Acid-catalysed Rearrangements of Steroid Alkenes. Part 1. Rearrangement of 5α-Cholest-7-ene

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In the presence of boron trifluoride–diethyl ether or anhydrous toluene-*p*-sulphonic acid–acetic acid, 5α-cholest-7-ene (**1**) is transformed into 5α-cholest-8(14)-ene (**2a**) and 5α-cholest-14-ene (**3a**) and then *via* c-ring contraction into the ring c/D-rearranged 12(13→14)*abeo*-5α-cholest-13(17)-ene (**4a**). Isomerisation at C-20 in the cholestene (**4a**) occurs giving compound (**4b**). Both can then undergo a reversal of the c-ring contraction, regenerating the cholestenes (**2a**) and (**3a**) and also forming (20*S*)-5α-cholest-8(14)-ene (**2b**) and -14-ene (**3b**). Two other rearrangement products have been identified as 14β-methyl-18-nor-5α,13β-cholest-17(20)-enes (**6a,b**). They may be formed *via* 14β-methyl-18-nor-5α-cholest-12-enes and -13(17)-enes (**5a,b**). Experiments with anhydrous toluene-*p*-sulphonic acid–*O*-deuteriated acetic acid indicate that the rearrangement occurs by a predominantly stepwise process.

Turner *et al.*[1] described the rapid conversion of 5α-cholest-7-ene (1) with toluene-*p*-sulphonic acid in acetic acid–cyclohexane at 85 °C into a non-crystalline material in which 5α-cholest-8(14)-ene (**2a**) predominated. Prolonged treatment gave rise to an oily compound which was subsequently identified as the ring C/D-rearranged 12(13→14)*abeo*-5α-cholest-13(17)-ene (**4a**).[2] As part of a wider study of the occurrence of the rearrangement in nature, we presented preliminary results for isomerisation at C-20 in the cholestene (**4a**) giving compound (**4b**) and identified both isomers and their 24-methyl (and presumed 24-ethyl) homologues in sediments with a mild thermal history.[3] In addition to isomerisation at C-20 in the cholestene (**4a**), other rearrangement processes occur and a fuller description of the rearrangement of 5α-cholest-7-ene (1) is now given.

Figure 1*a* illustrates the typical product distribution from initial treatment of 5α-cholest-7-ene (**1**) with boron trifluoride–diethyl ether (BF_3–OEt_2). The major product (63%) had a mass spectrum characteristic of the cholestene (**4a**),[2] whereas the other two significant products (16 and 7%) had spectra characteristic of authentic 5α-cholest-8(14)-ene (**2a**) and 5α-cholest-14-ene (**3a**), respectively. These three components were isolated either by silver ion-impregnated silica t.l.c. or by h.p.l.c. and their structures were confirmed by ^{1}H n.m.r. spectroscopy. The ^{13}C n.m.r. spectrum of the cholestene (**4a**) exhibited 26 signals (Table 1); sp^3-hybridised carbon types were distinguished by the DEPT technique. The ^{13}C chemical shifts of 5α-cholestane[4] were used as reference for assignment of C-1 to C-7, C-9, C-10, and C-19 and those of 5β,14β-dimethyl-18,19-dinor-8α,9β,10α-cholest-13(17)-ene [diacholest-13(17)-ene (**7a**)][5] for C-20 to C-27; C-8, C-14, and C-18 were assigned by default (the only remaining methine, quaternary, and methyl carbons, respectively), leaving four unassigned methylene resonances (C-11, C-12, C-15, and C-16) and the two unassigned sp^2-hybridised carbon resonances (C-13 and C-17).

When the reaction time was increased additional products were formed (Figure 1*b*). Silver ion t.l.c. afforded three major fractions containing mainly the cholestenes (**4a,b**) unknowns (**6a,b**), and compound (**2a**) and unknown (**2b**). H.p.l.c. on the total product afforded compounds (**2a,b**), (**3a**), (**4a,b**), and (**6a,b**) in sufficient purity for ^{1}H n.m.r. studies.

Component (**4b**) had an identical mass spectrum to the cholestene (**4a**) and was shown to be (20*S*)-12(13→14)*abeo*-5α-cholest-13(17)-ene from its ^{1}H n.m.r. spectrum which showed a 0.01 p.p.m. shielding of the 21-H_3 doublet compared with its (20*R*) counterpart (**4a**) (confirmed by running the spectrum of a mixture of the two added in different abundances[3]). The ^{13}C n.m.r. spectrum of this mixture displayed an additional 6 signals over the (20*R*)-cholestene (**4a**) itself, these being assigned to C-8, C-21, C-22, C-23, and two from C-11, C-12, C-15, and C-16 (Table 1). The isomerisation at C-20 in the 12(13→14)*abeo*-5α-cholest-13(17)-enes is analogous to that reported in the diacholest-13(17)-enes (**7a,b**).[6]

Components (**6a,b**) had almost identical mass spectra, with the major ion at *m/z* 257 corresponding to loss of the side-chain. The ^{1}H n.m.r. spectra showed the presence of a vinylic methyl at δ 1.591 (t, *J* 1.9 Hz) in compound (**6a**) and at δ 1.519 (multiplet) in compound (**6b**), assigned as the 21-H_3 resonances of the *E*- and *Z*-isomers of a $\Delta^{17(20)}$ system by comparison with (*E*)- and (*Z*)-cholesta-5,17(20)-dien-3β-ol.[7,8] Irradiation of a multiplet at δ 2.18 (16-H_2) in compound (**6a**) collapsed the vinylic methyl to a singlet. A similar experiment on compound (**6b**) resulted, however, in a somewhat broad vinylic methyl resonance. This 'extra' coupling to 21-H_3 in compound (**6b**) suggested the presence of a hydrogen at C-13 and hence a rearranged C/D ring junction. Oxidation of a mixture of compounds (**6a,b**) with osmium tetroxide followed by reduction with lithium aluminium hydride and then further oxidation with lead tetra-acetate gave an androstanone (**8**). Two methyl resonances were observed at δ 0.738 and 0.971 in the ^{1}H n.m.r. spectrum and a carbonyl stretch at 1 741 cm^{-1} in the i.r. spectrum. These properties are consistent with those previously reported for the androstanone (**8**).[9] The mass spectrum had the major ion at *m/z* 97 as expected from comparison with that of 5α,14β-androstan-15-one.[10] From these studies, compounds (**6a,b**) were assigned as the *E*-and *Z*-isomers of 14β-methyl-18-nor-5α,13β-cholest-17(20)-ene. The structure of the cholestene (**6b**) was confirmed by a combination of two-dimensional (COSY) and n.O.e. enhancement difference studies. Irradiation of the 14β-Me signal gave enhancements of 8β-H, 13β-H, and 16β-H, thereby confirming the stereochemistry at the C/D ring junction.

Component (**2b**) had an identical mass spectrum to that of compound (**2a**). The ^{1}H n.m.r. spectrum showed, however, different chemical shifts for the 18-H_3 and 21-H_3 resonances, which were shielded by 0.008 and 0.058 p.p.m. These differences are explicable in terms of isomerism at C-20. Component (**2b**) is, therefore, (20*S*)-5α-cholest-8(14)-ene. Component (**3b**) had an identical mass spectrum to that of compound (**3a**). Although it

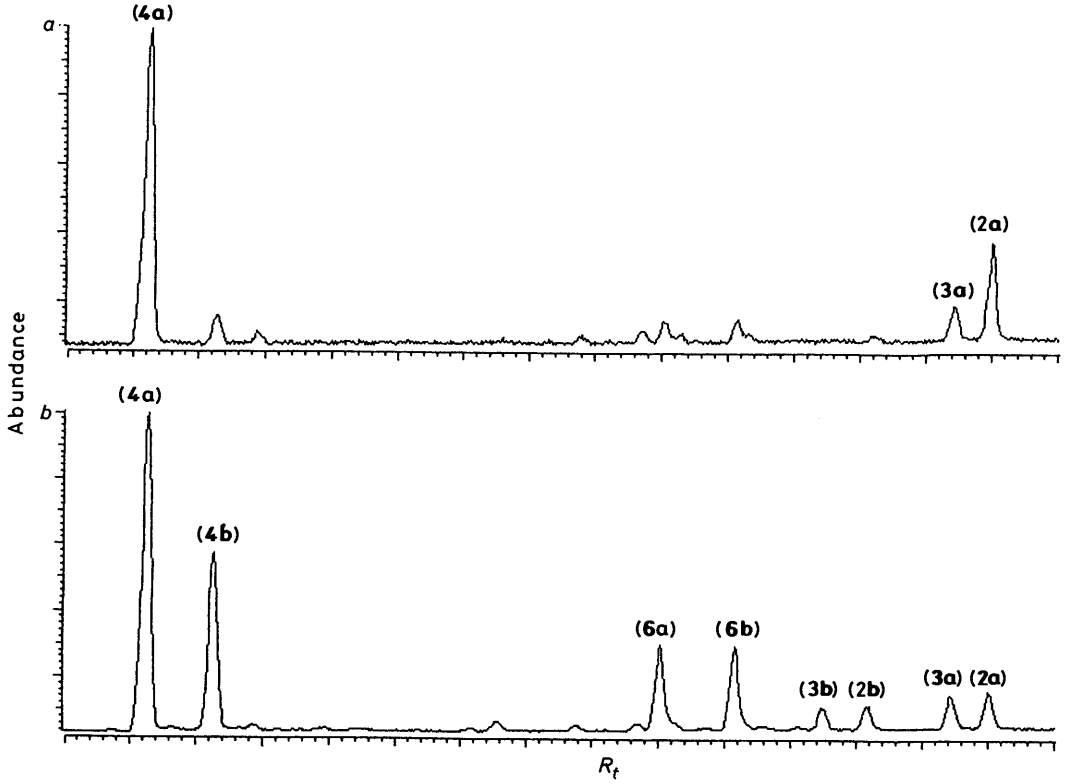


Figure 1. Reconstructed ion current chromatograms (g.l.c.–m.s., 30 m DB-17) of products from isomerisation of 5α-cholest-7-ene (**1**) with BF_3–OEt_2: *a*, short-term treatment (20 min) and *b*, longer-term treatment (45 min)

was not isolated in sufficient purity for ^1H n.m.r. analysis, the structural relationship between the other components (*i.e.*, isomerism at C-20) indicates that compound (**3b**) is (20*S*)-5α-cholest-14-ene.

The transformations were conveniently followed using anhydrous TsOH–HOAc for periods of up to 12 days. The products were analysed by g.l.c. using *n*-C_{24} as internal standard. No significant loss of steroidal material occurred and the product distributions are summarised in Table 2.

Further information about the transformations was obtained by following the rearrangement in anhydrous TsOH–*O*-deuteriated acetic acid (DOAc)[11] (*cf.* Table 2). The deuterium contents of the major fragment ions of the components (gas liquid chromatography–mass spectrometry, g.l.c.–m.s.) over the heating periods are summarised in Table 3. The 7-day reaction was repeated and the products were fractionated by silver ion t.l.c. The ^1H n.m.r. spectrum of the mixture of compounds (**4a,b**) confirmed substantial deuterium incorporation (*cf.* Table 3), with the resonances for 16-H_2, 18-H_3, 20-H, and 21-H_3 having essentially disappeared. The spectrum of the mixture of compounds (**6a,b**) displayed similar features. The ^{13}C n.m.r. spectrum of the mixture of compounds (**4a,b**) (Table 1) established the sites of incorporation at C-7 to C-9, C-11, C-12, C-15, C-16, C-18, and C-20 to C-22 (Figure 2). Similar sites of incorporation would be expected in the other components (*cf.* Table 3).

The rearrangement products can be envisaged as being formed by a series of carbocation–alkene interconversions.[11] Thus, the double bond in 5α-cholest-7-ene (**1**) can migrate from C-7 to C-8(14) and then to C-14 (Scheme). The incorporation of up to 9 deuterium atoms in the ring system of compounds (**2a**) and (**3a**) after only 8 hours treatment with anhydrous TsOH–DOAc (Table 3) suggests the presence of other short-lived alkene intermediates [Δ^8, $\Delta^{9(11)}$, in addition to the Δ^7 alkene]. The observation that the $\Delta^{8(14)}$ and Δ^{14} components are the most stable of the non-rearranged alkenes within this series is in agreement with recent molecular mechanics calculations.[12] Before equilibration of compounds (**2a**) and (**3a**) is reached, rearrangement to compound (**4a**) occurs *via* a 12-CH_2 shift to a C-14 carbocation.[2] The equilibrium ratio of compounds (**2a**):(**3a**) would appear to be reached only after a significant proportion of compounds (**4a,b**) are formed and is taken as 53:47 (Figure 1*b*).

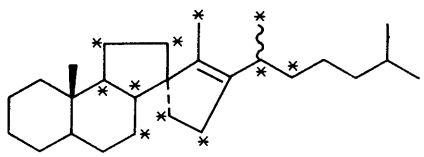
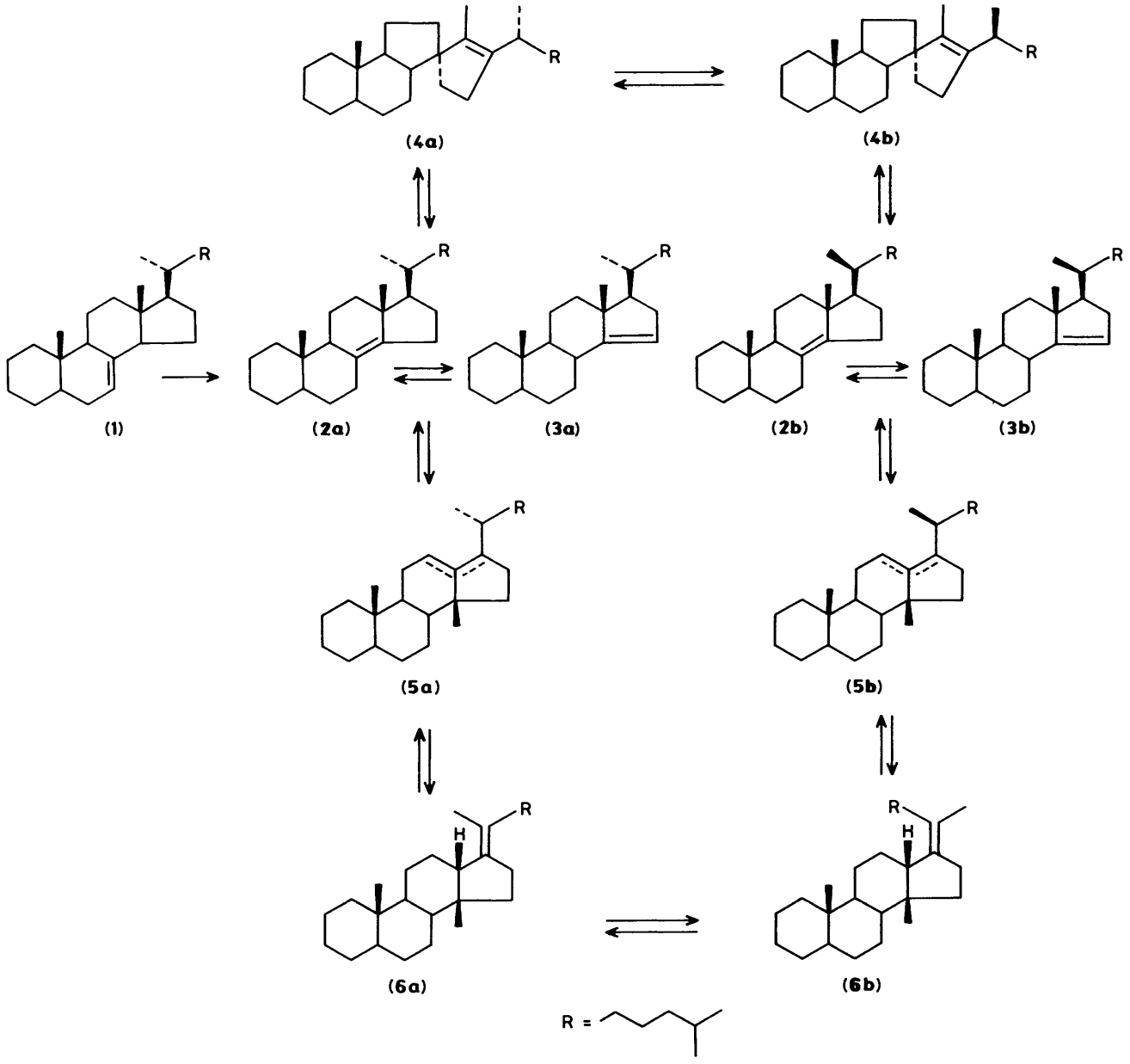


Figure 2. Location of deuterium (*) in 12(13→14)*abeo*-5α-cholest-13(17)-enes (**4a,b**) from rearrangement of 5α-cholest-7-ene (**1**) with anhydrous TsOH–DOAc (70 °C, 7 days)

Isomerisation at C-20 in the cholestene (**4a**) may then proceed in an analogous manner to that reported for the diacholest-13(17)-enes (**7a,b**) *via* transient $\Delta^{17(20)}$, Δ^{20}, and $\Delta^{20(22)}$ species,[11] a hypothesis confirmed by deuterium incorporation at C-20, C-21, and C-22 (Table 1).

Protonation at the α-face of C-17 in the cholestenes (**4a,b**) followed by a reversal of the C-ring contraction step is required to account for the appearance of the cholestenes (**2b**) and (**3b**) and the presence of deuterium in the side-chain of the cholestenes (**2a,b**), (**3a,b**) (compare *m/z* 370 *vs. m/z* 257 in Table 3). Thus, compound (**4a**) can regenerate the cholestenes (**2a**) and (**3a**), and compound (**4b**) gives rise to the cholestenes (**2b**) and (**3b**). Similarly, protonation at the β-face of C-17 in compounds (**4a,b**) followed by a reversal of the C-ring contraction step could give rise to 17β(H)-steroid 8(14)-enes and -14-enes (**9a,b** and **10a,b**). Although these alkenes were not observed, evidence for their presence as minor products of the rearrangement came

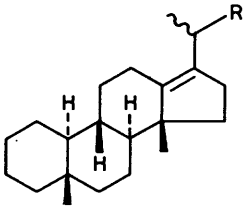


Scheme. Acid-catalysed rearrangement of 5α-cholest-7-ene (**1**)

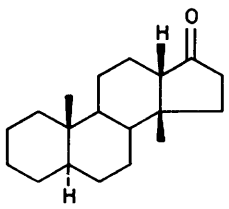
from hydrogenation of compounds (**4a,b**) in acidic media (see later).

The $\Delta^{17(20)}$ components (**6a,b**) may be formed *via* intermediates of type (**5**) (although these are rather strained[2]). A two-step concerted process from compounds (**9a,b** and **10a,b**) can also be envisaged involving a 13-Me shift to a C-14 carbonium ion, a 1,2-H shift from C-17, and finally loss of the proton from C-20. Treatment of compound (**10a**) itself with TsOH–HOAc, however, gave identical product distributions to those obtained from 5α-cholest-7-ene (**1**) (*cf.* Table 2) which would seem to indicate a preference through intermediates of type (**5**). The presence of such intermediates would account for deuterium incorporation at C-12 (Figure 2; Table 1). Since compounds (**6a,b**) were always present in a *ca.* 1:1 ratio (Table 2), even when the 12(13→14)*abeo*-5α-cholest-13(17)-enes were only *ca.* 20% isomerised to each other (*e.g.* 24-h reaction in Table 2), then it is likely that they are rapidly isomerised to each other. The transformation pathways resulting from acid-catalysed rearrangement of the cholestene (**1**) are summarised in the Scheme. The $\Delta^{17(20)}$ components would appear to be the most thermodynamically stable species observed under the conditions used. Longer-term treatment of the cholestene (**1**), however, with BF_3–OEt_2 (or by carrying out the rearrangement with trifluoroacetic acid) resulted in the formation of further unidentified rearrangement products,[13] suggesting that thermodynamic equilibrium has not been reached at the stage of the 12-day reaction in Table 2.

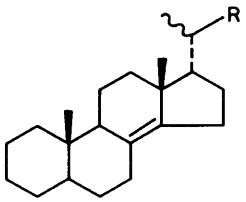
Prior to our identification of compounds (**4a,b**) and homologues in sediments with a mild thermal history,[3] the interest in such species lay in their proposed intermediacy in the transformation of steroidal 7-, 8(14)-, and 14-enes into 17β(H)-steroid 14-enes.[14–17] Indeed, treatment of the cholestene (**1**) with hydrogen chloride at low temperatures always gave (after dehydrochlorination) small amounts of compound (**4a**) in addition to varying amounts (as previously described[14,15]) of compounds (**10a**) and (**3a**).



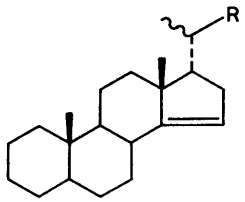
(20*R*)-(**7a**)
(20*S*)-(**7b**)



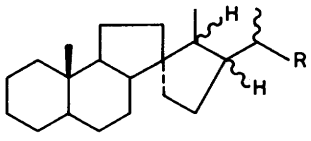
(**8**)



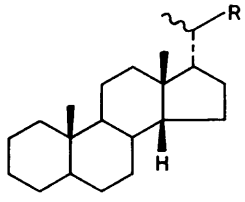
(20*R*)-(**9a**)
(20*S*)-(**9b**)



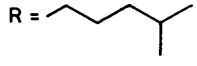
(20*R*)-(**10a**)
(20*S*)-(**10b**)



(**11**)



(20*R*)-(**12a**)
(20*S*) (**12b**)



Hydrogenation of 17β(H)-steroid 14-enes yields 5α,14β,17β(H)-steroids.[14,18] Hydrogenation of a mixture of compounds (**4a,b**) under acidic conditions afforded 10 major components. Eight had almost identical mass spectra and may be 12(13→14)*abeo*-5α-cholestanes (**11**) isomeric at C-13, C-17, and C-20. The other two had mass spectra and g.l.c. retention times characteristic of 5α,14β,17β(H)-cholestanes (**12a,b**).[19,20] Presumably they result from hydrogenation of the cholestenes (**10a,b**) which were formed under the acidic conditions in the hydrogenation and 'trapped-out' by reduction to the cholestanes (**12a,b**). 5α-Cholestane and (20*S*)-5α-cholestane were also recognised as minor hydrogenation products [being formed from compounds (**3a,b**)] from their mass spectra and g.l.c. retention times. The significance of these observations is in accord with our recent hypothesis regarding the natural formation of 5α,14β,17β(H)-steroid alkanes in sediments.[21,22]

Experimental

N.m.r. spectra were obtained on a variety of instruments: a Jeol FX90Q spectrometer operating at 22.5 MHz for ^{13}C; a Jeol FX200 operating at 200 MHz, a Jeol GX270 operating at 270 MHz and a Bruker WH-400 operating at 400 MHz for ^{1}H. Spectra were recorded in $CDCl_3$ using Me_4Si as internal standard; 2-D and n.O.e. enhancement experiments were performed on the Bruker WH-400. I.r. spectra were obtained on a Perkin-Elmer 1420 spectrophotometer as liquid films on NaCl plates. G.l.c. was performed on a Carlo Erba Mega 5160 chromatograph (on-column injection) fitted with a 25 m OV-1 fused silica capillary column obtained from Hewlett Packard. Hydrogen was the carrier gas. Samples were injected in hexane at 40 °C and programmed to 300 °C at 4 °C min^{-1}. G.l.c.–m.s. was performed on a Carlo Erba Mega 5160 chromatograph fitted with either a 25 m OV-1 fused silica capillary column from Hewlett Packard or a 30 m DB-17 fused silica capillary column obtained from J & W. The g.l.c. conditions were similar to those described above. The chromatograph was interfaced to a Finnigan 4000 mass spectrometer (ionising temperature *ca.* 250 °C; electron energy 35 eV; emission current 350 μA; accelerating voltage *ca.* 2 kV). The scan range was *m/z* 50—450 with a cycle time of 1 s. Data collection was performed using a Finnigan Incos 2300 data system. Semi-preparative h.p.l.c. was performed using a Waters 6000A pump fitted with a Rheodyne 7125 injector (25 μl loop). A LDC Refractometer III was used as detector. The column (Spherisorb 5W ODS2; 250 mm × 10 mm i.d.) was obtained from Phase Separations Ltd. The mobile

Table 1. ^{13}C N.m.r. assignments for 12(13→14)*abeo*-5α-cholest-13(17)-enes (**4a,b**) and compounds used to aid assignments[4,5]

Carbon	5α-Cholestane	(**7a**)	(**4a**)	(**4b**)	(**4a**) + (**4b**)[a]
1	39.2		39.9	39.9	39.9
2	22.4		21.8	21.8	21.9
3	27.1		27.2	27.2	27.2
4	29.4		28.4	28.4	28.4
5	47.2		47.3	47.3	47.3
6	29.6		29.5	29.5	29.3[b,c]
7	32.4		32.8	32.8	*d*
8			45.1	45.0	*d*
9	47.1		54.6	54.6	*d*
10	36.4		36.5	36.5	36.5
11			*e*	*e*	*d*
12			*e*	*e*	*d*
13			*f*	*f*	*d*
14			60.0	60.0	*d*
15			*e*	*e*	*d*
16			*e*	*e*	*d*
17			*f*	*f*	*d*
18			9.5	9.5	*d*
19	12.3		11.4	11.4	11.4
20		31.5	32.6	32.6	*d*
21		20.3	19.7	19.9	19.6/19.8[b,g]
22		35.9	35.9	35.7	*d*
23		25.5	25.6	25.5	25.5/25.6[c]
24		39.1	39.2	39.2	39.2
25		28.0	28.0	28.0	28.0
26		22.6	22.6	22.6	22.6
27		22.7	22.6	22.6	22.6

[a] Rearrangement of 5α-cholest-7-ene (**1**) with anhydrous TsOH–DOAc (70 °C, 7 days). [b] Isotope shift due to deuterium incorporation at adjacent carbon. [c] Intensity slightly reduced compared with non-deuteriated species. [d] No resonance observed. [e] (**4a**): 22.2, 26.4, 28.6, or 35.2. (**4b**) 22.1, 26.4, 28.6, or 35.1. [f] 134.0 or 139.7. [g] Intensity greatly reduced compared with non-deuteriated species.

Table 2. Product distributions[a] from rearrangement[b] of 5α-cholest-7-ene (**1**)

Reaction time	Component (%) (**2a**) + (**3a**)[c]	(**2b**) + (**3b**)[c]	(**4a**)	(**4b**)	(**6a**)	(**6b**)
4 h	36	*d*	61	*d*	*d*	*d*
8 h	17	*d*	81	*d*	*d*	*d*
24 h	15	3	61	12	3	3
2 days	13	5	52	17	6	6
3 days	9	5	46	21	9	9
7 days	3	3	19	18	25	28
12 days	*d*	*d*	13	10	35	35

[a] Calculated from peak areas using g.l.c. on OV-1. [b] Anhydrous TsOH–HOAc at 70 °C. [c] Co-elution on column used. [d] Not detected.

Table 3. Deuterium contents (min., mode, max.)[a] of ions of components formed by rearrangement[b] of 5α-cholest-7-ene (**1**)

Reaction time	Component	121	206	219	257	370
4 h	(**2a**) + (**3a**)[c]	*d*	*d*	*d*	1,5,7	1,5,7
	(**4a**)	0,2,4	0,2,4	0,2,5	*d*	1,5,7
8 h	(**2a**) + (**3a**)[c]	*d*	*d*	*d*	1,6,9	2,6,9
	(**4a**)	0,3,5	0,3,5	0,3,6	*d*	1,6,9
24 h	(**2a**) + (**3a**)[c]	*d*	*d*	*d*	1,9,13	4,9,13
	(**4a**)	1,5,8	1,5,8	1,5,9	*d*	4,9,13
	(**4b**)	3,7,10	3,7,11	7,10,14	*d*	7,10,16
3 days	(**2a**) + (**3a**)[c]	*d*	*d*	*d*	7,11,15	9,12,15
	(**2b**) + (**3b**)[c]	*d*	*d*	*d*	8,11,15	11,13,19
	(**4a**)	4,7,10	4,7,10	4,7,11	*d*	7,11,16
	(**4b**)	6,9,12	6,9,13	6,9,14	*d*	10,13,20
	(**6a**)	*d*	*d*	*d*	7,11,14	11,15,19
	(**6b**)	*d*	*d*	*d*	7,11,14	10,15,19
7 days	(**2a**) + (**3a**)[c]	*d*	*d*	*d*	7,12,15	12,17,21
	(**2b**) + (**3b**)[c]	*d*	*d*	*d*	8,12,15	12,17,21
	(**4a**)	7,11,13	7,13,15	7,13,16	*d*	12,17,20
	(**4b**)	7,11,13	7,13,15	8,13,16	*d*	12,17,21
	(**6a**)	*d*	*d*	*d*	8,12,15	12,17,21
	(**6b**)	*d*	*d*	*d*	8,12,15	11,17,21

[a] Determined from g.l.c.–m.s. on OV-1. [b] Anhydrous TsOH–DOAc at 70 °C. [c] Co-elution on column used. [d] Ion absent.

phase was 10% water–acetone at 4 ml min^{-1}. Typical loading was 2 mg of steroid alkenes in CH_2Cl_2.

Typical Work-up.—This involved dilution with water, followed by extraction with CH_2Cl_2 (×3). The combined extracts were neutralised with aqueous $NaHCO_3$, dried (Na_2SO_4), filtered, and the solvent evaporated under reduced pressure. The residue was chromatographed on alumina. Elution with hexane afforded the steroid alkene products.

Isomerisation of 5α-Cholest-7-ene (**1**) *with* BF_3–OEt_2.—*Short-term treatment.* BF_3–OEt_2 (5 ml) was added to 5α-cholest-7-ene (**1**) (1.0 g) in dry toluene (100 ml) and the solution shaken, left for 20 min, and worked up. Silver ion-impregnated silica t.l.c. (5% $AgNO_3$; hexane development) on an aliquot afforded 2 major bands. The lower (R_F 0.31—0.46) contained 12(13→14)*abeo*-5α-cholest-13(17)-ene (**4a**) in 94% purity (g.l.c.) and the upper (R_F 0.69—0.75) 5α-cholest-8(14)-ene (**2a**) in 86% purity. H.p.l.c. of aliquots afforded 3 components, all in >95% purity: 12(13→14)*abeo*-5α-cholest-13(17)-ene (**4a**) (R_t 26 min); 5α-cholest-14-ene (**3a**) (R_t 38 min); and5α-cholest-8(14)-ene (**2a**) (R_t 39 min).

12(13→14)*abeo*-5α-Cholest-13(17)-ene (**4a**) had: *m/z* 370 ($M^{+\cdot}$, 2%), 219 (14, cleavage through C_8–C_{14} and C_9–C_{11}), 206 (100, cleavage through C_8–C_{14} and C_{11}–C_{12}), and 121 (56, cleavage from *m/z* 206 through C_{20}–C_{22}); δ_H(200 MHz) 0.748 (3 H, s, C-19), 0.835 (6 H, d, *J* 6.4 Hz, C-26 and -27), 0.932 (3 H, d, *J* 6.8 Hz, C-21), 1.470 (3 H, dd, *J* 2 Hz, C-18), *ca.* 2.0 (2 H, m, C-16), and *ca.* 2.5 (1 H, m, C-20).

5α-Cholest-8(14)-ene (**2a**) had: *m/z* 370 ($M^{+\cdot}$, 100%), 355 (32, $M^{+\cdot}$ – Me), 257 (40, cleavage through C_{17}–C_{20}), 231 (23, cleavage through C_{13}–C_{17} and C_{15}–C_{16}), and 215 (56, cleavage through C_{13}–C_{17} and C_{14}–C_{15}); δ_H(200 MHz) 0.650 (3 H, s, C-19), 0.826 (3 H, s, C-18), 0.853 (6 H, d, *J* 6.6 Hz, C-26 and -27), and 0.920 (3 H, d, *J* 6.6 Hz, C-21). These were identical with those for a sample prepared by a standard method.[23]

5α-Cholest-14-ene (**3a**) had: *m/z* 370 ($M^{+\cdot}$, 3%), 355 (2, $M^{+\cdot}$ – Me), and 257 (100, cleavage through C_{17}–C_{20}); δ_H(200 MHz) 0.792 (3 H, s, C-19), 0.867 (6 H, d, *J* 6.6 Hz, C-26 and -27), 0.898 (3 H, s, C-18), 0.910 (3 H, d, *J* 6.6 Hz, C-21), and 5.15 (1 H, br s, C-15). These were identical with those for a sample prepared by a standard method.[23]

Longer-term treatment. BF_3–OET_2 (5 ml) was added to 5α-cholest-7-ene (**1**) (1.0 g) in dry toluene (100 ml) and the solution shaken, left for 45 min, and worked up. Silver ion t.l.c. on an aliquot afforded 3 major bands. The lowest (R_F 0.26—0.47) contained mainly 12(13→14)*abeo*-5α-cholest-13(17)-enes (**4a,b**), the middle (R_F 0.68—0.83) mainly 14β-methyl-18-nor-5α,13β-cholest-17(20)-enes (**6a,b**), and the upper (R_F 0.86—0.93) mainly 5α-cholest-8(14)-enes (**2a,b**). H.p.l.c. of aliquots afforded 7 components, all in >85% purity: 12(13→14)*abeo*-5α-cholest-13-(17)-ene (**4a**) (R_t 26 min); (20*S*)-12(13→14)*abeo*-5α-cholest-13(17)-ene (**4b**) (R_t 27.5 min); 14β-methyl-18-nor-5α,13β-cholest-17(20*E*)-ene (**6a**) (R_t 30 min); 14β-methyl-18-nor-5α,13β-cholest-17(20*Z*)-ene (**6b**) (R_t 31 min); (20*S*)-5α-cholest-8(14)-ene (**2b**) (R_t 35.5 min); 5α-cholest-14-ene (**3a**) (R_t 38 min); and 5α-cholest-8(14)-ene (**2a**) (R_t 39 min).

(20*S*)-12(13→14)*abeo*-5α-Cholest-13(17)-ene (**4b**) had [*cf.* (**4a**)]: *m/z* 370 (2%), 219 (15), 206 (100), and 121 (57); δ_H(200 MHz) 0.746 (3 H, s, C-19), 0.835 (3 H, d, *J* 6.6 Hz, C-27), 0.841 (3 H, d, *J* 6.6 Hz, C-26), 0.922 (3 H, d, *J* 7.1 Hz, C-21), 1.469 (3 H, dd, *J* 2 Hz, C-18), *ca.* 2.0 (2 H, m, C-16), and *ca.* 2.5 (1 H, m, C-20).

14β-Methyl-18-nor-5α,13β-cholest-17(20*E*)-ene (**6a**) had: *m/z* 370 ($M^{+\cdot}$, 45%), 355 (11, $M^{+\cdot}$ – Me), and 257 (100, cleavage through C_{17}–C_{20}); δ_H(200 MHz) 0.721 (3 H, s, C-19), 0.833 (3 H, d, *J* 0.4 Hz, 14β-Me), 0.854 (6 H, d, *J* 6.6 Hz, C-26 and -27), 1.591 (3 H, t, *J* 1.9 Hz, C-21), and *ca.* 2.18 (2 H, m, C-16).

14β-Methyl-18-nor-5α,13β-cholest-17(20*Z*)-ene (**6b**) had [*cf.* (**6a**)]: *m/z* 370 (45%), 355 (11), and 257 (100); δ_H(400 MHz) 0.721 (3 H, s, C-19), 0.828 (3 H, d, *J* 0.4 Hz, 14β-Me), 0.856 (3 H, d, *J* 6.6 Hz, C-27), 0.858 (3 H, d, *J* 6.6 Hz, C-26), 1.519 (3 H, m, C-21), *ca.* 1.97 (1 H, m, C-8), *ca.* 1.71 (1 H, m, C-13), and *ca.* 2.17 (2 H, m, C-16).

(20*S*)-5α-Cholest-8(14)-ene (**2b**) had [*cf.* (**2a**)]: *m/z* 370 (100%), 355 (37), 257 (42), 231 (21), and 215 (59); δ_H(270 MHz) 0.650 (3 H, s, C-19), 0.818 (3 H, s, C-18), 0.856 (6 H, d, *J* 6.6 Hz, C-26 and -27), and 0.862 (3 H, d, *J* 6.6 Hz, C-21).

(20*S*)-Cholest-14-ene (**3b**) had [*cf.* (**3a**)]: *m/z* 370 (2%), 355 (2), and 257 (100).

Isomerisation of 5α-Cholest-7-ene (**1**) *with Anhydrous* TsOH–HOAc (DOAc).—Anhydrous TsOH–HOAc was prepared by heating TsOH (10 g) under reflux in HOAc (350 ml) and cyclohexane (100 ml) in a distillation apparatus until the temperature reached 117 °C. The remaining solution was allowed to cool and used as required. A series of reacti-vials (1 ml; Pierce) containing 5α-cholest-7-ene (**1**) (5 mg) and anhydrous TsOH–HOAc (DOAc) (0.5 ml) was heated at 70 °C (heating block) for various periods of time. The contents of each vial were then worked up. The large-scale isomerisation of 5α-cholest-7-ene (**1**) (200 mg) with anhydrous TsOH–DOAc (200 ml) was carried out in a sealed flask (70 °C, 7 days). After work-up, the alkene products were fractionated by silver ion t.l.c. as described above.

Oxidation of 14β-Methyl-18-nor-5α,13β-cholest-17(20)-enes (**6a,b**).—OsO_4 (50 mg) was added to the alkenes (20 mg) in dry pyridine (5 ml) and the mixture left at ambient temperature (7 days). After evaporation of solvent under reduced pressure, the residue was heated under reflux (2 h) with $LiAlH_4$ (20 mg) in fresh, dry Et_2O (15 ml). The reaction mixture was worked up by dropwise addition of wet methanol to destroy the excess of reagent, addition of HCl (1M, 10 ml), extraction with CH_2Cl_2, neutralisation with aqueous $NaHCO_3$, drying (Na_2SO_4), and then evaporation of solvent to afford the crude diols (20 mg). These were treated (24 h) with $Pb(OAc)_4$ (160 mg) in t-butyl alcohol–HOAc (1:1, v/v, 5 ml) at room temperature. The reaction mixture was worked up by addition of a few drops of ethanediol to destroy the excess of reagent, dilution with water

(10 ml), extraction with CH_2Cl_2, neutralisation with aqueous $NaHCO_3$, drying (Na_2SO_4), and then evaporation of the solvent. The residue was chromatographed on a small column of alumina. Elution with hexane–CH_2Cl_2 (10:1, v/v) afforded the crude 14β-methyl-18-nor-5α,13β-androstan-17-one (**8**) which had: *m/z* 274 ($M^{+\bullet}$, 12%), 259 (7, $M^{+\bullet}$ − Me), and 97 (100, cleavage through C_8–C_{14} and C_{12}–C_{13}); δ_H(200 MHz) 0.739 (3 H, s, C-19) and 0.971 (3 H, s, 14β-Me); $\nu_{max.}$ 1 741 cm^{-1} (C=O).

Hydrogenation of 12(13→14)abeo-5α-*Cholest*-13(17)-*enes* (**4a,b**).—The alkenes (5 mg) in HOAc (5 ml) containing a few drops of $HClO_4$ were hydrogenated (2 h) over PtO_2 (50 mg). After work-up, the products were analysed by g.l.c.–m.s. Eight of the products (90%) typically had: *m/z* 372 ($M^{+\bullet}$, 35—41%), 357 (5—7, $M^{+\bullet}$ − Me), 259 (9—26, cleavage through C_{17}–C_{20}), and 189 (100, cleavage through C_{13}–C_{14} and C_{14}–C_{15}). The other two major products (6%) (**12a,b**) had: *m/z* 372 ($M^{+\bullet}$, 15%), 357 (7, $M^{+\bullet}$ − Me), 217, 218, and 219 (42, 100, and 33, cleavage through C_{13}–C_{17} and C_{14}–C_{15}).

Isomerisation of 5α-*Cholest*-7-*ene* (**1**) *with* HCl.—HCl gas was bubbled (6 h) through a solution of 5α-cholest-7-ene (**1**) (200 mg) in OEt_2 (20 ml) at various temperatures (−30 to −78 °C). The reaction product was allowed to warm to room temperature and worked up. The residue was stirred (24 h) with $NaHCO_3$–acetone at room temperature and worked up. G.l.c.–m.s. analysis of the steroid alkene products always indicated the presence of 12(13→14)*abeo*-5α-cholest-13(17)-ene (**4a**) (*ca.* 8%), 5α-cholest-14-ene (**3a**), and 5α,17β(H)-cholest-14-ene (**10a**) in varying abundances depending on the temperature [(**3a**) predominating at −30 °C and (**10a**) at −78 °C].[14,15] Compound (**10a**) had: *m/z* 370 ($M^{+\bullet}$, 6%), 355 (38, $M^{+\bullet}$ − Me), and 257 (100, cleavage through C_{17}–C_{20}); δ_H(200 MHz) 0.814 (3 H, d, *J* 6.6 Hz, C-21), 0.827 (3 H, s, C-19), 0.868 (6 H, d, *J* 6.6 Hz, C-26 and -27), 1.102 (3 H, s, C-18), and *ca.* 5.07 (1 H, br s, C-15).

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