RING TRANSFORMATION OF HETEROCYCLES VIA N-IMIDE INTERMEDIATES: FROM NICOTINE TO HEXAHYDROPYRIDO[3,4-b]-1,2-DIAZOCINE

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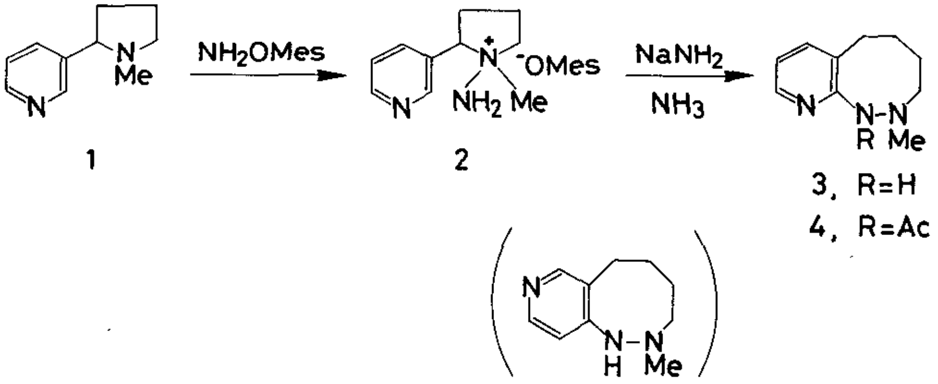
Abstract —— Treatment of the N-amino derivative of nicotine with sodium amide in liquid ammonia gave 2-methylhexahydropyrido[3,4-b]-1,2-diazocine.

The Sommelet-Hauser rearrangement ([2,3]-sigmatropic rearrangement)[1] has been utilized to the ring enlargement of a variety of heterocycles.[2] In connection with our interest in the ring transformation of heterocycles via ylide intermediates,[3,4] we have applied this reaction to the ring expansion of nicotine (1)[5] which is an important alkaloid available commercially.



1

2

3, R=H
4, R=Ac

5

According to the procedure of Lednicer and Hauser,[6] the N-aminopyrrolidinium salt 2[3] was treated with sodium amide in liquid ammonia to give a single crystalline product, m.p. 67-68°C (from n-hexane), in 52% yield, which was assigned the structure 3 by its spectral properties. Elemental analysis and mass spectrum (M^+

177) of **3** indicated the molecular formula $C_{10}H_{15}N_3$. Its i.r. spectrum ($CHCl_3$) showed an NH stretching band at 3280 cm^{-1} and the n.m.r. spectrum revealed three doublets of doublets centered at δ 7.81 (1H, H-9, J = 5 and 2 Hz), 7.09 (1H, H-7, J = 7.5 and 2 Hz) and 6.45 (1H, H-8, J = 7.5 and 5 Hz). In addition, a broad signal assignable to NH at δ 5.65 (disappeared by treatment with D_2O), an *N*-methyl singlet at δ 2.56, and three multiplets assignable to H-3 (δ 3.1-3.4), H-6 (δ 2.6-2.9), and H-4 and 5 (δ 1.4-2.0) were observed. Acetylation of **3** with acetic anhydride in pyridine at room temperature gave the *N*-acetate **4**, m.p. 110-111°C, in 90% yield.

The reaction is site-specific and no isomeric product **5** was detected.

REFERENCES AND FOOTNOTES

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2. E. Vedejs, M.J. Arco, D.W. Powell, J.M. Renga, and S.P. Singer, *J. Org. Chem.*, **43**, 4831 (1978) and the references cited therein; T. Tsuchiya and H. Sashida, *Chem. Pharm. Bull.* (Tokyo), **29**, 1887 (1981) and the references cited therein.
3. This compound was prepared by the reaction of **1** with *O*-mesitylenesulfonylhydroxylamine [Y. Tamura, J. Minamikawa, Y. Kita, J.H. Kim, and M. Ikeda, *Tetrahedron*, **29**, 1063 (1973)].
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5. Only recorded example of the ring transformation reaction of nicotine is the thermal conversion of nicotine 1'-oxide to 2-methyl-6-(3-pyridyl)tetrahydro-1,2-oxazine, a Stevens-type rearrangement product [C.H. Rayburn, W.R. Harlan, and H.R. Hanmer, *J. Am. Chem. Soc.*, **72**, 1721 (1950)].
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