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PHOTOLYSIS OF PYRIDYL, QUINOLYL, AND ISOQUINOLYL AZIDES IN HYDROHALOGENOIC ACIDS

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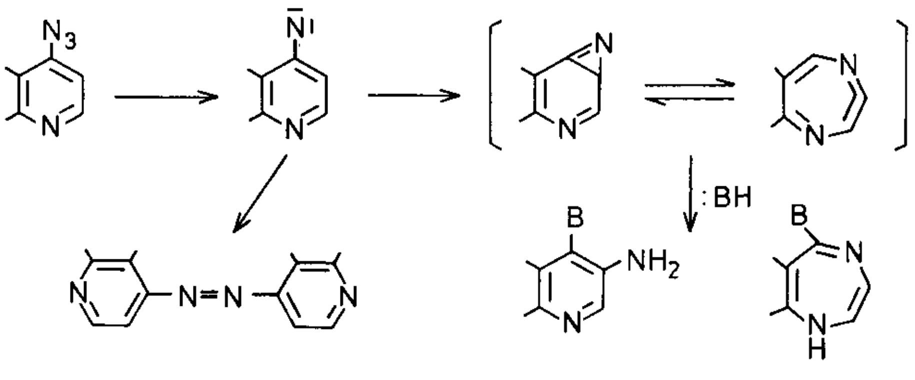
Abstract —— Photolysis of 4-azido-pyridine and -quinoline in hydrohalogenoic acids gave the 3-amino-4-halogeno compounds (2) via azirine or azacycloheptatetraene intermediates, whereas their N-oxides (4), under similar conditions, gave the 4-amino-3-halogeno compounds (5) presumably via nitrenium ion intermediates. In the 3-azidoquinoline and 4-azidoisoquinoline series, both free bases (6a, 8a) and N-oxides (6b, 8b) gave similar results to 4-azido-pyridine and -quinoline N-oxides (4).

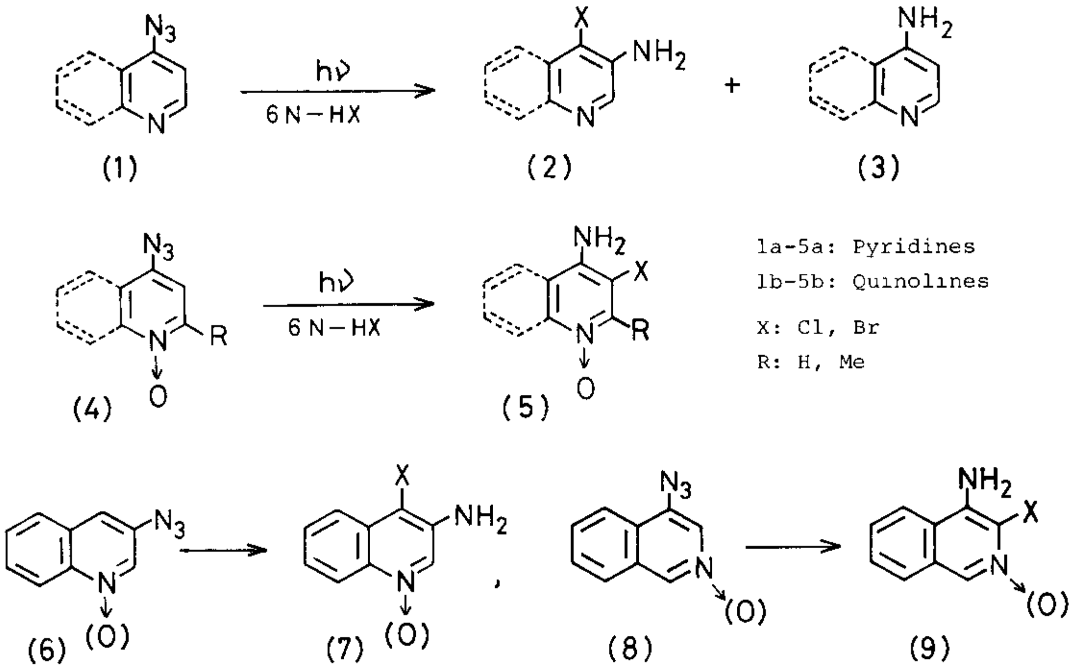
Azides have been widely used as reactive intermediates in organic syntheses[1] and the photochemical behavior of azidoazines has also received much attention in connection with those of phenyl azides.[1,2] For example, it has been shown that irradiation of azidoquinolines in the presence of bases such as alkoxides and amines gives the corresponding ring-expansion products and/or ortho-substituted



Scheme 1

amino derivatives via azirine or azacycloheptatetraene intermediates as illustrated in Scheme 1.[3] Azidoquinolines are also known to undergo dimerization to give azo compounds by irradiation in neutral conditions.[4] However, the photochemical behavior of azidoazines in acidic medium has not been reported. We now report our new results of the photolysis of some azido-pyridines, -quinolines, and -isoquinolines in hydrohalogenoic acids.

Irradiation (200 W, halogen lamp, Pyrex filter) of 4-azidopyridine (1a) and -quinoline (1b)[5] in 6 $\underline{\underline{N}}$ hydrochloric or hydrobromic acid at room temperature gave the correponding 3-amino-4-halogeno compounds (2) in 10-15% yields, analogous to the behavior observed for the photolysis in the presence of bases.[3] Besides 2, 4-amino compounds (3) were also obtained in 25-35% yields. In contrast, under similar conditions, 4-azido-pyridine (4a) and -quinoline N-oxides (4b) showed a different behavior to give the corresponding 4-amino-3-halogeno compounds (5) in high yields (80-95%),[6] respectively. The positions of the halogen and amino group in the

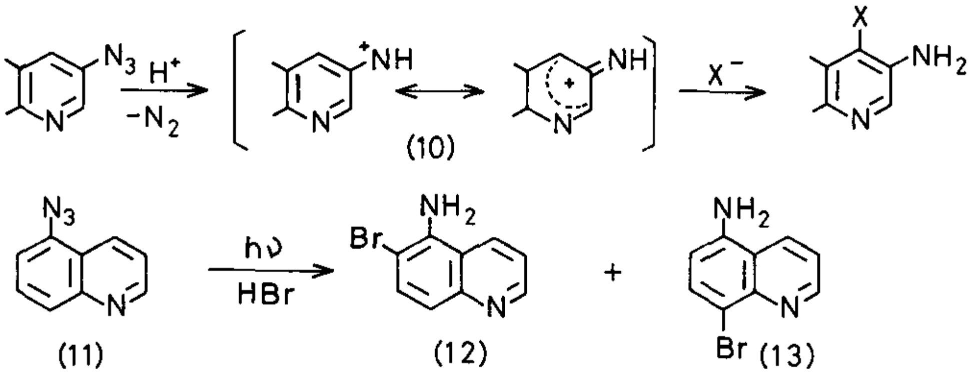


1a-5a: Pyridines
1b-5b: Quinolines

X: Cl, Br
R: H, Me

6a–9a : Free Bases
6b–9b : N-Oxides

Scheme 2



Scheme 3

products (5) are different from those in 2. Namely, the azido group in the starting N-oxides (4) is converted into the amino group and the halogen atom is introduced in the ortho-position of the original azido group.[7]

On the other hand, in the cases of 3-azidoquinolines (6) and 4-azidoisoquinolines (8), both free bases (6a, 8a) and N-oxides (6b, 8b) gave the similar results to those for 4-azidopyridine N-oxides (4), giving the corresponding halogenoamino compounds (7, 9) in 30-60% yields, respectively.

The formation of the halogenoamines (5,7,9) from the azides (4,6,8) may involve the resonance stabilized nitrenium ion intermediates (10). It is not clear at this stage whether the key intermediates (10) are derived from the conjugate acids of azides[1c] formed initially by protonation to the azides or from the singlet nitrenes by protonation,[2b] the singlet nitrenium ions[8] thus formed may then react with a halogen anion to give the products as illustrated in Scheme 3. This mechanistic proposal would be supported by the fact that the photolysis of 5-azidoquinoline (11) in hydrobromic acid resulted in the formation of both 6- (12) and 8-bromo-5-aminoquinoline (13) in the ratio of <u>ca</u>. 1:1. In the cases of 5-azido-pyridine (1a) and -quinoline (1b), the protonation might be unable to take place because the electron density of the azide or nitrene moiety is decreased by the electron-withdrawing effect of the conjugated ring nitrogen. Thus the formation of either azirine intermediates or reduction products from the singlet nitrenes may predominate over that of the nitrenium ion intermediates (10). In contrast, the electron -donating effect of the N-oxide group may cause the high yields of the products (5) in the cases of the N-oxides (4).

It is known that the thermal decomposition of phenyl azides in hydrohalogenoic acids gives halogenoanilines.[2] Heating of 4-azidoquinoline N-oxide (4b) in hydrochloric acid at 180-200° in a sealed tube gave also 5b in 40-50% yield. However, the thermolysis requires more drastic conditions and gives lower yields of the products than those for the photolysis. Studies on the detailed mechanism and on synthetic applications to other systems are in progress.

REFERENCES AND FOOTNOTES

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5. The starting azido compounds used in the present reactions were prepared from the corresponding chloro compounds by treatment either with sodium azide or with hydrazine hydrate followed by diazotization, according to the reported method [cf., T. Itai and S. Kamiya, *Chem. Pharm. Bull*., 1961, **9**, 871].
6. A solution of 6-10 N acids is most favorable to the present photolysis. When 2 N acids were used, yields of 5 decreased in 20-30%.
7. The structures of the products reported were confirmed by comparison with authentic samples or by NMR spectral analyses of the halogeno compounds obtained by deamination of these products.
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