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PHOTOLYSIS OF N-NITROSOAMINES*

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A recent communication by Burgess and Lavanish[1] has prompted us to disclose our results on the relevant photolysis of N-nitrosamines. Photochemical generation of alkoxy (from alkylnitrite)[2] and amine radicals (from N-haloamines and N-haloimides)[3,4] and intramolecular abstraction of unactivated hydrogen by such radicals has been utilised for various elegant syntheses. The following result shows that nitrosamines follow a substantially different photolytic course under the conditions specified below than in the above photolyses.

Simple N-nitrosodialkylamines were found to be quite stable to photolysis (Hannovia lamp type 30620) in solvents such as ether, cyclohexane or water and also to hydrolysis in dilute hydrochloric acid solutions (less than 1N).

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* This communication was sent to the Editor of the Proceedings of the Chemical Society on April 27, 1964, prior to the publication of Burgess and Lavanish's communication.[1] Upon appearance of the above paper, the editor advised resubmission of this communication to the Tetrahedron Letters.

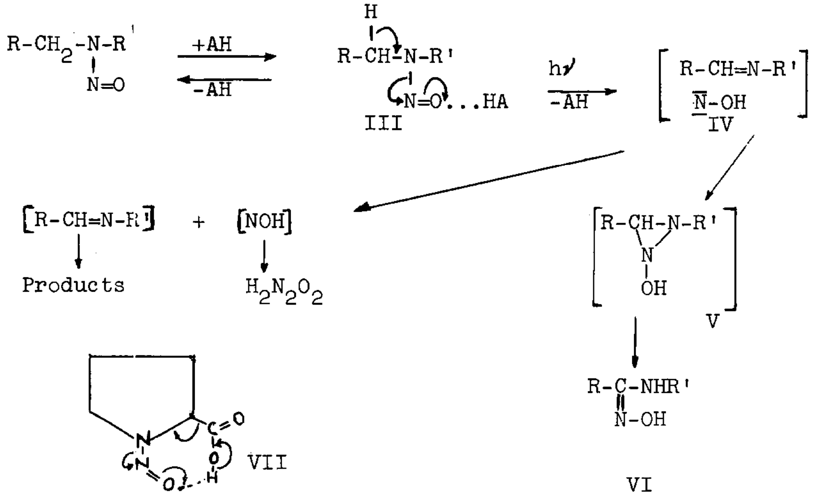
The typical ultraviolet absorption for an N-nitrosodialkylamine in the 330-350 mμ region was, however, found to disappear rapidly when an acidic solution (less than 0.3N in hydrochloric acid) of such a compound was photolysed in a pyrex flask. The corresponding amidoxime and the imine (or further products from the latter) derived from the sec-amine were produced. Typical examples of the photolysis are described below.

The photolysis of N-nitroso-N-methylcyclohexylamine in a water-methanol solution (1:4) which is 0.06N in hydrochloric acid at 20° gave cyclohexanone (56%, isolated as 2,4-DNPH), cyclohexylamine (9.5%) and N-methylcyclohexylamine (8%). In addition, a small amount of N-cyclohexylformamidoxime (m.p. 81-85°, $\nu_{max.}$ 3380 and 1650 cm^{-1}) was obtained. The crude product was hydrolysed under basic conditions to N-cyclohexylformamide. N-Nitrosodibutylamine in aqueous methanol (1:1) which is 0.2N in hydrochloric acid was photolysed to give butyraldehyde (9%, isolated as 2,4-DNPH), N-butylbutyramidoxime (I, b.p. 158-160°/12 mm., $C_8H_{18}N_2O$, 66%) and dibutylamine (21%), the last compound possibly being formed by hydrolysis. The structure of Compound I was proved by the elemental analysis, infrared spectrum (absorption at 3400-3300 and 1660 cm^{-1} in liquid film) and n.m.r. spectrum (τ-values at 0.8, 4.8, 6.99, 7.99 and 9.15 in the ratio of 1:1:2:2:3) and by a basic hydrolysis to N-butylbutyramide. N-Nitroso-3-azabicyclo[3,2,2]nonane was photolysed in water-methanol (1:3) solution containing 0.14N hydrochloric acid to give some polymers and 2-oximino-3-azabicyclo-

[3,2,2]nonane which was identified as the hydrochloride (25% $C_8H_{14}N_2O$:HCl, m.p. 230-240°, $\nu_{max.}$ 3250, 3120, 1670 cm^{-1}). The n.m.r. spectrum in D_2O displays signals at 5.9τ (2H, doublet J=3.6 cps.) 6.8τ (1H) and 7.13τ (1H).

The photolysis of N-nitrosopiperidine provided some valuable information on the nature of the reaction and, therefore, was investigated in more detail. In 0.24N hydrochloric acid solution at 20° the products were tetrahydropyridine trimer (41%, m.p. 95-96°; lit.[5] 97-98°) and 2-piperidonoxime (II, 50%, $C_5H_{10}N_2O$., m.p. 121-123°, $\nu_{max.}$3380, 3060, 1648 and 1350 cm^{-1}). The n.m.r. confirmed the assignment of the structure; the signals in $CDCl_3$ being at 6.80τ (poorly resolved triplet, 2H), 7.73τ (triplet, 2H) and a diffused multiplet at 8.2τ (4H) and in benzene solution at 0τ (1H) and 4.5τ (1H) in addition to other signals. The ratio of the two products can be varied by changing the photolysis temperature and/or by adding methanol as a co-solvent. In this way 2-piperidonoxime (75-77%) was obtained when the photolysis was carried out at 90° or when 1:1 aqueous methanol which was 0.24N in hydrochloric acid was used as the photolysis medium at 50°. Variation of the acid concentration in the photolysis medium did not appreciably change the rate of the disappearance of the 347 mμ peak (less than 20%)[6]. The photolyses of nitrosamines in aprotic solvents have been described[1].

The role played by the acid in the photolysis is not clear at this stage. Nitrosamines(Pk_b ca. -3)[7] have been shown, however, to form hydrogen bonded 1:1 complexes with an acid ($\lambda_{max.}$ 340 mμ ε, ca. 100) in cyclohexane.[7] Furthermore the first complexing site with methyl carbonium ion has been demonstrated to be at the nitroso oxygen.[8] These facts suggest that the entity undergoing the excitation may be a complex such as III and that the mechanism of the photolysis is probably as follows:



The overall reaction thus appears to be a photoelimination reminiscent of ionic elimination, though the mechanism of the transformation from III to IV can be visualised in several ways. A free radical mechanism appears unlikely inasmuch as the photolysis was not altered by the presence of oxygen. One possibility is the elimination of an α-proton as indicated to give caged IV. The species [NOH], the fictitious hyponitrous acid monomer, can be visualised as a biradical analogue of the well established[9] [NH] and would be expected to add to a double bond in a similar manner[10] to give V within the cage which, in turn, rearranges to an amidoxime. Alternatively, dimerisation to the stable hyponitrous acid dimer would be expected if [NOH] diffuses out of the cage. In support of the latter alternative the presence of $H_2N_2O_2$ in the N-nitrosopiperidine photolysate was demonstrated by ultraviolet spectroscopy [11] ($\lambda_{max.}$ 230 $m\mu$ at pH 9 and 208 $m\mu$ at pH 4), and by its decomposition product[11] N_2O (45%) which was trapped and identified by mass spectrometry. Efforts to trap transient [NOH] with various scavengers have not been successful.

Application of this photolysis to some nitrosamines derived from natural products is currently in progress. For example, photolysis of N-nitrosoproline‡ in 0.1N aqueous hydrochloric acid solution gave 2-pyrrolidonoxime, which was also obtained in a similar photolysis of N-nitrosopyrrolidin, isolated and characterized as the hydrochloride ($C_4H_8N_2O{:}HCl$, m.p. 197-200°, $\nu_{max.}$ 3200, 3310, 1695, cm^{-1} and n.m.r.τ-value in D_2O at 6.27, 7.1, and 7.73 in 1:1:1 ratio). The facile decarboxylation suggests an intervention of a cyclic mechanism such as VII. The details of this process together with others will be discussed in the full paper to be published at a later date. The I.R. spectra were taken in nujol and n.m.r. in $CDCl_3$ using TMS as internal standard unless specified otherwise. A Varian A-60 spectrometer and Metropolitan-Vickers MS-2 mass spectrometer were used. All compounds whose molecular formulae are given showed satisfactory analyses. The spectra were recorded by Mr. R. N. Swindlehurst to whom the Author is much indebted.

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‡ In agreement with the proposed intermediate III, this compound undergoes photolysis alone in ether solution to give the same product.