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

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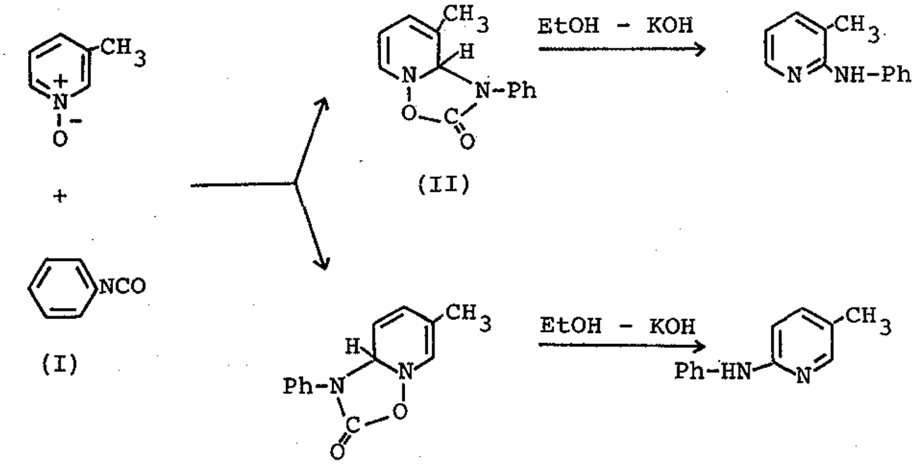
3,5-Dibromopyridine N-oxide (IV) reacted with phenyl isocyanate (I) at 110° in DMF to give 2,3-dihydro-2-oxo-3-phenyl-6-bromooxazolo[4,5-b]-pyridine (V) in 70% yield, although it was noticed that the reaction of pyridine N-oxide with I directly affords α-anilinopyridine and that 3-picoline N-oxide under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

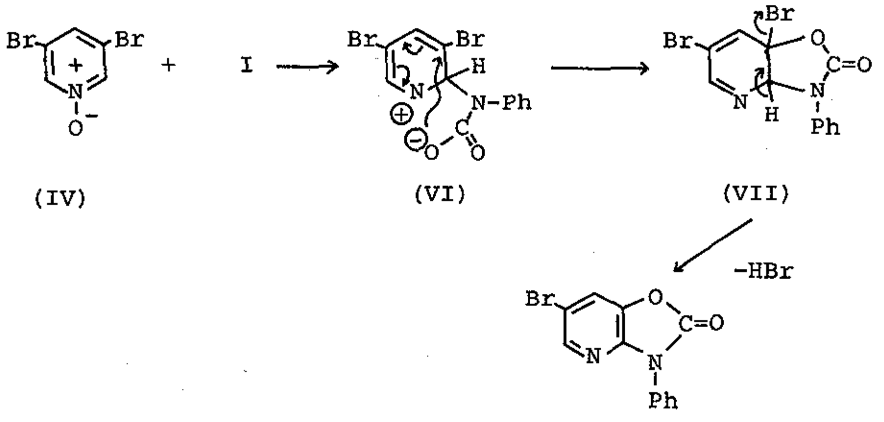
The previous papers from our laboratory[1] described that 3-picoline N-oxide reacted with phenyl isocyanate (I) at 110° in DMF to afford primary cycloadducts, II and III, in 34 and 24% yields, respectively. Although these compounds were easily converted into the corresponding α-amino derivatives on reflux 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 the 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 hydrogen 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.

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