HETEROCYCLES, Vol. 2, No. 2, 1974

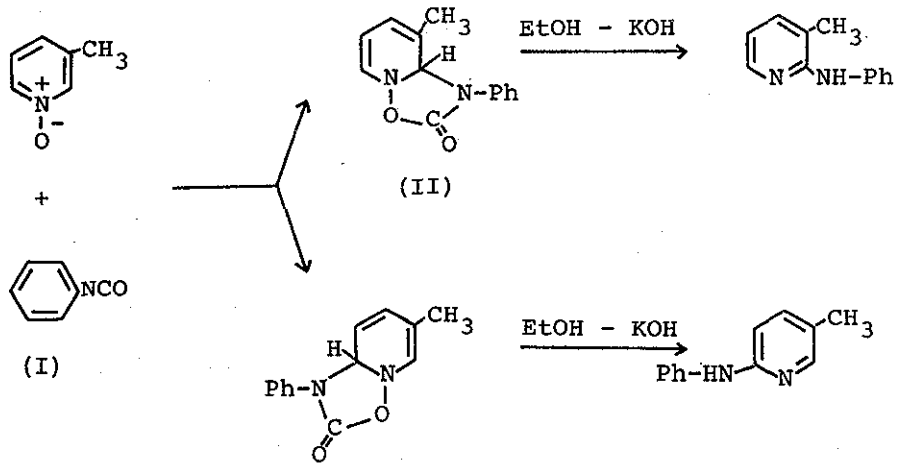
THE REACTION OF 3,5-DIBROMOPYRIDINE N-OXIDE WITH PHENYL ISOCYANATE

Takuzo Hisano, Toshikazu Matsuoka, and Masataka Ichikawa
Faculty of Pharmaceutical Sciences, Kumamoto University
Oe-hon-machi, Kumamoto, Japan

3,5-Dibromopyridine N-oxide (IV) reacted with phenyl isocyanate (I) at 110° in DMF to give 2,3-dihydro-2-oxo-3-phenyl-6-bromooxazolo[4,5-b]-pyridine (V) in 70% yield, although it was noticed that the reaction of pyridine N-oxide with I directly affords α-anilinopyridine and that 3-picoline N-oxide under the similar reaction two isomeric 1,3-cyclo-adducts (II and III).

The previous papers from our laboratory[1] described that 3-picoline N-oxide reacted with phenyl isocyanate (I) at 110° in DMF to afford primary cycloadducts, II and III, in 34 and 24% yields, respectively. Although these compounds were easily converted into the corresponding α-amino derivatives on reflux in alcoholic potassium hydroxide, they are stable to heating at 150-160° in DMF (no decomposition to the amine such as an

anilino-pyridine). The successful isolation of such dihydropyridines is apparently due to the stabilizing effect of th electron-donating β-methyl group.

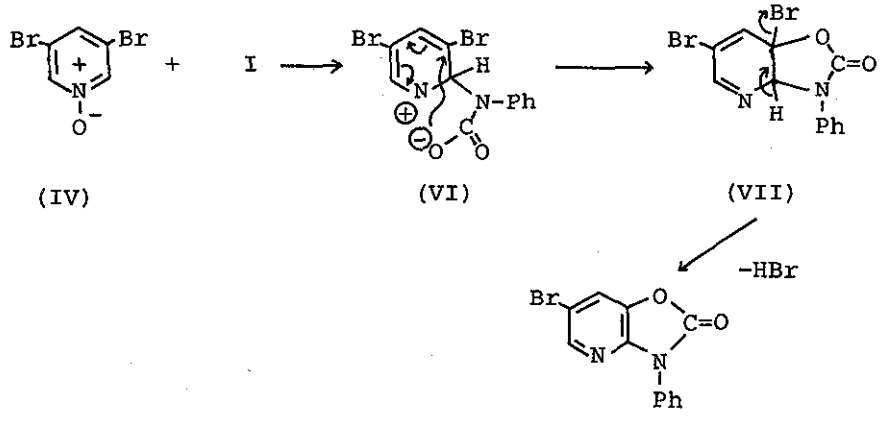


As an extension of this work, we selected 3,5-dibromopyridine N-oxide (IV) as a pridine N-oxide bearing electron-attracting group on β-position contrary to 3-picoline N-oxide and examined the reaction with I under the same condition, obtaining another novel cyclic compound.

3,5-Dibromopyridine N-oxide (IV) was heated with phenyl isocyanate (I) at 110° in DMF for 7 h to afford a product (V), mp 155-156°, as colorless needles in 70% yield, which was stable to heating to 150° in DMF, no decomposition being noticed. The analytical values were in agreement with the empirical formula $C_{12}H_7O_2N_2Br$, and its mass spectrum showed peaks at m/e 290 and 292 (M^+; relative intensity, 1 : 1), 246 and 248 ($M^+ - CO_2$), and 167 ($M^+ - CO_2$ - Br). These data demonstrate that one molar hydro-

gen bromide had been lost from an 1 : 1 adduct of IV and I during the reaction. Its ir spectrum exhibited a carbonyl absorption at 1790 cm^{-1}, but did not display any bands ascribable to a carboxylic acid group. The nmr spectrum (in 5% $CDCl_3$ solution, 100 Mc) showed an α-proton of pyridine nucleus as a narrow doublet at τ1.65 (1H, d, J=1.6 Hz, C_2-H) and the six remaining aromatic protons as a complex multiplet at τ 2.05-2.60.

On the basis of these observations, we deduced the compound V to be 2,3-dihydro-2-oxo-3-phenyl-6-bromooxazolo[4,5-b]pyridine. The formation of V may be reasonably explained by the course which involves the extrusion of N-O bond of primary cycloadduct (VI) and concerted attack by the carbamate anion thus formed at the electron-deficient 3-position to give a second cyclic intermediate (VII) followed by the elimination of a hydrogen bromide molecule.



(IV) (VI) (VII) (V)

We are continuing to examine the factors governing the processes of these cycloadducts.

ACKNOWLEDGEMENT The authors wish to thank the members of the Analytical Department of this Faculty for the micro-analyses and spectral measurements. They also are grateful to Mr. M. Nakatomi, President of Hisamitsu Pharmaceutical Co., Inc., for the supply of several chemicals.

REFERENCES

1 T. Hisano, S. Yoshikawa, and K. Muraoka, Organic Preparations and Procedures Internationals, 5(3), 95 (1973); T. Hisano, S. Yoshikawa, and K. Muraoka, Chem. Pharm. Bull. (Tokyo) in press.

Received, 5th February, 1974