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The Intramolecular Ene Reaction of 5-(Prop-2-enyl)-2ξ-hydroxy-5α-cholestan-3-one.

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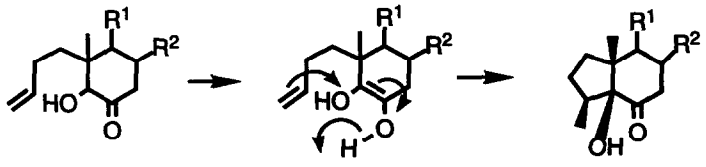
Abstract: The title unsaturated acyloin undergoes the relatively low temperature (110°C) intramolecular ene reaction to give the 2,5-ethano-acyloin (17) which rearranges to the 3,5-ethano-isomer (16).

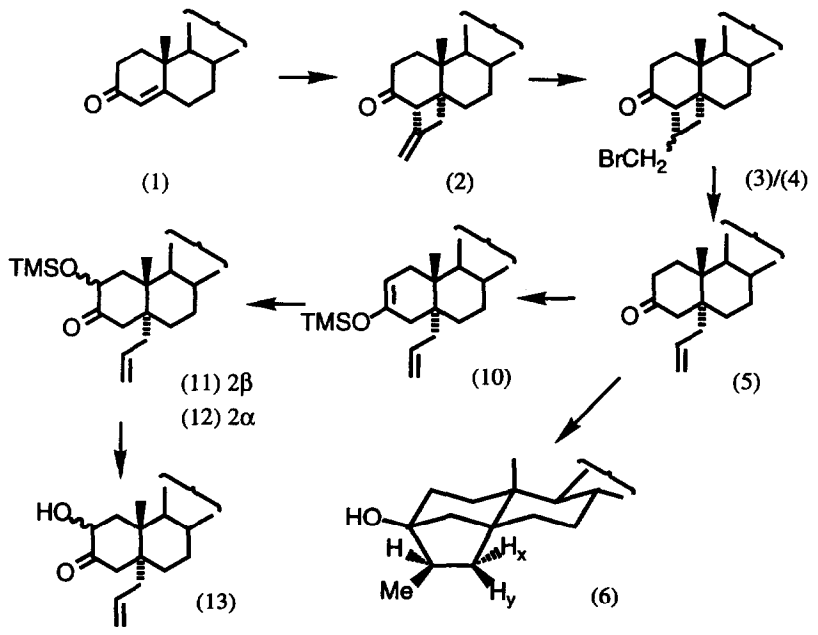
Intramolecular ene reactions are recognised as efficient carbocyclisation reactions which profit from entropic advantage relative to the intermolecular equivalents.[1] We have recently reported[2,3] examples of facile ene reactions of unsaturated acyloins (Scheme 1) in which the much lower reaction temperatures, compared with those required for unsaturated ketones can possibly be ascribed, in part, to the electron rich nature of the ene (enediol). An additional important factor is probably the ease with which the reacting conformation may be achieved.



Scheme 1

We report here an investigation of the ene reaction of steroidal unsaturated acyloins (13) to further explore the influence of conformational mobility. A preliminary account of some of this work has been reported.[4]

The unsaturated acyloins (13) were prepared according to Scheme 2. Photoaddition of allene[5,6] to cholest-4-en-3-one (1) in hexane at -60°C gave the adduct (2). A signal at δ 5.07 (m, $W_{1/2}$ 8Hz) in the ^1H n.m.r. spectrum confirmed the presence of the exomethylene group. The 4α, 5α-stereochemistry and methylene regiochemistry were assigned by comparison with similar known steroid photo-adducts.[5] The photochemically initiated anti-Markovnikov addition of hydrogen bromide to the adduct (2) gave a mixture of the isomeric bromides (3) and (4). The bromides were usually used as a mixture but could be separated by flash column chromatography.



Scheme 2

The less polar isomer (3) had important 1H signals in its 360 MHz ^{1}H n.m.r. spectrum at δ 3.45 (q,RCH_2Br, J 3.6 and 9Hz), 3.01 (q, RCH_2Br, J 9 and 10.8 Hz) and 2.85 (m, R_2 C*H* CH_2 Br). Double irradiation of the signal at δ 3.45 causes the signal at δ 3.01 to collapse to a doublet (J 10.8 Hz) illustrating the vicinal coupling between the cyclobutane ring methine proton and one of the bromomethyl group protons. Double irradiation of the ring methine signal at δ 2.85 causes the signal at δ 3.45 to collapse to a doublet (J 9Hz) illustrating the geminal coupling of the bromomethyl protons. The COSY 45 ^{1}H n.m.r. spectrum clearly shows the coupling of these protons to each other.

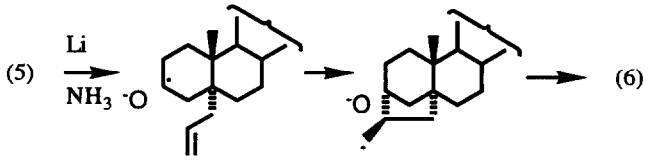
The more polar isomer (4) had important signals in its 360 MHz ^{1}H m.n.r. spectrum at δ 3.55 (q, RCH_2Br, J 6.3 and 9.9 Hz), 3.40 (t, RCH_2Br, J 9.9 Hz) and 2.46 (m R_2 C*H*-CH_2Br). Double irradiation of the signal at δ 2.46 causes the signals at δ 3.55 and 3.40 to collapse to doublets (J 9.9 Hz) illustrating the geminal coupling between the bromomethyl protons. The coupling between these protons was clearly confirmed in the COSY 45 ^{1}H n.m.r spectrum.

The bromides (3) and (4) were reductively cleaved with lithium in liquid ammonia and T.H.F to give the required allyl ketone (5) (75%). A by-product of this reaction was an alcohol (6), the yield of which could be reduced by the use of a minimum amount of lithium and a short reaction time.

The allyl ketone (5) had infrared (υ_{max}. 3080, 1640 ($RCH{=}CH_2$), 1710 (C=0) cm^{-1}.) and ^{1}H n.m.r (δ 5.4 - 6.1, m and 5.1, m, $RCH{=}CH_2$) spectra which confirmed the presence of the allyl and ketone groups. The mass spectrum showed a molecular ion at m/z 426 and a fragment ion at m/z 385 $[M\text{-}C_3H_5]^+$.

The alcohol (6) was identified from its infrared spectrum which had $\upsilon_{max.}$ 3500 (OH) cm^{-1}. The 360 MHz ^1H n.m.r spectrum had a signal at δ 0.92 (d, J 7Hz) for the bridge methyl and a signal at δ 2.36 (m) which was assigned to the bridge methylene proton, H_x. The COSY 45 ^1H n.m.r. spectrum shows the spin-spin coupling of this bridge methylene proton, H_x (δ 2.36 to its geminal neighbour Hy (δ 0.79, dd, J 5 and 14 Hz). The lowfield position of the signal for H_x is presumed to be due to the steric crowding it suffers from the 7α - and 9α - protons. The mass spectrum (6) showed a molecular ion at m/z 428 and fragment ions at m/z 413 $[M\text{-}Me]^+$ and m/z 385 $[M\text{-}C_3H_7]^+$.

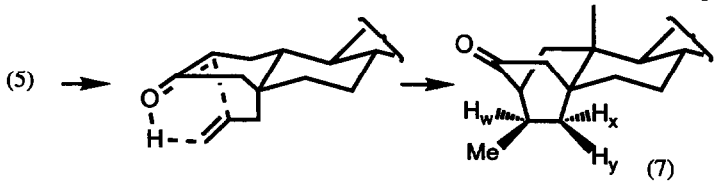
It is proposed that the alcohol (6) arises from a reductive anion radical mediated cyclisation of the allyl ketone (5) (Scheme 3) and that the bridge methyl will take up the less hindered *exo* configuration. Evidence for this mechanism was provided by treating the allyl ketone (5) with lithium in liquid ammonia resulting in the isolation of the alcohol (6) (46%) and some starting material.



Scheme 3

This cyclisation is particularly efficient when compared to the cyclisation of 4,5-secocholest-3-en-5-one reported by Pradhan[7,8] presumably owing to the close proximity of the allyl chain to the reacting centre.

The allyl ketone (5) when heated in decalin solution in a sealed tube at 330°C, underwent an ene reaction (Scheme 4) giving the 2,5-ethano-ketone (7) (79%). Cyclisation could also be achieved at temperatures as low as 250°C although the conversion was reduced to 57% over the same period (4 hours).

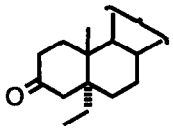


Scheme 4

The ketone (7) had υ_{max} 1728 (C=0) cm^{-1} in its infrared spectrum and the 360 MHz ^1H n.m.r spectrum had a doublet (J 7Hz) at δ 0.93 for the bridge methyl which is spin-spin coupled to H_w (δ2.0,m). The 4-methylene group gave a double doublet at δ 2.25 (J 19Hz and 3Hz) and a doublet at δ1.74 (J 19Hz). The lower field signal is assigned to the 4β- proton which suffers long range (W) spin-spin coupling with the bridge methylene proton H_x (δ 2.67, m). The COSY 45 ^1H n.m.r. spectrum shows the spin-spin coupling of H_x (δ 2.67) to the 4β-H and to H_y (δ 0.71, dd, J 14 and 3 Hz). A signal at δ 2.13 (brd s, $W_{1/2}$ 7 Hz) was assigned to the 2β- proton. The mass spectrum showed a molecular ion at m/z 426 and a fragment ion at m/z 411 $[M\text{-}Me]^+$. The regiochemistry and methyl stereochemistry were assigned on the basis of the proposed mechanism and by comparison with the similar reaction of 5-vinyl-5α-cholestan-3-one (8) to give the 2,5- methano-ketone (9)[9].

The allyl ketone (5) was converted to the enol silyl ether (10) by treatment with trimethylsilyl chloride and triethylamine in refluxing dimethylformamide.[10] The infrared (υ_{max} 1665 (RCH=CR=OSiMe) cm^{-1}) and the ^1H n.m.r. (δ 4.7, brd s) spectra confirmed the presence of an enol ether.

Oxidation with *m*-chloroperbenzoic acid in anhydrous hexane[11] and non-aqueous work up gave a mixture of the silyloxy ketones (11) and (12). Careful flash column chromatography on silica gave the less polar epimer, 2β-(trimethylsilyloxy-5-(prop-2-enyl)-5α-cholestan-3-one (11) as an oil, and the more polar epimer 2α-(trimethylsilyloxy)-5-(prop-2-enyl)-5α -cholestan-3-one (12) which was crystalline. The C2-stereochemistry was assigned on the basis of the spin-spin coupling for the 2-H in the ^1H n.m.r. spectra. The spectrum for compound (11) has a quartet at δ 4.10 (2α-H, J 7 and 3 Hz) whereas that for compound (12) had a quartet at δ 4.15 (2β-H, J 11 and 7 Hz). The larger coupling constant observed for (12) is attributed to an axial-axial coupling. The 2β-silyloxy-ketone (11) hydrolysed on standing, but the 2α-silyloxy-ketone (12), when pure, appeared quite stable. Deprotection of the mixture of epimers (11) and (12) with tetrabutylammonium flouride/silica in chloroform gave initially the acyloins (13) which were converted very quickly in the presence of air into the diosphenol (14). The diosphenol (14) had υ_{max} 3400, (OH) 1710 (C=O) and 1665 (C=C(OH)-C=O) cm^{-1} in its infrared spectrum. The ^1H n.m.r. spectrum had important 2H singlets at δ 6.1 (1-H) and 5.7 (4-H). The mass spectrum showed a molecular ion at m/z 440. The analogous oxidation of 2α-hydroxy-cholestan-3-one in alkaline solution has been reported.[12] It is unusual that this autoxidation occurs rapidly and without base catalysis.



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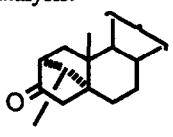

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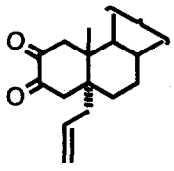
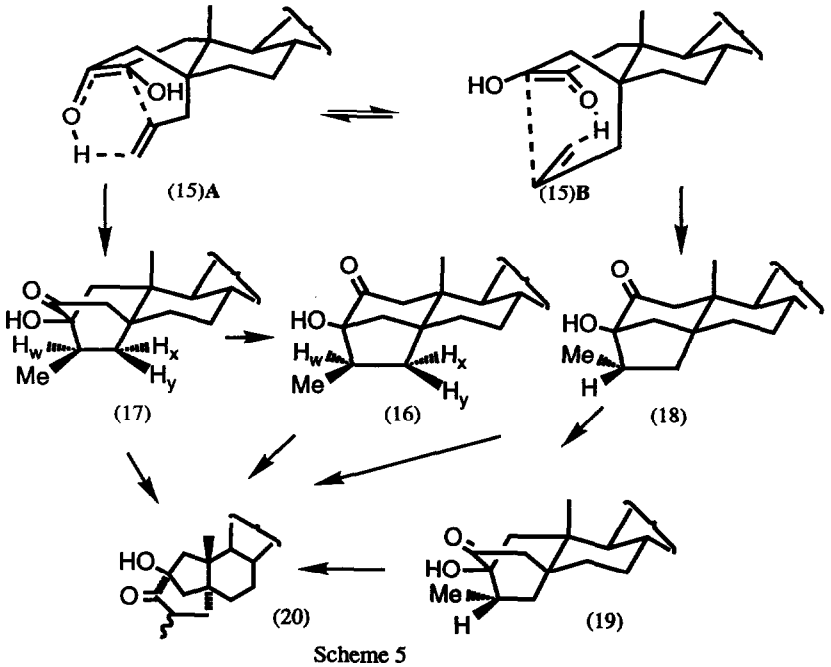


(14)

Deprotection of the silyloxy-ketones (11) and (12) with $Bu_4N^+F^-/SiO_2$ in a refluxing solution of deoxygenated toluene under an atmosphere of argon (18 hours) afforded two products. Separation by preparative thin layer chromatography gave the 3α,5α-ethano-compound (16) (6%) and the 2α, 5α–ethano-compound (17) (33%). Similar yields of (16) (7%) and (17) (27%) were obtained by heating a solution of the silyloxy-ketones (11) and (12) in decalin with $Bu_4N^+F^-/SiO_2$ in a sealed tube at 200°C (4 hours).

Two primary ene reaction products (17) and (18) may be formed from the unsaturated acyloins (13) arising respectively from the dienediol (15) in conformations A and B (Scheme 5). Acyloin arrangement of (17) could afford the isomer (16) while the similar rearrangement of (18) would give (19). Other possible acyloin rearrangement products (20) may also arise in principle but the spectroscopic evidence supported the assigned structures (16) and (17). In particular, the infrared spectrum of the minor isomer (16) [υ_{max} 3495 (OH), 1705 (C=0) cm^{-1}] differed from that of the major isomer (17) [υ_{max} 3500 (OH), 1725 (C=0) cm^{-1}] suggesting a different carbon skeleton rather than simply a difference in the configuration of the bridge carbon atom bearing methyl.



Scheme 5

The 360 MHz ^1H n.m.r. spectrum of the minor isomer (16) showed a doublet (J7Hz) at δ 1.05 for the bridge methyl. The 1-methylene protons gave an AB quartet at δ 2.25 (J15 Hz) in which the upfield branch was slightly broadened. The bridge methylene proton, H_x appeared at low field (δ 2.64, quartet xd, J 14, 9 and 3 Hz). The general splitting pattern compared with that of the bridge methylene proton, H_x in alchohol (6). The COSY 45 ^1H n.m.r spectrum showed the spin-spin coupling of H_x to proton H_w (δ 1.8, m) and the other bridge methylene proton, H_y (δ 1.22). A sharp singlet at δ 3.6 was assigned to the hydroxyl proton. The absence of any n.O.e of the 1-methylene on double irradiation of the bridge methyl resonance (δ 1.05) confirmed the assigned methyl stereochemistry. In the alternative structure (18) a significant n.O.e between the 1α-H and the bridge methyl would be expected. The mass spectrum of compound (16) showed a molecular ion at m/z 422 and a fragment ion at m/z 398 $[M\text{-}CH_3CHO]^+$. That the 3,5-ethano compound (16) may be formed from the 2,5-ethano compound (17) was demonstrated by t.l.c of the product of heating (17) in decalin at 200°C for 4 hours in a sealed tube.

The major isomer (17) showed a doublet (J7Hz) in the 360 MHz ^1H n.m.r. spectrum at δ 0.85 for the bridge methyl. The 4-methylene gave a double doublet at δ 2.45 (J 19 Hz) and a doublet at δ 1.92 (J 19 Hz). The lower field signals were assigned to the 4β-H which suffers long range spin-spin coupling (W) with the bridge methylene proton, H_x (δ2.91) [cf. ketone (7)]. The COSY 45 ^1H n.m.r spectrum shows the spin-spin coupling of proton H_x (δ 2.91, m, J 3, 10 and 15 Hz) to the 4β–H, the proton H_w, (δ 2.03, m) and the other bridge methylene proton, H_y (δ 0.90). The spin-spin coupling between proton H_w and the bridge methyl is also apparent. The signal for the hydroxyl proton appeared as a sharp singlet at δ 3.50. The mass spectrum showed a molecular ion at m/z 422 and a fragment iron at m/z 398 $[M\text{-}CH_3CHO]^+$.

The ene reaction at 110° of acyloins (13) is a further example of the increased reactivity of acyloins compared to ketones. This enhanced reactivity is probably owed to the relatively election rich nature of the

ene. The increased reactivity of (13) versus the related acyloins (Scheme 1)[2,3] is probably owed to the relatively favourable entropy associated with the ring closure of the more conformationally restricted system in (13).

Experimental

Solutions were dried over anhydrous magnesium sulphate and solvents were removed under reduced pressure with a rotary evaporator. Preparative t.l.c was performed on Kieselgel $60PF_{254}$ and PF_{360}. Flash chromatography was carried out with Merck silica gel (230-240 mesh). I.r. spectra were recorded for nujol mulls (solids) or thin films with a Perkin-Elmer 177 spectrometer. ^{1}H n.m.r spectra were determined for solutions in $CDC1_3$ with tetramethylsilane as internal standard at 60 MHz (Varian EM360A) or 90 MHz (Perkin-Elmer R32) or 360 MHz (Bruker EM360) spectrometers. Mass spectra were recorded with a Kratos MS80 spectrometer, with DS55 data system. Melting points were determined with a Kofler hot-stage microscope. Optical rotations were measured for solutions in chloroform with an Optical Activity automatic digital polarimeter AA-10.

4α,5-(1'-Methylene-ethano)-5α-cholest-3-one. (2) A solution of cholest-4-en-3-one (1) (6.0g) and allene (14g) in n-hexane (300 ml, HPLC grade) was irradiated (Hanovia 100W medium pressure Hg arc lamp) for 3 hrs at -60° C. The solvent was removed *in vacuo* and the crude product recrystallised from dichloromethane/methanol to yield the title compound (2) (4.3g, 65%), m.p. 158-159° C; $[\alpha]_D$ + 62° (c=1.3) ; υ_{max} 1695 (C=0), 1675 (C=C) cm^{-1} ; δ 5.07 (m, 2H, $R_2C{=}CH_2$, W $1/_2$ 8Hz, 0.84 (s, 3H, 10β-Me) and 0.68 (s, 3H, 13β-Me). (Found: m/z 424.3699 ($M^{+\cdot}$). C, 85 1; H, 11.4% $C_{30}H_{48}0$ requires M 424.3705). C, 84.8; H, 11.4%).

4α,5-(1'-Bromomethylethano)-5α-cholestan-3-one (3)/(4). Anhydrous HBr was bubbled through an irradiated (Hanovia 100W medium pressure Hg arc lamp) solution of the allene photo adduct (2) (3.0g) in n-hexane (100 ml) for 2 hrs. The solution was washed with aqueous sodium bicarbonate (100 ml), aqueous sodium thiosulphate (100 ml) and H_20 (100 ml), dried and evaporated *in vacuo*. Recrystallisation from dichloromethane/methanol gave a mixture of epimeric bromides (3)/(4) (3.4g, 95%) which could be used directly in the next step. Flash column chromatography (SiO_2, petrol/ether, 4:1) gave as the less polar isomer, bromide (3), m.p. 128-130° C (dichloromethane/methanol) ; $[\alpha]_D$ +98° (c 0.42) ; υ_{max} 1690 (C=0) cm^{-1}; δ 3.45 and 3.01 (m, 2H, CH_2Br), 0.81 (s, 3H, 10β-Me) and 0.66 (s, 3H, 13β-Me). (Found: m/z 506.2929/504.2944 ($M^{+\cdot}$). C,71.2;9.9% $C_{30}H_{49}0Br$ requires M 506.2947/504.2967. C, 71.1; H, 9.9%). and the more polar isomer, bromide (4), m.p. 156-158° C; $[\alpha]_D$ +24° (c 0.58); υ_{max} 1695 (C=0) cm^{-1}; δ 3.55 and 3.40 (m, 2H, CH_2Br), 0.77 (s, 3H, 10β-Me), and 0.65 (s, 3H, 13β-Me). (Found: m/z 506.2941/504.2961 ($M^{+\cdot}$) C, 71.5; H, 9.9% $C_{30}H_{49}0Br$ requires M 506.2947/504.2967. C, 71.1; H, 9.9%).

5-(Prop-2-enyl)-5α-cholestan-3-one (5) A solution of bromides (3) and (4) (8.6g) in THF (60 ml) was added dropwise to a solution of lithium (0.56g) in liquid ammonia (150 ml) and THF (60 ml) over 10 mins. Stirring was continued for an additional 15 mins then the excess lithium was quenched by addition of solid ammonium chloride. The ammonia was allowed to evaporate under a stream of nitrogen and the reaction mixture diluted with ether (150 ml). The ether solution was washed with aqueous sodium bicarbonate (50 ml) and H_20 (50ml), dried and evaporated *in vacuo*. Flash column chromatography ($Si0_2$, petrol/ether, 6:1) gave the title compound (5) (4.3g, 75%), m.p. 124-125° C (acetone) ; $[\alpha]_D$ +50° (c 0.54) ; υ_{max} 3080 (C=C-H), 1710 (C=0), 1640 (C=C) cm^{-1}; δ 5.4-6.1 (m, 1H, $RCH{=}CH_2$), 5.1 (m, 2H, $RCH{=}CH_2$), 1.21 (s, 3H, 10β-Me)

and 0.69 (s, 3H, 13β-Me). (Found: m/z 426.3852 ($M^{+\cdot}$). C, 84.1; H, 11.8% $C_{30}H_{50}0$ requires M 426.3861. C, 84.,4; H, 11.8%), and *3α,5-(1'-methylethano)-5α-cholestan-3β-ol* (6) (1.15g, 20%), m.p. 184° C (ethyl acetate); $[\alpha]_D$ +21° (c 0.77); υ_{max} 3 500 (OH) cm^{-1} ; δ 0.92 (d, 3H, bridge methyl, J=7 Hz), 0.91 (s, 3H, 10β-Me) and 0.64 (s, 3H, 13β-Me). (Found: m/z 428.4026 ($M^{+\cdot}$) C, 83.7; H, 12.2% $C_{30}H_{52}0$ requires M 428.4018. C, 84.1; H, 12.2%).

3-(Trimethylsilyloxy)-5-(prop-2-enyl)-5α-cholest-2-ene (10). Ketone (5) (2.5g) was dissolved in dimethylformamide (60 ml), triethylamine (5 ml) and trimethylsilyl chloride (5ml) and heated to reflux for 24 hrs. The cooled solution was diluted with petroleum ether (100 ml) and washed with aqueous sodium bicarbonate (50 ml). The aqueous layer was re-extracted with petroleum ether (50 ml) and the combined organic extracts were washed with dilute HCl (1M, 50 ml), aqueous sodium bicarbonate (50 ml twice) and H_20 (50 ml), dried and evaporated *in vacuo*. Recystallisation from acetone gave the title compound (10) (2.0g, 68%), m.p. 103-118° C; $[\alpha]_D$ +38° (c 0.58); υ_{max} 3080 (C=C-H), 1665 (C=C-OSiMe$_3$), 1640 (C=C) cm^{-1}; δ 5.5-6.1 (m, 1H, C*H*=CH_2), 4.7-5.2 (m, 3H, C2-H, CH=C*H*$_2$), 0.81 (s, 9H, 10β-Me, 25-Me$_2$), 0.67 (s, 3H, 13β-Me) and 0.18 (s 9H, OSiMe$_3$). (Found:m/z 498.4248 ($M^{+\cdot}$) $C_{33}H_{58}OSi$ requires 498.4258).

2ξ-(Trimethylsilyloxy)-5-(prop-2-enyl)-5α-cholestan-3-one (11) and (12). A solution of silyl enol ether (10) (2.0g) in hexane (20 ml) was added dropwise to a suspension of *m*-chloroperbenzoic acid (1.04g) in hexane (50 ml) at 0°C. The solution was warmed to room temperature and stirred for 5 hrs. The suspension was filtered and filtrate evaporated *in vacuo*. Flash column chromatography ($Si0_2$, petrol/ether, 10:1) gave the title compounds (11)/(12) (1.3g, 62%) as an oil. Further careful chromatography allowed separation of the epimers, giving as the less polar epimer *2β-(trimethylsilyloxy)-5-(prop-2-enyl)-5α-cholestan-3-one* (11), an oil; υ_{max} 1728 (C=0) cm^{-1};δ 5.5-6.0 (m, 1H, C*H*=CH_2), 4.85-5.1 (m, 2H, CH=C*H*$_2$), 4.10 (brd dd, 1H, 2α-H, J=3, 7Hz), 1.17 (s, 3H, 10β-Me); and *2α-(trimethylsilyloxy)-5-(prop-2-enyl)-5α-cholestan-3-one* (12), m.p. 131-133°C (methanol); $[\alpha]_D$ +36° (c 0.22); υ_{max} 1728 C=0) cm^{-1}; δ 5.5-6.0 (m, 1H, C*H*=CH_2), 4.85-5.1 (m, 2H, CH=C*H*$_2$), 4.15 (dd, 1H, 2β-H, J=7, 11 Hz), 0.90 (s, 3H, 10β-Me) and 0.13 (s, 9H, OSiMe$_3$). (Found: m/z 514.4197 ($M^{+\cdot}$). C, 77.0;H, 11.3% $C_{33}H_{58}0_2Si$ requires M 514.4206. C, 77.0; H, 11.6%).

Reductive cyclisation of 5-(prop-2-enyl)-5α-cholestan-3-one (5). A solution of the allyl ketone (5) (0.3g) in THF (10 ml) was added dropwise with stirring to a solution of lithium (0.019g, 4 mol. equiv.) in liquid ammonia (30 ml). Stirring continued for thirty minutes then the excess lithium was destroyed by the addition of ammonium chloride. The ammonia was removed under a stream of nitrogen and the resulting reaction mixture diluted with ether (50 ml). The ether solution was washed with sodium bicarbonate (15 ml) and water (15 ml), dried and evaporated *in vacuo*. Flash column chromatography [$Si0_2$, petrol:ether, 6:1, (v/v)] gave the allyl ketone (5) (0.115g, 38%) and *3α,5-(1'-methylethano) 5α- cholestan-3β-ol* (6) (0.139, 46%).

Thermal cyclisation of 5-(prop-2-enyl)-5α-cholestan-3-one (5). 5-(Prop-2-enyl)-5α-cholestan-3-one (0.25g) in decalin (2 ml) was heated in a sealed tube at 330°C for four hours. The decalin was evaporated *in vacuo*. Flash column chromatography [$Si0_2$, petrol:ether, 6:1 (v/v)] gave *2α, 5-(1'-methylethano-5α-cholestan-3-one* (7) (1.98g, 79%), m.p. 92-94° C (methanol); $[\alpha]_D$ +52° (c 0.765), υ_{max} 1725 (C=0) cm^{-1}, δ 0.93 (d, 3H, bridge methyl, J=7Hz), 0.86 (s, 3H, 10β-Me) and 0.67 (s, 3H, 13β-Me). (Found: m/z 426.3871 ($M^{+\cdot}$). C, 84.6; H, 12.2% $C_{30}H_{50}0$ requires M 426.3861. C, 84.4; H 12.2%).

Hydrolysis and thermal cyclisation of 2ξ-(trimethylsilyloxy)-5-(prop-2-enyl)-5α-cholestan-3-one (11) and (12).

a) In a sealed tube: a solution of the α-silyloxy-ketones (11) and (12) (1.1g) in deoxygenated decalin (20 ml) was sealed in a tube containing tetrabutylammonium fluoride on silica (2 mol. equiv. F^-) and heated at 200°C for four hours. The suspension was filtered and the filtrate washed with water (2 ml), dried and evaporated *in vacuo*. Preparative thin layer chromatography [SiO_2, petrol:ether, 3:1 (v/v)] gave *3α, 5-(1'-methylethano)-3β-hydroxy-5α-cholestan-2-one* (16) (0.59g, 7%), m.p. 139-141° (methanol), $[\alpha]_D$ +48° (c 0.682); υ_{max} 3495 (OH), 1705 (C=0) cm^{-1}, δ 3.6 (s, OH), 2.64 (quartetxd, IH, 2-H, J=14, 9 and 3Hz.), 2.25 (q, 2H, 1-H_2, J =15 Hz),1.05 (d, 3H,1'-Me, J=7 Hz), 0.91 (s, 10β-Me) and 0.65 (s, 13β- Me). (Found: m/z 422.3824 ($M^{+\cdot}$). $C_{30}H_{50}O_2$ requires M^+ 442.3811) and *2α, 5 (1'-methylethano) - 2β-hydroxy-5α-cholestan-3-one* (17) (0.230g, 27%), m.p. 110-112°C (methanol), υ_{max} 3500(OH), 1725 (C=0) cm^{-1}, δ 3.50 (s, OH), 2.91 (m, 1H, 2-H), 2.45(dd, 1H,4β-H, J = 19Hz and 3 Hz), 1.92 (d, 1H,4α-H, J = 19 Hz), 0.90 (s, 3H, 10β-Me), 0.85 (d, 3H, l'-Me, J=7Hz) and 0.66 (s, 3H, 13β-Me). (Found: m/z 442.3819 ($M^{+\cdot}$). C, 81.6; H, 11.4 % $C_{30}H_{50}O_2$ requires M^+ 442.3811. C, 81.4; H 11.4%).

b) In refluxing toluene: tetrabutylammonium fluoride on silica (2 mol. equiv. F^-) was added to a solution of the α-silyloxy ketones (11) and (12) (0.20g) in deoxygenated toluene (25 ml). The solution was heated under reflux for eighteen hours under argon, then filtered, washed with water (10 ml) dried and evaporated *in vacuo* . Preparative thin layer chromatography [SiO_2, petrol:ether, 3:1 (v/v)] *gave 3α, 5-(1'-methylethano) -β-hydroxy-5α-cholestan-2-one* (16) (0.006g, 3%) and *2α, 5-(1'-methylethano)-2β-hydroxy-5α-cholestan-3-one (17)* (0.057g, 33%).

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