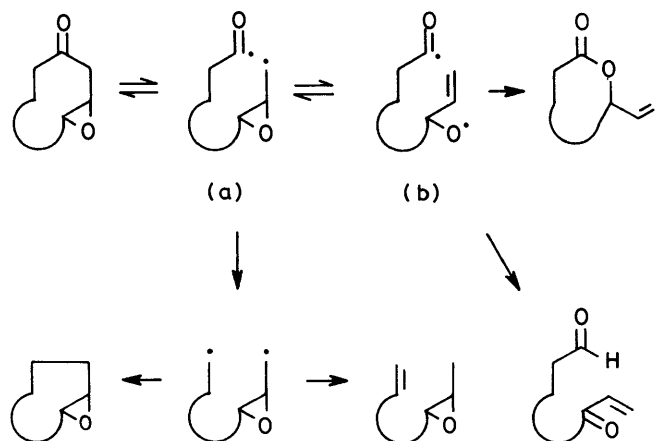


Steroids Part 22.¹ Photochemistry of 5,6-Epoxy-4,4-dimethylcholestan-3-ones and 5,6-Epoxy-17-hydroxy-4,4-dimethylcholestan-3-ones

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The β,γ -epoxy ketones (5), (6), (7), and (8) photolyse essentially as the equivalent ketones, e.g. (9), in methanol in that little evidence of epoxide cleavage is detected and the major products are the methyl 5-isopropyl-4-nor-3,5-secoesters. In ether, the 3-keto 5 β ,6 β -epoxide (8) photodecarbonylates *via* a double hydrogen shift (C-2 \rightarrow C-4 and C-1 \rightarrow C-2) and it is suggested that epoxide photocleavage in β,γ -epoxy ketones may be subject to stereoelectronic control.

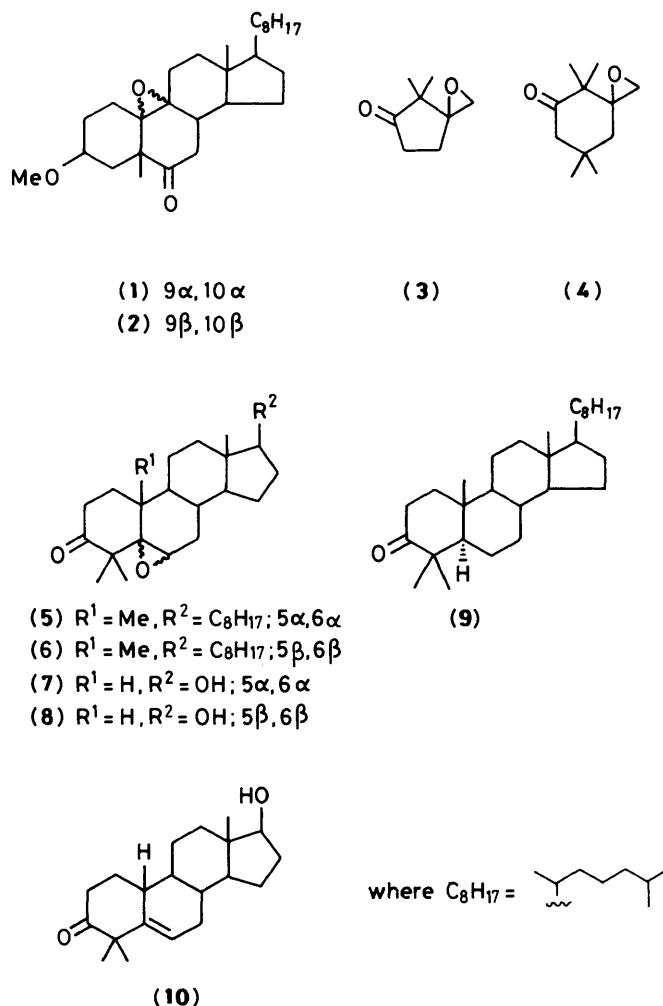
The photoreactions of the 9,10-epoxy-19-norcholestan-6-ones (1) and (2)² are not fully rationalised by the general Scheme 1 proposed³ for the photolyses of β,γ -epoxy ketones of this type. In particular, there is a significant difference in reactivity between isomers (1) and (2) and the decarbonylation of compound (2) in ether appears to involve an unusual 1,5-hydrogen transfer.² The absence of products arising from cleavage of the epoxide moiety is interesting since, in general, the radicals (a) (Scheme 1) might be expected⁴ readily to give oxide radicals (b) especially since stereoelectronic effects have been reported to be unimportant in this type of reaction.⁵ The photoreactions of the 1-oxaspiro[2.*n*]alkan-5-ones (3) and (4) are reported⁶ to be adequately accounted for by a reaction scheme which is analogous to Scheme 1. We report here an investigation of the photoreactions of the 5,6-epoxy-4,4-dimethylcholestan-3-ones (5)⁷ and (6),⁷ their 19-nor analogues (7) and (8), and 4,4-dimethyl-5 α -cholestan-3-one (9)⁸ in an attempt to evaluate further the proposed general reaction schemes and to elucidate any other important controlling factors.



Scheme 1.

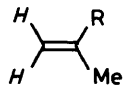
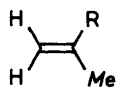
The 3-keto 19-nor-5 α ,6 α -epoxide (7) was prepared by monopero-phthalic acid oxidation of the Δ^5 -compound (10) and the 5 β ,6 β -epimer (8) was obtained from the latter by successive treatment with *N*-bromosuccinimide (NBS)-aqueous perchloric acid and potassium acetate. The 6-H doublets in the ¹H n.m.r. spectra of the epoxides (7) and (8) respectively at δ 3.14 (*J* 5 Hz) and 3.18 (*J* 3 Hz) confirmed the assigned stereochemistry.⁹

Photolysis of the 3-keto 5 α ,6 α -epoxide (5) in ether solution in Pyrex apparatus, using a medium-pressure Hg lamp, afforded an extremely complex inseparable mixture. The absence of the

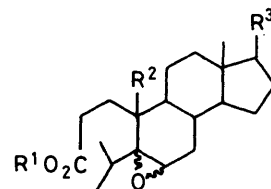


6-H doublet in the ¹H n.m.r. spectrum of the crude product suggested that the epoxide moiety had been cleaved. Similar photolysis of the 3-keto 5 β ,6 β -epoxide (6) led to rapid decarbonylation and the unsaturated 5 β ,6 β -epoxide (11) (29%) and the 4-nor-5 β ,6 β -epoxide (12) (12%) were isolated after preparative t.l.c. (p.l.c.). The ¹H n.m.r. spectrum of the unsaturated 5 β ,6 β -epoxide (11) confirmed (i) that the epoxide moiety was intact (δ 3.04, d, *J* 2 Hz, 6-H) and (ii) the presence of the ethenyl group [δ 5.88, dd, *J* (apparent) 11 and 18 Hz, 1-H, and 5.08, m, *J*_{gem} 2 Hz, 2-H₂]. The 5-isopropyl group of compound (11) gave rise to two doublets (*J* 7 Hz) in the ¹H n.m.r. spectrum at δ 0.72 and 0.85. The latter signal was only

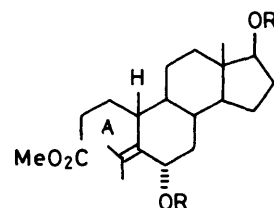
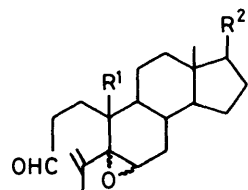
Table. Selected ^1H n.m.r. data for unsaturated epoxides (19)–(21)

Compound	δ			
			R'CHO	6-H
(19)	4.92, 5.08 br s	1.85 br s	9.78 br s	2.85 d, $J \sim 5$ Hz
(20)	4.8, 4.95 br s	1.96 br s	9.78 br s	3.25 d, $J \sim 2$ Hz
(21)	4.86, 5.05 br s	1.8 br s	9.72 br s	2.76 d, $J \sim 6$ Hz

resolved in a 220 MHz spectrum. The 4-nor-5 β ,6 β -epoxide (12) was shown by its mass spectrum to be isomeric with compound (11), having a molecular formula $\text{C}_{28}\text{H}_{48}\text{O}$, and the ^1H n.m.r. spectrum confirmed that the epoxide moiety was intact (δ 3.05, d, J 2 Hz, 6-H). The i.r. spectra of both (11) and (12) confirmed the absence of a carbonyl group. A sample of the 2-deuterated 3-keto 5 β ,6 β -epoxide (6) ($^2\text{H}_2$ 80%, $^2\text{H}_1$ 16%, $^2\text{H}_0$ 4%), obtained by treatment of the 3-keto 5 β ,6 β -epoxide (6) with $\text{NaOD}-\text{D}_2\text{O}$ -dioxane, was photolysed in ether and afforded the deuterated unsaturated 5 β ,6 β -epoxide (11) ($^2\text{H}_2$ 77.5%, $^2\text{H}_1$ 13.5%, $^2\text{H}_0$ 7%) and the deuterated 4-nor-5 β ,6 β -epoxide (12) ($^2\text{H}_2$ 80%, $^2\text{H}_1$ 17%, $^2\text{H}_0$ 3%). The 220 MHz ^1H n.m.r. spectrum of the former compound showed singlets for the methyl groups of the 5-isopropyl group (δ 0.72 and 0.85), confirming that deuterium is transferred from C-2 to C-4 in the photolysis. This was further confirmed by the simplification of the olefinic proton multiplet at δ 5.08 to two doublets at δ 5.06 (J 18 Hz) and 5.13 (J 11 Hz) corresponding to the *E*- and *Z*-isomer (11a) and (11b) respectively. Additionally, the double doublet ($w_{\frac{1}{2}}$ 29 Hz) at δ 5.88 became two superimposed doublets ($w_{\frac{1}{2}}$ 18 Hz, J 11 and 18 Hz) corresponding to a mixture of isomers (11a) and (11b).

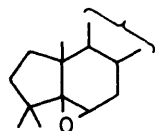
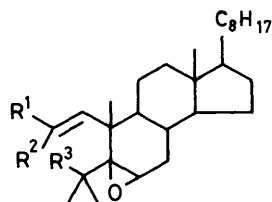


- (13) $\text{R}^1 = \text{R}^2 = \text{Me}$, $\text{R}^3 = \text{C}_8\text{H}_{17}$; 5 α , 6 α
 (14) $\text{R}^1 = \text{R}^2 = \text{Me}$, $\text{R}^3 = \text{C}_8\text{H}_{17}$; 5 β , 6 β
 (15) $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{H}$, $\text{R}^3 = \text{OH}$; 5 α , 6 α
 (16) $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{H}$, $\text{R}^3 = \text{OH}$; 5 β , 6 β
 (17) $\text{R}^1 = \text{R}^2 = \text{H}$, $\text{R}^3 = \text{OH}$; 5 α , 6 α
 (18) $\text{R}^1 = \text{R}^2 = \text{H}$, $\text{R}^3 = \text{OH}$; 5 β , 6 β



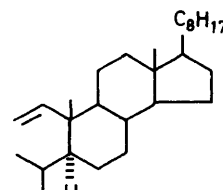
- (19) $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{C}_8\text{H}_{17}$; 5 α , 6 α
 (20) $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{C}_8\text{H}_{17}$; 5 β , 6 β
 (21) $\text{R}^1 = \text{H}$, $\text{R}^2 = \text{OH}$; 5 α , 6 α

- (22) $\text{R} = \text{H}$
 (23) $\text{R} = \text{Ac}$

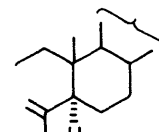


- (11) $\text{R}^1 = \text{R}^2 = \text{R}^3 = \text{H}$
 (11a) $\text{R}^1 = \text{R}^3 = ^2\text{H}$, $\text{R}^2 = \text{H}$
 (11b) $\text{R}^1 = \text{H}$, $\text{R}^2 = \text{R}^3 = ^2\text{H}$

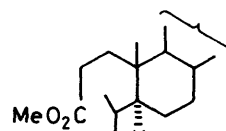
(12)



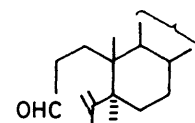
(24)



(25)



(26)



(27)

Photolysis of the 3-keto 5 α ,6 α -epoxide (5) in methanol afforded the methyl epoxy ester (13) (43%) and the unsaturated aldehyde (19) (22%). Similarly, the 3-keto 5 β ,6 β -epoxide (6) gave the methyl epoxy ester (14) (48%) and the unsaturated aldehyde (20) (12%). Other minor products were not identified. The ^1H n.m.r. spectra of the methyl epoxy esters (13) and (14) showed important singlets at δ 3.67 and 3.69 respectively (CO_2Me), and doublets at δ 2.84 ($J \sim 5$ Hz) and 3.16 ($J \sim 2$ Hz) respectively (6-H) confirmed the presence of the epoxide moiety in each. The ^1H n.m.r. spectra of the unsaturated aldehydes (19) and (20) showed important peaks confirming the presence of the disubstituted double bond, the aldehyde function, and the epoxide moiety (Table).

Photolysis of the 19-nor-3-keto 5 α ,6 α -epoxide (7) in ether gave a complex mixture which could not be resolved and a similar result was obtained with the 19-nor-3-keto 5 β ,6 β -epoxide (8) but the reaction was considerably slower. A similar qualitative difference in photolysis rates was observed for

isomers (7) and (8) in methanol and the major products were respectively the methyl epoxy esters (15) (56%) and (16) (48%). The spectroscopic data for the methyl epoxy esters (15) and (16) were similar to those for the related compounds (13) and (14), and hydrolysis afforded the epoxy acids (17) and (18)

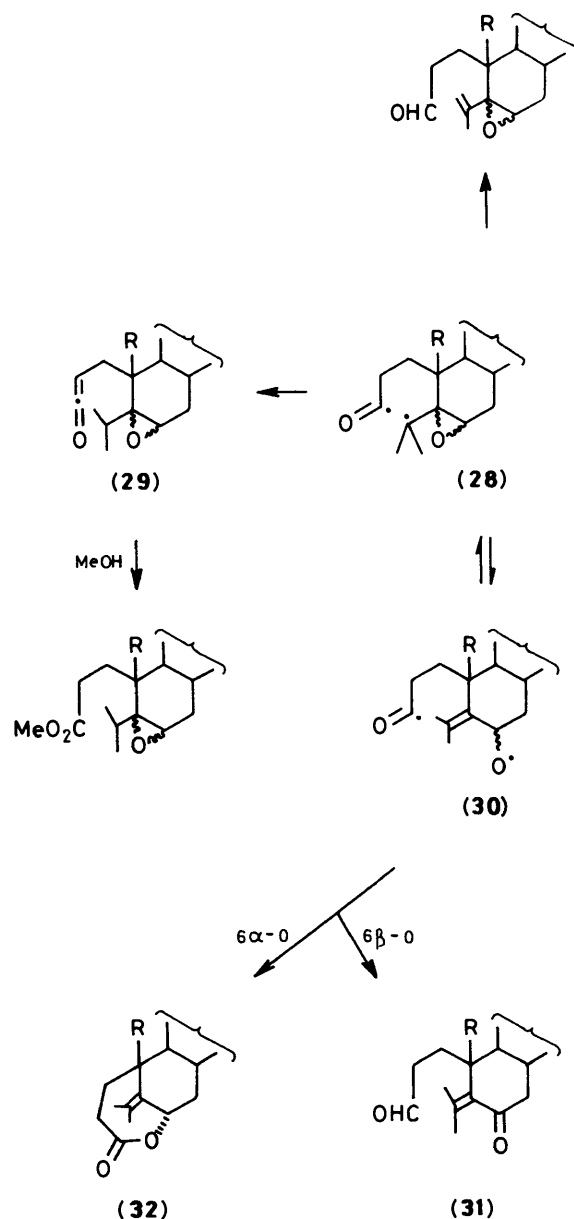
respectively. The minor products of photolysis of (7) and (8) in methanol were difficult to purify. However, in one experiment the 19-nor-3-keto 5 α ,6 α -epoxide (7) afforded the unsaturated aldehyde (21) (11%) (Table) and the allylic alcohol (22) (13%). Important signals in the ^1H n.m.r. spectrum of the allylic alcohol (22) at δ 1.70 and 1.75 (s, $\text{Me}_2\text{C}=\text{}$), 3.65 (s, CO_2Me), and 4.86 (br d, $J \sim 9$ Hz, 6-H) confirmed the structural assignment, and acetylation gave the diacetate (23). The ^1H n.m.r. spectrum of compound (23) showed the 6-H signal at $\delta \sim 5.93$ (br d, $J \sim 8$ Hz) and confirmed the presence of the 6 α -OH group in compound (22). The 6-H signal in the ^1H n.m.r. spectra of compounds (22) and (23) suggested that the B-ring adopts a skew-boat conformation presumably to relieve steric repulsion between the *syn*-methyl group (A) and the substituent at C-10.

Photolysis of the ketone (9) in ether rapidly gave a mixture from which the olefins (24) (12%) and (25) (6%) were obtained by p.l.c. Other impure fractions were not fully characterised. The olefin (24) had a ^1H n.m.r. spectrum similar to that of the unsaturated epoxide (11), and that of the olefin (25) was similar to those of the unsaturated aldehydes (Table). The major product (71%) of photolysis of the ketone (9) in methanol was the ester (26), as expected, and a minor product (*ca.* 10%) was the unsaturated aldehyde (27) which, though clearly identified from its spectroscopic data, could not be fully purified.

Discussion

In general, the major photochemical processes of the 3-keto 5,6-epoxides (5)–(8) in methanol are the same as observed for cyclic ketones,¹⁰ giving rise to methyl esters and unsaturated aldehydes through the biradical intermediate (28) (Scheme 2). The unsaturated aldehydes produced in these reactions and in the photolysis of the ketone (9) appear to be formed through a formal 1,7-hydrogen shift rather than the more usual 1,5-shift. Such 1,7-shifts have been recorded in the photolysis of limonin¹¹ and other α,α -dimethylketones.¹² The expected 1,5-shift is presumably involved in the formation of the ketene (29). The reaction course is hardly modified by the stereochemistry of the epoxide or the absence of the 10-methyl group even though this might be expected to change the conformation of the A-ring considerably (see below). It is surprising that hydrogen transfer in the diradical (28) competes with epoxide ring opening since it would be expected that this would take place rapidly and that the equilibrium between (28) and (30) would favour the latter,⁴ presuming the absence of stereoelectronic effects.⁵ The failure of conversion of the diradical (30) into other possible products (31) and (32) appears to depend critically on the considerable conformational changes required.³ The competing ketene- and unsaturated aldehyde-forming processes require only modest conformational changes in diradical (28) to bring the appropriate H atoms close to the reacting radical centres. Possibly, the position of the equilibrium between (28) and (30) is not very important in the presence of methanol since this has a major directing influence in trapping the ketene (29). That some epoxide-opened products are probably formed from the 3-keto 5,6-epoxides (5), (6), and (7) is indicated by the slightly lower yields of methyl esters obtained *versus* that obtained from the ketone (9). The yield of methyl ester from the 19-nor-3-keto 5,6-epoxide (8) seems relatively high since considerable unchanged starting material remained in the product.

In the photolyses in ether, it is presumed that the cleavage of the epoxide linkage in the 3-keto epoxides (5), (7) and (8) is responsible in part for the complexity of the product mixture. The alternative and more energetic C-5–C-6 bond cleavage may also be a complicating factor. The decarbonylation of the 3-keto 5 β ,6 β -epoxide (6) is significant and it involves the analogous 1,5-hydrogen shift to that reported earlier² for the 6-keto 9 α ,10 α -epoxide (1). Accordingly, the diradical (28; R = Me, 5 β ,6 β) is

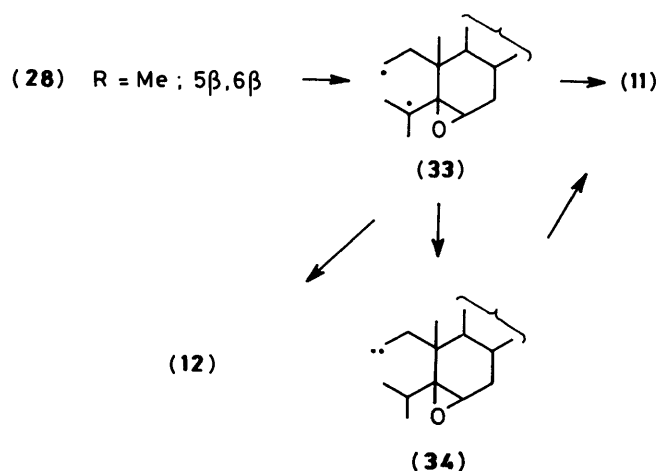


Scheme 2.

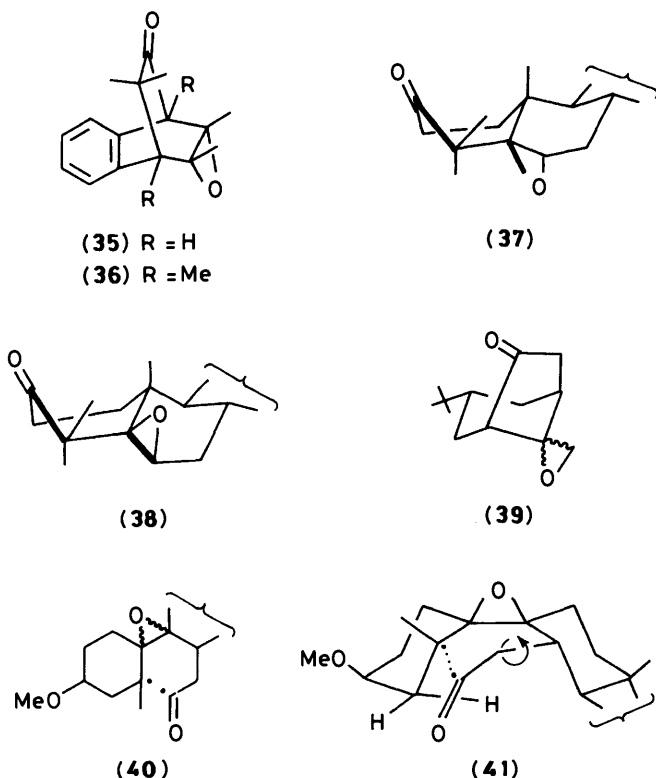
converted into the diradical (33) which may undergo synchronous or stepwise hydrogen shifts from C-2 to C-4 and C-1 to C-2 leading to the unsaturated epoxide (11) directly or *via* the carbene (34) (Scheme 3).

Possibly, this mechanism is quite general and is involved in the decarbonylation of the ketone (9) and certain other carbonyl compounds. That it is not the exclusive mechanism for photo-decarbonylation of β,γ -epoxy ketones has been established in the study¹³ of the benzo-fused bicyclo[2.2.2]octene derivatives (35) and (36).

By analogy with the 3-keto 4,4-dimethyl- Δ^5 -steroids, it may be assumed that the preferred conformation of the A-ring of the 3-keto 5,6-epoxides (5) and (6) is a skew-boat owing to the steric interaction between the 10-methyl group and the 4 β -methyl group in the normal chair conformation.¹⁴ Thus, in conformation (37) of the 3-keto 5 α ,6 α -epoxide (5), the C-3–C-4 bond is antiperiplanar with the C-5–O bond whereas in conformation (38) of the 5 β ,6 β -epoxide (6) this is not so. Perhaps this difference is responsible for the failure of the epoxide to open, since in β -



Scheme 3.



scission of a radical it is generally recognised that the semi-occupied orbital of the radical should be coplanar with the bond being broken for efficient reaction.¹⁵ Assuming that rotation around the C-4-C-5 bond in the diradicals (28; R = Me) is relatively slow owing to the steric interaction between the 4-methyl groups and either the 10-methyl group or the 1-methylene group, then in diradical (28; R = Me, 5 β ,6 β) decarbonylation may be able to compete with epoxide ring opening. In the diradicals (28; R = H) derived from the 19-norepoxides (7) and (8), which probably have preferred α -ring conformations close to the normal chair, the greater degree of rotational freedom around C-4-C-5 owing to the absence of the 10-methyl group results in rather complex reaction products presumed to be derived from epoxide ring opening. That the photoreactions of the 3-keto 5,6-epoxides (5)–(8) depend on stereoelectronic factors is in contradiction to the observations of Agosta and co-workers⁵ with the β,γ -epoxy ketones (39).

However, similar effects may also allow rationalisation of our earlier observations on the photochemistry of the 6-keto 9,10-epoxides (1) and (2). The diradical (40; 9 α ,10 α) would not readily achieve the planar conformation at C-5 in which the semi-occupied orbital is coplanar with the C-9-O bond owing to a severe steric interaction between the 5-methyl group and the 7-methylene group. However, hydrogen atoms at C-7 would become available for abstraction by rotation around the C-7-C-8 bond. In the diradical (40; 9 β ,10 β) a similar constraint operates in the alignment of the semi-occupied orbital at C-5 and the C-9-O bond. Additionally, rotation around the C-7-C-8 bond is impeded by steric interaction between the CO group and the 4-methylene group [see conformation (41)]. Accordingly, much of the diradical (40; 9 β ,10 β) most probably re-forms the starting material.

Experimental

Solutions were dried over anhydrous magnesium sulphate and solvents were removed under reduced pressure on a rotary evaporator. Plates (0.75 mm thick) of Kieselgel PF 254 (Merck) were used for p.l.c. In certain experiments the silica gel was impregnated with AgNO₃ (10%). I.r. were determined with a Perkin-Elmer 177 spectrophotometer. ¹H N.m.r. spectra were routinely determined for solutions in deuteriochloroform at 60 MHz with a Varian EM 360A, or at 90 MHz with a Perkin-Elmer R32 spectrometer. Those at 220 MHz were determined at the Physico-Chemical Measurements Unit using a Varian HR 220 spectrometer. Low-resolution mass spectra were recorded with an A.E.I. MS12 spectrometer and accurate mass measurements were determined at the Physico-Chemical Measurements Unit. Rotations were determined for solutions in chloroform with a Bendix polarimeter 143C. Photolyses were carried out in deoxygenated solvents in an atmosphere of nitrogen using a 125 W Hanovia medium-pressure mercury lamp in a water-cooled Pyrex photoreactor.

5,6 α -Epoxy-17 β -hydroxy-4,4-dimethyl-5 α -estrane-3-one (7).—17 β -Hydroxy-4,4-dimethylestr-5-en-3-one (10)¹⁵ (0.4 g, 1.32 mmol) was dissolved in chloroform (3 ml) and ether (10 ml), and the solution was cooled to 0 °C. An ethereal solution of monopero-phthalic acid (6.6 mmol) was added and the solution was kept in a refrigerator overnight. After being washed successively with water, saturated aqueous sodium hydrogen carbonate, and water, the organic phase was dried and evaporated to afford a white crystalline solid. Crystallisation from ether-light petroleum (b.p. range 40–60 °C) gave the 3-keto 5 α ,6 α -epoxide (7) (318 mg, 75%), m.p. 183–188 °C. Two further recrystallisations from acetone-cyclohexane raised the m.p. to 187–188 °C, [α]_D –14.7° (c 4.0); ν_{\max} . 1 719 (C=O) and 3 510 cm⁻¹ (OH); δ 0.75 (s, 13 β -Me), 0.88 (s, 4 α -Me), 1.28 (s, 4 β -Me), 3.14 (d, *J* 5 Hz, 6-H), and 3.65 (t, *J* 8 Hz, 17-H) (Found: C, 75.5; H, 9.8%; *M*⁺, 318. C₂₀H₃₀O₃ requires C, 75.45; H, 9.5%; *M*, 318).

5,6 β -Epoxy-17 β -hydroxy-4,4-dimethyl-5 β -estrane-3-one (8).—A solution of compound (10)¹⁵ (0.5 g, 1.82 mmol) in dichloromethane (2 ml), *t*-butyl alcohol (14 ml), and water (2 ml) was stirred and cooled to 0 °C. Perchloric acid [2 ml from 60% perchloric acid (0.43 ml) in water (40 ml)] was added, followed by NBS (0.59 g, 3.65 mmol), and the mixture was stirred for 15 min at 0 °C. An aqueous solution of sodium sulphate containing sodium metabisulphate was added, and the mixture was extracted with dichloromethane. The organic layer was washed with water, dried, and evaporated to afford a pale yellow oil, which was dissolved in absolute ethanol (350 ml) containing potassium acetate (8 g) and the solution was heated under reflux for 2.5 h. After cooling, the excess of ethanol was removed under reduced pressure. Water was added to the residue, and

extraction with chloroform gave a yellow oil, which was purified by p.l.c. with light petroleum (40–60 °C)–ether (15:85) as eluant. Crystallisation of the major component from acetone–cyclohexane gave the 3-keto 5 β ,6 β -epoxide (**8**) (230 mg, 44%), m.p. 186–188 °C; $[\alpha]_D + 19.6^\circ$ (*c* 2.68); ν_{\max} . 1 700 (C=O) and 3 500 cm⁻¹ (OH); δ 0.75 (s, 13 β -Me), 1.02 (s, 4 β -Me), 1.1 (s, 4 α -Me), 3.18 (d, *J* 3 Hz, 6-H), and 3.65 (t, *J* 8 Hz, 17-H) (Found: C, 75.3; H, 9.8%; M^+ , 318).

Photolysis of the 3-Keto 5 β ,6 β -Epoxide (6) in Ether.—A solution of epoxy ketone (**6**) (200 mg) in dry ether was irradiated for 1 h. Removal of the solvent gave an oil (212 mg), the i.r. spectrum of which revealed that decarbonylation had occurred. The crude reaction mixture was separated by p.l.c. with benzene–ethyl acetate (95:5) as eluant ($\times 2$), and afforded 5,6 β -epoxy-4 ϵ -methyl-2,3-seco-5 β -cholest-1-ene (**11**) (54 mg, 29%), m.p. 56–58 °C (from methanol–acetone); ν_{\max} . 1 630 cm⁻¹ (CH₂=CHR); δ 0.63 (s, 13 β -Me), 0.72 (d, *J* 7 Hz, MeCHMe), 0.85 (d, *J* 7 Hz, MeCHMe), 1.05 (s, 10 β -Me), 3.04 (d, *J* 2 Hz, 6-H), 5.08 (m, *J*_{gem} 2 Hz, CH=CH₂), and 5.88 (dd, *J* 11 and 18 Hz, CH=CH₂) (Found: M^+ , 400.3705. C₂₈H₄₈O requires *M*, 400.3705) and 5,6 β -epoxy-3,3-dimethyl-4-nor-5 β -cholestane (**12**) (23 mg, 12%), m.p. 76–78 °C (from acetone–methanol); δ 0.65 (s, 13 β -Me) and 3.05 (d, *J* 2 Hz, 6-H) (Found: M^+ , 400.3701. C₂₈H₄₈O requires *M*, 400.3705). Other bands isolated from the plate were impure.

Preparation and Photolysis of the Deuteriated Analogue of the 3-Keto 5 β ,6 β -Epoxide (6).—The epoxy ketone (**6**) (1 g) was dissolved in dry dioxane (40 ml) and the solution was heated under reflux with 30% sodium deuterioxide in deuterium oxide for 2 days. After the solvent had been removed the residue was extracted with chloroform (25 ml $\times 2$). The combined extracts were evaporated to dryness. The residue was subjected to this treatment four times and finally was recrystallised from acetone to give the deuteriated 3-keto 5 β ,6 β -epoxide (**6**) (486 mg, 49%), m.p. 198–200 °C; low-resolution mass spectra established the deuterium content was ²H₂ 80%, ²H₁ 16%, ²H₀ 4%.

Irradiation of the deuteriated epoxy ketone (**6**) (120 mg) in ether (100 ml) as above for 1 h gave an oil (128 mg), which was separated by p.l.c. on silica gel impregnated with AgNO₃, with benzene–ethyl acetate (95:5) as eluant. The two major components were the deuteriated 4-nor-5 β ,6 β -epoxide (**12**) (23 mg, 20%) and the deuteriated unsaturated 5 β ,6 β -epoxide (**11**) (36 mg, 29%) which were shown, by low-resolution mass spectrometry, to contain ²H₂ 77.5%, ²H₁ 13.5%, ²H₀ 7% and ²H₂ 80%, ²H₁ 17%, ²H₀ 3% respectively (see Discussion section for changes in ¹H n.m.r. spectra).

Photolysis of the 3-Keto 5 α ,6 α -Epoxide (5) in Methanol.—A solution of the epoxy ketone (**5**) (400 mg) in methanol (750 ml) was irradiated for 3 h. Evaporation of the methanol gave an oil (446 mg), p.l.c. of which with ether–light petroleum (40–60 °C) (15:85) as eluant gave methyl 5,6 α -epoxy-4,4-dimethyl-3,4-seco-5 α -cholestan-3-oate (**13**) (185 mg, 43%), $[\alpha]_D - 21.7^\circ$ (*c* 2.0); ν_{\max} . 1 740 cm⁻¹ (C=O); δ 0.63 (s, 13 β -Me), 0.76 (d, *J* 7 Hz MeCHMe), 0.95 (d, *J* 7 Hz, MeCHMe), low-field branch resolved), 1.02 (s, 10 β -Me), 2.84 (d, *J* 5 Hz, 6-H), and 3.67 (s, CO₂Me) (Found: M^+ , 460.3922. C₃₀H₅₂O₃ requires *M*, 460.3916) and 5,6 α -epoxy-4-methyl-4-methylene-3,4-seco-5 α -cholestan-3-al (**19**) (90 mg, 22%); ν_{\max} . 1 640 (CH₂=CR₂), 1 720 (C=O), and 2 710 cm⁻¹ (CHO); δ 0.63 (s, 13 β -Me), 1.08 (s, 10 β -Me), 1.85 (br s, CH₂=CMe), 2.85 (d, *J* 5 Hz, 6-H), 4.92 and 5.08 (br s, CH₂=CMe), and 9.78 (br s, CHO) (Found: M^+ , 428.3652. C₂₉H₄₈O₂ requires *M*, 428.3654). Other impure bands were not characterised.

Photolysis of the 3-Keto 5 β ,6 β -Epoxide (6) in Methanol.—A solution of epoxy ketone (**6**) (300 mg) in methanol (750 ml) was

irradiated as above for 3 h. Removal of the solvent afforded a yellowish oil (338 mg), which on p.l.c. with ether–light petroleum (40–60 °C) (15:85) as eluant gave methyl 5,6 β -epoxy-4,4-dimethyl-3,4-seco-5 β -cholestan-3-oate (**14**) (156 mg, 48%), m.p. 69–70 °C (from methanol); $[\alpha]_D - 5.1^\circ$ (*c* 2.0); ν_{\max} . 1 740 cm⁻¹ (C=O); δ 0.61 (s, 13 β -Me), 0.80 (d, *J* 7 Hz, MeCHMe), 0.98 (d, *J* 7 Hz, MeCHMe, high-field branch resolved), 1.01 (s, 10 β -Me), 3.16 (d, *J* 2 Hz, 6-H), and 3.69 (s, CO₂Me) (Found: M^+ , 460.3922. C₃₀H₅₂O₃ requires *M*, 460.3916) and 5,6 β -epoxy-4-methyl-4-methylene-3,4-seco-5 β -cholestan-3-al (**20**) (35 mg, 12%); ν_{\max} . 1 640 (CH₂=CR₂), 1 720 (C=O), and 2 710 cm⁻¹ (CHO); δ 0.63 (s, 13 β -Me), 1.11 (s, 10 β -Me), 1.96 (br s, CH₂=CMe), 3.25 (d, *J* 2 Hz, 6-H), 4.8 and 5.05 (br s, CH₂=CMe), and 9.78 (br s, CHO) (Found: M^+ , 428.3652. C₂₉H₄₈O₂ requires *M*, 428.3654). Other impure bands were not characterised.

Photolysis of the 19-Nor-3-keto 5 α ,6 α -Epoxide (7) in Methanol.—A solution of the epoxy ketone (**7**) (270 mg) in methanol (600 ml) was irradiated as above for 7.5 h. Removal of the solvent, and p.l.c. ($\times 3$) with ether–light petroleum (40–60 °C) (70:30) as eluant, gave methyl 5,6 α -epoxy-17 β -hydroxy-4,4-dimethyl-3,4-seco-5 α -estran-3-oate (**15**) (166 mg), $[\alpha]_D + 2.4^\circ$ (*c* 1.0); ν_{\max} . 1 740 (C=O) and 3 450 cm⁻¹ (OH); δ 0.71 (d, *J* 7 Hz, MeCHMe), 0.72 (s, 13 β -Me), 0.98 (d, *J* 7 Hz, MeCHMe), 2.93 (d, *J* 6 Hz, 6-H), 3.63 (t, *J* 8 Hz 17-H), and 3.67 (s, CO₂Me) (Found: M^+ , 350. C₂₁H₃₄O₄ requires *M*, 350). Hydrolysis of the ester (**15**) in 10% methanolic KOH gave the acid (**17**), m.p. 177–180 °C (Found: C, 71.7; H, 10.1. C₂₀H₃₂O₄ requires C, 71.4; H, 9.6%).

In one experiment other fractions isolated were 5,6 α -epoxy-17 β -hydroxy-4-methyl-4-methylene-3,4-seco-5 α -estran-3-al (**21**) (30 mg, 11%); ν_{\max} . 1 640 (CH₂=CR₂), 1 725 (C=O), and 3 460 cm⁻¹ (OH); δ 0.73 (s, 13 β -Me), 1.8 (br s, CH₂=CMe), 2.76 (d, *J* 6 Hz, 6-H), 3.64 (t, *J* 8 Hz, 17-H), 4.86 and 5.05 (br s, CH₂=CMe), and 9.72 (br s, CHO) (Found: M^+ , 318. C₂₀H₃₀O₃ requires *M*, 318) and methyl 6 α ,17 β -dihydroxy-4,4-dimethyl-3,4-secoestr-4-en-3-oate (**22**) (40 mg, 13%); ν_{\max} . 1 725 (C=O) and 3 430 cm⁻¹ (OH); δ 0.71 (s, 13 β -Me), 1.7 and 1.75 (s, Me₂C=C), 3.64 (t, *J* 8 Hz, 17-H), 3.65 (s, CO₂Me), and 4.86 (br d, *J* 9 Hz, 6-H) (Found: M^+ , 350. C₂₁H₃₄O₄ requires *M*, 350). Acetylation with acetic anhydride and pyridine gave the diacetate (**23**), δ 0.78 (s, 13 β -Me), 1.69 and 1.82 (s, Me₂C=C), 2.02 and 2.05 (s, MeCO₂), 3.66 (s, CO₂Me), 4.6 (t, *J* 7 Hz, 17-H), and 5.93 (d, *J* 8 Hz, 6-H) (Found: *m/z*, 374.2452. C₂₃H₃₄O₄ requires $M^+ - \text{CH}_3\text{CO}_2\text{H}$, 374.2457).

Photolysis of the 19-Nor-3-keto 5 β ,6 β -Epoxide (8) in Methanol.—A solution of the epoxy ketone (**8**) (400 mg) in methanol (700 ml) was photolysed for 13 h. Removal of the solvent, and p.l.c. with ether–chloroform (95:5) as eluant, gave methyl 5,6 β -epoxy-17 β -hydroxy-4,4-dimethyl-3,4-seco-5 β -estran-3-oate (**16**) (210 mg), $[\alpha]_D + 21.4^\circ$ (*c* 6.0); ν_{\max} . 1 740 (C=O) and 3 460 cm⁻¹ (OH); δ 0.71 (d, *J* 7 Hz, MeCHMe), 0.74 (s, 13 β -Me), 0.98 (d, *J* 7 Hz, MeCHMe), 3.17 (d, *J* 3 Hz, 6-H), 3.56 (t, *J* 8 Hz, 17-H), and 3.66 (s, CO₂Me) (Found: M^+ , 350. C₂₁H₃₄O₄ requires *M*, 350). Hydrolysis of the ester (**16**) in 10% methanolic KOH gave the acid (**18**), m.p. 253–254 °C (Found: *m/z* 293.1746. C₂₀H₃₂O₄ requires $M^+ - \text{C}_3\text{H}_7$, 293.1746). A second band (173 mg) was largely unchanged ketone (**8**) containing aldehydic material which could not be purified.

Photolysis of the Ketone (9) in Ether.—A solution of the ketone (**9**) (200 mg) in ether (100 ml) was photolysed as above for 1 h. Removal of the solvent gave an oil (218 mg), which on p.l.c. with ether–light petroleum (40–60 °C) (5:95) as eluant gave one major band (55 mg) and other minor bands which were not satisfactorily purified. The major bands from three

experiments were combined and subjected to p.l.c. with light petroleum (40–60 °C) on silver nitrate-impregnated silica gel to afford 4ξ-methyl-2,3-seco-5α-cholest-1-ene (**24**) (68 mg, 12%); ν_{\max} . 1 635 cm^{-1} ($\text{CH}_2=\text{CHR}$); δ 0.65 (s, 13β-Me), 0.75 (d, J 7 Hz, MeCHMe), 0.82 (d, J 7 Hz, MeCHMe), 0.90 (s, 10β-Me), 4.95 (m, J_{gem} 2 Hz, $\text{CH}=\text{CH}_2$) and 5.5 (dd, J 11 and 18 Hz, $\text{CH}=\text{CH}_2$) (Found: M^+ , 386.3904. $\text{C}_{28}\text{H}_{50}$ requires M , 386.3912) and 4-methyl-2,3-seco-5α-cholest-3-ene (**25**) (35 mg, 6%), ν_{\max} . 1 630 cm^{-1} ($\text{CH}_2=\text{CR}_2$); δ 0.64 (s, 13β-Me), 0.82 (s, 10β-Me), 1.73 (br s, $\text{CH}_2=\text{CMe}$), and 4.67 and 4.83 (br s, $\text{CH}_2=\text{CMe}$) (Found: M^+ , 386.3896). Other bands were not satisfactorily purified.

Photolysis of the Ketone (9) in Methanol.—A solution of the ketone (**9**) (200 mg) in methanol (100 ml) was photolysed as above for 3.5 h. Removal of the solvent, and p.l.c. with ether-light petroleum (40–60 °C) (15:85) as eluant, gave methyl 4,4-dimethyl-3,4-seco-5α-cholestan-3-oate (**26**) (153 mg, 71%), m.p. 66–67 °C (from methanol); $[\alpha]_D + 6.1$ °C (c 2.0); ν_{\max} . 1 745 cm^{-1} (C=O); δ 0.65 (s, 13β-Me), 0.82 (d, J 7 Hz, MeCHMe, upfield branch resolved), 0.85 (s, 10β-Me), 0.91 (d, J 7 Hz, MeCHMe, low-field branch resolved), and 3.62 (s, CO_2Me) (Found: M^+ , 446.4142. $\text{C}_{30}\text{H}_{54}\text{O}_2$ requires M , 446.4126) and the impure unsaturated aldehyde (**27**) (22 mg, 10%); ν_{\max} . 1 640 ($\text{CH}=\text{CR}_2$), 1 735 (C=O), and 2 730 cm^{-1} (CHO); δ 4.65 and 4.82 (br s, $\text{CH}_2=\text{CMe}$) and 9.68 (br s, CHO).

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