

The Rearrangement of *N*-Chloroisoquinuclidine

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THE unusual absence of alkyl migration in the Stieglitz rearrangement of hydroxylamines and in the related rearrangement of *N*-halogeno-amines has recently been noted.^{1,2} We report here an example of such an alkyl migration in the rearrangement of an *N*-chloro-amine.

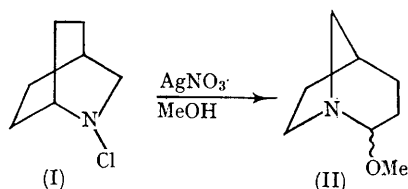
Treatment of isoquinuclidine with *t*-butyl hypochlorite readily afforded *N*-chloroisoquinuclidine (I). When a methanolic solution of (I) and silver nitrate was refluxed for two hours, silver

chloride was precipitated and a 60% yield of 2-methoxy-1-azabicyclo[3,2,1]octane (II) was obtained.³

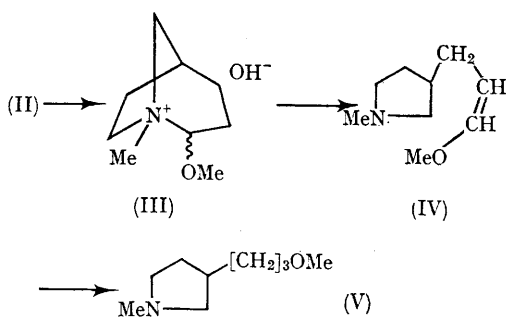
The rearrangement product (II) was a clear colourless liquid, n_D^{25} 1.4722. A picrate was readily prepared, m.p. 175—178°.

The structure of (II) was elucidated by partial degradation, coupled with synthesis of the degradation product as shown below. Formation of the quaternary methiodide of (II) followed by

passage of a methanolic solution of the salt through IRA 400 ion-exchange resin yielded the syrupy quaternary ammonium hydroxide (III). Pyrolysis

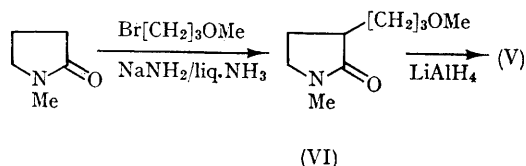


of (III) yielded 1-methyl-3-(*cis*-3-methoxyprop-2-enyl)pyrrolidine (IV), n_D^{24} 1.4618. The *cisoid* nature of the substituents on the double bond was evident from the n.m.r. coupling constant of 6.3 c./sec. between the olefinic hydrogens.⁴ Catalytic hydrogenation of (IV) yielded the saturated ether (V). An independent synthesis of (V) was accomplished as outlined.

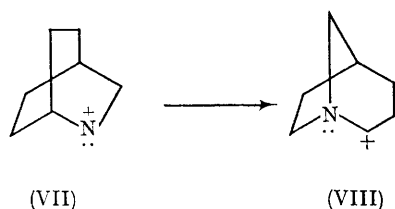


Trimethylene oxide was readily converted into 1-bromo-3-methoxypropane by standard procedures.⁵ Addition of the bromide to a solution of the anion formed from sodium amide and *N*-methylpyrrolidone in liquid ammonia yielded the alkylated pyrrolidone (VI). Reduction of crude

(VI) with lithium aluminium hydride gave the degradation product (V) in 42% overall yield for the alkylation and reduction steps.⁶



The rearrangement of (I) to (II) can be compared to other reactions in which carbon-nitrogen bonds are formed from nitrenium-ion precursors.^{7,8} In these cases the reaction pathway probably involves hydride abstraction by the nitrenium ion prior to C-N bond formation.⁷ The nature of our product precludes a similar mechanistic route in the rearrangement of (I) to (II).



Whether (I) ionizes directly to the nitrenium ion (VII) followed by subsequent rearrangement to the carbonium ion (VIII) or whether a concerted rearrangement-loss of chloride ion is involved in this reaction has not been determined. Since this type of rearrangement may be very useful in the synthesis of complex compounds containing nitrogen (*i.e.*, alkaloids), a detailed investigation of the mechanism and scope of the reaction is in progress.

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¹ P. A. S. Smith in "Molecular Rearrangements," Vol. 1, P. de Mayo, ed., Interscience, New York, 1963, pp. 480—482.

² For recent reviews of rearrangements involving charged nitrogen intermediates, see R. A. Abramovitch and B. A. Davis, *Chem. Rev.*, 1964, **64**, 149 and P. A. S. Smith in "Molecular Rearrangements," Vol. 1, P. de Mayo, ed., Interscience, New York, 1963, pp. 457—483.

³ The same product was obtained when the reaction was carried out in the dark at 10° for prolonged periods of time. The fact that this reaction occurs in the dark and in the absence of acid indicates that this rearrangement is not mechanistically related to the free-radical Hofmann-Löffler-Freytag rearrangement of protonated *N*-halogenoamines.

⁴ L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon, New York, 1959, p. 85.

⁵ S. Searles and C. F. Butler, *J. Amer. Chem. Soc.*, 1954, **76**, 56; L. I. Smith and J. A. Sprung, *J. Amer. Chem. Soc.*, 1943, **65**, 1276.

⁶ A detailed study of the alkylation of *NN*-dialkylamides has been carried out in connection with the synthesis of β -substituted alkylamines. These studies will be the topic of a subsequent publication.

⁷ O. E. Edwards, D. Vocelle, J. W. ApSimon, and F. Haque, *J. Amer. Chem. Soc.*, 1965, **87**, 678.

⁸ G. Adam and K. Schreiber, *Angew. Chem.*, 1964, **76**, 752.