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SOLVOLYSIS AND REARRANGEMENT OF HOLARRHENINE MESYLATE UNDER REDUCING CONDITIONS

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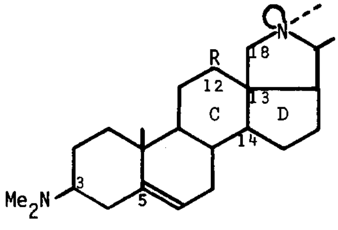
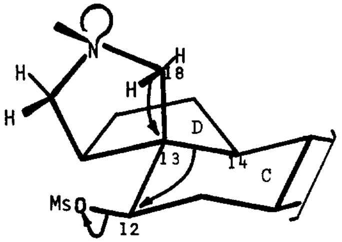
Some years ago, by analogy with the course of the solvolysis of rockogenine 12-tosylate (1), Uffer emitted the hypothesis that a C-nor-D-homo rearrangement occurs when holarrhenine tosylate (IV) is treated with lithium aluminium hydride in ether and proposed structure (V) for the resulting product (2).

Our reinvestigation of Uffer's experiment led to a finding which could, we hope, have a more general utility.

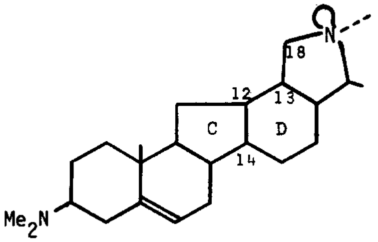
The preparation of the rearranged product (V) needed some improvement as the yields mentioned by the author (2) are rather low. It is to be noted that, even with a large excess of tosylchloride, the conversion of holarrhenine (I) into its tosylate (IV) is very slow and that the reaction mixture cannot be readily resolved; on the contrary, the quantitative preparation of holarrhenine mesylate (III) revealed much easier.

The reduction of both tosylate (IV) and mesylate (III) by means of lithium aluminium hydride in ether always afforded mixtures of holarrhenine (I) and rearranged product (V), this indicates concurrent O-S and C_{12}-O bond cleavages although no conessine (II) was detected. Surprisingly, the issue of an experiment with tetrahydrofuran as a solvent was the reverse, holarrhenine (I) being recovered almost quantitatively.





	R	
(I)	H , β-OH	
(II)	H_2	
(III)	H , β-OMs	m.p.:146-7°C $\vert\alpha\vert_D$=-11° (Chl)
(IV)	H , β-OTs	m.p.:144-5°C



(V) m.p.:91-2°C $|\alpha|_D$ = -16.5° (Chl)

The predominance of the rearranged product (V) and the absence of conessine (II) in the reaction mixture when ether was used as a solvent points to the intermediate formation of a rapidly rearranging carbonium ion or to the immediate formation of a rearranged item via a concerted cleavage of C_{12}-O and C_{13}-C_{14} linkages.

Consequently, we thought it would be useful to work out conditions favouring the unimolecular C_{12}-O bond cleavage of the sulphonate.

It was indeed verified that the rearrangement of holarrhenine mesylate (III) is complete without occurrence of O-S bond cleavage, when the reaction is performed in anhydrous alcohols using an excess of sodium borohydride. We think this procedure could be a choice method to convert 12β-hydroxy steroids with a normal skeleton into the corresponding saturated C-nor-D-homo derivatives when the reaction with lithium aluminium hydride and the Bamford-Stevens reaction on 12-keto steroids (4) fail.

Recently it was reported (5a) that 12β-tosyloxyconanine (IV, H_2 at C_3, 5α-H) rearranges in the same way with lithium aluminium hydride-aluminium chloride as a reagent in ether. Mechanistic studies including deuterium labeling afforded a strong evidence that the rearrangement as outlined above is followed by a hydride shift from C_{18} to C_{13} on the rear side of the molecule, which could be assisted by the electron pair of the nitrogen atom (5b).

Reduction of holarrhenine mesylate (III) with sodium borodeuteride in O-deuteroethanol or in O-deutero-*i*-propanol led to a 97% monodeuterated rearranged product (V, 18α-d) with at least 80% deuterium incorporation at C_{18} (NMR, MS). These results are in good agreement with the findings of the French authors.

Further details on the experiments and spectroscopic as well as chemical evidence for the suggested structure (V) will be presented soon in a full publication.

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