The Cholestane Backbone Rearrangement: Isomerisation at C-20

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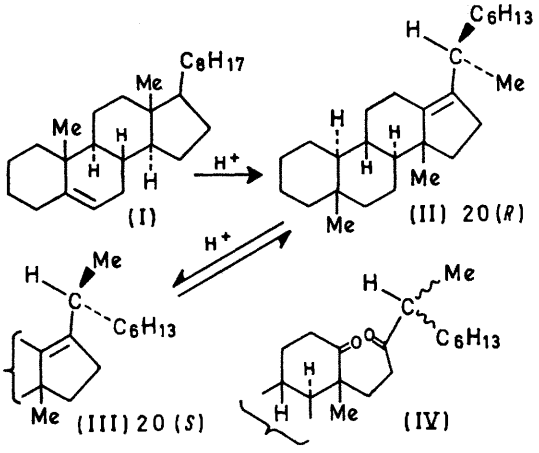
Summary The backbone-rearranged cholest-13(17)-ene (II) undergoes epimerisation at C-20 under acidic conditions to give a 1 : 1 mixture of 20(*R*)- and 20(*S*)-isomers.

CHOLEST-5-ENE (I) suffers "backbone-rearrangement" with toluene-*p*-sulphonic acid in refluxing acetic acid, to give the 5β,14β-dimethyl-18,19-bisnor-13(17)-ene (II).[1] G.l.c. examination of samples from the reacting mixture shows that a second olefin is also formed, reaching *ca.* 30% of the mixture when (I) is no longer detectable. Continued reaction leads to equilibration of these isomers (*ca.* 1 : 1), only traces of other products being present.

The new olefin has now been identified as the 20(*S*)-isomer (III) of the rearranged olefin (II). The olefins were separated in 20 mg quantities (as gums) by preparative g.l.c. Both compounds exhibited the n.m.r. characteristics of the 13(17)-olefinic system:[1,2] the doublet due to the C-21 methyl group collapsed to a singlet with a superimposed frequency *ca.* 90 Hz downfield, corresponding to C-20–H (spectra in $CDCl_3$, at 60 MHz). The two spectra were indistinguishable apart from the C-21-methyl doublet [τ 9·11, 9·00 in (II); 9·17, 9·05 in (III)]. Mass spectra were virtually identical, the main peak (*m/e* 257) representing loss of the entire cholestane side-chain. U.v. spectra were similar (λ_{max} 197 nm; ϵ 11,000) but c.d. curves showed different Cotton effects (λ_{max} 210 nm; II, $\Delta\epsilon$ −9·5; III; $\Delta\epsilon$ −7·1), interpreted tentatively in terms of the side-chain conformations indicated (II and III), with the C-20–H bond eclipsing the 13(17)-olefinic bond. Assuming the C_6H_{13} chain to have a larger perturbing effect than the C-21-methyl on the $n \rightarrow \pi^*$ transition, the observed Cotton effects obey Scott's octant rule[3] for olefins. The similar conformations (II) and (III) also explain the near-identity of n.m.r. spectra.



Hydroxylation of each olefin with osmium tetroxide gave a corresponding 13,17-diol, easily distinguished by t.l.c. and g.l.c. Each diol afforded a 13,17-seco-13,17-dione (IV) on cleavage with lead tetra-acetate. The diketones were virtually indistinguishable their n.m.r. spectra; upfield shifts of only the 14β- and C-21-methyl groups in benzene[4] agree with the structures (IV). G.l.c. retention times for the diketones differed very slightly.

The very close similarities between olefins (II) and (III), and between the derived diketones, are consistent only with identity of their tetracyclic structures, leaving C-20 as the one remaining possible centre of difference. The concept of the backbone rearrangement as leading to the least strained olefinic product[1,5] demands the same conclusion.

Isomerisation at C-20 seems likely to occur *via* a C-20-carbonium ion derived by transient double bond migration from 13(17) to the less stable 17(20)-position.

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