Tetracyclic Triterpenes. Part 13.[1] A New Synthesis of 4β-Demethyl-24,25-dihydrolanosterol

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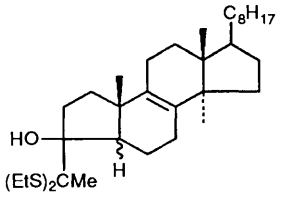
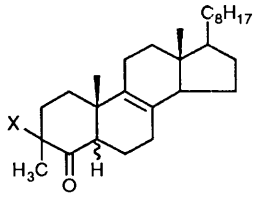
The reaction of 3β-hydroxy-3α-acetyl-14α-methyl-4-nor-5α-cholest-8-ene toluene-*p*-sulphonylhydrazone **10** under Bamford–Stevens conditions resulted in formation of 4α,14α-dimethyl-5α-cholest-8-en-3-one (4β-demethyldihydrolanosterol) and a mixture of 3,14α-dimethyl-4-oxo steroids. Thermal deoxygenation of **10** leading to the ketal **11** is explained by the intramolecular reduction mechanism involving the steroidal diimide.

In the previous paper[2] we reported the sulphur-mediated ring expansion reactions of α-hydroxy dithioacetals, derivatives of 3-acetyl-3-hydroxy-14α-methyl-4-nor-5α- and 5β-cholest-8-ene. The purpose of the work was to find a new and effective method for synthesizing 4β-demethyllanostane derivatives. Lewis acid catalysed reactions of hydroxythioacetals **1** proceeded without exception with undesired regioselectivity. Thus ring expansion accompanied by migration of the C(2)–C(3) bond led to 3-methyl-4-ketones **2**.[2] Acid- or base-catalysed rearrangement

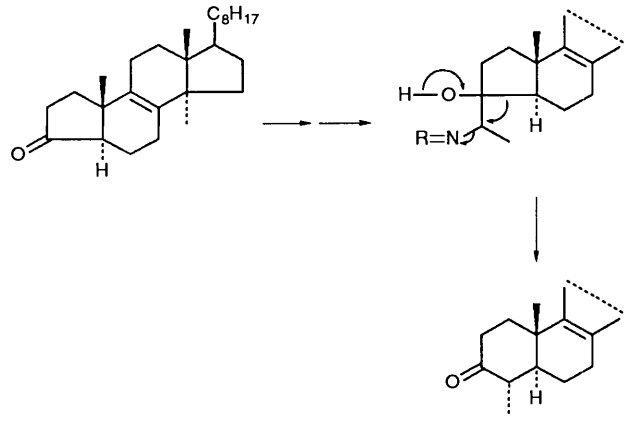


1a 5α
1b 5β
1c 5β, $\Delta^{7,9(11)}$



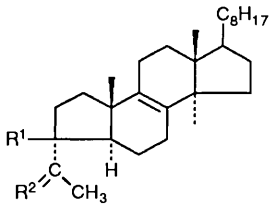
2 X = SC_2H_5
3 X = OH

of 3α-acetyl-3β-hydroxy-14α-methyl-4-nor-5α-cholest-8-ene **4** gave products of structure **3** also resulting from the migration of C(2)–C(3) bond.[3] In continuation of these synthetic efforts toward 4β-demethyllanosterol we decided to study nitrogen-mediated reactions which might possibly be accompanied with expansion of ring A in 4-nor-cholestane derivatives (Scheme 1).

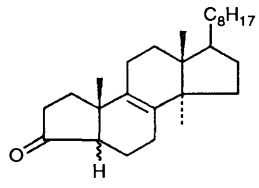


Scheme 1

The simplest solution to the problem appeared to be the reaction of 4-nor-5α-lanost-8-en-3-one **5**, readily available from lanosterol,[4] with diazoethane, followed by the expansion of the ring A. However, ketones **5** and **6** were unreactive toward

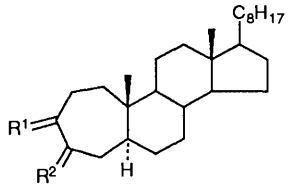


4 R^1 = OH, R^2 = O
10 R^1 = OH, R^2 = N–NH–Ts
12 R^1 = H, R^2 = O

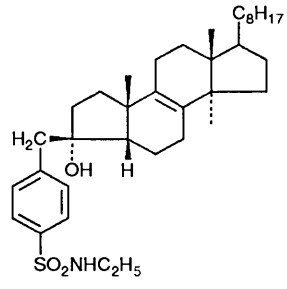


5 5α
6 5β

diazoethane in various conditions [uncatalysed or Lewis acid ($ZnCl_2$, BF_3·Et_2O, $AlCl_3$) catalysed reactions]. In similar reaction conditions it was possible to transform effectively a model ketone, 5α-cholestan-3-one, into a mixture of ring expanded, 7-membered α-methyl ketones **7** and **8** in 92% total yield.



7 R^1 = O, R^2 = CH_3, H
8 R^1 = CH_3, H, R^2 = O



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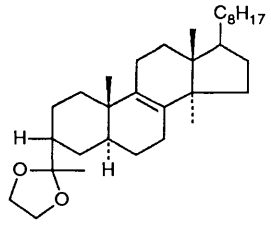
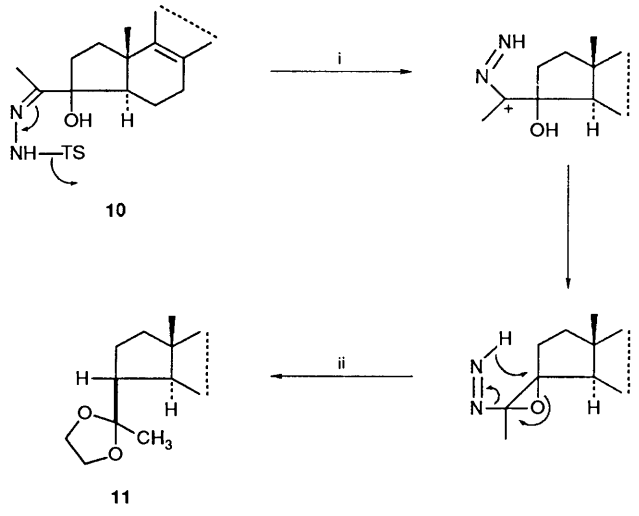
The attempted addition of the carbanion,[5] generated from diazoethane by the action of lithium diisopropyl amide (LDA), to the ketone **6** also failed. When **6** reacted with *N*-ethyl-*N*-nitrosotoluene-*p*-sulphonamide in the presence of LDA a product of addition of the benzyl carbanion was isolated in 45% yield. Spectral data of this compound were consistent with structure **9**.

The availability of the acyloin **4**, which could be prepared from the ketone **5** *via* **1a** in three steps,[2] prompted us to study reactions of the hydroxy tosylhydrazone **10**. In the steroid literature, the ring expansion of a tosylhydrazone derivative of the 17-hydroxypregnan-20-one has been described.[6] In that example, migration of the quaternary carbon C(13) resulted in the formation of 17-oxo-17aβ-methyl-D-homoandrostane (39% yield) along with the product of the secondary carbon C(16) migration (49% yield).



11

The tosylhydrazone **10** was prepared from **4** in 94% yield. The thermal reaction of **10** in boiling ethylene glycol without base gave a deoxygenation product **11**. Its formation is explained by the reduction mechanism involving the transient 'diimide' (Scheme 2). The decomposition of the tosylhydrazone involving

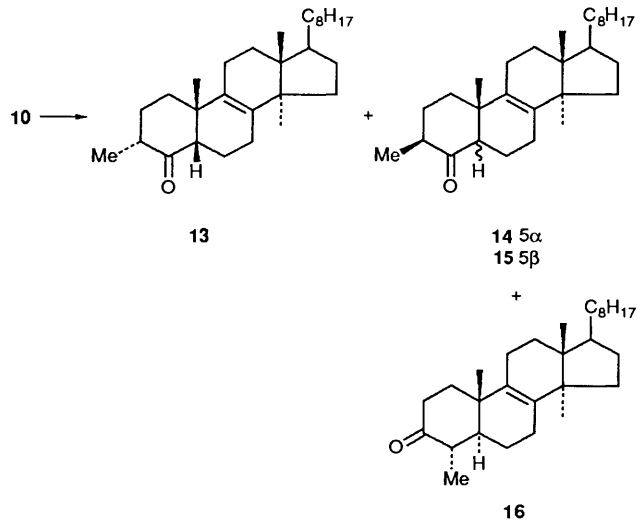


Scheme 2 *Reactions and conditions:* i, 200 °C; ii, $HOCH_2CH_2OH$

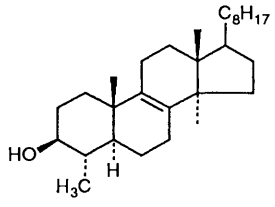
a carbene as an intermediate is less probable in protic solvents.[7] The acetal **11** is hydrolysed in acidic acetone to the thermodynamically more stable ketone **12** with the pseudo-equatorial acetyl group at C(3). This was indicated by a weak positive Cotton effect ($\Delta\varepsilon = +0.09$ at $\lambda = 296$ nm) which is characteristic of similar steroidal compounds.[8]

The tosylhydrazone **10** did not react with potassium t-butoxide in boiling t-butyl alcohol. However, in Bamford–Stevens conditions[9] (sodium ethylene glycolate in refluxing ethylene glycol) the tosylhydrazone **10** gave a mixture of ring-expanded α-methyl ketones. After chromatographic separation the following compounds were obtained: 3α-methyl-4-ketone **13** (16%), an inseparable mixture of **14** and **15** (1:1, 25%), and 4α-methyl-3-ketone **16** (34%) (Scheme 3). In repeated experiments, including large scale preparation (12 g of **10**), the desired ketone **16** was isolated in a similar yield. Spectral properties of **16** were in full agreement with those reported.[10] The reduction of the ketone **16** with lithium tri(t-butoxy)aluminohydride gave, quantitatively, 4β-demethyl-24,25-dihydrolanosterol **17**.

3α,14α-Dimethyl-5α-cholest-8-en-4-one is excluded as a product of the rearrangement, since it should exhibit a pronounced negative Cotton effect.[11] 5β-Configuration of compound **13** is assigned on the basis of the almost negligible Cotton effect in the region of $n \longrightarrow \pi^*$ transition ($\Delta\varepsilon = -0.05$) and of characteristic absorption of carbon atoms C(19), C(5) and C(10) in the ^{13}C NMR spectrum (δ_C 28.5, 54.7 and 41.3, respectively). Compound **13** was also obtained on an independent route.[3] The characteristic ^1H and ^{13}C NMR signals of compound **15** were obtained by substracting the spectra of the known ketone **14**[2] from those of the mixture **14** + **15**. Thus the proportion of compounds **14** and **15** in their



Scheme 3



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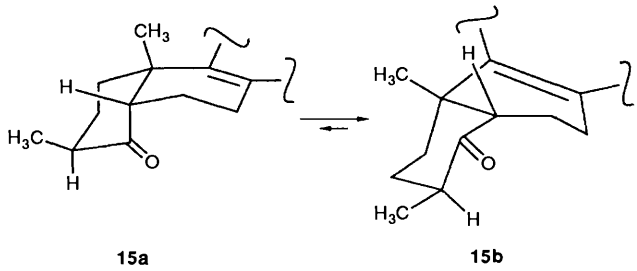
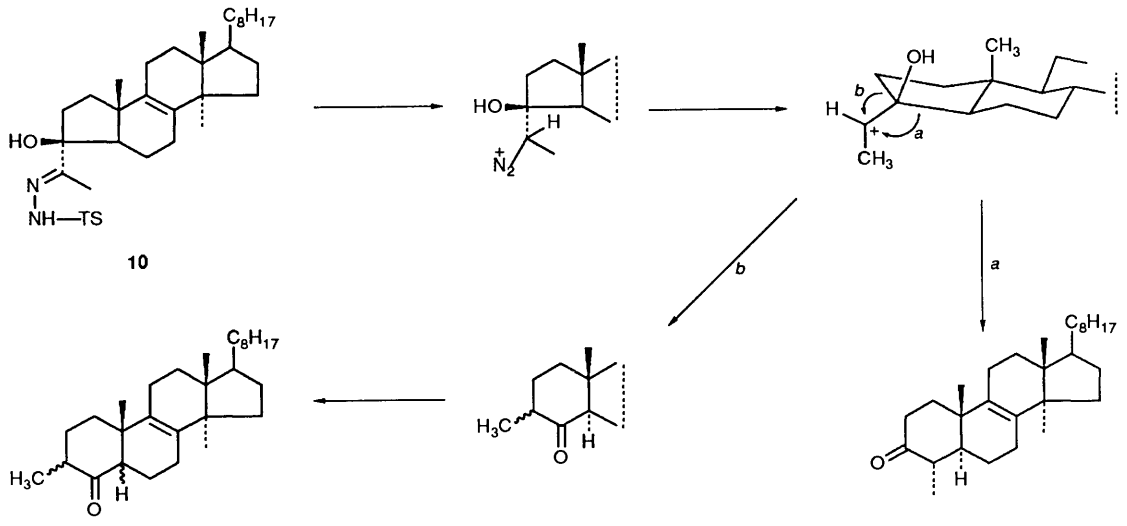
mixtures could also be estimated. The structure of compound **15** is proposed on the basis of the following reasoning. It could not be the 4α-H epimer of **16**, which should be unstable in the reaction conditions.[12] The two remaining structures were those having a carbonyl group in position 4 with 3α-CH_3,5α-H or 3β-CH_3,5β-H arrangement. The chemical shifts (δ_H 0.97; δ_C 24.0) of the C-19 methyl group in compound **15** do not conform with the 5α-configuration and rather suggest the 5β-H configuration[13] proposed for this compound.

The basic conditions of the Bamford–Stevens rearrangement of **10** caused the equilibration of 3-methyl-4-ketones **13**, **14** and **15**. This was confirmed when a 1:1 mixture of **14** and **15** was treated with alcoholic potassium hydroxide to give **13** (35%) and a 1:1 mixture of **14** and **15** (58%). Similar composition of the equilibrium mixture [**13** (40%) and **14** + **15** (60%)] was obtained when pure **13** was left in $CDCl_3$ solution at 5 °C for 40 days. At first sight, the absence of 3β-H,5α-H-isomer in the equilibrium mixture of 3-methyl-4-oxo steroid is surprising. The presence of 3β-methyl-4-oxo isomer **15** could be explained if we assumed that



15a **15b**

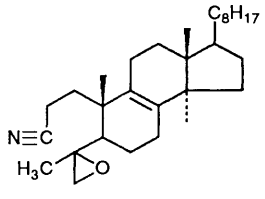
this compound exists in solution in the inverted chair conformation **15b** instead of the classical conformation **15a**.[14] Only very recently similar inverted chair conformation was proposed for 5β-steroids possessing conjugated double bonds in position 8 and 14.[15] Thus, all the four α-methyl ketones **13**–**16** produced in the rearrangement of **10** under basic conditions have the methyl substituent in the equatorial position.



Scheme 4

In the rearrangement of the tosylhydrazone **10** the two modes of carbon–carbon bond migration to the carbocationic centre formed from the tosylhydrazone[7] are realized (Scheme 4). The electronically favoured migration of the more electron-rich C(3)–C(5) bond gives **16** through a sterically unfavourable boat-like transition state, even though the migration of C(2)–C(3) bond is still a slightly predominating process.

The total yield of the eight-step transformation of dihydrolanosterol to its 4β-demethyl analogue described here and in the previous papers[2,4] is about 17% and is comparable with that obtained in the Holker–Pinhey method.[10a,16] The advantage of the present method is that it does not require the use of a strong acid at any stage of the synthesis. This eliminates difficulties encountered in the Pinhey method and associated with the possible isomerization of the 8,9-double bond to position 7.[17] We have found that when the secoepoxynitrile **18** is treated with a Lewis acid (BF_3·Et_2O or $SnCl_4$), besides the desired compound **16**, the isomeric oxo olefin **19** is formed in up to 30%. This is in agreement with other work reporting a low yield of the cyclization of secoepoxynitriles similar to **18**.[18]



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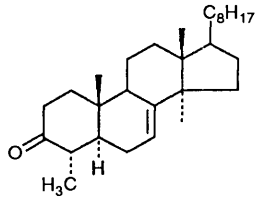

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Experimental

M.p.s were determined on a Kofler hot-stage apparatus and are uncorrected. IR Spectra were determined with a Perkin-Elmer 580 grating spectrophotometer for solutions in chloroform. ^1H and ^{13}C NMR Spectra were recorded with a JEOL FX90Q spectrophotometer operating in the Fourier transform mode using solutions in deuteriochloroform. Coupling constants *J* are given in Hz, and the chemical shifts (δ) are expressed in ppm relative to tetramethylsilane. The SFORD technique along with extensive substituent effect comparison in the lanostane series[2,19] was used for ^{13}C signal assignments. Electron impact mass spectra were recorded with a JEOL JMS-D 100 spectrometer. CD Spectra were recorded with a Jobin-Yvon Dichrograph Mark III for solutions in dioxane. Column chromatography was performed by using silica gel 60 (Merck 70-230 mesh, no. 7734). The progress of reactions was monitored by TLC using a precoated aluminium-backed silica plates (E. Merck, no. 5554).

Reaction of 5α-cholestan-3-one with Diazoethane.—(*a*) *Generated* in situ.To a solution of 5α-cholestan-3-one (230 mg, 0.6 mmol) and lithium hydroxide monohydrate (200 mg, 4.8 mmol) in propanol (10 cm^3), stirred at 0 °C, was added a solution of *N*-ethyl-*N*-nitrosotoluene-*p*-sulphonamide (228 mg, 1 mmol) in propanol (5 cm^3) dropwise over 15 min. The reaction mixture was left at 0 °C for 18 h. Acetic acid (2 cm^3) was added and the solution concentrated *in vacuo*. The residue was dissolved in benzene (50 cm^3) and the solution washed with water, aqueous sodium hydrogen carbonate (5%), dried with potassium carbonate and solvent was evaporated to leave 236 mg of a crude product which was chromatographed on silica gel (15 g) with benzene as the eluent to give: 5α-cholestan-3-one (34 mg, 14%) and a mixture of *4-methyl-A-homo-5α-cholestan-3-one* **7** and *3-methyl-A-homo-5α-cholestan-4-one* **8** (199 mg, 80%), m.p. 95–97 °C (from methanol–diethyl ether); ν_{max}/cm^{-1} 1695; CD Δε (λ/nm) + 1.67 (293); δ_H 2.85–2.31 (2 H, m), 1.04 (3 H, d, *J* 7), 0.92, 0.89, 0.86, 0.82, 0.74 and 0.65; *m/z* 414 (M), 399, 260, 152, 109 and 101 (Found: C, 83.8; H, 12.2. $C_{29}H_{50}O$ requires C, 84.0; H, 12.15%).

(*b*) *Generated* ex situ. To a solution of 5α-cholestan-3-one (110 mg, 0.29 mmol) in anhydrous Et_2O (20 cm^3) stirred at −78 °C was added a solution of diazoethane in Et_2O. The mixture was kept at −15 °C for 46 h. The work-up as above and chromatography (SiO_2, 7 g) gave a mixture of **7** and **8** (109 mg, 92%) with spectral properties as in (*a*).

3β-(N-Ethyl-p-benzenesulphonamide)methyl-3α-hydroxy-14α-methyl-4-nor-5β-cholest-8-ene **9**.—To a solution of lithium diisopropylamide (1.2 mmol) in tetrahydrofuran (THF) (10 cm^3) stirred at −78 °C was added a solution of *N*-ethyl-*N*-nitroso-toluene-*p*-sulphonamide in THF (3 cm^3), followed by addition of the ketone **6** (93 mg, 0.242 mmol) dissolved in THF (2 cm^3). The reaction mixture was stirred at −78 °C for 2 h, then left at −15 °C for 20 h. Acetic acid (1 cm^3) was added and solvents were removed *in vacuo*. The residue was dissolved in benzene (50 cm^3) and washed successively with brine, water 5% aqueous sodium hydrogen carbonate and water again. The organic layer was dried ($MgSO_4$) and concentrated *in vacuo* to yield a solid residue (126 mg) which was purified by colunn chromatography

on silica gel (7 g). Elution with methylene chloride afforded the unreacted ketone **6** (39 mg) and *compound* **9** (64 mg, 45%), m.p. 157–158 °C (from methanol); ν_{max}/cm^{-1} 3620, 3550, 3385, 3285, 3030, 3015, 1602, 1495, 1330, 1160, 1095, 1060, 1020 and 847; δ_H 7.78 (2 H, d, *J* 8.3), 7.42 (2 H, d, *J* 8.3), 4.67 (1 H, t, *J* 6.1, NH), 2.92 (4 H, m, $w_{h/2}$ 30 Hz), 1.09 (3 H, t, *J* 7.2, NCH_2CH_3), 1.07 (3 H, s, 19-H) and 0.90, 0.83 and 0.72 (3 H, s, 18-H); *m/z* 583 (M^+), 568, 565, 550, 384, 367, 199, 159 and 145 (Found: C, 74.0; H, 9.8; N, 2.4. $C_{36}H_{57}NO_3S$ requires C, 74.05; H, 9.8; N, 2.4%).

3α-*Acetyl*-3β-*hydroxy*-14α-*methyl*-4-*nor*-5α-*cholest*-8-*ene Toluene*-p-*sulphonylhydrazone* **10**.—To a hot solution of the ketone **4** (8.98 g, 20.96 mmol) in acetic acid (30 cm^3) was added, dropwise, a solution of toluene-*p*-sulphonylhydrazine (7.4 g, 39.8 mmol) in acetic acid (20 cm^3) and the mixture was stirred at 80 °C for 1 h. To the cooled reaction mixture benzene (120 cm^3) and hexane (50 cm^3) were added and the solution washed with brine (3 ×), aqueous 5% $NaHCO_3$, and water (2 ×). After drying the solution ($MgSO_4$), the solvents were evaporated to dryness. The residue (12.31 g) was purified by column chromatography on silica gel (170 g) with methylene chloride as eluent. This gave *compound* **10** (11.82 g, 94%), m.p. 192–194 °C (from methanol–methylene chloride); ν_{max}/cm^{-1} 3480, 3295, 3215, 3025, 1600, 1340, 1185, 1165, 1085, 915, 880 and 810; δ_H 7.83 (2 H, d, *J* 8.3), 7.63 (1 H, br s, NH), 7.31 (2 H, d, *J* 8.3), 2.43 (3 H, s, $ArCH_3$), 1.78 (3 H, s, $N{=}C{-}CH_3$), 1.08 (3 H, s, 19-H), 0.90, 0.86, 0.83 and 0.72 (3 H, s, 18-H); *m/z* 596 (M^+), 578, 563, 441, 423, 412, 397, 379, 231, 156 and 119 (Found: C, 72.6; H, 9.7; N, 4.7. $C_{36}H_{56}O_3N_2S$ requires C, 72.4; H, 9.5; N, 4.7%).

3-(1′,1′-*Ethylenedioxy*)*ethyl*-14α-*methyl*-4-*nor*-5α-*cholest*-8-*ene* **11**.—A solution of compound **10** (60 mg, 0.1 mmol) in ethylene glycol (5 cm^3) was heated at reflux under argon for 5 min. TLC Indicated the formation of one product. The mixture was cooled to room temperature, then benzene (30 cm^3) and hexane (20 cm^3) were added and the solution washed with brine (3 ×) and water (3 ×). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo* to give a white solid, which was chromatographed on silica gel (3 g) with benzene as eluent. *Compound* **11** (41 mg, 89%) had m.p. 86–88 °C (from methanol); ν_{max}/cm^{-1} 1145, 1115, 1055, 1045, 1035 and 948; δ_H 3.93 (4 H, br s, OCH_2CH_2O), 1.29 [3 H, s, $CH_3{-}C{-}(O)_2$], 0.91 (3 H, s, 19-H), 0.90, 0.86, 0.83 and 0.72 (3 H, s, 18-H); *m/z* 456 (M^+), 441, 369, 354 and 149 (Found: C, 81.3; H, 11.6. $C_{31}H_{52}O_2$ requires C, 81.5; H, 11.5%).

3α-*Acetyl*-14α-*methyl*-4-*nor*-5α-*cholest*-8-*ene* **12**.—A solution of the acetal **11** (20 mg, 0.044 mmol) and toluene-*p*-sulphonic acid (20 mg) in an acetone (5 cm^3)–water (0.1 cm^3) mixture was heated under reflux for 2 h. The solution was concentrated *in vacuo*, benzene (30 cm^3) was added and the resulting solution washed with brine, 5% aqueous $NaHCO_3$, and water. The organic layer was dried ($MgSO_4$) and concentrated *in vacuo* to give *compound* **12** (15 mg, 83%), m.p. 73–75 °C (from methanol); ν_{max}/cm^{-1} 1712, 1235, 1138, 1020 and 973; CD Δε (λ/nm) +0.09 (296); δ_H 2.16 (1 H, s, CH_3CO), 0.90 and 0.88 (3 H, s, 19-H) and 0.83 and 0.72 (3 H, s, 18-H); *m/z* 412 (M^+), 397, 243, 133, 119 and 105 (Found: C, 84.5; H, 11.8. $C_{29}H_{48}O$ requires C, 84.4; H, 11.7%).

Bamford–Stevens Reaction of the Tosylhydrazone **10**.—To a mixture of compound **10** (920 mg, 1.54 mmol) and ethylene glycol (25 cm^3) a solution of sodium monoglycolate prepared from sodium (160 mg) and ethylene glycol (4 cm^3) was added. The reaction mixture was refluxed for 5 min. After cooling it was poured into brine (100 cm^3) and extracted with benzene (3 × 60 cm^3). The combined benzene solutions were washed with water (3 ×), dried ($MgSO_4$) and evaporated *in vacuo* to yield a white solid, which was chromatographed on silica gel (50 g) with benzene as eluent. This gave 3α,14α-*dimethyl*-5β-*cholest*-8-*en*-4-*one* **13** (88 mg, 16%), m.p. 115–117 °C (from methanol); ν_{max}/cm^{-1} 1695; CD Δε (λ/nm) −0.05 (292); δ_H 2.12 (1 H, m, $w_{h/2}$ 14 Hz), 1.19 (3 H, s, 19-H), 0.98 (3 H, d, *J* 6.4, 3α-CH_3), 0.90, 0.83, 0.77 and 0.70; δ_C [3] 54.7 (C-5), 41.3 (C-10) and 28.6 (C-19); *m/z* 412 (M^+), 397, 285, 243, 231 and 149 (Found: C, 84.2; H, 11.4. $C_{29}H_{48}O$ requires C, 84.4; H, 11.7%); a mixture of 3β,14α-*dimethyl*-5α-*cholest*-8-*en*-4-*one* **14** [2] and 3β,14α-*dimethyl*-5β-*cholest*-8-*en*-4-*one* **15** (136 mg, 25%), m.p. 96–98 °C (from methanol); signals of compound **15**; δ_H 2.28 (m, $w_{h/2}$ 7 Hz, 5-H), 1.02 (d, *J* 6.3, 3β-CH_3), 0.97 (3 H, s, 19-H) and 0.74 (3 H, s, 18-H); δ_C [3] 58.4 (C-5), 40.6 (C-10) and 24.0 (C-19) (Found: C, 84.3; H, 11.8); and 4α,14α-dimethyl-5α-cholest-8-en-3-one **16** (180 mg, 34%), m.p. 105–107 °C (needles from methanol) or 108–110.5 °C (needles from acetonitrile) (lit.,[10a] m.p. 109–111 °C, lit.,[10b] m.p. 105–108 °C); ν_{max}/cm^{-1} 1705; CD Δε (λ/nm) +0.76 (290); δ_H 2.34 (1 H, m, $w_{h/2}$ 16 Hz, 4-H), 1.20 (3 H, s, 19-H), 1.02 (3 H, d, *J* 6.4, 4α-CH_3), 0.90, 0.87, 0.83 and 0.74.

Isomerization of Compounds **13**, **14** *and* **15**.—(*a*) A solution of the mixture containing the ketones **14** and **15** (1:1), (95 mg) and potassium hydroxide (100 mg) in ethanol (96%, 5 cm^3) was refluxed for 45 min. Benzene (30 cm^3) and hexane (10 cm^3) was added and the mixture washed with brine and water. Evaporation *in vacuo* gave a white solid which was chromatographed on silica gel (5.5 g) with benzene–hexane as eluent to give: ketone **13** (34 mg, 35%) (characterized by its ^1H NMR spectrum) and a mixture of **14** and **15** (54 mg, 58%, approx. 1:1, estimated from ^1H and ^{13}C NMR spectra).

(*b*) The pure crystalline ketol **13** was dissolved in $CDCl_3$ and left at 5 °C for 40 days. TLC Showed a new spot of R_f identical with that found for compounds **14** and **15**. ^1H and ^{13}C NMR spectra showed the presence of compounds **13**, **14** and **15** in approx. ratio 4:3:3.

Reduction of the Ketone **16** *with Lithium Tri*(*t-butoxy*)-*aluminohydride*.—To the stirred under argon solution of $LiAlH_4$ (380 mg) in Et_2O (100 cm^3) was added t-butyl alcohol until the evolution of hydrogen ceased. After 10 min the mixture was cooled to −78 °C and a solution of the ketone **16** (1.36 g) in Et_2O (20 cm^3) was added dropwise. Stirring was continued for 30 min and the temperature was raised to 20 °C during 1 h. Saturated aqueous magnesium sulphate was added, the organic layer was separated, washed with brine and water (2 ×), dried ($MgSO_4$) and evaporated *in vacuo* to give pure 4α,14α-dimethyl-5α-cholest-8-en-3β-ol **17** (1.33 g, 97%), m.p. 140–141 °C (from methanol) (lit.,[18a] m.p. 140.5–142 °C); ν_{max}/cm^{-1} 3580, 3470 and 1160; δ_H 3.10 (1 H, m, $w_{h/2}$ 26 Hz, 3α-H), 1.00 (3 H, s, 19-H), 0.90 and 0.86 (3 H, d, *J* 6.2, 4α-CH_3) and 0.83 and 0.72 (3 H, s, 18-H); *m/z* 414 (M^+), 399, 381 and 169 (Found: C, 83.7; H, 12.2. Calc. for $C_{29}H_{50}O$: C, 84.0; H, 12.15%).

Reaction of Secoepoxynitrile **18** *with Lewis Acids*.—To a solution of the mixture of (4*R*)- and (4*S*)-4,30-epoxy-3,4-seco-5α-lanost-8-en-3-one **18** (1.21 g, 2.75 mmol) (prepared according to the literature method [10a]) in dry toluene (160 cm^3) stirred under argon at 100 °C was added a solution of $SnCl_4$ (2.40 g, 9.2 mmol) in toluene (10 cm^3). The solution was refluxed for 6 h, then cooled to 0 °C and washed with brine (2 ×), water, aqueous 5% sodium hydrogen carbonate (2 ×) and water. The organic layer was dried (K_2CO_3) and concentrated *in vacuo* to give a pale yellow solid, which was chromatographed on silica gel (30 g) with benzene as eluent. The combined chromatographically pure fractions gave a white solid (0.68 g, 56%) which consisted of the ketone **16** and its Δ^7-isomer in approx. 4:1 ratio (estimated from the integration curve of the ^1H NMR spectrum). The IR and mass spectra of the mixture were very

similar to those of pure **16**. The ^1H NMR spectrum, besides featuring the signals characteristic of the ketone **16**, showed the following signals of the ketone **19** at δ_H 5.20 (0.2 H, m, $w_{h/2}$ 12 Hz, 7-H), 1.09 (0.6 H, s, 19-H), 1.00 (0.6 H, d, *J* 6.4, 4α-CH_3), 0.86 (0.6 H, s, 14α-CH_3) and 0.68 (0.6 H, s, 18-H).

Repeating the reaction of **18** with $SnCl_4$ or BF_3·Et_2O as catalysts gave a similar mixture containing **16** and up to 30% of compound **19**.

Acknowledgements

Financial support of this work from the Program RP II.13 is gratefully acknowledged.

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Paper 0/04502K
Received 4*th October* 1990
Accepted 15*th October* 1990