Tetracyclic triterpenes. Part 16.[1] Synthesis of 31-norcucurbitane and fusidane derivatives in the skeletal rearrangements of 9,11-epoxy-4β-demethyl-5α-lanostanes

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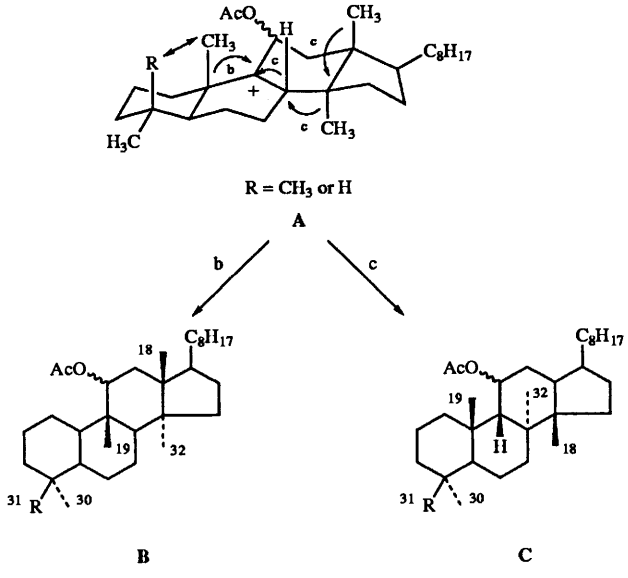
The BF_3·Et_2O-catalysed rearrangement of 9β,11β-epoxy-4β-demethyl-5α-lanostan-7-one derivatives 11 and 12 in acetic anhydride resulted in formation of 19(10→9β)*abeo* compounds (31-norcucurbitanes) 20–22 or 23 and 24, respectively. The extent of a rearrangement was dependent on the substituent at position 3 of the steroid. Reaction of the 9α,11α-epoxide 17 under similar conditions gave fusidenone 25 (31-norprotostane) in high yield which had the carbon skeleton characteristic of the steroidal antibiotic, fusidic acid.

As a continuation of our investigations on rearrangements of C-9 carbocations derived from 9,11-epoxylanostanes we have been focusing our attention on 4β-demethyl-5α-lanostane derivatives. From a synthetic point of view, the rearrangement of the carbocation **A** (Scheme 1, R = H) would potentially give compounds **B** (path b) and/or **C** (path c) with 31-norcucurbitane or 31-norprotostane (fusidane) skeletons, respectively.

Compounds with protostane and fusidane skeletons have been isolated from plants,[2] including the biologically significant helvolic and fusidic acids.[3,4] The pharmacological activity of fusidic acid led to investigations towards its partial and total synthesis.[3,5,6] The rearrangement of lanostane derivatives to compounds with the fusidane[6a] or protostane[6b] skeleton has been reported; however, the resulting dienes were unstable.[7] The cucurbitacins[8] are tetracyclic triterpenes of plant origin long known to have weak tumour-inhibitory activity and recently, 31-norcucurbitacin glycosides have been isolated from natural sources.[9] 4α,14α-Dimethylsterols such as these are rather rare in plants and the isolation of these compounds[10] pointed to the possibility that in some plants the 4β-methyl group is removed before the 14α-methyl group in the degradation pathway leading to sterols. Also of interest was the influence of the steric compression of the angular 10β-methyl group and axial 4β-substituent (Scheme 1, R = H or CH_3) on the migratory aptitude of the 10β-methyl group in the rearrangements of the 9,11-epoxides under study.[11]

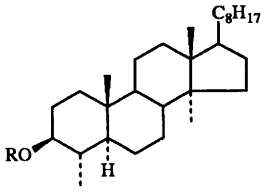
A new approach to 4β-demethyl-24,25-dihydrolanosterol **1** has recently been reported from our laboratory.[12] This compound served as the starting material for the synthesis of 9β,11β-epoxy-4α,14α-dimethyl-7-oxo-5α-cholestan-3β-yl acetate **11**, one of the lanostanes required for the rearrangements. Thus, acetylation of **1** and epoxidation of **2** gave the epoxide **3** which upon treatment with boron trifluoride–diethyl ether afforded the diene **4** in 74% yield. Oxidation of this diene with chromium trioxide in AcOH–$CHCl_3$–H_2O solution[13] furnished a mixture of two principal products which were separated chromatographically and characterized as the unconjugated enone **5** and the enedione **7** in 46 and 28% yield, respectively. The ^1H NMR spectrum of **5** showed signals for the characteristic protons 3α-H (δ_H 4.42), 8β-H (δ_H 2.93) and 11-H (δ_H 5.44) and the ^{13}C NMR spectrum of **5** (Table 1) correlated well with the published data for its 4,4-dimethyl analogue.[14] Epoxidation of **5** with *m*-chloroperbenzoic acid (MCPBA) resulted in formation of only one stereoisomer, 9β,11β-epoxide **11**, thus confirming the effect of the 7-carbonyl group upon the stereochemistry of epoxidations at 9,11-double bonds, which has been described by us.[15] However, in the epoxidations of 9(11)-en-7-ones reported so far, the respective 9α,11α-epoxides were also formed



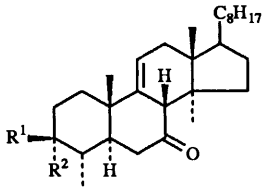
Scheme 1

in about 20% yield besides the major 9β,11β-product. In addition to the evident effect of the 7-carbonyl group, the unprecedented exclusive β-attack of the peracid upon the 9,11-double bond in a steroid like **5** is most probably a result of the less pronounced steric hindrance for β-attack and of the absence of steric compression of substituents at C-4 and C-10, both being a consequence of the absence of the axial 4β-methyl group. Indeed, molecular mechanics calculations (PC MODEL)[16] showed that the distance between the 10- and 13-methyl groups in **5** increases by approx 0.13 Å when compared with the 4,4-dimethyl analogue of **5**. It was also interesting to examine the epoxidation of **6** in which an additional carbonyl group at position 3 was present. The expected epoxide **12** would be another promising substrate for a rearrangement. Thus, epoxidation–dehydration of the enone **13** gave the diene **14** (66%) accompanied by the diene lactone **18** (21%). In the oxidation of **14** with chromium trioxide, the enedione **6** and the enetrione **8** were obtained in 22 and 28% yield, respectively. As in the case of the enone **5**, epoxidation of **6** with MCPBA was a slow reaction[15a] in which again only β-epoxidation occurred. However, the β-epoxide **12** was formed in low yield (15%), the Baeyer–Villiger oxidation product **19** being the predominant product (36%). In the epoxidations of enones **5** and **6** the respective 9α,11α-epoxides were not found among the reaction

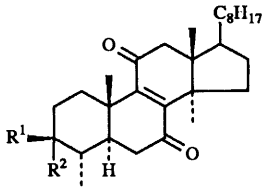
products. These results further support the role of the carbonyl group in the steroid skeleton upon the stereochemistry of enone epoxidation.[15] It is interesting to note, that in the epoxidation of 4β-demethyl-5α-lanost-9(11)-en-3β-yl acetate **15** the exclusive product was the respective 9α,11α-epoxide **16** (94% yield).[6] As the yields of **6** and **12** were low, the alternative route to **12** was attempted. The epoxide **11** gave, upon treatment with lithium tri-*tert*-butoxyaluminium hydride in tetrahydrofuran, the 3-hydroxy derivative with the preserved, base sensitive 9β,11β-epoxy-7-oxo functionality. The resulting alcohol could be cleanly oxidized to the 3,7-diketo epoxide **12** in 91% overall yield.



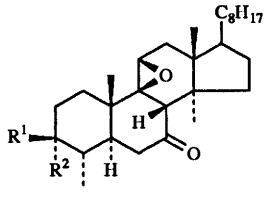
1 R = H, Δ^8
2 R = Ac, Δ^8
3 R = Ac, 8α,9α-epoxy
4 R = Ac, $\Delta^{7,9(11)}$



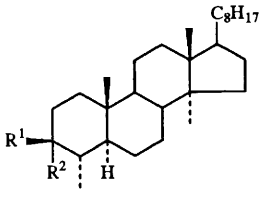
5 R^1 = AcO, R^2 = H
6 R^1, R^2 =O



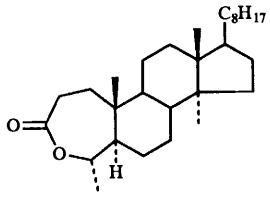
7 R^1 = AcO, R^2 = H
8 R^1, R^2 =O
9 R^1 = AcO, R^2 = H, 8,9-dihydro
10 R^1, R^2 =O, 8,9-dihydro



11 R^1 = AcO, R^2 = H
12 R^1, R^2 =O

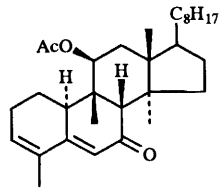


13 R^1, R^2 =O, Δ^8
14 R^1, R^2 =O, $\Delta^{7,9(11)}$
15 R^1 = AcO, R^2 = H, $\Delta^{9(11)}$
16 R^1 = AcO, R^2 = H, 9α,11α-epoxy
17 R^1, R^2 =O, 9α,11α-epoxy



18 $\Delta^{7,9(11)}$
19 7-oxo, 9β,11β-epoxy

BF_3-catalysed rearrangement of the epoxide **11** carried out in acetic anhydride solution at room temperature gave a complicated mixture of products. Column and preparative thin layer chromatography allowed for the isolation of four compounds: the known diketone **9**[17] (9%), the dienone **20** (43%), the trienol acetate **21** (12%) and the dienol acetate **22** (5%). The structures of the new compounds with the rearranged carbon skeleton were proposed on the basis of spectral data. The IR (ν_{max} 1643 and 1624 cm^{-1}) and UV (λ_{max} 288 nm, ε 19 100 dm^3 mol^{-1} cm^{-1}) spectra of **20** showed absorptions characteristic of a conjugated dienone chromophore. In its ^1H NMR spectrum a one proton singlet at δ_H 2.63 ascribed to a 8β proton was in accordance with the (10→9β) migration of the 10β-methyl group. Two signals at δ_H 6.15 and 6.05 of protons



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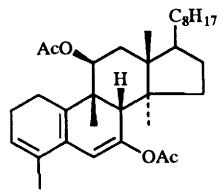

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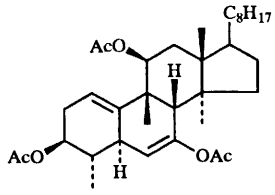

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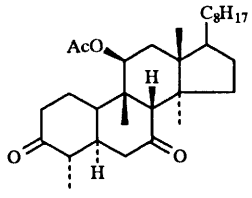
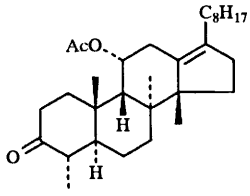


23 $\Delta^{1(10)}$
24 Δ^1



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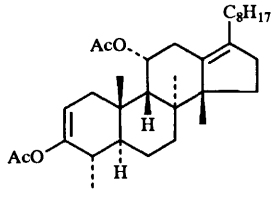

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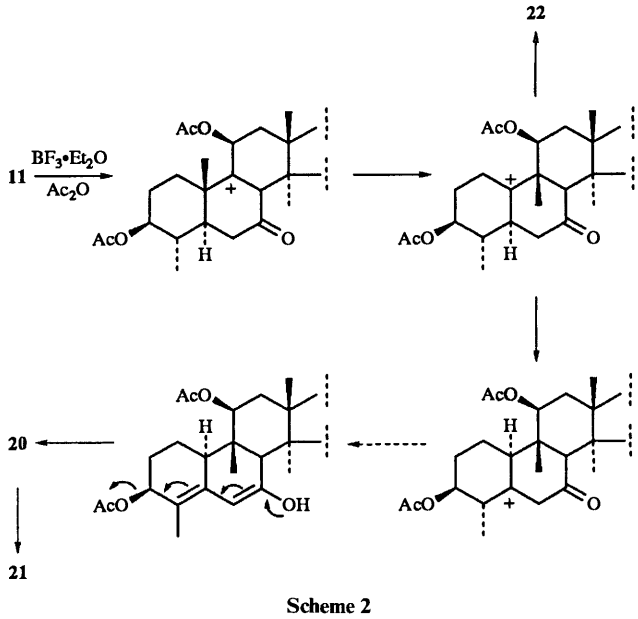
in vinylic positions (C-3 and C-6) and a three-proton signal at δ_H 1.86, ascribed to the methyl group at C-4, also suggested the formation of the 3,5-dien-7-one system. This was supported by the presence of signals at δ_H 5.34 (11α-H) and 2.06 (acetate methyl protons) originating from only one acetate group. The facile elimination of the axial 3β-acetoxy group leading to **20** is in accordance with the 10α-configuration of the likely intermediates (Scheme 2).



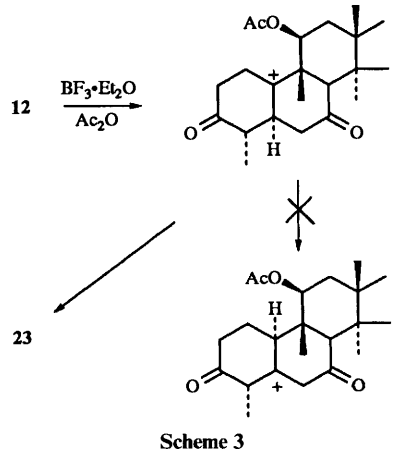
Scheme 2

With the structure of the major product **20** established, the spectral data of the next most abundant product suggested the structure of **21**. Thus, the UV spectrum (λ 340 nm, ε 21 250 dm^3 mol^{-1} cm^{-1}) suggested conjugated double bonds, but excluded the 3,5,7-triene system. In the IR spectrum, two intense bands of the acetate carbonyl groups at 1742 and 1721 cm^{-1} and weak absorption bands of carbon–carbon double bonds at 1638 and 1595 cm^{-1} were found. In the ^1H NMR spectrum, two low-field signals in the olefinic region (δ 6.53 and 6.11) and a signal of 11α-proton at δ 5.32 were observed. Other important signals

were a singlet at δ 2.63 for a 8β-proton and two singlets of acetate methyl groups at δ 2.20 (7-acetate) and δ 2.05 (11-acetate). All these data are in accordance with structure **21**. Supporting chemical evidence was obtained in a separate experiment, when the enol acetate **21** was obtained from the enone **20** under the conditions used for the rearrangement reaction. The structure of the least abundant product **22** was evident from the analysis of its ^{1}H NMR spectrum. It showed a three proton multiplet at δ 5.85–5.95 including signals for two protons at sp^2 carbon atoms, C-1 and C-6, and for the 11α-proton. Also one additional signal for a proton bound to acetoxy-carrying carbon was found at δ 4.77. The respective signals of protons belonging to acetate methyl groups were found at δ 2.14, 2.05 and 1.99. The absence of absorption bands characteristic of conjugated double bonds in IR and UV spectra further confirmed the structure **22**.

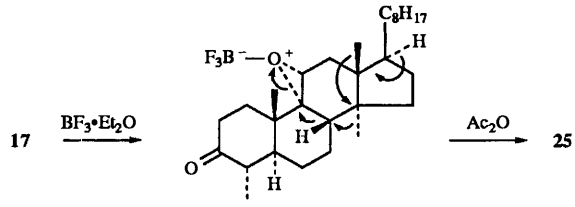
The BF_3-catalysed rearrangement of 3-ketoepoxide **12** carried out under standard conditions (acetic anhydride, room temp., 15 min) gave a very complicated mixture of several products (TLC test), most probably resulting from rearrangements and formation of enol acetates. However, a short reaction time (10 s) gave the major kinetic product **23** (73%), accompanied by the ketone **10** (17%) and the conjugated enone **24** (4%). The structure of compound **23** was deduced from its spectral data. The UV and IR spectra excluded the presence of an α,β-unsaturated ketone moiety and in the IR spectrum, strong absorption bands at 1718 and 1700 cm^{-1} characteristic of acetate and cyclohexanone carbonyls were observed. In the ^{1}H NMR spectrum, two signals, one proton each, at δ 5.74 and 6.04 were in accordance with the presence of an 11β-acetoxy group and a trisubstituted double bond, respectively. These data are consistent with the 10-methyl group migration resulting in formation of the 19(10→9β)*abeo* compound **23**. The structure of the triketone **10** was readily assigned from spectral data (Experimental section). ^{13}C NMR spectra of compounds **10** and **23** (Table 1) correlated well with the published data for 4,4-dimethyl analogues.[14]

The results of the rearrangements of epoxides **11** and **12** indicate that steric compression of axial methyl groups at the 4β and 10β positions is not an important factor and the effective migration of the 19-methyl group occurs in the case of 9β,11β-epoxides with both lanostane[18] and 4β-demethyllanostane skeletons. However, in the case of 4β-demethyllanostane epoxides **11** and **12**, the structure of the rearrangement products evidently depends upon the functionality of the ring A in the steroid. Thus, 3-ketone **12** gives the 1(10)-enone **23** as a major kinetic product of the rearrangement, while Δ^4 or Δ^5 conjugated ketones are not produced. This indicates a high energy barrier between C-10 and C-5 carbocations, which are potential intermediates in the rearrangement of diketoepoxide **12** (Scheme 3). On the other hand, the major product **20** arises from the 3-acetate **11** *via* formation of a C-5 carbocation-like intermediate followed by elimination of acetic acid (Scheme 2).



Scheme 3

In view of the results obtained in the rearrangement of 3,7-dioxo-4β-demethyllanostane epoxide **12** it was of interest to examine the rearrangement of 3-oxo-4β-demethyllanostane 9α,11α-epoxide **17**. This was prepared from the known 3β-acetoxy derivative **16**.[6] The rearrangement of **17** was carried out under standard conditions for 15 s to give three products which were isolated by chromatography. The least polar, minor product (6%) was the already prepared diene **14**. The major product (68%) analysed for $C_{31}H_{50}O_3$ and the full assignment of its ^{1}H and ^{13}C NMR spectral data has been published in a separate paper.[19] From these data the structure **25** was inferred, having a rearranged, fusidane (31-norprotostane)-type carbon skeleton. The *R* configuration of the side-chain carbon atom C-20 of **25** was assigned on the basis of the characteristic position of the 20-methyl group (labelled C-21) signal at δ_H 0.93 in the ^{1}H NMR spectrum.[20] Thus skeletal rearrangement of **17** is not accompanied with isomerization at C-20 observed in reactions leading to diacholestanes.[20-22] The third product (15%) had the fusidane carbon skeleton and was assigned structure **26** on the basis of spectroscopic data (Experimental section). The structure was confirmed when the enol acetate **26** was hydrolysed with aq. HCl to the parent ketone **25**. The rearrangement of **17** carried out for 15 min gave a very complicated mixture, which was not examined further. The rearrangement of **17** induced by 9,11-epoxide cleavage proceeds toward ring D, the direction found in rearrangements of 9α,11α-epoxy-5α-lanostane derivatives.[6,7] The real importance of the reaction of **17** is the excellent yield (total 83%) of compounds with the fusidane skeleton possessing the 11α-hydroxy substituent and the 3-oxo group which may be easily reduced to a 3α-alcohol. These features are characteristic of a steroidal antibiotic, fusidic acid. As the migrating methyl groups and hydrogen atoms and leaving group are all *trans* to each other and the reaction is very fast at room temperature, it is conceivable that the rearrangement of the epoxide **17** is a concerted process (Scheme 4) with a low activation energy and



Scheme 4

concurrent 'axial cleavage' of the epoxide ring[23] and that the formation of a fully developed carbocation at C-9 is not required. On the other hand, a stepwise process (Scheme 2 and 3) is postulated in the rearrangement of **11** and **12**. In these reactions, a 1,2-*cis* relationship between the 10-methyl group and 9β epoxide oxygen requires that the formation of a fully developed carbocation at C-9 is followed by the migration of C-19. The alternative migration of 8β hydrogen is not observed as it would result in formation of α-ketocarbocation of high energy. Also in the reactions of β-epoxides **11** and **12** preferential 'axial cleavage' of the epoxide takes place.

Experimental

For the general experimental conditions see ref. 12. For most of the new compounds described in this paper the full assignment of signals in ^{13}C NMR spectra was possible (Table 1).

4α,14α-Dimethyl-5α-cholest-8-en-3β-yl acetate 2

To a solution of the alcohol **1**[12] (1.205 g, 3.13 mmol) in benzene (50 cm^3), pyridine (10 cm^3) and acetic anhydride (20 cm^3) were added and left at room temp. for 16 h. The usual workup gave **2** (1.13 g, 85%), mp 99–101 °C (from methanol–acetone) (lit.,[17]

Table 1 ^{13}C NMR chemical shifts for the 31-nor-5α-lanostane and 31-norcucurbitane derivatives

	2	**3**	**4**	**5**	**6**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**20**[d]	**22**[e]	**23**
C-1	34.7	31.8	34.5	34.7	37.1	35.3	35.0	37.0	30.4	32.8	37.2	37.3	35.2	28.6	31.0	25.2	116.8	115.6
C-2	27.3	26.7	27.5	27.0	37.7[a]	37.5	26.8	37.4	26.3	36.9	38.0	38.0	27.4[a]	26.6	37.0	36.4	30.4	40.3
C-3	78.8	78.4	78.3	77.6	210.8	210.4	77.5	210.6[a]	77.3	210.3	213.1	212.5	78.7	78.2	211.6	136.9	77.3	210.3
C-4	36.2	36.1	36.7	37.8	45.7	44.1	36.1	44.8	38.6	46.4	45.1	45.1	36.5	36.1	44.9	132.7	40.8[a]	48.7
C-5	47.3	40.4	45.7	45.2	47.7	48.9	49.7	52.3	41.7	44.4	49.8	48.8	49.5	46.7	48.8	155.9	41.9[a]	38.9
C-6	20.8	19.6	26.5	42.3	43.2	39.0	41.7	42.7	42.6	43.6	22.1	27.6	24.2	25.2[a]	26.6[a]	122.3	113.6	41.3
C-7	25.5	23.0	117.5[a]	212.0	210.9	202.3	209.4	209.2[a]	212.9	212.1	25.5	118.3[a]	27.3[a]	26.3[a]	26.1[a]	202.1	149.7	211.8
C-8	133.5	67.6	143.1[b]	56.3	56.3	150.2	53.0	53.0	55.3	55.2	132.5	142.4[b]	41.6	38.5	38.7	58.5	48.7	58.0
C-9	135.0	69.4	143.2[b]	141.9	140.8	151.9	58.9	58.3	66.4	65.8	135.7	143.4[b]	146.2	67.7	67.4	44.5[a]	44.8[b]	44.9[a]
C-10	36.3	37.3	38.0	37.8	38.0	38.6	36.3	36.3	36.7	36.9	36.7	38.0	38.6	38.2	38.4	42.0	145.1	144.9
C-11	21.8	22.2	119.0[a]	119.0	119.9	200.1	208.2	207.2	59.7	59.7	21.9	119.0[a]	116.6	54.2	54.4	72.8	73.3	73.3
C-12	31.2	26.9	36.3[c]	37.5	37.5[a]	51.5	52.5	52.5	35.4	35.2	31.1	36.7	37.5	34.9	34.8	35.8	36.1	35.2
C-13	44.6	43.7	43.8	44.6	44.6	47.4	46.5	46.6	43.8	43.7	44.6	43.8	44.4	44.9	44.9	41.4[a]	43.2[b]	42.3[a]
C-14	50.0	48.9	50.5	47.7	47.6	49.1	49.2	49.2	48.6	48.6	50.0	50.4	47.2	46.5	46.4	48.8	50.7	49.7
C-15	30.8	31.9	31.6	34.5	34.4	32.1	33.1	33.1	33.0	32.9	30.9	31.5	34.0	35.2	35.2	34.8	34.2	34.1
C-16	28.2	28.4	27.9	28.1	28.0	27.3	28.6	28.5	27.6	27.5	28.2	27.9	28.1	28.1	28.1	27.7	27.9	27.5
C-17	50.6	48.4	51.2	50.0	50.0	49.2	48.7	48.8	51.6	51.6	50.6	51.1	51.2	51.0	51.0	50.4	51.0	50.4
C-18	15.8	16.1	15.8	15.4	15.3	15.8	16.2	16.3	19.3	19.3	15.9	15.8	14.5	16.1	16.2	19.6	17.6	19.5
C-19	18.1	16.1	20.6	18.0[a]	17.7[b]	26.1	12.3	11.7	15.0	14.5	17.5	20.2	20.4	16.8	16.5	17.1[b]	28.4	28.9
C-20	36.5	36.4	36.3	36.2	36.1	36.2	35.8	35.7	36.0	36.0	36.5	36.3	36.2	35.9	35.9	36.0	36.1	36.0
C-21	18.8	19.0	18.6	18.5	18.4	18.6	18.5	18.5	18.5	18.4	18.8	18.5	18.5	18.5	18.5	18.8	18.8	18.8
C-22	36.5	36.5	36.5[c]	36.5	36.5	36.3	35.8	36.4	36.3	36.2	36.5	36.5	36.6	36.5	36.5	36.2	36.4	36.4
C-23	24.2	24.1	24.2	24.1	24.1	24.0	24.0	24.0	24.1	24.1	24.1	24.1	24.2	24.1	24.1	24.1	24.1	24.0
C-24	39.6	39.5	39.6	39.5	39.5	39.4	39.4	39.5	39.5	39.4	39.6	39.5	39.6	39.6	39.6	39.4	39.5	39.4
C-25	28.0	28.0	28.1	28.0	28.0	28.0	28.0	28.0	28.0	28.0	28.0	28.0	28.0	28.0	28.0	27.9	28.0	28.0
C-26	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5
C-27	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.7
C-30	15.1	15.1	15.1	14.8	11.1	11.6	14.9	11.4	14.7	11.3	11.5	11.4	15.3	15.1	11.6	20.6	16.4	12.1
C-32	24.4	19.9	25.7	17.9[a]	17.9[b]	16.9	17.7	17.7	17.4	17.5	24.4	25.5	18.5	18.2	18.2	17.8[b]	17.2	18.0
CH_3CO	21.2	21.2	21.2	21.2			21.2		21.1				21.2	21.2			21.2	21.2
CH_3CO	170.8	170.5	170.6	170.6			170.6		170.6				170.6	170.4			170.7	170.1

[a,b,c] These signals may be interchanged. [d] 11-Acetate: 21.2 and 170.1. [e] 7- and 11-acetate: 21.4, 21.3, 169.1 and 170.2.

mp 98–98.5 °C); δ_H 4.41 (1 H, m, $w_{h/2}$ 30 Hz, 3α-H), 2.04 (3 H, s, Ac), 0.98 (3 H, s, 10-Me), 0.86 (3 H, d, *J* 6.4, 4-Me), 0.71 (3 H, s, 13-Me), 0.90 and 0.83 (other methyl signals).

8α,9α-Epoxy-4α,14α-dimethyl-5α-cholestan-3β-yl acetate 3

To a solution of **2** (2.60 g, 5.70 mmol) in methylene dichloride (200 cm^3), *m*-chloroperbenzoic acid (MCPBA) (1.88 g, 6.0 mmol, 55%) was added and the mixture was left at room temp. for 4 h. The solution was washed with aq. sodium thiosulfate (10%), aq. $NaHCO_3$ (5%; 2 ×) and water (2 ×). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure to give the *epoxide* **3** as a solidifying oil (2.663 g) which was crystallized from methanol (containing 20 ppm of pyridine), mp 132–134 °C; ν_{max}/cm^{-1} 1723, 1252, 1023, 974, 915 and 898; δ_H 4.35 (1 H, m, $w_{h/2}$ 30 Hz, 3α-H), 2.02 (3 H, s, Ac), 1.08 (3 H, s, 10-Me), 0.85 (3 H, d, *J* 6.5, 4-Me), 0.82 (3 H, s, 13-Me), 0.89 and 0.82; *m/z* 472 (M^+), 454 ($M^+ - H_2O$), 412, 379, 291, 134, 122, 107, 95, 57 and 43 (Found: C, 78.8; H, 11.1. $C_{31}H_{52}O_3$ requires C, 78.76; H, 11.09%).

4α,14α-Dimethyl-5α-cholesta-7,9(11)-dien-3β-yl acetate 4

To a solution of epoxide **3** (0.553 g, 1.17 mmol) in benzene (150 cm^3), $BF_3{\cdot}Et_2O$ (0.30 cm^3) was added at room temp. and the mixture was stirred for 10 min. Pyridine (1 cm^3) was added and the solution was washed with brine and water (3 ×). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (20 g) with benzene as eluent to give the *diene* **4** (393 mg, 74%), mp 119–120.5 °C (from methanol); ν_{max}/cm^{-1} 1720, 1422, 1255, 1025, 976 and 915; λ_{max}(EtOH)/nm 237 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 12 100), 244 (14 800) and 252 (10 400); δ_H 5.40 (2 H, m, $w_{h/2}$ 10 Hz, 7-H and 11-H), 4.37 (1 H, m, $w_{h/2}$ 26 Hz, 3α-H), 2.04 (3 H, s, Ac), 0.95 (3 H, s, 10-Me), 0.58 (3 H, s, 13-Me), 0.90 and 0.83; *m/z* 454 (M^+), 439 ($M^+ - CH_3$), 379, 299, 239, 145, 95, 69, 57 and 43 (Found: C, 81.9; H, 11.1. $C_{31}H_{50}O_2$ requires C, 81.88; H, 11.08%).

Oxidation of the diene 4 with chromium trioxide

To a solution of the diene **4** (135 mg, 0.297 mmol) in ethanol-free chloroform (1.7 cm^3) and acetic acid (0.25 cm^3), a solution of chromium trioxide (58 mg, 0.58 mmol) in acetic acid (1.5 cm^3) and water (0.20 cm^3) mixture was added dropwise over 2 h. The temperature of the reaction mixture was kept at 47–49 °C. The mixture was cooled to 0 °C and methanol (0.5 cm^3), hexane (10 cm^3) and benzene (20 cm^3) were added. The organic layer was washed with brine (2 ×) and water (2 ×), dried ($MgSO_4$) and concentrated under reduced pressure to give a solidifying oil (131 mg), which was chromatographed on silica gel (6 g) with benzene–hexane (2:1) as eluent to give 4α,14α-*dimethyl*-7-*oxo*-5α-*cholest*-9(11)-*en*-3β-*yl acetate* **5** (64 mg, 46%), mp 163–165 °C (from methanol–diethyl ether); ν_{max}/cm^{-1} 1715, 1255, 1160, 1024, 983 and 975; CD $\Delta\varepsilon$ (λ/nm) +0.28 (296); δ_H 5.44 (1 H, m, $w_{h/2}$ 8 Hz, 11-H), 4.42 (1 H, m, $w_{h/2}$ 24 Hz, 3α-H), 2.93 (1 H, br s, $w_{h/2}$ 4 Hz, 8β-H), 2.06 (3 H, s, Ac), 1.06 (3 H, s, 10-Me), 0.75 (3 H, s, 14-Me), 0.69 (3 H, s, 13-Me), 0.90, 0.86 and 0.83; *m/z* 470 (M^+), 455 ($M^+ - CH_3$), 410, 377, 357, 315, 303, 264, 207, 145, 133, 107, 95, 55 and 43 (Found: C, 78.9; H, 10.8. $C_{31}H_{50}O_3$ requires C, 79.10; H, 10.71%) and the dione **7** (40 mg, 28%), mp 149–151 °C (from methanol); ν_{max}/cm^{-1} 1723, 1668, 1255, 1171, 1060, 1027, 980 and 917; δ_H 4.42 (1 H, m, $w_{h/2}$ 25 Hz, 3α-H), 2.83 (1 H, d, *J* 17, 12β-H), 2.58 (1 H, d, *J* 16, 6α-H), 2.05 (3 H, s, Ac), 1.32 (3 H, s, 10-Me), 1.20 (3 H, s, 14-Me), 0.82 (3 H, s, 13-Me), 0.91 and 0.83; *m/z* 484 (M^+), 424 (M^+ – AcOH), 302, 278, 173, 133, 107, 69, 55 and 43 (Found: C, 76.8; H, 10.1. $C_{31}H_{48}O_4$ requires C, 76.81; H, 9.98%).

9β,11β-Epoxy-4α,14α-dimethyl-7-oxo-5α-cholestan-3β-yl acetate 11

To a solution of **5** (194 mg, 0.413 mmol) in chloroform (50 cm^3) containing a drop of pyridine, MCPBA (160 mg, 0.696 mmol, 75%) was added and the solution kept in the dark at room temp. for 94 h. Chloroform (30 cm^3) was added and the solution was washed with aq. sodium thiosulfate (10%), aq. $NaHCO_3$ (5%; 2 ×) and water (2 ×). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure to give a residue which was chromatographed on silica gel (10 g) with methylene dichloride (containing 20 ppm pyridine) as eluent. The pure fractions were collected and crystallized from methanol–diethyl ether (1:1) to give the *epoxide* **11** (135 mg, 67%), mp 239–242 °C; ν_{max}/cm^{-1} 1725, 1695, 1300, 1253, 1184, 1156, 1123, 1028 and 985; CD $\Delta\varepsilon$ (λ/nm) +1.31 (313), +1.48 (302) and +1.17 (293); δ_H 4.40 (1 H, m, $w_{h/2}$ 27 Hz, 3α-H), 3.51 (1 H, br s, $w_{h/2}$ 4 Hz, 11α-H), 2.86 (1 H, br s, $w_{h/2}$ 3 Hz, 8β-H), 2.48 (1 H, dd, J_1 17, J_2 7, 6β-H), 2.06 (3 H, s, Ac), 0.96 (3 H, s, 19-H), 0.92, 0.89 and 0.83; *m/z* 486 (M^+), 471 ($M^+ - CH_3$), 411, 345, 253, 221, 206, 121, 109, 95, 55 and 43 (Found: C, 76.8; H, 10.4. $C_{31}H_{50}O_4$ requires C, 76.50; H, 10.35%).

9β,11β-Epoxy-4α,14α-dimethyl-5α-cholestane-3,7-dione 12

To a solution of **11** (74.8 mg, 0.154 mmol) in anhyd. THF (10 cm^3), $LiAlH_4$ (10 mg, 0.264 mmol) was added and the mixture was stirred under argon at room temp. for 10 min. Saturated aq. $MgSO_4$ (5%) was added dropwise followed by benzene (40 cm^3) and the mixture was washed with brine and water (2 ×). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure to give a white solid (69.4 mg) which was dissolved in acetone (10 cm^3) and titrated with Jones' reagent. After completion of the oxidation, methanol (0.5 cm^3) and pyridine (4 drops) were added, the mixture was evaporated under reduced pressure and the residue was dissolved in benzene (50 cm^3), washed with brine, aq. $NaHCO_3$ (5%) and water. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure to give pure *epoxy diketone* **12** (61.9 mg, 91%), mp 241–244 °C (from ethanol); ν_{max}/cm^{-1} 1702, 1243, 1207, 1123, 1105, 1080, 988 and 890; CD $\Delta\varepsilon$ (λ/nm) +2.15 (312), +2.86 (302) and +2.61 (293); δ_H 3.47 (1 H, br s, $w_{h/2}$ 5 Hz, 11α-H), 2.91 (1 H, br s, $w_{h/2}$ 3 Hz, 8β-H), 2.56 (1 H, dd, J_1 17, J_2 6, 6β-H), 1.20 (3 H, s, 10-Me), 1.03 (3 H, d, *J* 6.4, 4-Me), 0.94 (3 H, s, 13-Me), 0.89 and 0.82; *m/z* 442 (M^+), 427 ($M^+ - CH_3$), 413, 301, 221, 209, 121, 109, 95, 69, 55 and 43 (Found: C, 78.6; H, 10.6. $C_{29}H_{46}O_3$ requires C, 78.68; H, 10.47%).

9α,11α-Epoxy-4α,14α-dimethyl-5α-cholestan-3-one 17

To a solution of epoxide **16**[6] (154 mg, 0.326 mmol) in anhyd. THF (15 cm^3), $LiAlH_4$ (20 mg, 0.526 mmol) was added and the mixture was stirred at room temp. under argon for 10 min. After work-up as in the preceding experiment the crude product (145 mg) was oxidized with Jones' reagent. The work-up gave a residue which was chromatographed on silica gel (25 g) with benzene as eluent to give epoxide **17** (119 mg, 85%), mp 138–139 °C (from methanol); ν_{max}/cm^{-1} 1702, 1237, 1142, 986, 952 and 905; δ_H 3.14 (1 H, dd, J_1 5, J_2 1.5, 11β-H), 1.36 (3 H, s, 10-Me), 1.00 (3 H, d, *J* 6.4, 4-Me), 0.88 (3 H, s, 14-Me), 0.83 (3 H, s, 13-Me), 0.90 and 0.83; *m/z* 428 (M^+), 413 ($M^+ - CH_3$), 287, 221, 121, 109, 107, 95, 81, 69, 55 and 43 (Found: C, 81.1; H, 11.1. $C_{29}H_{48}O_2$ requires C, 81.25; H, 11.29%).

Oxidation–dehydration of 13

To a solution of **13**[12] (270 mg, 0.655 mmol) in methylene dichloride (30 cm^3) containing pyridine (3 drops), MCPBA (250 mg, 1.09 mmol, 75%) was added and the mixture left at room temp. for 2 h. Methylene dichloride (50 cm^3) was added and the solution was washed with aq. sodium thiosulfate (10%), aq. $NaHCO_3$ (5%; 2 ×) and water (2 ×). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure to give a crude product which was dissolved in benzene (100 cm^3). $BF_3{\cdot}Et_2O$ (0.30 cm^3) was added and the solution stirred for 5 min. After addition of pyridine (1 cm^3), the solution was washed with water (3 ×), dried ($MgSO_4$) and concentrated

under reduced pressure to give a solid residue which was chromatographed on silica gel (10 g) with benzene as eluent to afford two compounds: 4α,14α-*dimethyl*-5α-*cholesta*-7,9(11)-*dien*-3-*one* **14** (209 mg, 66%), mp 116–118 °C (from acetone–methanol); ν_{max}/cm^{-1} 1703, 1630, 1170, 1132, 1100, 1068, 895 and 813; λ_{max}(EtOH)/nm 237 (ε/dm^3 mol^{-1} cm^{-1} 12 800), 244 (14 600) and 252 (10 100); δ_H 5.44 (2 H, m, $w_{h/2}$ 13 Hz, 7-H and 11-H), 1.20 (3 H, s, 10-Me), 1.02 (3 H, d, *J* 6.6, 4-Me), 0.88 (3 H, s, 14-Me), 0.61 (3 H, s, 13-Me), 0.90 and 0.84; *m/z* 410 (M^+), 395 ($M^+ - CH_3$), 297, 255, 243, 230, 119, 69, 55 and 44 (Found: C, 84.7; H, 11.4. $C_{29}H_{46}O$ requires C, 84.81; H, 11.29%) and 4aα,14α-*dimethyl*-4-*oxa*-4aα-*homo*-5α-*cholesta*-7,9(11)-*dien*-3-*one* **18** (59 mg, 21%), mp 176–178 °C (from methanol); ν_{max}/cm^{-1} 1722, 1292, 1252, 1163, 1118, 1085, 1062, 1005 and 980; λ_{max}(EtOH)/nm 238 (ε/dm^3 mol^{-1} cm^{-1} 10 700), 246 (15 900) and 254 (10 200); δ_H 5.44 (2 H, m, $w_{h/2}$ 15 Hz, 7-H and 11-H), 4.54 (1 H, m, $w_{h/2}$ 20 Hz, 4a-H), 2.70 (1 H, m, $w_{h/2}$ 18 Hz, 5-H), 1.32 (3 H, d, *J* 6.6, 4-Me), 1.05 (3 H, s, 10-Me), 0.88 (3 H, s, 14-Me), 0.57 (3 H, s, 13-Me), 0.90 and 0.83; *m/z* 426 (M^+), 411 ($M^+ - CH_3$), 313, 259, 246, 171, 95, 69, 55 and 44 (Found: C, 81.4; H, 11.0. $C_{29}H_{46}O_2$ requires C, 81.63; H, 10.87%).

Oxidation of the dienone 14 with chromium trioxide

To a stirred solution of **14** (686 mg, 1.66 mmol) in chloroform (8.6 cm^3) and acetic acid (1.3 cm^3), a solution of chromium trioxide (345 mg, 3.45 mmol) in acetic acid (7.7 cm^3) and water (0.9 cm^3) was added dropwise over 2 h while maintaining the temperature at 47–49 °C. The mixture was cooled to 0 °C, methanol (0.5 cm^3), hexane (50 cm^3) and benzene (50 cm^3) were added and the solution was washed with brine (3 ×) and water (2 ×). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure to give a solidifying oil, which was chromatographed on silica gel (35 g) with benzene–methylene dichloride (1:1) as eluent to afford two compounds: 4α,14α-*dimethyl*-5α-*cholest*-9(11)-*ene*-3,7-*dione* **6** (158 mg, 22%), mp 157–159 °C (from methanol); ν_{max}/cm^{-1} 1708, 1282, 1235, 1155, 1134 and 978; CD Δε (λ/nm) −0.28 (322), +0.30 (302), +0.23 (293); δ_H 5.48 (1 H, m, $w_{h/2}$ 8 Hz, 11-H), 3.00 (1 H, d, *J* 1.8, 8β-H), 1.30 (3 H, s, 10-Me), 0.98 (3 H, d, *J* 6.4, 4-Me), 0.74 (3 H, s, 14-Me), 0.71 (3 H, s, 13-Me), 0.90 and 0.83; *m/z* 426 (M^+), 411 ($M^+ - CH_3$), 313, 271, 220, 207, 147, 121, 95, 69, 55 and 44 (Found: C, 81.9; H, 11.0. $C_{29}H_{46}O_2$ requires C, 81.63; H, 10.87%) and 4α,14α-*dimethyl*-5α-*cholest*-8-*ene*-3,7,11-*trione* **8** (209 mg, 28%), mp 110–112 °C (from methanol); ν_{max}/cm^{-1} 1708, 1672, 1230, 1170, 1132, 1027 and 980; λ_{max}(EtOH)/nm 269 (ε/dm^3 mol^{-1} cm^{-1} 7460); δ_H 2.71 (1 H, d, *J* 17, 12β-H), 2.52–2.40 (4 H, m), 1.49 (3 H, s, 10-Me), 1.20 (3 H, s, 14-Me), 1.05 (3 H, d, *J* 6.8, 4-Me), 0.90 and 0.83; *m/z* 440 (M^+), 425 ($M^+ - CH_3$), 411, 273, 234, 138, 95, 83, 69, 55 and 44 (Found: C, 78.8; H, 10.1. $C_{29}H_{44}O_3$ requires C, 79.04; H, 10.06%).

Reaction of compound 6 with MCPBA

To a solution of **6** (46 mg, 0.108 mmol) in chloroform (50 cm^3) containing pyridine (3 drops), MCPBA (50 mg, 0.159 mmol, 55%) was added and the mixture left in the dark at room temp. until the substrate disappeared (62 h, TLC test). Chloroform (50 cm^3) was added and the solution was washed with aq. sodium thiosulfate (10%), aq. $NaHCO_3$ (5%; 2 ×) and water (2 ×). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure to give a solid which was chromatographed on silica gel (2.5 g) and gave three compounds: the substrate **6** (10.7 mg, 23%); the epoxide **12** (7.0 mg, 15%) identical with the sample described above (by ^{1}H NMR) and 9β,11β-*epoxy*-4aα,14α-*dimethyl*-4-*oxa*-4aα-*homo*-5α-*cholestane*-3,7-*dione* **19** (17.9 mg, 36%), mp 259–262 °C (from methanol); ν_{max}/cm^{-1} 1730, 1697, 1330, 1283, 1245, 1170, 1125, 1111, 1050 and 980; δ_H 4.41 (1 H, m, $w_{h/2}$ 16 Hz, 4-H), 3.48 (1 H, br s, $w_{h/2}$ 4 Hz, 11-H), 2.91 (1 H, br s, $w_{h/2}$ 3 Hz, 8β-H), 1.34 (3 H, d, *J* 6.4, 4-Me), 1.04 (3 H, s, 10-Me), 0.83 (3 H, s, 13-Me), 0.90 and 0.83; *m/z* 458 (M^+), 443 ($M^+ - CH_3$), 440 ($M^+ - H_2O$), 379, 319, 239, 221, 158, 139, 107, 95, 69, 55 and 44 (Found: C, 75.7; H, 10.1. $C_{29}H_{46}O_4$ requires C, 75.94; H, 10.11%).

BF_3·Et_2O catalysed rearrangement of epoxide 11

To a solution of epoxide **11** (75 mg, 0.154 mmol) in acetic anhydride (10 cm^3) stirred under argon at room temp., BF_3·Et_2O (0.08 cm^3) was added. After 10 min pyridine (5 cm^3) and benzene (150 cm^3) were added. The solution was washed with brine (150 cm^3), aq. $NaHCO_3$ (5%; 2 ×) and water (2 ×). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure to give a thick oil which was chromatographed on silica gel (6 g) with benzene–CH_2Cl_2 (1:1) as eluent and gave four compounds of increasing polarity: the diketone **9** (6.5 mg, 9%), mp 180–181 °C (lit.,[17] mp 180.5–181 °C); IR and ^{1}H NMR spectra were in accordance with those published;[17] 7-*oxo*-31-*nor*-10α-*cucurbita*-3,7-*dien*-11β-*yl acetate* **20** (31.0 mg, 43%), oil, ν_{max}/cm^{-1} 1722, 1643, 1624, 1595, 1255, 1155, 1020, 982 and 930; λ_{max}(EtOH)/nm 288 (ε/dm^3 mol^{-1} cm^{-1} 19 100); δ_H 6.15 (1 H, m, $w_{h/2}$ 8 Hz, 3α-H), 6.05 (1 H, br s, $w_{h/2}$ 3 Hz, 6-H), 5.34 (1 H, m, $w_{h/2}$ 8 Hz, 11α-H), 2.63 (1 H, br s, $w_{h/2}$ 2 Hz, 8β-H), 2.06 (3 H, s, Ac), 1.86 (3 H, d, *J* 1.2, 4-Me), 0.99 (3 H, s, 9-Me), 0.92, 0.89 and 0.82; *m/z* 468 (M^+), 408 (M^+ − AcOH), 393, 274, 175, 134, 105, 95, 55 and 43 (Found: C, 79.6; H, 10.4. $C_{31}H_{48}O_3$ requires C, 79.44; H, 10.31%); 31-*norcucurbita*-3,5(10),6-*triene*-7β,11β-*diyl diacetate* **21** (9.5 mg, 12%), oil, ν_{max}/cm^{-1} 1742, 1721, 1638, 1595, 1292, 1248, 1158, 1022, 975 and 883; λ_{max}(EtOH)/nm 340 (ε/dm^3 mol^{-1} cm^{-1} 21 250); δ_H 6.53 (1 H, br s, $w_{h/2}$ 3 Hz, 6-H), 6.11 (1 H, m, $w_{h/2}$ 6 Hz, 3-H), 5.32 (1 H, m, $w_{h/2}$ 9 Hz, 11-H), 2.63 (1 H, m, $w_{h/2}$ 2 Hz, 8β-H), 2.20 (3 H, s, 7-Ac), 2.05 (3 H, s, 11-Ac), 1.98 (3 H, br s, 4-Me), 0.98 (3 H, s, 9-Me), 0.90 and 0.82; *m/z* 510 (M^+), 468, 450, 275, 215, 121, 95, 69, 55 and 43 (Found: C, 77.4; H, 9.9. $C_{33}H_{50}O_4$ requires C, 77.60; H, 9.87%); and 31-*nor*-5α-*cucurbita*-1(10),6-*diene*-3β,7,11β-*triyl triacetate* **22** (4.4 mg, 5%), oil, ν_{max}/cm^{-1} 1745, 1725, 1252, 1138, 1120, 1100, 1075, 1018, 972 and 965; δ_H 5.85–5.45 (3 H, m, 1-H, 6-H and 11-H), 4.77 (1 H, m, $w_{h/2}$ 18 Hz, 3α-H), 2.57 (1 H, br s, 8β-H), 2.14 (3 H, s, 7-Ac), 2.05 (3 H, s, 11-Ac), 1.99 (3 H, s, 3-Ac), 1.12 (3 H, s, 9-Me), 0.97, 0.89 and 0.82; *m/z* 570 (M^+), 528, 510, 468, 450, 393, 207, 174, 149, 95, 83, 69, 55 and 43 (Found: C, 74.0; H, 9.5. $C_{35}H_{54}O_6$ requires C, 73.65; H, 9.53%).

Enol-acetylation of 20

To a solution of **20** (5.0 mg, 0.011 mmol) in acetic anhydride (3 cm^3), BF_3·Et_2O (0.02 cm^3) was added and the mixture left at room temp. for 1.5 h. The usual work-up and purification on a preparative TLC plate (silica gel) gave compound **21** (2.6 mg, 41%) as an oil, the UV and ^{1}H NMR spectra for which were identical with those obtained for **21** in the preceding experiment.

BF_3·Et_2O catalysed rearrangement of epoxide 12

To a solution of epoxide **12** (228 mg, 0.515 mmol) in acetic anhydride (50 cm^3) stirred at room temp. under argon, BF_3·Et_2O (0.50 cm^3) was added. After 15 s pyridine (5 cm^3) was added and the crude product was isolated as for **11**. Chromatography on silica gel (12 g) with methylene dichloride as eluent gave: 4α,14α-*dimethyl*-5α-*cholestane*-3,7,11-*trione* **10** (38 mg, 17%), mp 174–175 °C (from methanol); ν_{max}/cm^{-1} 1703, 1302, 1270, 1230, 1195, 1152, 1126, 1080 and 900; δ_H 2.82–2.10 (9 H, m), 1.48 (3 H, s, 9-Me), 1.22 (3 H, s, 14-Me), 0.99 (3 H, d, *J* 6.6, 4-Me), 0.75 (3 H, s, 13-Me), 0.90 and 0.83; *m/z* 442 (M^+), 427, 329, 277, 220, 193, 123, 95, 69, 55 and 44 (Found: C, 78.5; H, 10.3. $C_{29}H_{46}O_3$ requires C, 78.68; H, 10.47%); 3,7-*dioxo*-31-*nor*-5α-*cucurbit*-1(10)-*en*-11β-*yl acetate* **23** (134 mg, 59%) as an oil, ν_{max}/cm^{-1} 1718, 1700, 1250, 1200, 1167, 1105, 1018 and 975; δ_H 6.04 (1 H, m, $w_{h/2}$ 6 Hz, 1-H), 5.74 (1 H, m, $w_{h/2}$ 12 Hz, 11α-H), 3.04–2.42 (6 H, m), 2.08 (3 H, s, Ac), 1.12 (3 H, d, *J* 6.6, 4-Me), 1.11 (3 H, s, 9-Me), 0.99 (3 H, s, 14-Me), 0.89 and 0.82; *m/z*

484 (M^+), 469 ($M^+ - CH_3$), 424 (M^+ – AcOH), 409, 311, 234, 207, 191, 135, 121, 95, 55 and 43 (Found: C, 77.1; H, 10.0. $C_{31}H_{48}O_4$ requires C, 76.81; H, 9.98%) and an unseparable mixture (41 mg, 18%) of **23** and 3,7-*dioxo*-31-*nor*-5α-*cucurbit*-1-*en*-11β-*yl acetate* **24** (in the ratio of 4:1, as estimated from ^1H NMR spectrum); ν_{max}/cm^{-1} 1640, 1575 and 1125; λ_{max}/nm 231; δ_H 6.56 (br s, 1-H) and 5.33 (m, $w_{h/2}$ 10 Hz, 11-H).

Isomerization of enone 23 with *p*-TsOH

To a solution of **23** (15 mg, 0.031 mmol) in benzene (5 cm^3), *p*-TsOH (20 mg) was added and the mixture stirred under argon at room temp. for 23 h. The usual work-up gave an oil (13.8 mg), the ^1H NMR spectrum for which showed the presence of compounds **23** and **24** in the approx. ratio 4:1.

BF_3·Et_2O catalysed rearrangement of epoxide 17

To a solution of epoxide **17** (103.2 mg, 0.241 mmol) in acetic anhydride (35 cm^3) stirred under argon at room temp., BF_3·Et_2O (0.30 cm^3) was added. After 15 s pyridine (2 cm^3) and benzene (70 cm^3) were added. The solution was washed with brine, aq. $NaHCO_3$ (5%; 2×) and water. The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure to give a thick oil, which was chromatographed on silica gel (6 g) with benzene or benzene–CH_2Cl_2 (1:1) as eluents to give the following compounds: the ketone **14** (5.9 mg, 6%), mp 115–117 °C, whose identity was proved by UV and ^1H NMR spectra; 31-*nor*-5α-*protosta*-2,13(17)-*dien*-3,11α-*diyl diacetate* **26** (18.2 mg, 15%), oil, ν_{max}/cm^{-1} 1745, 1723, 1315, 1255, 1230, 1127, 1055, 1045 and 918; δ_H 5.30–5.15 (2 H, m, 2-H and 11β-H), 2.70–2.20 (5 H, m), 2.11 (3 H, s, 3-Ac), 1.98 (3 H, s, 11-Ac), 1.15 (3 H, s, 8-Me), 1.10 (3 H, s, 14-Me), 1.05 (3 H, s, 10-Me), 0.96 (3 H, d, *J* 6.6, 4-Me), 0.93 (3 H, d, *J* 6.8, 20-Me) and 0.82 (6 H, d, *J* 6.2, 26-H and 27-H); *m/z* 512 (M^+), 452 (M^+ – AcOH), 437, 392, 339 ($M^+ - C_8H_{17}$ – AcOH), 205, 147, 133, 109, 95, 81, 69, 55 and 43 (Found: C, 77.1; H, 10.2. $C_{33}H_{52}O_4$ requires C, 77.30; H, 10.22%) and 3-*oxo*-31-*nor*-5α-*protost*-13(17)-*en*-11α-*yl acetate* **25** (77.1 mg, 68%), oil, ν_{max}/cm^{-1} 1722, 1702, 1256, 1237, 1185, 1108, 1015, 948 and 910; δ_H and δ_C (see ref. 19); *m/z* 470 (M^+), 410 (M^+ – AcOH), 395, 297 ($M^+ - C_8H_{17}$ – AcOH), 286, 221, 219, 147, 133, 119, 107, 95, 81, 55 and 43 (Found: C, 79.0; H, 10.7. $C_{31}H_{50}O_3$ requires C, 79.10; H, 10.71%).

Hydrolysis of enol acetate 26

To a solution of **26** (18.2 mg, 0.035 mmol) in dioxane (5 cm^3) and water (0.5 cm^3), one drop of conc. HCl was added. The mixture was stirred under argon at room temp. for 1 h followed by reflux for 15 min, after which it was extracted with benzene (50 cm^3). The organic layer was washed with brine, aq. $NaHCO_3$ (5%; 2×) and water (2×), dried ($MgSO_4$) and concentrated under reduced pressure to give an oil. Chromatography on silica gel (1 g) with CH_2Cl_2 as eluent gave the ketone **25** (13.3 mg, 79%) as an oil. Its ^1H NMR spectrum was identical with that of the authentic sample.

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References

1 Part 15. Z. Paryzek and J. Martynow, *J. Chem. Soc., Perkin Trans. 1*, 1994, 3047.
2 *Natural Products Chemistry*, eds. K. Nakanishi, T. Goto, S. Ito, S. Notori and S. Nozoe, Kodansha Ltd., Tokyo, Academic Press Inc., New York, 1974, vol. 1, p. 341 and references cited therein.
3 W. G. Dauben, C. R. Kessel, M. Kishi, M. Somei, M. Tada and D. Guillerm, *J. Am. Chem. Soc.*, 1982, **104**, 303.
4 D. J. Cram and N. L. Allinger, *J. Am. Chem. Soc.*, 1956, **78**, 5275; S. Iwasaki, M. I. Sair, H. Igarashi and S. Okuda, *J. Chem. Soc., Chem. Commun.*, 1970, 1119.
5 R. E. Ireland, R. Giger and S. Kamata, *J. Org. Chem.*, 1977, **42**, 1276; R. E. Ireland, P. Benslin, R. Giger, U. Hengartner, H. A. Kirst and H. Maeg, *J. Org. Chem.*, 1977, **42**, 1267; M. Tanabe, D. M. Yasuda and R. H. Peters, *Tetrahedron Lett.*, 1977, 1481.
6 (*a*) R. Kazlauskas, J. T. Pinhey and J. J. H. Simes, *J. Chem. Soc., Perkin Trans. 1*, 1972, 1243; (*b*) I. G. Guest and B. A. Marples, *J. Chem. Soc. C*, 1971, 1468.
7 Z. Paryzek and R. Wydra, *Bull. Pol. Acad. Sci., Chem.*, 1978, **26**, 591.
8 D. Lavie and E. Glotter, in *Fortschritte der Chemie Organischer Naturstoffe*, Springer Verlag, Berlin, 1971, p. 307.
9 M. R. Farias, E. P. Schenkel, R. Mayer and G. Rucker, *Planta Med.*, 1993, **59**, 272; L. M. M. Valante, A. A. L. Gunatilaka, T. E. Glass, D. G. I. Kingston and A. C. Pinto, *J. Nat. Prod-Lloydia*, 1993, **65**, 1772; E. Himeno, T. Nagao, J. Honda, H. Okabe, N. Irino and T. Nakasumi, *Chem. Pharm. Bull.*, 1993, **41**, 986; E. Himeno, T. Nagao, J. Honda, H. Okabe, N. Irino and T. Nakasumi, *Chem. Pharm. Bull.*, 1992, **40**, 2885.
10 T. Itoh, T. Ishi, T. Tamura and T. Matsumoto, *Phytochemistry*, 1978, **17**, 971; L. J. Goad, F. X. Garneau, J.-L. Simard, J. W. ApSimon and M. Girard, *Tetrahedron Lett.*, 1985, **26**, 3513; K. Ambia, L. J. Goad, S. Hkycko, F. X. Garneau, J. Belanger and J. W. ApSimon, *Comp. Biochem. Physiol.*, 1987, **86B**, 191; A. Ben Harref and J.-P. Lavergne, *Bull. Soc. Chim. Fr.*, 1985, 965.
11 O. E. Edwards and Z. Paryzek, *Can. J. Chem.*, 1975, **53**, 3498; J. W. ApSimon, R. R. King and J. J. Rosenfeld, *Can. J. Chem.*, 1969, **47**, 1989; J. Fried, J. W. Brown and M. Applebaum, *Tetrahedron Lett.*, 1965, 849.
12 Z. Paryzek and J. Martynow, *J. Chem. Soc., Perkin Trans. 1*, 1991, 243.
13 R. B. Boar, J. F. McGhie and D. A. Lewis, *J. Chem. Soc., Perkin Trans. 1*, 1972, 2590; E. V. Lassak, J. T. Pinhey and J. J. H. Simes, *Aust. J. Chem.*, 1973, **26**, 1051.
14 G. V. Baddeley, H. J. Samaan, J. J. H. Simes and T. H. Ai, *J. Chem. Soc., Perkin Trans. 1*, 1979, 7.
15 (*a*) Z. Paryzek, *J. Chem. Soc., Perkin Trans. 1*, 1978, 329; (*b*) Z. Paryzek and R. Wydra, *Monatsh. Chem.*, 1980, **111**, 1427.
16 PC MODEL 4.0, Serena Software, Box 3076, Bloomington, IN 47402-3076.
17 M. Naora (Namikawa), T. Murae, T. Tsuyuki and T. Takahashi, *Bull. Chem. Soc. Jpn.*, 1986, **59**, 1767.
18 Z. Paryzek, *J. Chem. Soc., Perkin Trans. 1*, 1979, 1222.
19 Z. Paryzek, J. Martynow and T. Shimo, *Magn. Reson. Chem.*, 1992, **30**, 579.
20 T. M. Peakman, K. Ellis and J. R. Maxwell, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1071; D. M. Tal, H. E. Gottlieb, C. Ben-Ari and Y. Mazur, *Tetrahedron*, 1981, **37**, 4331.
21 D. N. Kirk and P. M. Shaw, *J. Chem. Soc., Perkin Trans. 1*, 1975, 2284; T. M. Peakman and J. R. Maxwell, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1065.
22 T. M. Peakman and J. R. Maxwell, *Tetrahedron*, 1988, **44**, 1559.
23 M. Hartshorn and D. N. Kirk, *Tetrahedron*, 1965, **21**, 1547.

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