Novel Backbone Rearrangement of Steroids: Formation of (20*R* and 20*S*) 1β,14β-Dimethyl-18,19-dinor-5β,8α,9β,10α-cholest-13(17)-enes

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Two new 1-methyl rearranged sterenes were formed from cholestan-3β-ol and related compounds by a novel backbone reaction, catalysed by K10-montmorillonite; their structures were determined by ^1H and ^{13}C n.m.r. spectroscopy.

Under acidic conditions cholest-5-ene undergoes extensive isomerization reactions[1] leading, in particular, to $\Delta^{13(17)}$-compounds by the well known backbone rearrangement.[2—5] $\Delta^{13(17)}$ Rearranged sterenes ('diasterenes') have also been reported to occur in immature sediments where they are presumably formed by rearrangement of cholestenes catalysed by clay minerals.[5—7] Furthermore laboratory experiments have shown that montmorillonite clays are the most efficient catalysts for converting cholest-5-ene into backbone rearranged products.[8] We report here the occurrence of a novel backbone rearrangement of steroids leading to 1β,14β-dimethyl-18,19-dinor-5β,8α,9β,10α-cholest-13(17)-enes, the formation of which implies a carbocation migration pathway *via* C(1).

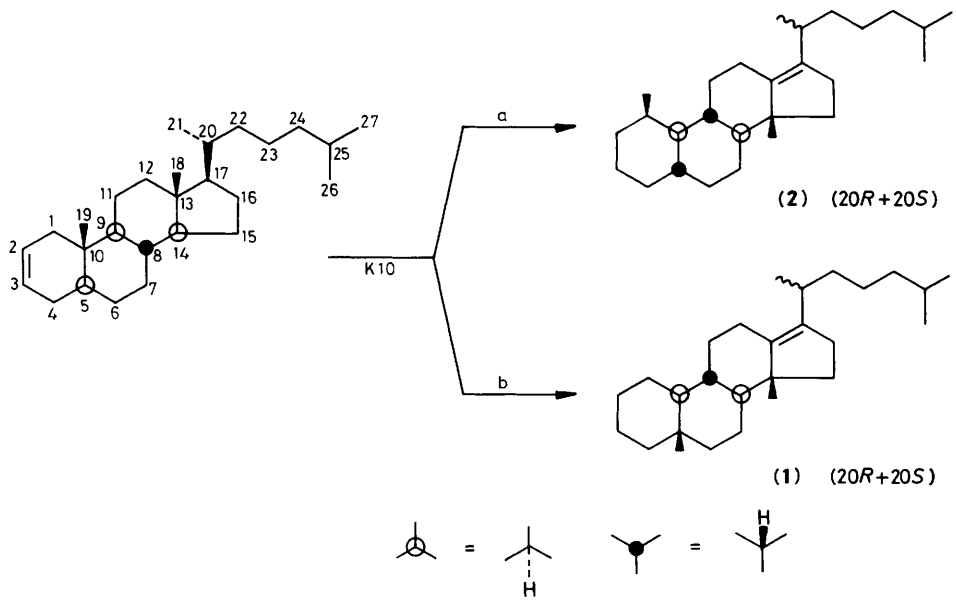
Typically, heating of cholestan-3β-ol (1 g) in refluxing cyclohexane (50 ml) for one hour in the presence of K10-montmorillonite (FLUKA; 5 g) produced cholest-2-ene which was in turn rapidly converted into a mixture of isomeric sterenes. After work-up[8] this mixture (85% of starting material) was shown by g.c. to contain four major components. Two of them (40% of the reaction product) were the previously described 5β,14β-dimethyl-18,19-dinor-8α,9β,10α-cholest-13(17)enes (20*R* and 20*S*), (**1**) ('diasterenes'). These compounds are formed by migration of a C(2) [or C(3)] carbenium ion towards C(5), followed by a classical backbone rearrangement and epimerization at C(20) (Figure 1).

The two other major products (30% of reaction mixture) were sterenes of unknown structures displaying the same mass spectra as diasterenes (**1**) [electron impact, 70 eV, *m/z* 370 (7%, M^+), 257 (100%, $M^+ - C_8H_{17}$)] from which it was difficult to separate them by usual chromatographic methods.

The same reaction mixture was obtained when cholestan-3β-ol was replaced by cholest-2-ene. However, when cholest-1-ene was used as the starting material the proportion of the new compounds was highly increased; they indeed became three times more important than diasterenes (**1**). With cholestan-1α-ol[9] they were the major products (30—40%) accompanied by only traces of (**1**).

These observations suggested, along with the similarity of chromatographic properties and mass spectra with those of (**1**), that the unknown sterenes were also backbone rearranged products, but formed by a different route implying a carbenium ion migration *via* C(1) instead of C(5). Indeed in such a rearrangement the angular C(19) methyl group would be shifted from C(10) to C(1) and the carbenium ion would migrate along the backbone as for classical diasterenes by a series of reversible carbocation–alkene interconversions[5,10,11] leading finally to the thermodynamically more stable products (Scheme 1).

The experiment with cholestan-1α-ol allowed the preparation of the new sterenes as a mixture of 20*R* and 20*S* diastereoisomers which were separated by t.l.c. ($AgNO_3$–SiO_2, elution with hexane–methylene chloride, 2:1) and further purified by reverse phase h.p.l.c. (RP-18, Merck, elution with acetone–water, 9:1). As in the case of the known diasterenes (**1**), the new products were obtained as oils. Their structure was established by ^1H and ^{13}C n.m.r. on the 20*S* isomer (**2**). Spectra and chemical shifts of (**2**) (20*S*) were



Scheme 1. Backbone rearrangement pathways of cholest-2-ene on K10 montmorillonite: (a) *via* C(1); (b) *via* C(5).

Table 1. ^{13}C and ^{1}H chemical shifts for classical (**1**) and new (20*S*)-diasterenes (**2**) in C_6D_6 solutions. Chemical shifts were measured with respect to C_6D_6 or to C_6HD_5 and converted to the Me_4Si scale by $\delta_C = \delta_{meas.} + 128$ p.p.m.; $\delta_H = \delta_{meas.} + 7.15$ p.p.m.

Carbon number	(20*S*)-Diasterene (**1**)		(20*S*)-Diasterene (**2**)	
	δ ^{13}C	δ ^{1}H	δ ^{13}C	δ ^{1}H
1	24.81	0.92—1.66	28.30	2.03
2	27.72	1.13—1.73	34.45	1.36—1.53
3	22.03	1.42—1.48	20.73	1.40
4	42.73	1.05—1.33	35.49	0.86—1.67
5	34.15		38.61	1.13
6	42.42	1.08—1.37	35.24	0.93—1.63
7	22.57	1.35—1.44	27.42	1.18—1.56
8	56.16	0.89	55.24	0.96
9	36.84	1.22	35.25	1.24
10	51.05	0.71	51.32	0.74
11	31.86	0.69—1.90	30.86	0.76—1.97
12	23.25	1.80—2.41	23.18	1.88—2.47
13	141.78		141.77	
14	50.82		50.66	
15	38.41	1.48—1.69	38.43	1.55—1.73
16	28.47	2.15—2.28	28.42	2.18—2.33
17	134.12		134.15	
18	18.43	0.96	18.66	0.97
19	17.16	0.85	12.68	0.85
20	32.14	2.49	32.12	2.53
21	20.06	0.98	20.04	1.02
22	36.05	1.30—1.34	35.97	1.33
23	26.14	1.24—1.30	26.11	1.23—1.38
24	39.53	1.17	39.43	1.19
25	28.35	1.53	28.36	1.55
26	23.04	0.91	22.93	0.91
27	22.90	0.91	22.79	0.91

compared with those of the known diasterene (**1**) (20*S*). For the latter the ^{13}C signal assignments were essentially in agreement with those published previously,[12] except for a notable difference observed for C(5), also pointed out recently by Peakman *et al.*[5] They resulted from 2D-INADEQUATE experiments, whereas the corresponding proton signal assignments were obtained from COSY δ ^{13}C/δ ^{1}H experiments (Table 1). The well resolved signals of H(12e), H(16), H(16'), H(11e), H(12a), H(15) and H(11a) (in $CDCl_3$ solution) allowed the measurements of the ^{3}J coupling constants, which were in agreement with a ring *C* in chair conformation and a *B*/*C trans* ring junction ($J_{11a—9a}$ 12.5 Hz; $J_{11e—9a}$ 4.1 Hz; $J_{11a—12a}$ 12.5 Hz; $J_{11a—12e}$ 4.0 Hz; $J_{11e—12a}$ 4.2 Hz; $J_{11e—12e}$ 2.4 Hz), and of the highly stereospecific ^{5}J coupling constants between H(12a) and H(16) and H(16') (4.4 and 2.0 Hz, respectively). The identity of the coupling patterns of diasterene (**1**) and of the new compound (**2**) clearly indicated that the *B*/*C* ring junction and the stereochemistry at C(14) were indeed preserved in the latter.

COSY $^{1}H/^{1}H$ and $^{13}C/^{1}H$ experiments enabled us to assign the signals of the remaining nuclei in rings *A* and *B* (Bruker AM 400, DISR 871 software) (Table 1). Significant differences were observed in the ^{13}C spectra of compounds (**1**) and (**2**) for several carbons of rings *A* and *B* only. From the ^{1}H and ^{13}C spectra, as well as from the above correlations it appeared that the C(19) methyl (δ ^{1}H = 0.85, d) was indeed shifted from C(10) to C(1).

J-spectroscopy allowed the determination of the fine structure of the signals corresponding to H(9) and H(10), and hence the nature of the *A*/*B* ring junction. Indeed H(9) was a quartet (*J* 10.6 Hz) further dedoubled (*J* 3.5 Hz), implying three *trans* and one *gauche* couplings, while H(10) appeared as a multiplet (*J* 10.8, 10.0, 4.0 Hz) corresponding to two *trans* and one *gauche* couplings. These values were consistent with H(9) being β, *trans* coupled with H(8) (α), H(11) (α), and H(10) (α), and *gauche* coupled with H(11) (β). They further showed that H(10) (α) was *trans* coupled to H(5) (β) and *gauche* coupled to H(1) (α), revealing an *A*/*B trans* ring junction and a C(19) methyl in an axial position.

These results therefore defined the new rearranged sterenes as being (20*R* and 20*S*) 1β,14β-dimethyl-18,19-dinor-5β,8α,9β,10α-cholest-13(17)-enes (**2**) (Scheme 1).

The C(19) methyl at C(1) remains axial most probably because the equatorial position is thermodynamically unfav-

oured due to periplanar interactions with ring *C*, a feature previously recognized in corresponding perhydrophenanthrenes.[13,14] Data obtained on graphics computer system by modelling based on molecular mechanics (program SYBYL, Tripos Assoc.) were in agreement with this statement. They indeed showed an energy difference of about 5 kcal/mol (cal = 4.184 J) in favour of the more stable axial epimer.

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