Oxidation of Steroidal 5-enes with Thallium Triacetate; a Westphalen-type Rearrangement of Epicholesterol

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Treatment of epicholesterol with thallium triacetate in acetic acid afforded mainly 3α,10α-epoxy-5-methyl-19-nor 5β-cholestan-6β-yl acetate (2b), accompanied by cholest-4-ene-3α,6β-diol 6-acetate (3b) and 5α-cholestane-3α,5,6β-triol 6-acetate (4b). The structure of compound (2b) was confirmed by conversion into known compounds belonging to the 'Westphalen' rearranged series. Similar treatment of cholest-5-ene and of cholesta-3,5-diene afforded compounds having the unrearranged cholestane-type skeleton. A mechanistic scheme involving the initial formation of a bridged organothallium intermediate is proposed. In complete contrast is the behaviour of cholesteryl and epicholesteryl acetate, which remained unchanged in the presence of thallium triacetate; the only product isolated from cholesterol was its acetate.

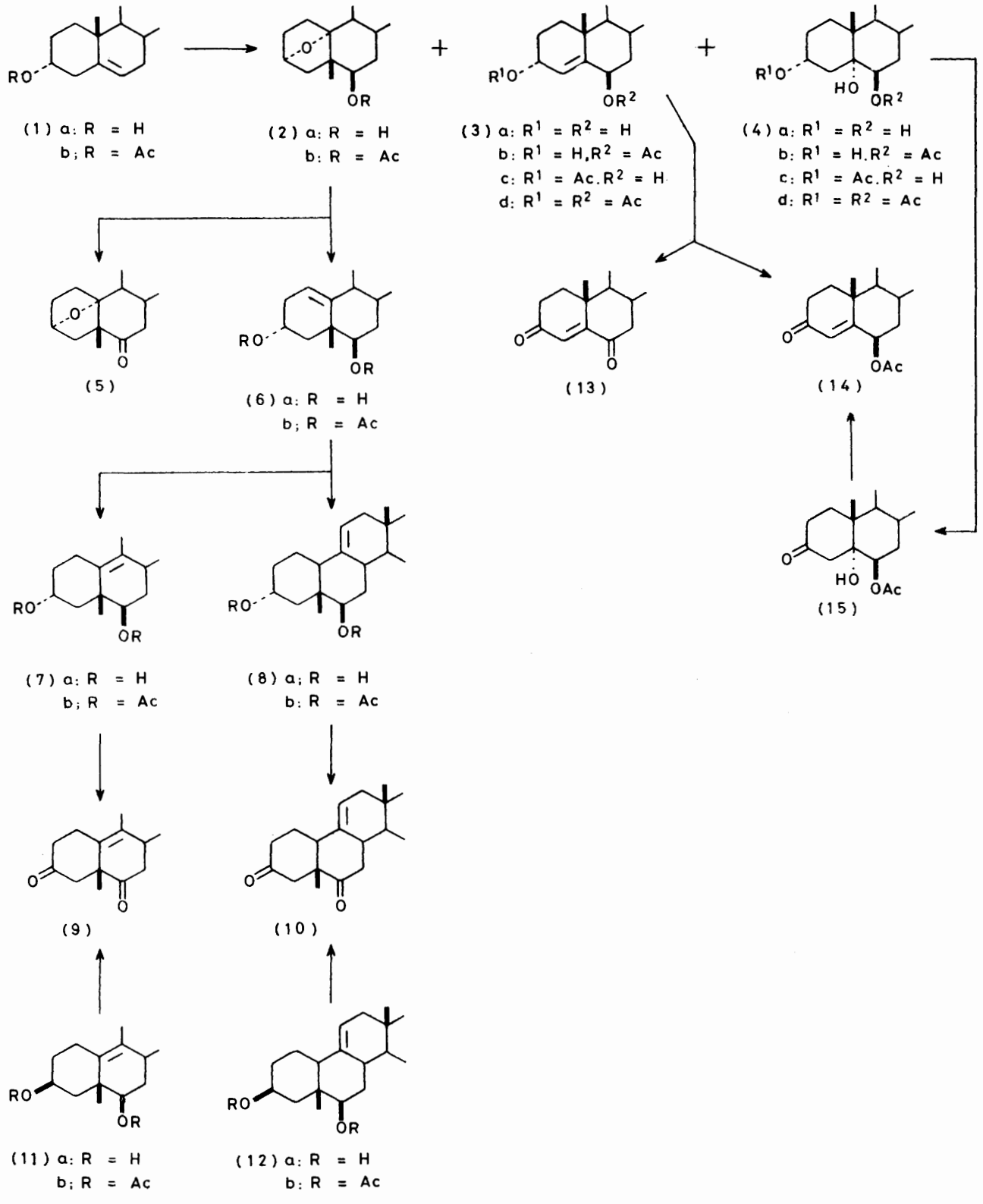
We have previously reported [1] that oxidation with thallium triacetate of the disubstituted double bond in several steroidal 2-enes afforded 2β,3β-diols, mainly as the corresponding 2-acetates. Best results were obtained with 5α-cholest-2-en-5-ol, suggesting that the electrophilic attack on the double bond is assisted by the homoallylic, axially oriented hydroxy-group. This finding prompted us to investigate the behaviour of a related system possessing a secondary axial hydroxy-group homoallylic to a trisubstituted double bond. The reaction with epicholesterol (1a) proceeded slowly at *ca.* 50 °C, to give a mixture of compounds (2b), (3b), and (4b), accompanied by some unchanged material (1a) and the corresponding acetate (1b).

The main product (2b) (*ca.* 60%) is apparently the first 1,4-epoxy-steroid with the oxygen bridge between C-3 and C-10 to be described. A related system is found in 2α,5α-epoxy-steroids (with the angular methyl group at the usual 10-position).[2a-e] The n.m.r. spectrum of compound (2b) shows two one-proton multiplets at δ 4.35 and 4.93, in addition to signals for an acetate methyl group and for the usual two tertiary and three secondary methyl groups found in any cholestane-type compound. Treatment of (2b) with methanolic potassium hydroxide afforded the alcohol (2a), characterised in the n.m.r. spectrum by two one-proton multiplets at δ 4.36 and 3.78, and a slight upfield shift of a tertiary methyl group [from δ 1.15 in (2b) to 1.08 in (2a)]. Oxidation of this alcohol afforded the ketone (5) having only one n.m.r. multiplet at 4.33 and the tertiary methyl signal at δ 1.30. The presence of an almost unchanged n.m.r. multiplet in the spectra of compounds (2a), (2b), and (5) suggested that it could be due to a proton attached to a secondary–tertiary epoxy-bridge. With the exception of the known 3α-5-epoxy-5α-cholestan-6β-yl-acetate,[2d] which possesses however, physical constants and spectral properties different from those of compound (2b), two structures could fit the above n.m.r. data: that of the as yet unknown 3α,9α-epoxy-5-methyl-19-nor-5β-cholestan-6β-yl acetate, which would not afford the olefin (6b) (see later) and structure depicted (2b), which agreed with the properties of this compound.

In order to confirm the assigned structure, compound (2b) was treated with reagents that could eventually open the epoxy-bridge. The material remained unchanged under relatively mild acidic conditions (perchloric or hydrobromic acid in acetone) but was smoothly cleaved with concentrated aqueous hydrobromic acid in acetic acid solution, at room temperature, to give mainly 5-methyl-19-nor-5β-cholest-1(10)-ene-3α,6β-diol diacetate (6b), accompanied by small amounts of the isomeric 9-ene (7b). Compound (6b) was characterised in the n.m.r. spectrum by a narrow multiplet at δ 5.42 for a vinylic proton and by two, partially overlapped, broad multiplets for C*H*OAc. The assignment of the δ 5.42 signal was confirmed by treatment with perbenzoic acid, leading to a mixture of the two 1,10-epoxides that was not further investigated. When the pure $\Delta^{1(10)}$-

[1] E. Glotter and A. Schwartz, *J.C.S. Perkin I*, 1976, 1660.

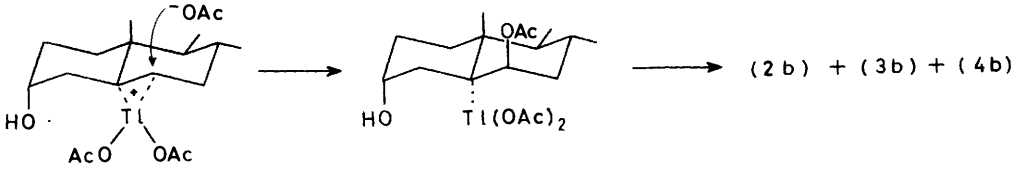
[2] (*a*) B. Ellis and V. A. Petrow, *J. Chem. Soc.*, 1939, 1078; (*b*) T. Komeno and H. Itani, *Chem. and Pharm. Bull.* (*Japan*), 1970, **18**, 608; (*c*) A. Ambles and R. Jacquesy, *Bull. Soc. chim. France*, 1972, 804; (*d*) P. Tsui and G. Just, *Canad. J. Chem.*, 1973, **51**, 3502; (*e*) P. Kocovsky and V. Cerny, *Coll. Czech. Chem. Comm.*, 1977, **42**, 163.


(1) a: R = H
b; R = Ac
(2) a: R = H
b: R = Ac
(3) a: R¹ = R² = H
b: R¹ = H, R² = Ac
c: R¹ = Ac, R² = H
d: R¹ = R² = Ac
(4) a: R¹ = R² = H
b: R¹ = H, R² = Ac
c: R¹ = Ac, R² = H
d: R¹ = R² = Ac
(5)
(6) a: R = H
b; R = Ac
(7) a: R = H
b; R = Ac
(8) a; R = H
b: R = Ac
(9)
(10)
(11) a: R = H
b; R = Ac
(12) a: R = H
b: R = Ac
(13)
(14)
(15)

derivative (6b), in acetic acid solution, was treated with a few drops of 45% hydrobromic acid in acetic acid at 60 °C, a mixture of the Δ^{9}- (7b) and the $\Delta^{9(11)}$- (8b) compounds was obtained. Similar isomerisations have been reported [3] for ' Westphalen '-type rearranged compounds.

Compounds (7b) and (8b) were hydrolysed with methanolic potassium hydroxide to the diols (7a) and (8a), which were oxidised to the diketones (9) [4] and (10),[3a] respectively. Mild oxidation (Jones reagent) of the diol (6a) took place with concomitant migration of the double bond, to give the diketone (9); such a migration did not occur during oxidation of 5-methyl-19-nor-5β-cholest-1(10)-ene-3β,6β-diol.[3b] The same diketones were obtained from the known compounds (11b) and (12b),[3a] respectively.

The structures assigned to the minor products (3b) and (4b) obtained from epicholesterol were confirmed by conventional transformations. Cholest-4-ene-3α,6β-diol 6-acetate (3b) was oxidised to the unsaturated ketone (14); [5] it was also converted into the known diacetate (3d),[6] then hydrolysed and oxidised to the unsaturated diketone (13).[7a] Cholestane-3α,5,6β-triol 6-acetate (4b) gave the diacetate (4d) [2d] and the triol (4a), alternatively obtained from 5,6α-epoxy-5α-cholestan-3α-ol, by treatment with perchloric acid in acetone. Oxidation of compound (4b) afforded the ketone (15),[2a] which was smoothly dehydrated on alumina to the unsaturated ketone (14).[5]



The formation of compounds (2b), (3b), and (4b) in the reaction of epicholesterol with thallium triacetate in acetic acid can be interpreted by assuming an initial electrophilic attack of the double bond from the less hindered side of the molecule, leading to a transient bridged organothallium intermediate, followed by attack of the anion of the solvent to give an intermediate possessing a weak C–Tl bond. Heterolysis of the C–Tl bond proceeds with the gradual development of a positive charge at C-5, stabilised by: (*a*) a Westphalen-type rearrangement involving migration of the 10-methyl group, followed by internal nucleophilic attack of the suitably oriented 3α-hydroxy-group (2b); (*b*) loss of a proton from the neighbouring C-4 (3b); (c) attack of water to give a 5α-hydroxy-group (4b).

Although such a scheme can give a reasonable interpretation of the formation of the above compounds, it cannot explain the role of the 3α-hydroxy-group. Under similar or even more drastic conditions, no reaction took place with cholesteryl and epicholesteryl acetates. The only reaction that occurred with cholesterol was the formation of the corresponding acetate. The inertness of the double bond in these compounds is in sharp contrast not only with the case of epicholesterol, but also with that of cholest-5-ene.

Three compounds, (3d), (17), and (18), accounting for more than 80% of the transformed material, could be isolated from the mixture obtained from cholest-5-ene (16), when exposed to thallium triacetate in acetic acid solution at 75 °C. The enol acetate structure of cholest-5-en-6-yl-acetate (17) ($\nu_{max.}$ 1 740 cm^{-1}) was confirmed by its quantitative conversion into 5α-cholestan-6-one (20).[7b] Compounds (3d) and (18) were identical with authentic samples.[6] When the reaction was performed at 60 °C, small amounts of 5α-cholestane-5,6α-diol 6-acetate (19) [8] were also obtained. The possibility of an isomeric 5β,6α-diol 6-acetate structure was ruled out by recording the n.m.r. spectrum in pyridine solution. The compound was identified by dehydration with thionyl chloride to cholest-4-en-6α-yl acetate (22).[9a] The formation of compounds (3d) and (18) can be explained by allylic oxidation of a cholest-4-en-6β-yl acetate intermediate. Indeed, when this compound (21) [9a] was treated with thallium triacetate, a mixture of compounds (3d) and (18) was obtained, in about the same ratio as from cholest-5-ene. No product arising from a Westphalen- or a backbone-type rearrangement was identified in the mixture obtained from compound (16).

Cholesta-3,5-diene (23) yielded mainly products of 1,4-addition [(3c), (3d), and (18)], accompanied by products of 1,2-addition [(24b) [10a,b] and (24c) [10a]]. Completely saturated, oxidised products that could not be fractionated, accounted for *ca.* 15% of the mixture. Acetylation of compound (3c) afforded the diacetate (3d). Compound (24c) gave the same diol (24a) and diacetate (24d) as compound (24b).[10] The 3α-acetoxy-derivative (3d) was not formed by isomerisation of the 3β-acetoxy-derivative (18).[6b] The latter remained unchanged when treated with thallium triacetate under conditions similar to those used in the reaction with the diene (23).

[3] (*a*) H. Aebli, C. A. Grob, and E. Schumacher, *Helv. Chim. Acta*, 1958, **41**, 774; (*b*) G. Snatzke and H. W. Fehlhaber, *Annalen*, 1964, **676**, 188.

[4] V. A. Petrow, O. Rosenheim, and W. W. Starling, *J. Chem. Soc.*, 1938, 677.

[5] T. Koga and M. Tomoeda, *J.C.S. Perkin I*, 1973, 1848, and references cited therein.

[6] M. P. Hartshorn and D. N. Kirk, *Tetrahedron*, (*a*) 1965, **21**, 1567; (*b*) 1966, **22**, 1415.

[7] L. Fieser and M. Fieser, ' Steroids,' Reinhold, New York, 1959, (*a*) p. 44; (*b*) p. 197; (*c*) P. C. Cherry, W. R. T. Cottrell, G. D. Meakins, and E. E. Richards, *J. Chem. Soc.* (*C*), 1967, 181.

[8] C. R. Narayana and M. R. Sarma, *Tetrahedron Letters*, 1968, 1553.

[9] (*a*) D. N. Jones, J. R. Lewis, C. W. Shoppee, and G. H. R. Summers, *J. Chem. Soc.*, 1955, 2876; D. Lavie, S. Greenfield, Y. Kashman, and E. Glotter, *Israel J. Chem.*, 1967, **5**, 151.

[10] (*a*) V. A. Petrow, O. Rosenheim, and W. W. Starling, *J. Chem. Soc.*, 1943, 135; (*b*) R. Lorne and S. Julia, *Bull. Soc. chim. France*, 1973, 1357.

In the light of the structures of the compounds obtained from this diene, it is difficult to decide whether the initial electrophilic attack took place at the disubstituted or at the trisubstituted double bond. While the only explanation for the formation of compounds (24b) and (24c) is through a 3,4-organothallium intermediate, the formation of compounds (3c), (3d), and (18) can be explained in both ways.

EXPERIMENTAL

M.p.s were taken with a Fisher–Johns apparatus. Optical rotations were recorded with an automatic Perkin-Elmer 141 polarimeter and refer to solutions in chloroform. I.r. spectra were recorded for solutions in chloroform with a Perkin-Elmer 237 grating spectrophotometer. N.m.r. spectra were determined with a Varian NV-14 instrument (60 MHz) for solutions in deuteriochloroform. T.l.c. was carried out on chromatoplates of silica gel G (Merck) and spots were developed with iodine vapour. Column chromatography was performed on silica gel 60 (Merck; 70—230 mesh). Petroleum refers to the fraction of b.p. 60—80 °C.

Treatment of Epicholesterol (1a) *with Thallium Triacetate.*—Thallium triacetate (2 g) was added to a solution of compound (1a) [11] (1 g) in glacial acetic acid (30 ml) and the solution was stirred for 50 h at 50 °C. After cooling to room temperature, N-hydrochloric acid (5 ml) and ether (150 ml) were added to precipitate most of the thallium salts. The precipitate was filtered off and washed with ether. The combined solutions were washed with aqueous 5% sodium hydrogen carbonate until a test for thallium ions was negative (no colouration with 10% potassium iodide), then washed with water (3 × 25 ml), dried (Na_2SO_4), and evaporated. The crude product (1.12 g) was chromatographed on silica (200 g); elution with benzene gave epicholesteryl acetate (1b) (50 mg). Elution with benzene–ethyl acetate (98 : 2) gave unchanged material (1a) (80 mg), followed by compound (2b) (650 mg). Elution with dichloromethane–ethyl acetate (4 : 1) gave compound (3b) (120 mg); further elution with ethyl acetate gave compound (4b) (100 mg). *3α,10α-Epoxy-5-methyl-19-nor-5β-cholestan-6β-yl acetate* (2b) had m.p. 118—119 °C (from methanol), $[\alpha]_D$ —27.7° (*c* 0.6); δ 0.65 [s, C(13)Me], 1.15 [s, C(5)Me], 2.00 (OAc), 4.35 (3β-H, m, $W_{\frac{1}{2}}$ 12 Hz), and 4.93 (6α-H, m, $W_{\frac{1}{2}}$ 20 Hz) (Found: M^+, 444.3577. $C_{29}H_{48}O_3$ requires *M*, 444.3552). Cholest-4-ene-3α,6β-diol 6-acetate (3b) could

[11] Y. Houminer, *J. Org. Chem.*, 1975, **40**. 1361.

not be crystallised; δ 1.08 [s, C(10)Me], 2.00 (OAc), 4.13 (3β-H, m, $W_{\frac{1}{2}}$ 12 Hz), 5.32 (6α-H, m, $W_{\frac{1}{2}}$ 8 Hz), and 5.85 (4-H, d, J 4.5 Hz). 5α-Cholestane-3α,5,6β-triol 6-acetate (4b) had m.p. 171—172 °C (lit.,[2d] 180—181 °C); δ 1.08 [s, C(10)-Me], 2.05 (OAc), 4.23 (3β-H, m, $W_{\frac{1}{2}}$ 10 Hz) (lit.,[2d] δ 3.8), and 4.77 (6α-H, m, $W_{\frac{1}{2}}$ 6 Hz) (lit.,[2d] δ 5.3). We believe that there is a mistake in the previously reported [2d] data. Further reactions confirm the structure of compound (4b) as given above.

Hydrolysis of Compound (2b) *to* 3α,10α-*Epoxy*-5-*methyl*-19-*nor*-5β-*cholestan*-6β-*ol* (2a).*—To a solution of compound (2b) (500 mg) in methanol (50 ml), methanolic 5% potassium hydroxide (30 ml) was added. After 24 h at room temperature, water was added, the solution neutralised with dilute hydrochloric acid, and the *product* isolated by filtration; m.p. 175—177 °C (from methanol), $[\alpha]_D$ −33.7° (*c* 0.8); δ 0.67 [s, C(13)Me], 1.08 [s, C(5)Me], 3.78 (6α-H, m, $W_{\frac{1}{2}}$ 20 Hz), and 4.36 (3β-H, m, $W_{\frac{1}{2}}$ 12 Hz) (Found: C, 80.4; H, 11.6. $C_{27}H_{46}O_2$ requires C, 80.55; H, 11.5%).

Oxidation of Compound (2a) *to* 3α,10α-*Epoxy*-5-*methyl*-19-*nor*-5β-*cholestan*-6-*one* (5).—To a solution of compound (2a) (250 mg) in acetone (50 ml), a solution of Jones reagent was added dropwise, with stirring at 15 °C. After 20 min the excess of reagent was destroyed with a few drops of methanol, most of the solvent was removed, water was added, and the *product* was isolated by filtration; m.p. 86—87° C (from methanol–hexane), $[\alpha]_D$ −13.9° (*c* 0.7); δ 0.72 [s, C(13)Me], 1.30 [s, C(5)Me], and 4.33 (3β-H, m, $W_{\frac{1}{2}}$ 12 Hz) (Found: C, 80.9; H, 11.2. $C_{27}H_{44}O_2$ requires C, 80.95; H, 11.1%).

Conversion of Compound (2b) *into* 5-*Methyl*-19-*nor*-5β-*cholest*-1(10)-*ene*-3α,6β-*diol Diacetate* (6b).—To a solution of compound (2b) (600 mg) in glacial acetic acid (20 ml), aqueous 40% hydrobromic acid (2 ml) was added. After 24 h at room temperature, the solution was neutralised with sodium carbonate, the product was extracted with ether, and the ethereal solution was washed with water and dried (Na_2SO_4). After evaporation, the crude product was chromatographed on silica (100 g). Elution with benzene–ethyl acetate (95 : 5) gave 5-methyl-19-nor-5β-cholest-9-ene-3α,6β-diol diacetate (7b) (30 mg), followed by *compound* (6b) (400 mg), m.p. 151—152 °C (from methanol), $[\alpha]_D$ +6° (*c* 0.7); δ 0.65 [s, C(13)Me], 1.26 [s, C(5)Me], 2.03 (2 × OAc), 4.7—5.3 (3β, and 6α-H, two partially overlapped broad multiplets), and 5.42 (1-H, m, $W_{\frac{1}{2}}$ 9 Hz) (Found: C, 76.4; H, 10.3. $C_{31}H_{50}O_4$ requires C, 76.5; H, 10.35%).

Conversion of Compound (6b) *into* 5-*Methyl*-19-*nor*-5β-*cholest*-9-*ene*-3,6-*dione* (9).[4]—The diacetate (6b) (150 mg) was hydrolysed with methanolic 5% potassium hydroxide as above. The diol (6a) showed one spot on a chromatoplate and had n.m.r. signals at δ 0.65 [s, C(13)Me], 1.13 [s, C(5)Me], 3.4—4.0 (3β- and 6α-H, two partially overlapped broad multiplets), and 5.42 (1-H, m, $W_{\frac{1}{2}}$ 9 Hz). The crude product (130 mg) was oxidised as described above. The diketone (9) was crystallised twice from methanol; m.p. 102—104 °C, $[\alpha]_D$ −46° (*c* 0.6) (lit.,[4] m.p. 105—106 °C, $[\alpha]_D$ −45.7°).

Migration of the Double Bond in Compound (6b) *to give* 5-*Methyl*-19-*nor*-5β-*cholest*-9-*ene*-3α,6β-*diol Diacetate* (7b), *and* 5-*Methyl*-19-*nor*-5β-*cholest*-9(11)-*ene*-3α,6β-*diol Diacetate* (8b).—To a solution of compound (6b) (160 mg) in glacial acetic acid (3 ml), 45% hydrobromic acid in acetic acid (12 capillary drops) was added. The solution was warmed for 2 h at 60 °C, and after cooling it was worked up as described for the conversion of (2b) into (6b). The crude product (140 mg) was chromatographed on silica (50 g). Elution with petrol–ethyl acetate (97 : 3) gave compound (7b) (45 mg); δ 0.80 [s, C(13)Me], 1.15 [s, C(5)Me], 2.03 and 2.07 (2 × OAc), and 4.6—5.1 (3β- and 6α-H, two partially overlapped multiplets). Further elution with the same solvent gave compound (8b) (80 mg); δ 0.62 [s, C(13)Me], 1.09 [s, C(5)Me], 2.00 and 2.08 (2 × OAc), 4.70 (6α-H, m, $W_{\frac{1}{2}}$ 6 Hz), 5.1 (3β-H, m, $W_{\frac{1}{2}}$ 16 Hz), and 5.47 (11-H, m, $W_{\frac{1}{2}}$ 8 Hz).

Hydrolysis of the Diacetates (7b) *and* (8b) *to the Diols* (7a) *and* (8a), *and Oxidation to the Diketones* (9) *and* (10).—Compound (7b) (30 mg) was hydrolysed with methanolic 3% potassium hydroxide. The diol (7a) showed one spot on a chromatoplate and had n.m.r. signals at δ 0.80 [s, C(13)Me], 1.05 [s, C(5)Me], and 3.3—4.1 (3β- and 6α-H, two partially overlapped multiplets). Oxidation of the crude diol (30 mg), as described above, afforded the diketone (9). The same diketone was obtained by hydrolysis of 'Westphalen diol diacetate' (11b) and oxidation. Similarly, hydrolysis of compound (8b) afforded the diol (8a), that showed one spot on a chromatoplate and had n.m.r. signals at δ 0.61 [s, C(13)Me], 1.15 [s, C(5)Me], 3.42 (6α-H, m, $W_{\frac{1}{2}}$ 7 Hz), 4.13 (3β-H, m, $W_{\frac{1}{2}}$ 18 Hz), and 5.43 (11-H, m, $W_{\frac{1}{2}}$ 8 Hz). Oxidation of the crude diol (45 mg) gave 5-methyl-19-nor-5β-cholest-9(11)-ene-3,6-dione (10), m.p. 105—107 °C (from methanol–water) (lit.,[3a] 112—113 °C); δ 0.67 [s, C(13)Me], 1.19 [s, C(5)Me], and 5.77 (11-H, m, $W_{\frac{1}{2}}$ 9 Hz). The same diketone was obtained by hydrolysis of 5-methyl-19-nor-5β-cholest-9(11)-ene-3β,6β-diol diacetate (12b) and subsequent oxidation with Jones reagent, as described above. The isomerisation of compound (11b) to (12b) was performed as described.[3a]

Oxidation of Compound (3b) *to* 3-*Oxocholest*-4-*en*-6β-*yl Acetate* (14).—Compound (3b) (150 mg) was oxidised with Jones reagent as described above to the ketone (14), m.p. 101—102 °C (lit.,[5] 103.5—104.5 °C), n.m.r. data as reported.[5]

Conversion of Compound (3b) *into Cholest*-4-*ene*-3,6-*dione* (13).—Compound (3b) (50 mg) was hydrolysed with methanlic 3% potassium hydroxide; the crude diol (one spot on a chromatoplate) was oxidised with Jones reagent to give the diketone (13), m.p. 122—124 °C (from acetone) (lit.,[6a] 125 °C).

Acetylation of Compound (3b) *to Cholest*-4-*ene*-3α,6β-*diol Diacetate* (3d).—Compound (3b) (150 mg) was acetylated with acetic anhydride (2 ml) and pyridine (3 ml) overnight at room temperature. Following the usual work-up, the diacetate (3d) was obtained, m.p. 101—102 °C (from methanol–water) (lit.,[6] 102—102.5 °C).

Acetylation of Compound (4b) *to* 5α-*Cholestane*-3α,5,6β-*triol* 3,6-*Diacetate* (4d).—Compound (4b) (100 mg) was acetylated as above to give the diacetate (4d), m.p. 85—86 °C (from methanol–petrol) (lit., [2d] 86—88 °C), n.m.r. data as reported.[2d]

Conversion of Compound (4b) *into Compound* (14).—Oxidation of compound (4b) (130 mg) with Jones reagent afforded 6β-acetoxy-5-hydroxy-5α-cholestan-3-one (15), m.p. 159—161 °C (from methanol) (lit., [2a] 161 °C); δ 1.32 [s, C(10)Me], 2.17 (OAc), and 4.70 (6α-H, m, $W_{\frac{1}{2}}$ 7 Hz). Compound (15) (100 mg) in benzene solution (25 ml) was introduced into a column of alumina (Alcoa F_{20}; 25 g). After 48 h the product was washed out with dichloromethane and

* *Note added in proof*: We inadvertently overlooked a paper (J. M. Coxon, M. P. Hartshorn, and C. N. Muir, *Tetrahedron*, 1969, **25**, 3925) describing the preparation of compound (2a) by treatment of 5,6β-epoxy-5β-cholestan-3α-ol with boron trifluoride–ether.

purified by chromatography on silica [elution with petrol–ethyl acetate (4 : 1)]. The product (50 mg), m.p. 100—101 °C (from methanol–water), was identical with compound (14).

Treatment of Cholest-5-ene (16) [12] *with Thallium Triacetate.*—The reagent (2 g) was added to a solution of compound (16) (1 g) in glacial acetic acid (40 ml) and the solution was stirred for 75 h at 75 °C. Following work-up as for compound (1a), the crude product was chromatographed on silica (200 g). Elution with petrol afforded unchanged material (280 mg); elution with petrol–ethyl acetate (97 : 3) gave cholest-5-en-6-yl acetate (17) (230 mg), which could not be induced to crystallise; $\nu_{max.}$ 1 740 cm^{-1}; δ 1.03 [s, C(10)Me], and 2.10 (OAc). Further elution with petrol–ethyl acetate (9 : 1) gave cholest-4-ene-3β,6β-diol diacetate (18) (160 mg), m.p. 130—131 °C (from methanol) (lit.,[6] 130—131 °C), followed by cholest-4-ene-3α,6β-diol diacetate (3d) (300 mg).

When the reaction was performed at 60 °C for 100 h, the following compounds were isolated by chromatography: unchanged material (290 mg) and compound (17) (190 mg); further elution with petrol–ethyl acetate (96 : 4) gave 5α-cholestane-5,6α-diol 6-acetate (19) (65 mg), m.p. 122—123 °C (from methanol) (lit.,[8] 117—118 °C); δ 1.00 [s, C(10)Me], 2.07 (OAc), and 4.95 [6β-H, m, $W_{\frac{1}{2}}$ 15 Hz); Δδ ($CDCl_3$ — C_5D_5N) of C(10)Me −0.01 p.p.m. Further elution gave compounds (18) (150 mg) and (3d) (270 mg.)

Hydrolysis of the Enol Acetate (17) *to 5α-Cholestan-6-one* (20).—A solution of compound (17) (200 mg) in methanolic 3% potassium hydroxide (25 ml) was left overnight, then neutralised with dilute hydrochloric acid. The product was isolated by filtration and crystallised from acetone, m.p. 97—98 °C (lit., [7b] 99 °C); δ 0.66 [s, C(10)Me] in $CDCl_3$ and 0.54 in C_6H_6.[7c]

Dehydration of Compound (19) *to Cholest-4-en-6α-yl Acetate* (22).—To a solution of compound (19) (25 mg) in dry pyridine (2 ml), at 0 °C, thionyl chloride (5 capillary drops) was added. After 30 min at 0 °C, ice was added, the product was extracted with ether, and the cold solution was washed with N-hydrochloric acid, then aqueous 5% sodium hydrogen carbonate, and water. The solvent was removed and the residue (22 mg) crystallised from petrol; m.p. 95—96 °C (lit.,[9a] 95—98 °C), n.m.r. spectrum as reported.[9b]

Treatment of Cholest-4-ene-6β-yl Acetate (21) [9a] *with Thallium Triacetate.*—Thallium triacetate (200 mg) was added to a solution of compound (21) (100 mg) in glacial acetic acid (10 ml) and the solution was stirred for 20 h at 75 °C. Following the usual work-up, the product was chromatographed on silica (50 g). Elution with petrol–ethyl acetate (9 : 1) gave compound (18) (30 mg), followed by compound (3d) (55 mg).

[12] J. Mauthner, *Monatsh.*, 1909, **30**, 635.

Treatment of Cholesta-3,5-diene (23) [13] *with Thallium Triacetate.*—Thallium triacetate (5 g) was added to a solution of compound (23) (2.5 g) in glacial acetic acid (130 ml), and the solution was stirred for 4 h at 50 °C. After work-up as before the crude product was chromatographed through silica (400 g). Elution with petrol gave unchanged material (300 mg). Elution with benzene–ethyl acetate (98 : 2) gave compound (18) (360 mg), followed by compound (3d) (1.1 g). Elution with dichloromethane–ethyl acetate (9 : 1) afforded compound (24c), m.p. 190—192 °C (from methanol (lit.,[10a] 194 °C); δ 1.23 [s, C(10)Me], 2.10 (OAc), 4.27 (4α-H, d, *J* 4 Hz), 4.77 (3α-H, m, $W_{\frac{1}{2}}$ 16 Hz), and 5.73 (6-H, m, $W_{\frac{1}{2}}$ 9 Hz). Elution with dichloromethane–ethyl acetate (85 : 15) gave compound (3c) (200 mg), which could not be induced to crystallise; δ 1.20 [s, C(10)Me], 2.03 (OAc), 4.23 (6α-H, m, $W_{\frac{1}{2}}$ 7 Hz), 5.17 (3β-H, m, $W_{\frac{1}{2}}$ 10 Hz), and 5.67 (4-H, d, *J* 4.5 Hz). Elution with dichloromethane–ethyl acetate (4 : 1) gave compound (24b) (120 mg), m.p. 157—159 °C (from methanol) (lit.,[10] 159—161 °C); n.m.r. data as described.[10b]

Acetylation of 3α-acetoxy-6β-hydroxycholest-4-ene (3c) afforded the diacetate (3d). Hydrolysis of compound (3c) with methanolic 3% potassium hydroxide afforded the diol (3a), which was subsequently oxidised with Jones reagent to cholest-4-ene-3,6-dione (13).

Acetylation of compounds (24b and c) gave the same diacetate (24d), m.p. 166—168 °C (from methanol–water) (lit.,[14] 169—170 °C); hydrolysis gave the same diol (24a), m.p. 178—179 °C (from methanol–water) (lit.,[14] 176—177 °C).

Treatment of Epicholesteryl Acetate, Cholesteryl Acetate, and Cholesterol with Thallium Triacetate.—To a solution of epicholesteryl acetate (1b) (100 mg) in glacial acetic acid (5 ml), thallium triacetate (200 mg) was added, and the solution was heated for 50 h at 50 °C. Following the usual work-up, only unchanged material (1b) was isolated quantitatively. The reaction was performed under the same conditions with cholesteryl acetate; the compound remained unchanged. The reaction with cholesterol was carried out with 250 mg samples, under the following conditions:

Time (h)	Temp. (°C)	Unchanged material (mg)	Cholesteryl acetate (mg)
4	80	160	50
10	90	110	85
7	Reflux	50	180

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[13] E. Caspi, *J. Org. Chem.*, 1956, **21**, 729.
[14] O. Rosenheim and W. W. Starling, *J. Chem. Soc.*, 1937, 377.