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THE REARRANGEMENT OF BOTH C-12 EPIMERS OF A BILE ACID DERIVATIVE TO AN ETIOJERVANE STRUCTURE[o]

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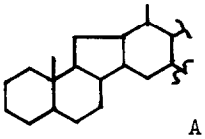
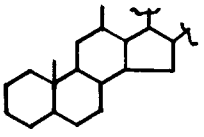
12-Oxo tosylhydrazones of several steroidal classes (1,2,3), the 12β-mesylate of rockogenin (1,2) and a 12β-amino spirostane (4) undergo Wagner-Meerwein type rearrangement to the C-nor-D-homo (etiojervane) ring structure A. As previously reported (5), 12α-mesyloxycholane is converted



A



B

by refluxing in collidine into a mixture of olefins, which consists largely of isomers of rearranged structure. The structure of the major component (I) as deduced from a derived crystalline diol, was regarded to have the 12-methyl-18-nor ring system B, based mainly on conformational considerations and by analogy.

We now wish to report the successful isolation of olefin I and evidence that it has the A structure, contrary to the earlier deductions. Furthermore, both the epimeric 12β-mesylate and 12-oxocholane tosylhydrazone reactions yield the same compound I as major product.

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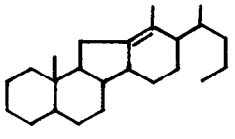
The oil (5) from the 12α-mesyloxycholane reaction after removal of 11-cholene by crystallization, responded to successive column and preparative thin-layer chromatography (tlc) on silver nitrate-impregnated adsorbents to give I as colorless crystals, $C_{24}H_{40}$;+ mp 55.8-56.4°; $[\alpha]_D$ +2.5°; with nmr spectrum showing singlets at 9.12 (3H, 19-methyl) and 8.44τ (3H, vinyl methyl), a doublet at 9.07τ (3H, 21-methyl) and no resonance in the olefinic region.

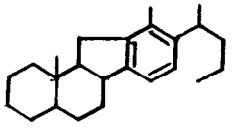
Dihydroxylation of I affords solely the major diol previously reported (5). This diol on oxidation gives a crystalline diketone, $C_{24}H_{40}O_2$;+ mp 54.0-54.8°; $[\alpha]_D$ +92°; λ max (CS_2) 5.72 (C_5-ring C=O) and 5.84 μ (aliphatic C=O); nmr signals, 9.33 (3H singlet, 19-methyl) and 7.83τ (3H singlet, methyl alpha to C=O).

I under aromatization conditions [palladium-charcoal-cymene reflux (6)] gives an oil which by column chromatography yielded a hydrocarbon (II), $C_{24}H_{36}$ (M^+324), not crystalline but homogeneous by tlc and gas chromatography (glc). It has $[\alpha]_D$ +40°; λ max (EtOH) at 267, 270, 276 mμ (identical to maxima of veratramine); and λ max (CCl_4) at 12.0 μ (aromatic). Its nmr spectrum shows a 2-proton multiplet centered at 3.20τ (aromatic), 3-proton doublet centered at 8.87τ, J=7 c/s (C-21 methyl), and 3-proton singlets at 7.84 (C-18 methyl) and 8.97τ(C-19 methyl). By double irradiation, the C-21 methyl signal (doublet) is shown to be coupled with a proton at 7.08τ (C-20, benzylic), indicating the side chain attachment on the aromatic ring.

The foregoing observations permit the assignment of structure 17-(1-methylbutyl)- $\Delta^{12,14,16}$-5β-etiojervatriene (7) to compound II, and consequently, 17β-(1-methylbutyl)- Δ^{12}-5β-etiojervene to compound I.



I



II

+ Satisfactory elemental analyses have been obtained.

12β-Mesyloxycholane (8), under similar conditions but in a much faster reaction, also gives a mixture of olefins. The major product isolated in crystalline form is identical (ir, nmr, tlc, glc, mp) with I; no 11-cholene was found in the total product. 12-Oxocholane tosylhydrazone (9) on alkaline decomposition affords a more complex mixture, but I is also the major olefin formed and 11-cholene is present. As determined by glc, yields (10) of I and 11-cholene, respectively, in the three reactions are as follows: 12α-mesylate reaction, 32 and 40%; 12β-mesylate reaction, 35 and 0%; 12-oxo tosylhydrazone reaction, 26 and 24%.

A speculation that jerveratrum alkaloids might arise biogenetically by a steroidal pathway, is based mainly on the observed "chemical" transformation of a 12β-hydroxy steroid into a C-nor-D-homo structure (1, 11). The results reported here embellish that speculation by affording the epimeric C-12 hydroxy compounds as alternate possible intermediates. In this connection, the occurrence in veratrum plants of the 12α-hydroxy steroidal alkaloid, rubijervine, as a companion of alkaloids of C-nor-D-homo structure, may be relevant.

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7. The numbering system follows that used for the jervcratrum alkaloids (L. F. Fieser and M. Fieser, "Steroids", Reinhold Publishing Corp., N. Y., 1959, p. 871).

8. mp 56.0-56.4°, crystalline but extremely unstable.

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10. Other olefinic components under study and details of the experiments will be described in a full paper.

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