cholestane-3,6-dione (II; R = C_8H_{17}) and a small amount of cholesta-3,5-dien-2-one (VII). With the same acid in methanol as solvent, the two major products were 3,3-dimethoxy-5α-cholestan-6-one,[8] and the aromatic 2-methoxy-4-methyl-19-norcholesta-1,3,5(10)-triene (III; R = C_8H_{17}).[9] The dimethyl acetal showed a negative Cotton effect curve, consistent with the presence of a free carbonyl group at C-6. Its identity with the compound obtained [8] by treatment of 6β-methoxy-, 6β-hydroxy-, or 6β-bromocholest-4-en-3-one or cholestane-3,6-dione with methanolic hydrochloric acid, was established by its m.p. and by its chemical reactions. 3-Methoxy-5α-cholest-2-en-4-one (VIII) was also isolated from this reaction. The structure was deduced from its analytical and spectral properties and confirmed by comparison with an authentic sample.[10]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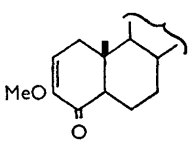
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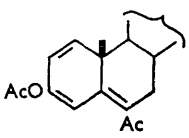
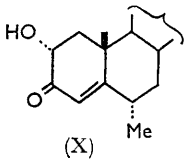

(IX)

Treatment of the hydroxy-ketone (IV) with perchloric acid in acetic anhydride–ethyl acetate gave a complex

[1] Part III, B. R. Davis and P. D. Woodgate, *J. Chem. Soc.* (*C*), 1968, 712.
[2] A. J. Waring, *Adv. Alicyclic Chem.*, 1966, **1**, 131.
[3] R. L. Clarke, *J. Amer. Chem. Soc.*, 1960, **82**, 4629.
[4] R. L. Clarke, *J. Amer. Chem. Soc.*, 1962, **84**, 467.
[5] B. R. Davis and T. G. Halsall, *J. Chem. Soc.*, 1962, 1833.
[6] A. W. Fort, *J. Org. Chem.*, 1961, **26**, 332.
[7] M. Tomoeda, M. Ishizaki, M. Kobayashi, S. Kanatomo, T. Toga, M. Inuzuka, and T. Furuta, *Tetrahedron*, 1965, **21**, 733.
[8] D. J. Collins and J. J. Hobbs, *Austral. J. Chem.*, 1964, **17**, 661.
[9] R. J. Conca and W. Bergmann, *J. Org. Chem.*, 1953, **18**, 1104.
[10] B. Camerino, B. Patelli, and R. Sciaky, *Gazzetta*, 1962, **92**, 709.

mixture of products from which was isolated, in 40% yield, the acetyl-enol acetate (IX) identified by its mass spectral molecular formula and i.r., u.v., and n.m.r. spectra.

When these rearrangements were carried out using 2α-hydroxy-6α-methylcholest-4-en-3-one (X) the chief product in each case was 6-methylcholesta-4,6-dien-3-one (VI; $R^1 = H$, $R^2 = Me$), although with perchloric acid in acetic anhydride–ethyl acetate, a small amount of the enol acetate (XI) was obtained as an unstable yellow oil.



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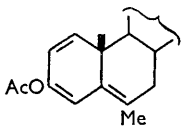

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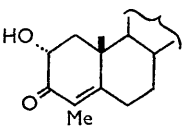

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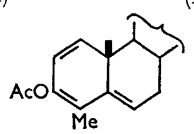

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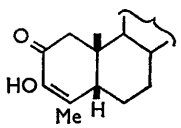


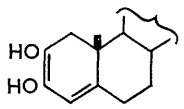
(XIV)

With the 4-methyl compound (XII), some of the linear 4,6-dien-3-one (VI; $R^1 = Me$, $R^2 = H$) was isolated from reactions carried out under the three conditions described above. Under enol acetylation conditions, a small amount of the enol acetate (XIII) was obtained, but with toluene-*p*-sulphonic acid in benzene, the diosphenol (XIV) was the major product.

The structures of all of these products were deduced from molecular formulae, established by combustion analysis or high resolution mass spectrometry, and by the use of i.r., u.v., and n.m.r. spectra.

The yields of products isolated are shown in the Table.

The course of these reactions may be rationalised in the following manner. α-Substituted ketones are known not to react readily by S_N1 processes, presumably because the intermediate carbonium ion would place a positive charge next to the positively charged end of the carbonyl group. However, in one enol form, such compounds bear an allylic substituent, more readily lost by ionisation. In the present instance, two possible enols may be formed; both (XV) and (XVI) may exist as the enol methyl ether or enol acetate depending on the solvent. In the case of the enol (XVI) the hydroxy-



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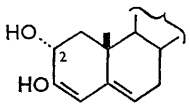
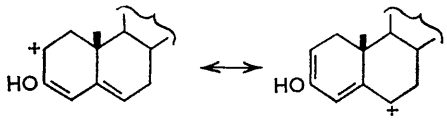


(XVI)

group at C-2 is now allylic and after protonation would be readily lost as water to give the ion (XVII). It appears that this ion reacts as if it more closely resembles (XVIIb); thus loss of a proton from C-7 and ketonisation



(XVIIa) (XVIIb)

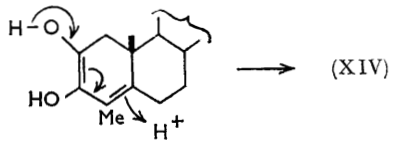
at C-3 would provide the linear dienones (VI); this is especially the case when a methyl group is present at C-6 to stabilise a positive charge at that site. The ion (XVIIa, b) may, alternatively, undergo attack by nucleophilic oxygen at C-6 to produce, finally, the 3,6-dione. It is known that 6α-hydroxycholest-4-en-3-one gives cholestane-3,6-dione on reaction with acid.[8] The oxygen atom may, in the case of solvent benzene, be water either from C-2 or from the toluene-*p*-sulphonic acid monohydrate.

The two trienol acetates (XI) and (XIII) can arise by formation of the enol acetates of type (XVI) followed by dehydration. In the case of the unsubstituted compound (IV), the first formed enol acetate may undergo substitution at C-6 by an acetyl group through an addition–elimination mechanism to give compound (IX).

Yields and products from rearrangements of 2-hydroxy-3-oxo-Δ^4-steroids

Substrate	Methanol–toluene-*p*-sulphonic acid	Benzene–toluene-*p*-sulphonic acid	Acetic anhydride–ethyl acetate–perchloric acid
2α-Hydroxycholest-4-en-3-one	2-Methoxy-4-methyl-19-nor-cholesta-1,3,5(10)-triene (16%) 3,3-Dimethoxycholestan-6-one (29%) 3-Methoxy-5α-cholest-2-en-4-one (29%)	Cholesta-3,5-dien-2-one (5%) Cholesta-4,6-dien-3-one (53%) Cholestane-3,6-dione (20%)	6-Acetyl-3-acetoxycholesta-1,3,5-triene (35%)
2α-Hydroxy-4-methylcholest-4-en-3-one	4-Methylcholesta-4,6-dien-3-one (70%)	4-Methylcholesta-4,6-dien-3-one (9%) 3-Hydroxy-4-methyl-5β-cholest-3-en-2-one (65%)	4-Methylcholesta-4,6-dien-3-one (67%) 3-Acetoxy-4-methylcholesta-1,3,5-triene (10%)
2α-Hydroxy-6α-methylcholest-4-en-3-one	6-Methylcholesta-4,6-dien-3-one (88%)	6-Methylcholesta-4,6-dien-3-one (49%)	6-Methylcholesta-4,6-dien-3-one (51%) 3-Acetoxy-6-methylcholesta-1,3,5-triene (4%)
2α-Acetoxycholesta-4,6-dien-3-one	Cholesta-1,4,6-trien-3-one (26%) 3-Methoxycholesta-3,5-dien-2-one (35%)		

The diosphenol (XIV) could arise from the enol (XV) by protonation at C-5 according to the scheme



(XIV)

The mode of formation of the aromatic compound is obscure, although a tentative mechanism for its formation has been advanced in the testosterone case.[4] Further experiments are in progress in this laboratory to clarify this point.

The reactions of this system show clear similarities with those of 6-halo- or 6-oxygenated steroidal Δ^4-3-ketones. Thus, Fieser and Romero [11] showed that 6β-bromocholest-4-en-3-one gave 2α-acetoxycholest-4-en-3-one with potassium acetate in acetic acid, a reaction which has been used in the synthesis of 2-hydroxylated steroid derivatives.[12–15] A more extensive study has been made [8] of the reactivity in acidic alcoholic solution or on alumina of 6β- and 6α-bromocholest-4-en-3-one. Although a number of products are common to the reactions of both the 2- and 6-substituted derivatives their proportions differ so widely that it is ununlikely that the reactions proceed by way of a common ion.

EXPERIMENTAL

For general experimental details see Part III.[1]

4β,5-Epoxy-5β-cholestan-3-one.—Hydrogen peroxide (30%; 10 ml.) and aqueous sodium hydroxide (4N; 10 ml.) were added slowly to a solution of cholest-4-en-3-one (2·0 g.) in ether (100 ml.) and methanol (300 ml.) and the solution was set aside for 2 hr. at 20°. Work up and chromatography gave the epoxide (1·90 g., 91%) as needles from methanol–chloroform, m.p. 118—118·5° (lit.,[7] 116—117°).

5-Acetonyl-4-hydroxycholestan-3-one (V).—Hydrogen peroxide (30%; 60 ml.) and aqueous sodium hydroxide (4N; 58 ml.), were added to cholest-4-en-3-one (6·0 g.) in methanol (120 ml.) and acetone (150 ml.). The solution was set aside at 45° for 2½ hr.; work up gave an oil (6·3 g.) which was chromatographed on alumina (180 ml.). Elution with light petroleum–ether (4 : 1) gave 4β,5-epoxy-5β-cholestan-3-one (2·4 g.), identical m.p. and spectral properties with the compound prepared above, while elution with light petroleum–ether (1 : 1) gave the *cholestanone* (V) as an oil (1·51 g.) (Found: C, 78·6; H, 10·9. $C_{30}H_{50}O_3$ requires C, 78·6; H, 10·9%), $\nu_{max.}$ 1710 (C-3 and acetonyl C=O) and 1170 cm.$^{-1}$ (C–OH), δ (CCl_4) 0·66 (C-18 Me), 0·83 (C-19 Me), 2·20 (MeCO), 2·20, 3·02 (2H, 2d, *J* 17 c./sec., $-CH_2CO$), 2·68 (1H, s, C-4 methine), 4·11 (1H, s, OH, disappears on deuteriation), $[\alpha]_D^{20}$ +15°.

2α-Hydroxycholest-4-en-3-one (IV).—4β,5-Epoxy-5β-cholestan-3-one (6·2 g.), acetone (200 ml.), water (10 ml.), and conc. sulphuric acid (4 ml.) were heated together under reflux for 2 hr. and the mixture was poured into water. Chromatography of the product gave the cholestenone (IV) (4·6 g., 74%) as needles from methanol, m.p. 143—146° (lit.,[7] 143—146°).

Rearrangements of 2α-Hydroxycholest-4-en-3-one (IV).—(a) *With toluene-p-sulphonic acid in benzene*. The cholestenone (IV) (0·22 g.) and toluene-*p*-sulphonic acid monohydrate (0·04 g.) in benzene (30 ml.) were heated under reflux for 3 hr. The solution was worked up to give an oil (0·197 g.) which was chromatographed on alumina (50 ml.) to give the following compounds. (i) Light petroleum–ether (43 : 7) gave cholesta-3,5-dien-2-one (VII) (0·01 g.) as needles from methanol–chloroform, m.p. 118—120° lit.,[5] 125—126°), $\nu_{max.}$ 1670 (C=O) and 1640 cm.$^{-1}$ (C=C), δ ($CDCl_3$) 0·71 (C-18 Me) and 0·82 (C-19 Me).

(ii) Light petroleum–ether (3 : 2) gave cholesta-4,6-dien-3-one (VI; $R^1 = R^2 = H$) (0·11 g.) as needles from methanol, m.p. and mixed m.p. 80—81° (lit.,[8] 80·5—81·5°), $\nu_{max.}$ 1660 (C=O), 1623 (C=C), and 885 cm.$^{-1}$, $\lambda_{max.}$ (cyclohexane) 276 mμ (ε 35,200), δ ($CDCl_3$) 0·76 (C-18 Me), 0·83 (C-19 Me), 5·70 (1H, C-4 vinyl), and 6·15 (2H, C-6 and C-7 vinyls).

(iii) Light petroleum–ether (2 : 3) gave, 5α-cholestane-3,6-dione (II; $R = C_8H_{17}$) (0·045 g.) as plates from aqueous ethanol, m.p. 167—169° (lit.,[8] 171—172°), $\nu_{max.}$ 1720 cm.$^{-1}$ (C=O), δ 0·69 (C-18 Me), and 0·82 (C-19 Me).

(b) *With perchloric acid in acetic anhydride–ethyl acetate*. Perchloric acid (4 drops, 70%) was added to a solution of the cholestenone (IV) (0·20 g.) in acetic anhydride (6 ml.) and ethyl acetate (25 ml.) which was then set aside at 24° for 4 hr. Water (40 ml.) was added and the mixture was set aside for a further 12 hr.; it was worked up to give an oil (0·24 g.) which was chromatographed on alumina (60 ml.). Elution with light petroleum–ether (8 : 2) gave 3-acetoxy-6-acetylcholesta-1,3,5-triene (IX) (0·082 g.) as pale yellow needles from chloroform–methanol, m.p. 146—147°, $[\alpha]_D^{20}$ −72° (Found: *M*, 466·3443. $C_{31}H_{46}O_3$ requires *M*, 466·3447), $\nu_{max.}$ 1770 (OAc), 1680 (conj. C=O), 1645, 1570 (C=C), 1305 cm.$^{-1}$, $\lambda_{max.}$ (cyclohexane) 345 mμ (ε 10,500), δ 0·72 (C-18 Me), 0·82 (C-19 Me), 2·25 ($OCOCH_3$), 2·27 ($COCH_3$), 5·55 (1H, C-4 vinyl), 6·01 (2H, C-1 and C-2 vinyls).

(c) *With toluene-p-sulphonic acid in methanol*. The cholestenone (IV) (3·15 g.) and toluene-*p*-sulphonic acid monohydrate (0·60 g.) in methanol (80 ml.) were heated together under reflux for 4 hr. Work up gave an oil (3·1 g.) which was chromatographed on alumina (100 ml.). Elution gave four compounds as follows. (i) Light petroleum gave 2-methoxy-4-methyl-19-norcholesta-1,3,5(10)-triene (0·48 g., 16%) as needles from methanol, m.p. 49—51° (lit.,[9] 51·5—52·5°), $\nu_{max.}$ 1604, 1310, 1143, and 1060 cm.$^{-1}$, δ (CCl_4) 0·70 (C-18 Me), 2·14 (aromatic Me), 3·70 (OMe), 6·47 and 6·63 (2H, 2d, *J* 2·5 c./sec., C-1 and C-3 aromatic H).

(ii) Light petroleum–ether (4 : 1) gave 3,3-dimethoxycholestan-6-one (0·95 g., 29%) as needles from ether–methanol, m.p. 77—79° (lit.,[8] 74·5—75·5°), $\nu_{max.}$ 1710, 1102, and 1057 cm.$^{-1}$; R.D. (*c* 5·24, $CHCl_3$) $[\phi]_{589}$ +118°, $[\phi]_{400}$ +185°, $[\phi]_{334}$ 0°, $[\phi]_{310}$ −1512°, $[\phi]_{294}$ 0°, $[\phi]_D^{20}$ +12·0° (lit.,[8] −1°), δ (CCl_4) 0·68 (C-18 Me), 0·72 (C-19 Me), and 3·06, 3·16 (6H, 2s, $C(OMe)_2$).

[11] L. F. Fieser and M. Romero, *J. Amer. Chem. Soc.*, 1953, **75**, 4716.
[12] F. Sondheimer, St. Kaufmann, J. Romo, H. Martinez, and G. Rosenkranz, *J. Amer. Chem. Soc.*, 1953, **75**, 4712.
[13] R. L. Clarke, Y. Dobriner, A. Mooradian, and C. M. Martini, *J. Amer. Chem. Soc.*, 1955, **77**, 661.
[14] P. N. Rao and L. R. Axelrod, *J. Amer. Chem. Soc.*, 1960, **82**, 2830.
[15] P. N. Rao, H. R. Gollberg, and L. R. Axelrod, *J. Org. Chem.*, 1963, **28**, 270.

(iii) Light petroleum–ether (1 : 6) eluate gave 3-methoxy-5α-cholest-2-en-4-one (VIII) (0·95 g., 29%) as needles from hexane, m.p. and mixed m.p. 144—146° (lit.,[10] 146—148°), $\nu_{max.}$ 1695, 1642, and 1108 cm.$^{-1}$, $\lambda_{max.}$ 261 mμ (ε 5500), δ (CCl_4) 0·66 (C-18 Me), 3·58 (OMe), 5·61 (C-2 vinyl H).

(iv) Light petroleum–ether (3 : 7) gave the cholestenone (IV) (0·74 g., 23%), identical i.r. spectrum and m.p. with an authentic specimen.

2α-Hydroxy-4-methylcholest-4-en-3-one (XII).—Hydrogen peroxide (30%; 20 ml.) and sodium hydroxide solution (4N; 20 ml.) were added to a solution of 4-methylcholest-4-en-3-one (4·0 g.) in methanol (600 ml.) and ether (200 ml.) and the mixture kept at 5° for 1 hr. and then at 15° for 48 hr. Work up gave a white solid (3·85 g.) which was chromatographed on alumina to yield an epimeric mixture of 4,5-epoxy-4-methylcholestan-3-ones, m.p. 70—85° (2·30 g., 60%), $\nu_{max.}$ 1710 cm.$^{-1}$, δ 0·68 (C-18 Me), 0·83 (C-19 Me), 1·35 (C-4 Me). 4,5-Epoxy-4-methylcholestan-3-one (0·18 g.) in acetone (15 ml.) and sulphuric acid (3M; 1·8 ml.) was heated under reflux for 2 hr. Addition of water and extraction with ether gave a yellow solid (0·17 g.) which was chromatographed on alumina to yield *2α-hydroxy-4-methylcholest-4-en-3-one* (XII) (0·10 g.) as needles from methanol–chloroform, m.p. 101—102° (Found: C, 81·1; H, 11·2. $C_{28}H_{46}O_2$ requires C, 81·1; H, 11·2%), $\nu_{max.}$ 3500 (OH), 1671 (C=O), 1615 (C=C), and 1072 cm.$^{-1}$ (C–OH), $\lambda_{max.}$ 252 mμ (ε 8630), δ ($CDCl_3$) 0·72 (C-18 Me), 0·83 (C-19 Me), 1·83 (C-4 Me), 4·25 (q, *J* 14 c./sec., *J* 5 c./sec., C-2β H), 3·72 (OH), $[\alpha]_D^{20}$ +64°.

Rearrangements of 2α-Hydroxy-4-methylcholest-4-en-3-one (XII).—(a) *With toluene-p-sulphonic acid in benzene.* The cholestenone (XII) (0·845 g.) and toluene-*p*-sulphonic acid monohydrate (0·210 g.) in benzene (70 ml.) were heated under reflux for 2¼ hr. The reaction mixture was washed with water and the solvent was evaporated to give an orange solid (0·810 g.) which was chromatographed on alumina (50 ml.). Elution gave the three compounds as follows.

(i) Light petroleum–ether (9 : 1) gave 4-methylcholesta-4,6-dien-3-one (VI; R^1 = Me, R^2 = H) (0·073 g.) as needles from methanol, m.p. 73—75° (lit.,[16] m.p. 74·5—75°), $\nu_{max.}$ 1650, 1620, and 1326 cm.$^{-1}$, $\lambda_{max.}$ (EtOH) 290 mμ (ε 22,300), δ ($CDCl_3$) 0·75 (C-18 Me), 0·82 (C-19 Me), 1·83 (C-4 Me), 6·15, 6·52 (2H, 2d, *J* 10·0 c./sec., C-6 and C-7 vinyls), $[\alpha]_D^{20}$ +50° (lit.,[16] +60°).

(ii) Ether–methanol (9 : 1) gave *3-hydroxy-4-methyl-5β-cholest-3-en-2-one* (XIV) (0·55 g.), needles from hexane, m.p. 158—159° (Found: C, 81·2; H, 11·2. $C_{28}H_{46}O_2$ requires C, 81·1; H, 11·2%), $\nu_{max.}$ 1660 (C=O) and 1640 cm.$^{-1}$ (C=C), $\lambda_{max.}$ (EtOH) 278 mμ (ε 7260), δ ($CDCl_3$) 0·66 (C-18 Me), 0·82 (C-19 Me), 1·85 (C-4 Me), 2·13 and 2·71 (2H, 2d, *J* 16 c./sec., C-1 methylene), 6·08 (1H, OH), $[\alpha]_D^{20}$ +27°.

(b) *With perchloric acid in acetic anhydride–ethyl acetate.* Perchloric acid (70%; 7 drops) was added to a solution of the cholestenone (XII) (0·57 g.) in ethyl acetate (50 ml.) and acetic anhydride (11 ml.) which was then set aside at 20° for 40 min. Work up gave a yellow oil (0·47 g.) which was chromatographed on alumina (45 ml.) to give two compounds as follows. (i) Light petroleum–ether (16 : 1) gave 3-acetoxy-4-methylcholesta-1,3,5-triene (XIII) (0·062 g.) as an unstable oil, $\nu_{max.}$ 1763 (OAc), 1655 (C=C), 1210 (OAc), and 1080 cm.$^{-1}$, $\lambda_{max.}$ (EtOH) 300, 314, and 329 mμ (ε 10,260, 11,390, and 7720).

(ii) Light petroleum–ether (9 : 1) gave 4-methylcholesta-4,6-dien-3-one, identical with authentic material (m.p. and spectra properties).

(c) *With toluene-p-sulphonic acid in methanol.* The cholestenone (XII) (0·17 g.) and toluene-*p*-sulphonic acid monohydrate (0·040 g.) in methanol (20 ml.) were heated under reflux for 12 hr. Work up and chromatography on alumina gave 4-methylcholesta-4,6-dien-3-one (VI; R^1 = Me, R^2 = H) (0·11 g.) [in the light petroleum–ether (19 : 1) eluate] identified by m.p. and spectral properties with authentic material.

4β,5-Epoxy-6α-methyl-5β-cholestan-3-one.—Hydrogen peroxide (30%; 4·5 ml.) and aqueous sodium hydroxide (4N; 5 ml.) were added dropwise to a cooled (5°) solution of 6α-methylcholest-4-en-3-one (1·0 g.) in methanol (150 ml.) and ether (50 ml.) and the mixture was set aside at 5° for 24 hr. Work up gave an oil (0·96 g.) which was chromatographed on silica gel (50 ml.). Elution with light petroleum–ether (17 : 3) gave the *4β,5-epoxide* (0·87 g.) as needles from acetone, m.p. 111—112° (Found: C, 81·1; H, 11·1. $C_{28}H_{46}O_2$ requires C, 81·1; H, 11·2%), $\nu_{max.}$ 1700 cm.$^{-1}$ (C=O), δ (CCl_4) 0·68 (C-18 Me), 0·70 (d, *J* 6 c./sec., C-6 Me), 0·83 (C-19 Me), 3·20 (1H, C-4 methine) $[\alpha]_D^{20}$ +116°.

2α-Hydroxy-6α-methylcholest-4-en-3-one.— 4β,5-Epoxy-6α-methyl-5β-cholestan-3-one (0·51 g.) in acetone (20 ml.) and sulphuric acid (4M, 1·5 ml.) was heated under reflux for 17 hr. Work up gave an oil (0·50 g.) which was chromatographed on alumina (30 ml.) to give the following compounds. (i) Light petroleum–ether (19 : 1) gave unchanged epoxide (0·15 g.).

(ii) Light petroleum–ether (3 : 2) gave *2α-hydroxy-6α-methylcholest-4-en-3-one* (X) (0·38 g.) as needles from methanol–chloroform, m.p. 94—96° (Found: C, 81·3; H, 11·0. $C_{28}H_{46}O_2$ requires C, 81·1; H, 11·2%), $\nu_{max.}$ 3500 (OH), 1680 (C=O), 1610 (C=C), and 1100 cm.$^{-1}$ (C–OH), δ ($CDCl_3$) 0·72 (C-18 Me), 0·82 (C-19 Me), 3·57 (OH), 4·37 (1H, C-2 methine), 5·87 (d, *J* 2 c./sec., C-4 vinyl), $[\alpha]_D^{20}$ +54°.

Rearrangements of 2α-Hydroxy-6α-methylcholest-4-en-3-one (X).—(a) *With toluene-p-sulphonic acid in benzene.* The cholestenone (X) (0·15 g.) and toluene-*p*-sulphonic acid monohydrate (0·06 g.) in benzene (20 ml.) were heated under reflux for 4 hr. Work up gave a yellow oil (0·125 g.) which was chromatographed on alumina (40 ml.) to give the following compounds. (i) Light petroleum–ether (4 : 1) gave 6-methylcholesta-4,6-dien-3-one (0·07 g.) as needles from methanol–ether, m.p. 91—92 lit.,[17] 91—92°), $\nu_{max.}$ 1650, 1620, and 1580 cm.$^{-1}$, δ (CCl_4) 0·73 (C-18 Me), 0·82 (C-19 Me), 1·82 (C-6 Me), 5·70 (s, C-4 vinyl), 5·90 (m, C-7 vinyl), $[\alpha]_D^{20}$ +30° (lit.,[17] +37°).

(ii) Starting material was isolated from later eluates.

(b) *With perchloric acid in acetic anhydride–ethyl acetate.* Perchloric acid (70%; 5 drops) was added to a solution of the cholestenone (X) (0·39 g.) in ethyl acetate (30 ml.) and acetic anhydride (7 ml.), which was then set aside at 20° for 45 min. Work up gave an orange oil (0·39 g.) which was chromatographed on alumina (50 ml.) to give the following compounds. (i) Light petroleum–ether (19 : 1) gave 3-acetoxy-6-methylcholesta-1,3,5-triene (XI), as an unstable yellow oil, $\nu_{max.}$ 1755 (OAc), 1665, 1625, 1580, and 1150 cm.$^{-1}$, $\lambda_{max.}$ 258, 290 mμ (ε 9180, 10,240).

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[17] B. Ellis, D. N. Kirk, V. Petrow, B. Waterhouse, and D. M. Williamson, *J. Chem. Soc.*, 1960, 2828.

(ii) Light petroleum–ether (9 : 1) gave 6-methylcholesta-4,6-dien-3-one (0·19 g.), identical with authentic material by m.p. and spectral evidence.

(c) *With toluene*-p-*sulphonic acid in methanol.* The cholestenone (X) (0·322 g.) and toluene-*p*-sulphonic acid monohydrate (0·06 g.) in methanol (10 ml.) were heated under reflux for 3 hr. Work up gave a yellow oil (0·334 g.) which was chromatographed on alumina (40 ml.) to give 6-methylcholesta-4,6-dien-3-one (0·27 g.) in the light petroleum –ether (9 : 1) eluate, identical with authentic material by m.p. and spectral evidence.

Rearrangement of 6α-*methyl*-4β,5-*epoxy*-5β-*cholestan*-3-*one.*—6α-Methyl-4β,5-epoxy-5β-cholestan-3-one (0·19 g.) and toluene-*p*-sulphonic acid monohydrate (0·065 g.) in methanol (20 ml.) were heated under reflux for 2 hr. Work up gave a yellow oil (0·17 g.) shown by t.l.c. to contain no 2α-hydroxy-6α-methylcholest-4-en-3-one. Chromatography of the product and elution with light petroleum–ether (4 : 1) gave 6-methylcholesta-4,6-dien-3-one (0·13 g.) identified as before.

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