>330°, in 47 and 76% yield respectively. The former compound was in all respects identical with the product prepared by Method A.

This procedure is a successful application of the known alloxazine synthesis[19] from 6-amino-1,3-dimethyluracil and nitrosobenzenes. However, it should be noted that the reaction of 6-alkylamino-1,3-dimethyluracils with nitrosobenzenes under the same conditions yields interestingly the corresponding 7-aryltheophyllines.[20]

Faculty of Pharmaceutical Sciences,
Kumamoto University
Oe-honmachi, Kumamoto

FUMIO YONEDA
YOSHIHARU SAKUMA

School of Medicine,
Keio University
Shinanomachi, Shinjuku-ku, Tokyo

MISUZU ICHIBA
KAZUKO SHINOMURA

Received March 31, 1972

19) E.C. Taylor, F. Sowinski, T. Yee, and F. Yoneda, *J. Am. Chem. Soc.*, **89**, 3369 (1967).
20) E.C. Taylor and F. Yoneda, unpublished results: see E.C. Taylor in "Topics in Heterocyclic Chemistry," ed. by R.N. Castle, Wiley-Intersciences, New York, 1969, p. 27.

[Chem. Pharm. Bull. 20(8)1834—1836(1972)]

UDC 547.821'781'861.1.657

Syntheses of 1-Pyrazylpyridinium Salts, and Pyrido[1',2':1,2]imidazo-[4,5-*b*]pyrazines, a New Type of Heterocyclic Compounds

In the course of our studies on pyrazine derivatives, we have synthesized a series of pyrazine derivatives (IIa—c, IIId—f) bearing pyridinium groups by reaction of pyrazine N-oxides (Ia—f) with tosyl chloride in the presence of pyridine.[1] The structure of these compounds was determined by their nuclear magnetic resonance (NMR) coupling constants

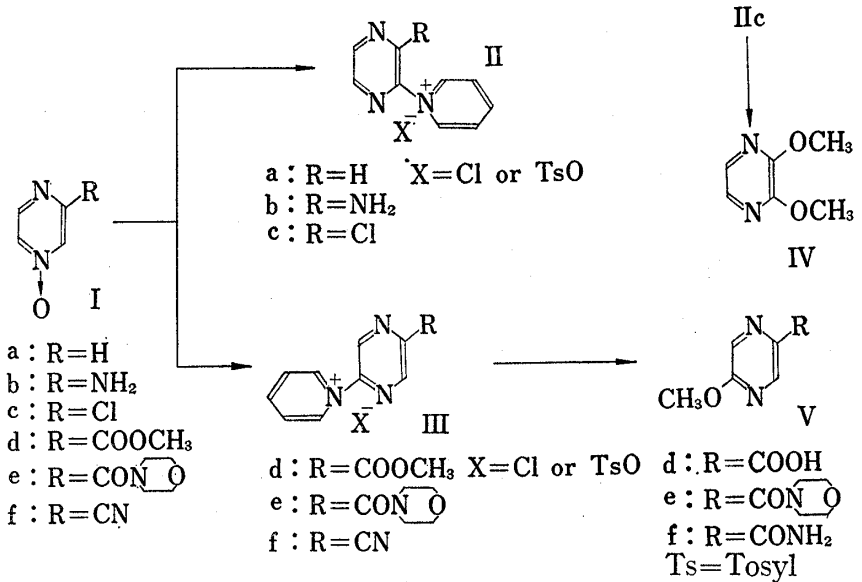

Chart 1

1) For the reaction in pyridine and quinoline N-oxides, see M. Hamana and K. Funakoshi, *Yakugaku Zasshi*, **84**, 23, 28 (1964).

and also by correlation with known substances such as (IV) and (Vd—f).[2] As a special case, the reaction of 2-aminopyrazine 4-oxide (Ib) with tosyl chloride in pyridine yielded a tricycli ccompound which belongs to a new ring system.

By the reaction of (Ib) with tosyl chloride in pyridine at room temperature we obtained pyridinium salt (IIb) in 41% yield. After heating under reflux for 4.5 hr, a compound showing negative color reaction of quaternary salt was obtained, and its structure was determined to be pyrido [1′,2′: 1,2]imidazo[4,5-*b*]pyrazine (VIa) on the basis of ultraviolet (UV), infrared (IR), NMR and mass (MS) spectra, analytical values and consideration of reaction mechanism. (VIa) was also formed by refluxing (IIb) in pyridine in a yield of 58%.

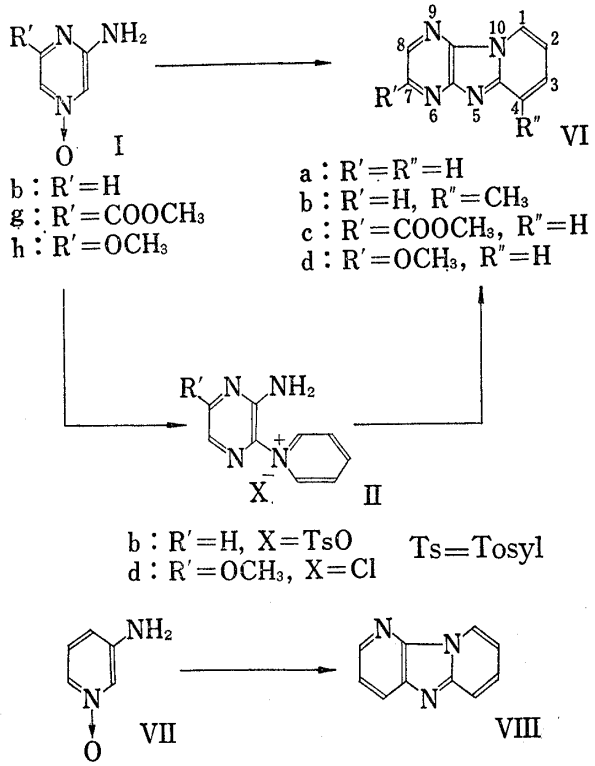

Chart 2

Recently Paudler and Blewitt have reported a detailed NMR spectral study on imidazo[1,2-*a*]pyridine derivatives.[3] Referring the data of the imidazo[1,2-*a*] pyridines, we assigned each proton signal and confirmed these assignments by decoupling experiment. These NMR spectral data agreed well to the above structure (VIa).

The scope and limitations of this reaction were further examined by using derivatives of (Ib). When β-picoline

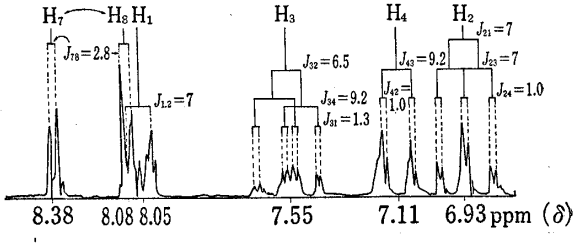

Fig. 1. NMR Spectrum of Pyrido[1′,2′: 1,2] imidazo[4,5-*b*] pyrazine (VI) (10% solution in D_2O, 100 MHz)

was used instead of pyridine, the methyl compound was similarly obtained. The methyl group was found to be in the position 4 by analysis of NMR data. 2-Amino-6-carbomethoxypyrazine 4-oxide yielded the 7-carbomethoxy derivative (VIc). In the case of 2-amino-6-methoxypyrazine 4-oxide, the desired product (VId) was prepared from the intermediate pyridinium salt (IId) by refluxing in pyridine.

On the other hand, 2-aminopyridine 4-oxide gave only a trace of the tricyclic compound, dipyrido[1,2-*a*: 2′,3′-*d*]imidazole (VIII) in a similar reaction. The formation of this compound (VIII) by the reaction of 3-acetoaminopyridine 1-oxide with 2-bromopyridine has been reported by Kajihara.[4]

With regard to the mechanism of this reaction, it appears likely that the lone pair of amino group of the intermediate (II) attacks initially the electron-deficient α-position of pyridinium ring as shown below.

2) F. Uchimaru, S. Okada, and T. Konno, Abstracts of Papers, The 91st Annual Meeting of Pharmaceutical Society of Japan, 1971, p. 616.
3) W.W. Paudler and H.L. Blewitt, *Tetrahedron*, **21**, 353 (1965).
4) S. Kajihara, *J. Chem. Soc. Japan*, **86**, 839 (1965).

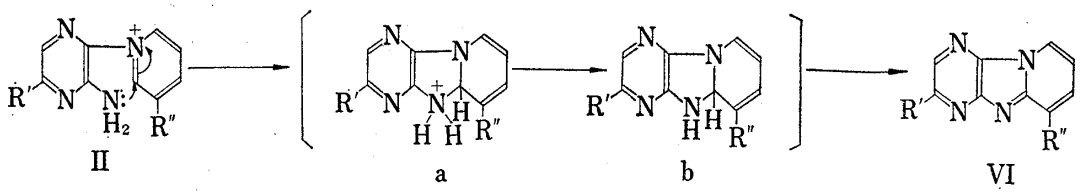

Chart 3

The authors are grateful to Prof. Toshihiko Okamoto of Tokyo University for his valuable discussions. The authors are also indebted to Dr. M. Shimizu, director of these Laboratories, Dr. T. Naito, Vice Director of these Laboratories and Dr. G. Ohta, Manager of Chemical Research Laboratory, for their kind encouragement throughout the course of this work.

Research Laboratories,
Daiichi Seiyaku Co., Ltd.
Minamifunabori-cho, Edogawa-ku, Tokyo

FUMIHIKO UCHIMARU
SEIZABURO OKADA
AKIRA KOSASAYAMA
TSUNEO KONNO

Received April 12, 1972

[Chem. Pharm. Bull. 20(8)1836—1838(1972)]

UDC 547.891.2.057 : 547.833.04

Synthesis of 3*H*-4,5-Dihydro-3-benzazepine Derivatives from Isoquinolines

Recently, we have been much interested in the formation and application of various kinds of stable dihydro-heteroaromatic amines, prepared ionically[1,2] or photochemically[3] from aromatic N-heterocycles possessing an electron-withdrawing group at the position β to the ring nitrogen, and have achieved the conversion of the stable dihydroquinolines into indole derivatives as reported in a previous paper.[2] We wish to describe here the ring expansion[4] of the isoquinoline system to 3*H*-4,5-dihydro-3-benzazepine derivatives (**2**, **3**, **5**) by utilizing the rearrangement through the carbonium ion initiated at the carbinol function of the photo-addition product (**1**).[3]

Mono-O-mesylation was effected when the photo-induced addition product (**1a**) between 4-cyanoisoquinoline and methanol was treated with mesyl chloride in a benzene-pyridine mixture at room temperature for a short period. The resulting mesylate was warmed, without further purification, with sodium methoxide in methanol at 60° for 2 hr, and comparison of the ultraviolet (UV) absorption spectrum (Table I) of the reaction product (**2a**) with the accumulated UV data of both the photo-addition product (**1**) and Grignard reaction products[1] (**4**) (Table II) suggested that the environment of the conjugated system was different from the original 1,2-dihydroisoquinolines, and the deuterium exchange study of NH in its nuclear magnetic resonance (NMR) spectrum clearly indicated the presence of the partial structure of CH_3O-$\dot{C}$H-CH_2-NH-CH=C$<$ in **2a** by the collapse of the doublet signal at 7.05 δ shown in the Table I to a singlet, as well as the appearance of the AB part of ABX pattern

1) M. Natsume and M. Wada, *Chem. Pharm. Bull.* (Tokyo), **20**, 1589 (1972).
2) M. Natsume and I. Utsunomiya, *Chem. Pharm. Bull.* (Tokyo), **20**, 1595 (1972).
3) M. Natsume and M. Wada, *Tetrahedron Letters*, **1971**, 4503.
4) Ring enlargement of 3,4-dihydroisoquinolinium salt and the 1,2,3,4-tetrahydroisoquinoline derivative was reported. *cf.* H.O. Bernhard and V. Snieckus, *Tetrahedron*, **27**, 2091 (1971); H. Irie, S. Tani, and H. Yamase, *Chem. Commun.*, **1970**, 1713.