Chromyl Halide Oxidation of Steroid Alkenes

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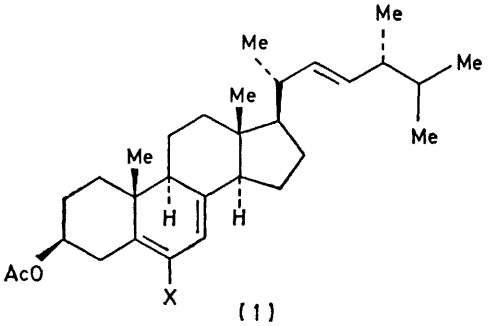
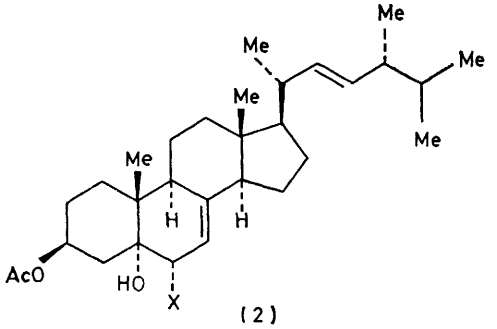
Ergosteryl acetate and CrO_2F_2 gave 3β-acetoxy-6α-fluoroergosta-7,22-dien-5α-ol. Cholesteryl acetate and CrO_2Cl_2 gave the α- and β-expoxides, the 5α-chloro-6-ketone, and both 5α,6β-chlorohydrins; *cis*-chlorohydrins were not detected. Cholesteryl acetate and CrO_2F_2 gave both epoxides and the 5α-fluoro-6β-alcohol. Unexpectedly, 9,11-dehydrotigogenin acetate and CrO_2F_2 gave only the 9,11-epoxides with the β-form predominating (5 : 1). The absence of *cis*-halogenohydrin formation from simple olefins and CrO_2X_2 (X = F, Cl) is in conflict with recent studies on acyclic and monocyclic alkenes.

REACTION of ergosteryl acetate (1a) and chromyl chloride has been shown to give the 5α-hydroxy-6α-chloro-derivative (2a).[1] Previously, the chromyl chloride oxidation of alkenes was reported to give *trans*-chlorohydrins.[2] Stairs *et al.* subsequently detected both *cis*- and *trans*-chlorohydrin formation with cyclohexene or cyclopentene.[3] In a recent study Sharpless has determined in detail the stereochemistry of the reaction and the sequence of product formation.[4] Acyclic or mono-



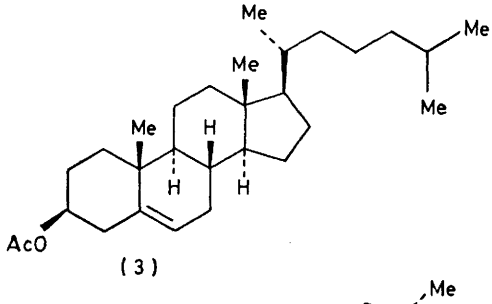
(1)
a ; X = H
b ; X = Cl
c ; X = F



(2)
a ; X = Cl
b ; X = F

cyclic alkenes and chromyl chloride at −78 °C gave epoxide, *cis*-chlorohydrin, and (sometimes) *cis* vicinal dichloride as the *primary* reaction products. Control experiments indicated that the *trans*-chlorohydrin was formed in a subsequent step *via* the epoxide and either HCl or a Lewis acid chromium(<VI) species. Secondary oxidation of chlorohydrins accounted for the formation of chloroketones. Typically cyclohexene gave epoxide (5%), *cis*-chlorohydrin (25%), *trans*-chlorohydrin (15%), and 2-chlorocyclohexanone (5%).

We were interested in examining the reactivity of chromyl fluoride which is conveniently prepared[5] from chromium(VI) oxide and cobalt(III) fluoride at 450 °C.



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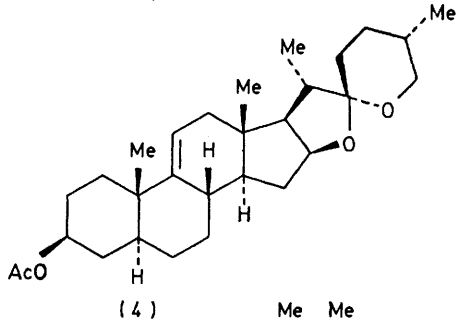

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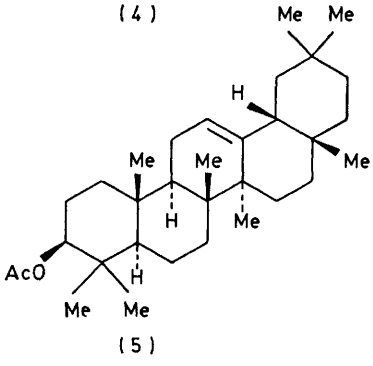


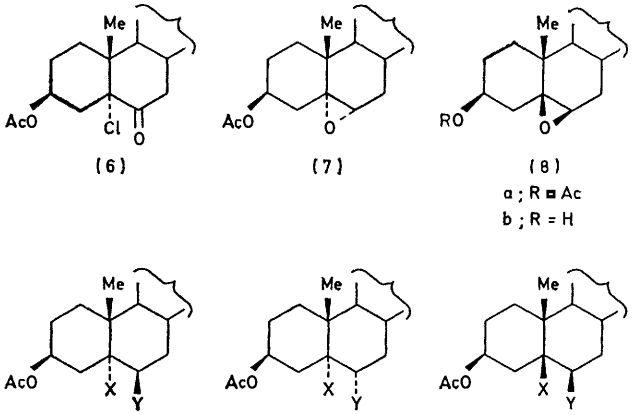
(5)

In order to clearly define the stereochemistry of the reaction, steroidal substances were chosen. The reactions of ergosteryl, cholesteryl, 9(11)-dehydrotigogenin, and β-amyrin acetates (1a), (3), (4), and (5) with both chromyl chloride and fluoride were studied and the unexpected stereochemistries elucidated.

RESULTS AND DISCUSSION

Chromyl fluoride rapidly and cleanly reacted with ergosteryl acetate (1a) to give 5α-hydroxy-6α-fluorosteroid (2b). Assignment of the stereochemistry followed from n.m.r. comparison with chlorohydrin (2a) [1] and facile dehydration. Addition of thionyl chloride and pyridine to the fluorohydrin (2b) gave an impure diene, plausibly [1] 6-fluoroergosteryl acetate (1c).

Although ergosteryl acetate (1a) was rapidly oxidised [1] by chromyl chloride at −78 °C, cholesteryl acetate (3) required a higher temperature to ensure reasonable consumption of alkene. Chromatography gave as major components starting material (3) (28%), 3β-acetoxy-5α-chlorocholestan-6-one (6) (12%), a mixture of α and β cholesteryl acetate epoxides (7) and (8a) (4%), 3β-acetoxy-6β-chlorocholestan-5α-ol (9a) (9%), and 3β-acetoxy-5α-chlorocholestan-6β-ol (9b) (18%).[6] Blank reactions suggested the epoxides (7) and (8a) were inert to chromyl chloride. However, chromyl chloride reduced by 2-methylpropene reacted with epoxides (7) and (8a) giving chlorohydrins (9a and b) but no chloroketone (6) (t.l.c.). This has literature precedent [4] with

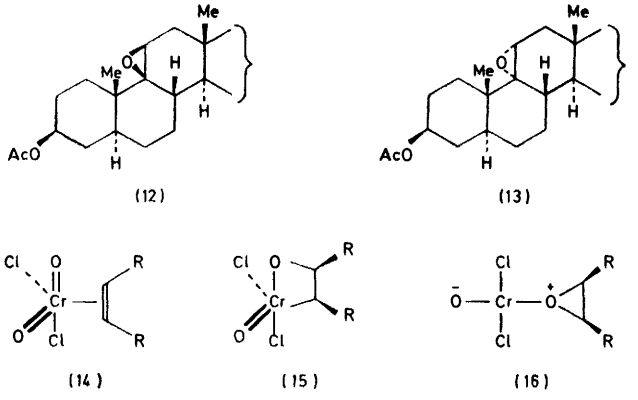


Compounds (6)—(11) are derivatives of cholesteryl acetate (3)

either HCl or a lower-valent chromium Lewis acid effecting epoxide cleavage. T.l.c. indicated the 5α-chloro-6-ketone (6) was formed from the chlorohydrin (9b) and further chromyl chloride oxidation. *cis*-Chlorohydrins (10a or b), (11a or b) were not isolated. It is not inconceivable that the 5α-chloro-6α-alcohol (10b), if formed, was rapidly oxidised and not observed. Given the observations of Sharpless, the epoxides (7) and (8a) were the only primary oxidation products. The optical rotation of the mixture ($[\alpha]_D^{22}$ −30°) suggested a 3 : 1 mixture of α-(7) ($[\alpha]_D^{18}$ −43.8°) and β-(8a) ($[\alpha]_D^{18}$ ±0°) epoxides.[6]

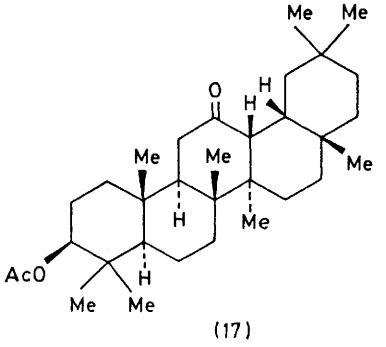
Cholesteryl acetate (3) was slow to react with chromyl fluoride and much starting material was recovered. Only α- and β-epoxides (7) and (8a) (1 : 1 from $[\alpha]_D$) (15%) and the known [7] 3β-acetoxy-5α-fluorocholestan-6β-ol (9c) (22%) were isolated.

9(11)-Dehydrotigogenin acetate (4) and chromyl chloride gave a complex mixture of products. Reaction with chromyl fluoride, although sluggish and incomplete, gave two analytically pure products. These were the β- (12) (major) and α- (13) (minor) epoxides.[8] The predominance of the β-epoxide is curious. Sharpless



Compounds (12) and (13) are derivatives of 9(11)-dehydrotigogenin acetate (4)

has invoked [4] intermediacy of complexes [(14), (15), and (16)] in epoxide formation. Such intermediates would give mostly α-epoxidation of both cholesteryl and 9(11)-dehydrotigogenin acetates (3) and (4). Yet β-epoxidation predominates in the latter. In addition, cholesteryl acetate (3) and CrO_2Cl_2 gave more 5α-chloro-6β-alcohol (9b) than the 6β-chloro-5α-alcohol (9a) in spite of the greater stability of the latter to further oxidation (tertiary alcohol). Cholesteryl acetate (3) and CrO_2F_2 gave the 5α-fluoro-6β-alcohol (9c) as the only isolated



fluorohydrin. The absence of *cis*-halogenohydrins and the stereochemistry of primary epoxidation are inconsistent with the Sharpless mechanism. Possibly the reaction may involve more than one molecule of chromyl halide in the product-forming step.

β-Amyrin acetate (5) reacted slowly with chromyl fluoride to give the known 12-ketone (17) as the only isolated product. This was presumably formed by the known [9] Lewis-acid-catalysed epoxide rearrangement.

Recently, Sharpless [10] has described the preparation of *cis* vicinal chloroacetates by the oxidation of alkenes using chromyl chloride and acetyl chloride. Thus, we examined the reactions of ergosteryl and cholesteryl acetates [(1a) and (3)] with this reagent. Ergosteryl acetate (1a) gave only the *cis*-chlorohydrin (2a) (40%).[1] Cholesteryl acetate (3) gave the 5α-chloro-6β-acetate (9d) as major product. No *cis* vicinal chloroacetates were detected. The by-product was the 5α-chloro-6β-alcohol (9b). These results are again not readily explicable by the Sharpless mechanism.

EXPERIMENTAL

M.p.s were determined on a Kofler hot stage. Optical rotations, and i.r., u.v., and n.m.r. spectra were recorded respectively on chloroform, carbon tetrachloride, cyclohexane, and deuteriochloroform or carbon tetrachloride (tetramethylsilane reference) solutions. All solvents and reagents were dried and purified before use. Light petroleum refers to the redistilled reagent with b.p. 40—60 °C. Organic extracts were dried over sodium sulphate. Generalised procedures are detailed in the first instance only. Both analytical and preparative (p.l.c.) thin layer chromatography were carried out on Merck Kieselgel GF_{254} films developed in ethyl acetate–benzene (1 : 9). Merck Kieselgel 60 was used for column chromatography; compounds are listed in sequence of elution.

Reaction of Ergosteryl Acetate (1a) *and Chromyl Fluoride.*—Chromium(VI) oxide (700 mg) and cobalt(III) fluoride (810 mg) were separately dried under vacuum at 110 and 50 °C, respectively, and intimately mixed (nitrogen dry-box). The mixture in a 20-mm bore Monel tube was heated to 200 °C under a stream of nitrogen for 10 min. The temperature was increased to 450 °C and the chromyl fluoride [5] gradually transferred with the nitrogen carrier gas. During 2 h the reagent was added to ergosteryl acetate (1a) (876 mg) in methylcyclohexane–1,1,2-trichlorotrifluoroethane (1 : 2) (120 ml) at −70 °C under nitrogen. After 3 h at −30 °C saturated ethanolic sodium borohydride (5 ml) was added. After 30 min, the then green solution was added to light petroleum (400 ml). The mixture was filtered, and the solids leached with benzene–light petroleum (1 : 1) (2 × 10 ml). The organic phase was washed with aqueous sodium hydrogencarbonate (5%), water (2 × 200 ml), dried, and evaporated. Trituration with benzene–light petroleum (1 : 1) gave the fluorohydrin (2b) (262 mg, 28%) as a crystalline solid. Chromatography of the mother-liquor gave [eluant benzene–ethyl acetate (9 : 1)] additional fluorohydrin (2b) (142 mg, 15%). Recrystallisation twice from ethyl acetate gave pure 3β-*acetoxy*-6α-*fluoroergosta*-7,22-*dien*-5α-*ol* (2b) (322 mg, 34%), m.p. 223—224 °C; $[\alpha]_D^{22}$ −10° (*c* 0.20 in benzene); $\nu_{max.}$ 3 590m, 3 440m, 2 960s, 2 870s, 1 733s, 1 468m, 1 370m, 1 245s, 1 030m, and 960m cm^{-1}; $\lambda_{max.}$, no absorption ⩾220 nm; τ 4.77 (2 H, m, 22- and 23-H), 4.97 (1 H, m, 7-H), 4.5—4.0 (2 H, m, 3α- and 6β-H), 7.99 (3 H, s, OAc), 8.94 (3 H, s, 10-Me), and 9.42 (3 H, s, 13-Me); *m/e* 474 (M^+), 456, 454, 436, 396, and 376 (Found: C, 75.95; H, 10.05; F, 4.1. $C_{30}H_{47}FO_3$ requires 75.9; H, 10.0; F, 4.0%). Reaction of ergosteryl acetate (1a) and chromyl fluoride in pure toluene or methylcyclohexane gave low yields of the fluorohydrin (2b).

Dehydration of 3β-*Acetoxy*-6α-*fluoroergosta*-7,22-*dien*-5α-*ol* (2b).—Thionyl chloride (350 mg) in dichloromethane (12 ml) was added to the fluorohydrin (2b) (237 mg) in pyridine (4 ml) and dichloromethane (20 ml) at −30 °C. After 35 min at 0 °C, the mixture was added to diethyl ether (50 ml) and the solution washed with water, 3% v/v cold hydrochloric acid, water, aqueous sodium hydrogencarbonate, and water, dried, and evaporated. Crystallisation from methanol–acetone gave 6-fluoroergosteryl acetate (1c) (139 mg, 64%), m.p. 164—165 °C; $[\alpha]_D^{22}$ −77° (*c* 0.265); $\nu_{max.}$ 2 968s, 2 880m, 1 740s, 1 682m, 1 465m, 1 375m, 1 240s, and 1 040s cm^{-1}; $\lambda_{max.}$ 265 (sh) (ε 7 600), 273 (8 700), 283 (7 900), and 295 (sh) nm (4 200); τ 4.54 (1 H, m, $W_{\frac{1}{2}}$ 8 Hz, 7-H), 4.8 (2 H, m, 22- and 23-H), 5.34 (1 H, m, $W_{\frac{1}{2}}$ 22 Hz, 3α-H), and 7.7 (3 H, s, OAc); *m/e* 456 (M^+), 396, 381, and 271 (Found: M^+, 456.3414. $C_{30}H_{45}FO_2$ requires *M*, 456.3423).

Oxidation of Cholesteryl Acetate (3) *with Chromyl Chloride.*—Chromyl chloride (930 mg) was added to a stirred solution of cholesteryl acetate (3) (1.28 g) in methylcyclohexane (150 ml) under nitrogen at −70 °C. After 3 h at −70 and 3 h at −30 °C, saturated ethanolic sodium borohydride (5 ml) was added. Work-up as above gave a yellow oil. P.l.c. gave, in sequence of increasing polarity, unreacted cholesteryl acetate (3) (360 mg); 3β-acetoxy-5α-chlorocholestan-6-one (6) (120 mg, 12%), m.p. 147—148 °C (from MeOH) (lit.,[11] 147—149 °C); $[\alpha]_D^{22}$ −100° (*c* 0.152) (lit.,[11] −98.5°); $\nu_{max.}$ 2 940s, 2 865m, 1 735s, 1 720s, 1 460m, 1 365m, 1 230s, and 1 040m cm^{-1}; τ 4.8 (1 H, m, $W_{\frac{1}{2}}$ 22 Hz, 3α-H), 7.24 (1 H, m, $W_{\frac{1}{2}}$ 22 Hz, 4α-H), 7.67 (3 H, s, OAc), and 9.03, 9.05, and 9.37 (methyl peaks); *m/e* 478 (M^+), 442, 418, and 382; cholesteryl acetate α- and β-epoxides (7) and (8a) (35 mg, 4%), m.p. 110—112 °C (from MeOH); $[\alpha]_D^{22}$ −30° (*c* 0.071) {lit.,[6] α-epoxide (7), m.p. 101—103 °C, $[\alpha]_D^{18}$ −43.8°; β-epoxide (8a), m.p. 111 °C, $[\alpha]_D^{18}$ ±0°}; $\nu_{max.}$ 2 940s, 2 869m, 1 460m, 1 360m, 1 235s, and 1 032m cm^{-1}; *m/e* 444 (M^+), 412, 384, and 369; 3β-acetoxy-6β-chlorocholestan-5α-ol (9a) (89 mg, 9%), m.p. 190—191 °C (from AcOEt–MeOH) (lit.,[6] 186—187 °C); $[\alpha]_D^{22}$ −29° (*c* 0.258) (lit.,[6] −26.7°); $\nu_{max.}$ 3 580m, 2 940s, 2 860m, 1 730s, 1 460m, 1 360m, 1 235s, 1 100m, and 1 029m cm^{-1}; τ 5.1 (1 H, m, $W_{\frac{1}{2}}$ 22 Hz, 3α-H), 6.27 (1 H, m, 6α-H), and 7.33 (1 H, m, $W_{\frac{1}{2}}$ 6 Hz, 7β-H?), 8.03 (3 H, s, OAc), and 8.77, 9.07, and 9.3 (methyl peaks); *m/e* 480 (M^+), 462, 444, and 412; and 3β-acetoxy-5α-chlorocholestan-6β-ol (9b) (185 mg, 18%), m.p. 190—191 °C [from light petroleum–THF (10 : 1)] (lit.,[6] 190—191 °C); $[\alpha]_D^{22}$ −27° (*c* 1.14) (lit.,[6] −24.3°); $\nu_{max.}$ 3 580m, 2 940s, 2 860m, 1 730s, 1 460m, 1 360m, 1 235s, 1 100m, and 1 029m cm^{-1}; τ 5.04 (1 H, m, $W_{\frac{1}{2}}$ 22 Hz, 3α-H), 6.27 (1 H, m, $W_{\frac{1}{2}}$ 8 Hz, 6α-H), 8.07 (3 H, s, OAc), 8.79 (3 H, s, 10-Me), and 9.36 (3 H, s, 13-Me); *m/e* 480 (M^+), 462, 444, 427, and 412. The identity of the products was further confirmed by undepressed mixed m.p. with authentic samples. Jones oxidation of alcohol (9b) gave ketone (6) (mixed m.p.), whereas alcohol (9a) was recovered unchanged.

Control Experiments in the Chromyl Chloride Oxidation of Cholesteryl Acetate (3).—(a) *Reaction of chromyl chloride with epoxides* (7) *and* (8a). Chromyl chloride (35 mg) was added with stirring to epoxides (7) and (8a) (3 : 1; 88 mg) *in* methylcyclohexane (15 ml) at −70 °C under nitrogen. After 2 h at −70 °C and 2 h at −20 °C normal work-up gave mostly unreacted epoxides (7) and (8a) contaminated by traces of the chlorohydrins (9a and b) (t.l.c.).

(b) *Reaction of chlorohydrins* (9a *and* b) *with chromyl chloride.* Reaction of the mixed chlorohydrins (9a and b) (94 mg) as in (a) gave some 5α-chloro-6-ketone (6); the epoxides (7) and (8a) were not formed (t.l.c.).

(c) *Reaction of epoxides* (7) *and* (8a) *with reduced chromyl chloride.* Chromyl chloride (0.04 ml) was added to dry 2-methylpropene (*ca.* 2 ml) in methylcyclohexane (20 ml) at −70 °C under nitrogen. After 1 h the solution was warmed up to −30 °C and additional 2-methylpropene added to discharge the remaining chromyl chloride. After 1 h at −30 °C the mixture was cooled to −70 °C and epoxides (7) and (8a) (1 : 1; 222 mg) in methylcyclohexane (5 ml) added. After 2 h at −70 and 2 h at −20 °C, the usual work-up gave a mixture of chlorohydrins (9a and b); the chloroketone (6) was not detected (t.l.c.). The chlorohydrins (9a and b) were recovered unchanged when reacted with the 2-methylpropene-reduced chromyl chloride.

Oxidation of Cholesteryl Acetate (3) *with Chromyl Fluoride.*—Chromyl fluoride [from chromium(VI) oxide (1.0 g) and cobalt(III) fluoride (1.1 g)] was added to cholesteryl acetate (3) (1.28 g) in methylcyclohexane (150 ml) at −30 °C under nitrogen. After 5 h at −30 and overnight at 0 °C (no further change in t.l.c. at 0 °C), work-up and p.l.c. gave cholesteryl acetate (3) (560 mg); α- and β-epoxides (7) and (8a) (105 mg, 15%), m.p. 111—112 °C, softens at 99 °C; $[\alpha]_D^{22}$ −20° (*c* 0.25); $\nu_{max.}$ 2 960m, 2 940s, 1 735s, 1 465m, 1 360m, 1 235s, and 1 030m cm^{-1}; an impure unidentified component (80 mg) inert to chromium(VI) oxide–pyridine; 3β-acetoxy-5α-fluorocholestan-6β-ol (9c) (173 mg, 22%), m.p. 168—169 °C (lit.,[7] 171—172 °C); $[\alpha]_D^{22}$ −11° (*c* 0.10) (lit.,[7] −9.0°); $\nu_{max.}$ 3 620m, 2 935s, 2 840m, 1 735s, 1 465m, 1 365m, 1 238s, and 1 029s cm^{-1}; τ 4.67 (1 H, m, $W_{\frac{1}{2}}$ 22 Hz, 3α-H), 6.2 (1 H, m, $W_{\frac{1}{2}}$ 7 Hz, 6α-H), and 7.97 (3 H, s, OAc); *m/e* 464 (M^+), 446, 444, 428, 412, 404, and 384 (Found: C, 75.2; H, 10.9. Calc. for $C_{29}H_{49}FO_3$: C, 74.95; H, 10.9%).

Oxidation of 9(11)-*Dehydrotigogenine Acetate* (4) *with Chromyl Fluoride.*—Oxidation of acetate (4) (1.368 g) as for cholesteryl acetate (3) and p.l.c. gave unreacted acetate (4) (1.15 g); α-epoxide (13) (15 mg, 7% *), m.p. and mixed m.p. 265—266 °C (from EtOAc–MeOH) (lit.,[8] 265—266 °C); $[\alpha]_D^{22}$ −74° (*c* 0.181) (lit.,[8] −74.6°); $\nu_{max.}$ 2 950s, 2 930s, 2 870m, 1 733s, 1 455m, 1 375m, 1 240s, 1 050s, 915m, and 897s cm^{-1}; *m/e* 472 (M^+), 454, 412, and 400 (Found: C, 73.35; H, 9.5. Calc. for $C_{29}H_{44}O_5$: C, 73.7; H, 9.35%); and β-epoxide (12) (85 mg, 37% *), m.p. and mixed m.p. 218—219 °C (from EtOAc) (lit.,[8] 216—217 °C); $[\alpha]_D^{22}$ −63° (*c* 0.203) (lit.,[8] −60°); $\nu_{max.}$ 2 950s, 2 930s, 2 860m, 1 735s, 1 455m, 1 375m, 1 240s, 1 050s, 920m, and 898s cm^{-1}; τ 5.6 (1 H, m, $W_{\frac{1}{2}}$ 22 Hz, 3α-H), 6.67 (2 H, m, 11α- and 16α-H), 8.07 (3 H, s, OAc), 9.0 (3 H, s, Me), and 9.4 (3 H, s, Me) (Found: C, 73.35; H, 9.55%).

Oxidation of β-*Amyrin Acetate* (5) *with Chromyl Fluoride.*—Chromyl fluoride oxidation of β-amyrin acetate (5) (0.82 g) and column chromatography gave (eluant benzene) starting material (5) (491 mg) and [eluant benzene–EtOAc (7 : 3)] a crystalline solid (311 mg). P.l.c. gave the 12-ketone (17) (135 mg, 41% *), m.p. and mixed m.p. 301—302 °C (lit.,[9] 293—295 °C); $[\alpha]_D^{22}$ −14° (*c* 0.254) (lit.,[9] −11°); $\nu_{max.}$ 2 940s, 2 860m, 1 733s, 1 699s, 1 460m, 1 365m, 1 268s, and 1 025m cm^{-1}; τ 5.55 (1 H, m, 3α-H), 7.27 (2 H, br d, 11α- and β-H), 7.97 (3 H, s, OAc), 8.87 (3 H, s, Me), 9.07 (6 H, s, Me), and 9.1 (6 H, s, Me); *m/e* 484 (M^+), 469, 424, and 409; and two unidentified polar components (35 mg each).

Oxidation of Ergosteryl Acetate (1a) *using Chromyl Chloride–Acetyl Chloride.*—Chromyl chloride (17 μl) was added with stirring to ergosteryl acetate (1a) (54 mg) in methylcyclohexane (16 ml) and acetyl chloride (8 ml) under nitrogen at −75 °C. After 1 h, quenching with ethanolic sodium borohydride, normal work-up, and crystallisation from diethyl ether gave the *cis*-chlorohydrin (2a) (27 mg, 40%), identical (m.p., mixed m.p., and $[\alpha]_D$) with authentic [1] material.

Oxidation of Cholesteryl Acetate (3) *with Chromyl Chloride–Acetyl Chloride.*—Chromyl chloride (38 μl) was added with stirring to cholesteryl acetate (3) (100 mg) in methylcyclohexane (15 ml) and acetyl chloride (7 ml) under nitrogen at −75 °C. After 3 h at −70 and 2 h at −30 °C ethanolic sodium borohydride quenching, work-up, and p.l.c. gave starting material (3) (7 mg); 3β,6β-diacetoxy-5α-chlorocholestane (9d) (56 mg, 46%), m.p. 113—115 °C (from MeOH) (lit.,[6] 112—113 °C); $[\alpha]_D^{22}$ −46° (*c* 0.54) (lit.,[6] −46°); $\nu_{max.}$ 2 950s, 2 880m, 1 745s, 1 470m, 1 370m, 1 235s, and 1 030s cm^{-1}; τ 4.65 (1 H, m, $W_{\frac{1}{2}}$ 22 Hz, 3α-H), 4.9 (1 H, m, $W_{\frac{1}{2}}$ 8 Hz, 6α-H), 7.95 (3 H, s, OAc), and 8.02 (3 H, s, OAc); *m/e* 522 (M^+); and 3β-acetoxy-5α-chlorocholestan-6β-ol (9b) (17 mg, 15%), m.p. 191—193.5 °C (from CH_2Cl_2–MeOH) (lit.,[6] 190—191°); $[\alpha]_D^{22}$ −29° (*c* 0.27) (lit.,[6] −24.3°); $\nu_{max.}$ 3 640m, 2 950s, 2 870m, 1 740s, 1 470m, 1 390m, 1 380m, 1 240s, and 1 030m cm^{-1}; τ 4.77 (1 H, m, $W_{\frac{1}{2}}$ 22 Hz, 3α-H), 6.14 (1 H, m, $W_{\frac{1}{2}}$ 10 Hz, 6α-H), and 8.03 (3 H, s, OAc); *m/e* 480 (M^+) (Found: C, 72.4; H, 10.35. Calc. for $C_{29}H_{49}ClO_3$: C, 72.4; H, 10.25%). The diacetate (9d) (24.5 mg) with potassium hydroxide (9 mg) in THF (1 ml) and methanol (1 ml) were heated to reflux for 1 h. The usual work-up gave the β-epoxide (8b) (15.7 mg, 77%), m.p. 131—133 °C (from MeOH) (lit.,[6] 131—132 °C); $[\alpha]_D^{20}$ +11° (*c* 0.51) (lit.,[6] +10°); $\nu_{max.}$ 3 620m, 2 950s, 2 870m, 1 470m, 1 370m, and 1 050m cm^{-1}. Chlorohydrin (9b) and potassium hydroxide gave the β-epoxide (8b), m.p. 131—133 °C (lit.,[6] 131—132 °C); $[\alpha]_D^{22}$ +13° (*c* 0.03) (lit.,[6] +11.5°). Alternatively chlorohydrin (9b) and ethanolic hydrogen chloride gave 5α-chlorocholestane-3β,6β-diol (9e), m.p. 170—171.5 °C (from MeOH) (lit.,[6] 170—171 °C), $[\alpha]_D^{22}$ −26° (*c* 0.053) (lit.,[6] −22.1°) (Found: C, 70.95; H, 10.85. Calc. for $C_{27}H_{47}ClO_2H_2O$: C, 70.95; H, 10.8%).

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REFERENCES

[1] D. H. R. Barton and R. K. Haynes, *J.C.S. Perkin I*, 1975, 2065.
[2] S. J. Cristol and K. R. Eilar, *J. Amer. Chem. Soc.*, 1950, **72**, 4353.
[3] R. A. Stairs, D. G. M. Diaper, and A. L. Gatzke, *Canad. J. Chem.*, 1963, **41**, 1059.
[4] K. B. Sharpless, A. Y. Teranishi, and J.-E. Bäckvall, *J. Amer. Chem. Soc.*, 1977, **99**, 3120.
[5] G. D. Flesh and H. J. Svec, *J. Amer. Chem. Soc.*, 1958, **80**, 3189.
[6] R. A. Baxter and F. S. Spring, *J. Chem. Soc.*, 1943, 613; J. Ruzicka and W. Bosshard, *Helv. Chim. Acta*, 1937, **20**, 244; P. N. Chakravorty and R. H. Levin, *J. Amer. Chem. Soc.*, 1942, **64**, 2317.
[7] H. B. Henbest and T. I. Wrigley, *J. Chem. Soc.*, 1957, 4765.
[8] D. H. R. Barton, Y. D. Kulkarni, and P. G. Sammes, *J. Chem. Soc.* (*C*), 1971, 1149 and references therein; Y. D. Kulkarni, D.I.C. Thesis, Imperial College, London, 1970.
[9] D. H. R. Barton and N. J. Holness, *J. Chem. Soc.*, 1952, 78; R. B. Boar, D. C. Knight, J. F. McGhie, and D. H. R. Barton, *J. Chem. Soc.* (*C*), 1970, 678.
[10] J. E. Bäckvall, M. W. Young, and K. B. Sharpless, *Tetrahedron Letters*, 1977, 3523.
[11] J. W. Blunt, M. P. Hartshorn, and D. N. Kirk, *Tetrahedron*, 1965, **21**, 559.