Solvolytic Rearrangement of Some Azabicyclic Chlorides

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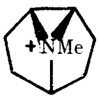
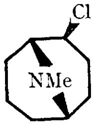
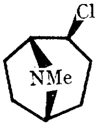
DESPITE the interest in solvolytic reactions of bridged bicyclic hydrocarbon derivatives, their heterocyclic analogues have received comparatively little attention. Apart from fragmentation processes,[1] the few reported instances of solvolytic rearrangement in azabicycloalkyl compounds have generally involved direct nitrogen participation,[2] *e.g.* the racemisation of (+)-L-tropan-2α-yl acetate *via* the tricyclic cation (I).[2a]



(I)



(II)



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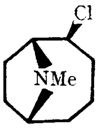


(IV)

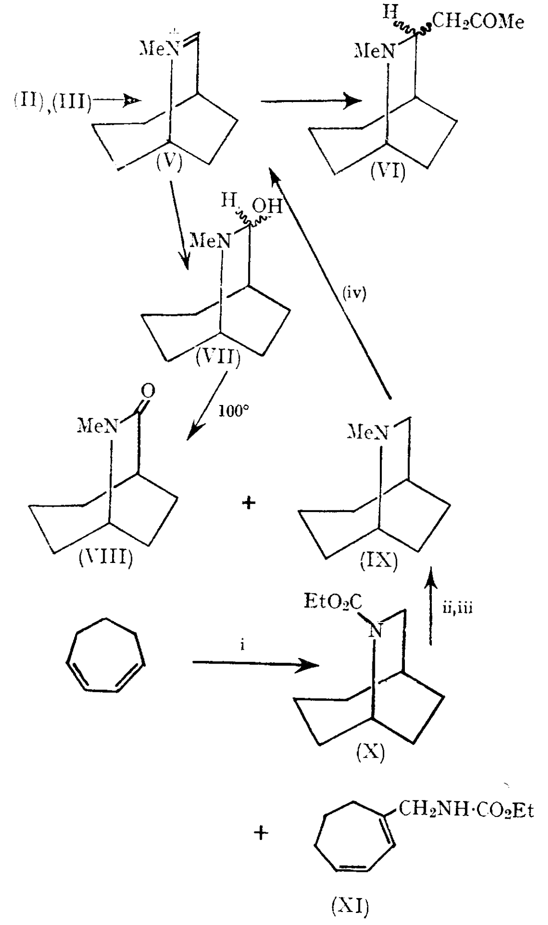
Since the configuration of the leaving group is often decisive in determining the course of rearrangement in bridged bicyclic systems,[3] it was of interest to examine the behaviour of the chlorides (II), (III), and (IV), in each of which the substituent has been assigned the *cis*- (*i.e.* β-) configuration relative to the nitrogen bridge.[4]

When the chlorides (II) and (III) were heated in aqueous acetone under reflux they were both converted into the same single product (VI), the i.r. and n.m.r. spectra of which indicated the incorporation of a molecule of acetone, but provided no evidence of skeletal rearrangement. However, solvolysis of the chlorides in aqueous dioxan gave, after basification, a liquid hydroxylic base which was converted into two new products upon being heated. This transformation was evidently the result of a disproportionation of the carbinolamine (VII), since one of these products was an amide (VIII), reducible (lithium aluminium hydride) to the other, (IX).

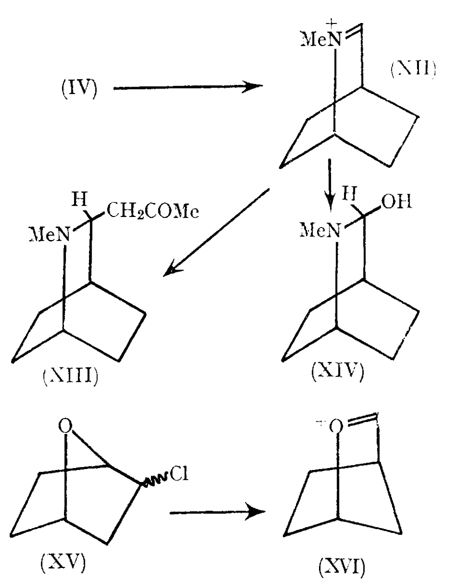
Confirmation that these compounds possessed the novel 6-azabicyclo[3,2,2]nonane skeleton was provided by synthesis. With methylenebisurethane in the presence of boron trifluoride,[5] cyclohepta-1,3-diene was converted into the 1,4-adduct (X) together with a small amount of the addition–abstraction product (XI). The structure of the latter follows from its spectra [λ_{max} 250 mμ (ϵ 9150); ν_{max} 3320 and 1700 cm.$^{-1}$; n.m.r.: apparent singlet at τ 4·3 (3 olefinic protons), and τ 6·25 (d, J 6 Hz, CH_2NH)] and those of its tetracyanoethylene adduct, the n.m.r. spectrum of which showed the presence of two olefinic protons.

The n.m.r. spectrum of the adduct (X) showed the expected features, including a quartet ($-N{\cdot}CH_2-$) centred at τ 6·67, only the low-field half of which was visibly coupled (J 4 Hz) to the bridgehead proton. Conversion of (X) into the perchlorate of (V) was effected by the route outlined; treatment of this immonium salt with acetone then afforded the original solvolysis product (VI).

Solvolysis of the lower homologue (IV) likewise led, *via* the immonium ion (XII), to 3-acetonyl-*N*-methyl-2-azabicyclo[3,3,1]nonane (XIII) in aqueous acetone, and to the carbinolamine (XIV) in aqueous dioxan; the latter afforded the perchlorate salt of (XII), the properties of which corresponded closely to those previously described[6] for this compound.



Reagents: i, $CH_2(NH{\cdot}CO_2Et)_2$–BF_3; ii, H_2–Pd; iii, $LiAlH_4$; iv, $Hg(OAc)_2$, then $HClO_4$.



A similar Wagner–Meerwein shift in a hetero-bicyclic system has been observed in solvolyses of the 7-oxabicyclo[2,2,1]heptyl chlorides (XV); in this case both epimers gave the rearranged intermediate (XVI).[7] However, in nitrogen-bridged ring systems, especially those having greater flexibility, direct participation of nitrogen in the ionisation of 2α-substituents would be anticipated,[2] leading presumably, in the case of the 2α-epimers of (II) and (III), to interconversion. The rearrangements described are thus regarded as characteristic of the 2β-chlorides, providing confirmation of their stereochemistry.

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