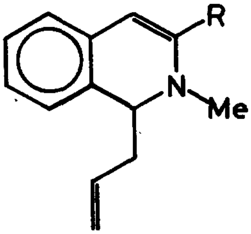
Tetrahedron Letters No. 27, pp 2231 - 2234, 1975. Pergamon Press. Printed in Great Britain.

UNUSUAL PRODUCTS IN AZA-COPE REARRANGEMENTS OF 1,2-DIHYDROISOQUINOLINES[1]

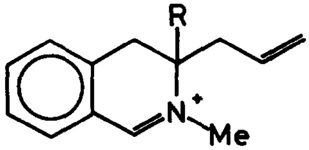
R.G.Kinsman* and S.F.Dyke*
School of Chemistry, University of Bath,
Claverton Down, Bath, Avon, England

(Received in UK 21 April 1975; accepted for publication 22 May 1975)

It has been found[2] that when a 1-allyl-1,2-dihydroisoquinoline such as (1a) is treated with hot dilute mineral acid, a rearrangement occurs rapidly, and in high yield, to a 3-allyl-3,4-dihydroisoquinoline derivative (2a). This reaction has been proved[3] to be intramolecular in nature, and is an example of a suprafacial sigmatropic[3,3] shift analogous to the Claisen and Cope rearrangements. The transition state might be expected to be as depicted in (3a).



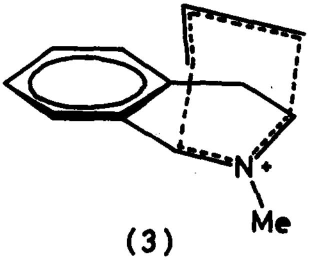
(1) a R = H
b R = Me



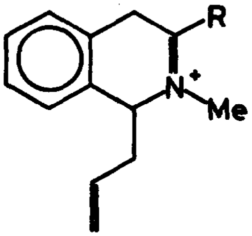
(2) a R = H
b R = Me

It has also been reported[1] that when 1-allyl-2,3-dimethyl-1,2-dihydroisoquinoline (1b) is similarly treated with acid, no rearrangement occurs. An examination of a model of this transition state (3b) demonstrates clearly that there should be no steric barrier to the migration reaction, and it was suggested[1] that in the equilibrium (4b) $\rightleftharpoons$ (2b), the protonated enamine (4b) is thermodynamically favoured.

During the above investigation, the enamine (1b) was heated under reflux with 2N HCl for a prolonged period of time. After 10 days the UV spectrum, which had become benzenoid in type, underwent no further change. Work-up of the acid solution gave a base, $C_{14}H_{18}NCl$ in high yield; no other product could be detected. The NMR spectrum ($CDCl_3$), which contained the following resonances (δ) : 7.3-6.9 m [4H] (aromatic protons); 4.1-3.6 m [2H]; 3.5-3.0 m [2H]; 2.8-1.9 m [4H]; 2.4 s [3H] ($N\text{-}CH_3$); 1.25 s [3H] ($C_1\text{-}CH_3$), is devoid of signals associated with an allyl group. In the mass spectrum of the base, a chlorine atom (but not HCl) is readily lost from the molecular ion; the succeeding fragmentations are closely



(3)

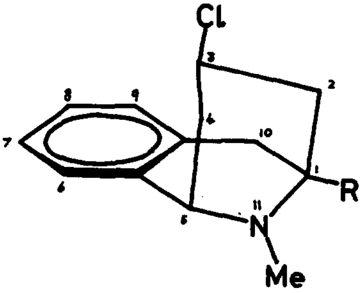


a R = H

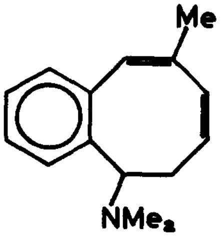
b R = Me

(4)

similar to those that we had observed previously for allyl-substituted dihydroisoquinolines.



(5)



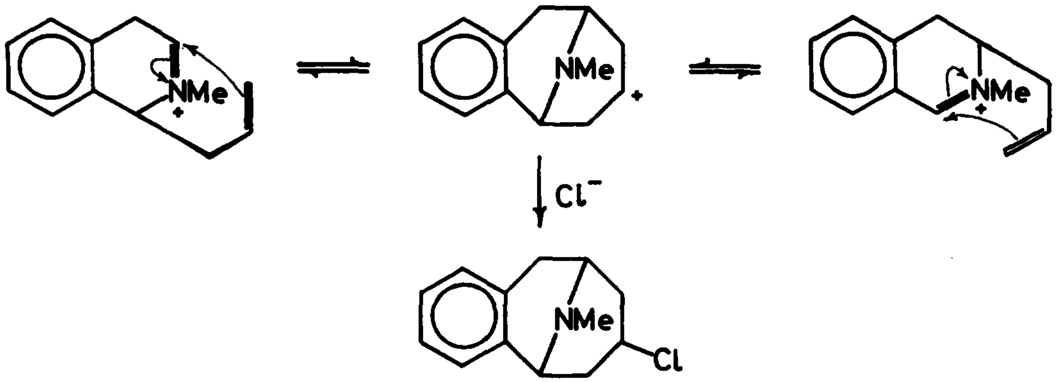
(6)

This data is consistent with structure (5b) for the new base. Further evidence was obtained by subjecting the methiodide to Hofmann degradation, when a chlorine-free product was obtained, the spectral characteristics of which are consistent with structure (6).

When 2-methyl-3-allyl-3,4-dihydroisoquinolinium chloride (2a) was subjected to similar conditions of acid treatment, reaction was complete after 14 days (UV spectrum). Work-up gave a high yield of a base (5a) which was purified by chromatography, sublimation and crystallisation. NMR: 7.3-6.9 m [4H] (aromatic protons): 4.1-3.6 m [2H] (C_3 + C_5 - protons); 2.9 d (J = 18Hz) [1H] and 2.6d (J = 18Hz) [1H] (C_{10} - protons); 2.4-1.7 m [4H] (C_2 + C_4 - protons); 2.3 s [3H] (N - CH_3). The mass spectral fragmentations lend further support^4 for structure (5a).

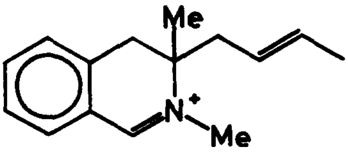
The formation of 3-chloro-11-azabenzo[f]bicyclo[3,3,1]nonanes such as (5a) and (5b) from either 1-allyl-1,2-dihydroisoquinolines or from 3-allyl-3,4-dihydroisoquinolines at similar rates under identical reaction conditions is best explained in terms of an intermediate carbonium ion, or developing carbonium ion, (Scheme I). Attack by chloride ion in an essentially irreversible reaction thus leads to the observed product. The relatively slow rate of formation of the bridged compounds, but high overall yield points to a low steady state concentration of the intermediate.

A similar cyclisation occurs when the 3,4-dihydroisoquinoline (7) is subjected to

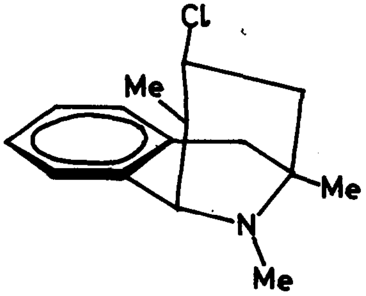


Scheme 1

prolonged acid treatment. The NMR spectrum of the product provides conclusive proof for structure (8), a geometry to be expected from the addition of chloride ion to an intermediate generated by a four-centred overlap of the allyl and imminium ion moieties. These compounds have structural similarities to the norharman derivatives obtained by Winterfeldt[5].



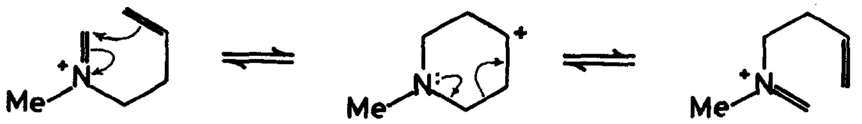
(7)



(8)

It is possible that the above two-step reaction is in competition with a concerted[6] rearrangement process, but we believe that the rearrangement itself is a two-step reaction[7]. The electrophilic character of the positively charged nitrogen atom may contribute uniquely to a mechanism involving a carbonium ion (Scheme 2).

Further investigations are in progress.



Scheme 2

References

1. R.G.Kinsman, S.F.Dyke and J.Mead, Tetrahedron, 29, 4303 (1973)

2. M.Sainsbury, D.W.Brown, S.F.Dyke, R.G.Kinsman and B.J.Moon, Tetrahedron, 24, 6695 (1968).

3. M.Sainsbury, S.F.Dyke, D.W.Brown and R.G.Kinsman, Tetrahedron, 26, 5265 (1970).

4. S.Shiotani and K.Mitsukashi, Chem.Pharm.Bull., 20, 1 (1972).

5. E.Winterfeldt and W.Franzischka, Chem.Ber., 101, 2938 (1968); and H.Rischke, J.D.Wilcock and E.Winterfeldt, Ibid., 106, 3106 (1973).

6. A.H.Andrist, J.Org.Chem., 38, 1772 (1973).

7. M.J.S.Dewar and L.E.Wade, J.Amer.Chem.Soc., 95, 290 (1973).