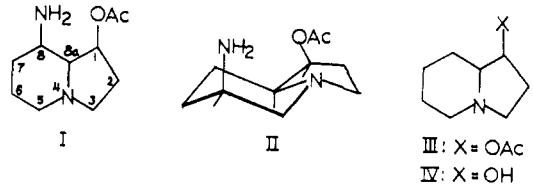
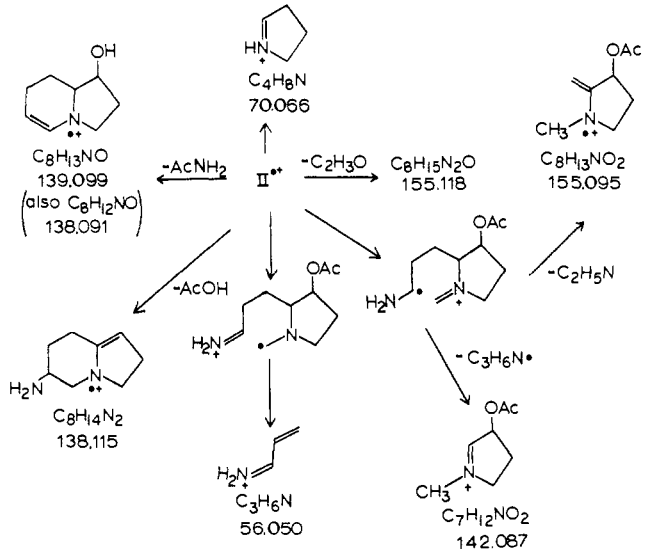


J = 6.5 Hz), is also coupled to one or more protons at 2.1 ppm (H-8) rather than to the -CHNAc proton. That proton (H-6, multiplet, 4.15 ppm) is coupled to H-5_{axial} (quartet, 3.21 ppm, $J_{5a,6}$ = 2.8 Hz), which in turn is coupled only to H-$5_{equatorial}$ (doublet, 3.90 ppm, $J_{5a,5e}$ = 13.0 Hz), establishing its location. The half-band width of H-6 is 7 Hz, consistent only with its equatorial nature.

The relative configuration at C-1 and C-9 is assigned by comparison of the nmr spectrum (100 MHz, $CDCl_3$ solution) of N-acetylslaframine[1] to those of the isomeric 1-acetoxyoctahydroindolizines (III) prepared from the corresponding isomeric 1-hydroxyoctahydroindolizines (IV), whose relative stereochemistry has recently been assigned.[4] The carbinyl acetate proton of N-acetylslaframine appears at 5.24 ppm with a half-band width of 13 Hz, while the carbinyl acetate proton of *cis*-III (H_1,H_{8a} *cis*) appears at 5.21 ppm with a half-band width of 13 Hz. The carbinyl acetate proton of *trans*-III appears at 4.76 ppm with a half-band width of 21 Hz. Moreover, the general shape of the spectrum of N-acetylslaframine is nearly identical with that of *cis*-III but quite different from that of *trans*-III. In particular, the splitting patterns for the carbinyl acetate protons are superimposable.

The absolute configuration at C-1 derives from application of Horeau's method.[5] Treatment of N-acetyl-O-deacetylslaframine[1,2] with α-phenylbutyric anhydride gave residual α-phenylbutyric acid of (−) rotation ($\alpha^{25}D$ −0.48°), thus assigning C-1 the *S* absolute configuration.

The high-resolution mass spectrum of slaframine[3] agrees with the major fragmentation pathways shown below. Except for the ions at *m/e* 155 and 138 the ions are essentially homogeneous. In deducing the origin of *m/e* 70 we were guided in part by the biosynthetic incorporation of nitrogen into slaframine.[6] The nitrogen in the C_4H_8N ion must come from the bridgehead (same ^{15}N enrichment from lysine-α-^{15}N and lysine-ϵ-^{15}N as the molecular ion, *m/e* 198, and the $C_7H_{12}NO_2$ ion, *m/e* 142).



Acknowledgment. This work was supported in part by Public Health Service Grants AI-04769 from the National Institute of Allergy and Infectious Diseases and AM-3156 from the National Institute of Arthritis and Metabolic Diseases.

(4) H. S. Aaron, C. P. Rader, and G. E. Wicks, Jr., *J. Org. Chem.*, **31**, 3502 (1966).

(5) (a) A. Horeau, *Tetrahedron Letters*, 506 (1961); (b) *ibid.*, 965 (1962).

(6) A. J. Aspen, H. P. Broquist, and K. L. Rinehart, Jr., submitted for publication.

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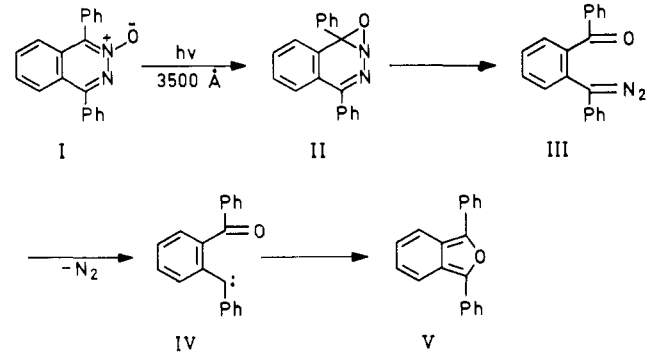
The Photolysis of 3,6-Diphenylpyridazine N-Oxide.[1] Detection of a Transient Diazo Compound

Sir:

As part of our continuing study of the photochemical behavior of aromatic amine N-oxides[2] we have examined the light-induced reactions of 1,4-diphenylphthalazine N-oxide (I) and 3,6-diphenylpyridazine N-oxide (VI). As previously reported,[3] photolysis of 1,4-diphenylphthalazine N-oxide (I) gave 1,3-diphenylisobenzofuran (V), 1,2-dibenzoylbenzene, the parent amine, an unidentified amorphous substance, and nitrogen. The 1,2-dibenzoylbenzene was assumed to arise by oxidation of 1,3-diphenylisobenzofuran. A tentative sequence leading to the isobenzofuran by way of the oxaziridine II, the diazo compound III, and the carbene IV is shown in Scheme I.

Scheme I



In the hope of further elucidating the mechanism of this novel reaction, we have examined the photolysis of 3,6-diphenylpyridazine N-oxide (VI),[4] which was

(1) Photochemical Studies. XIV. For paper XIII, see ref 2.

(2) O. Buchardt, P. L. Kumler, and C. Lohse, *Acta Chem. Scand.*, in press.

(3) O. Buchardt, *Tetrahedron Letters*, 1911 (1968).

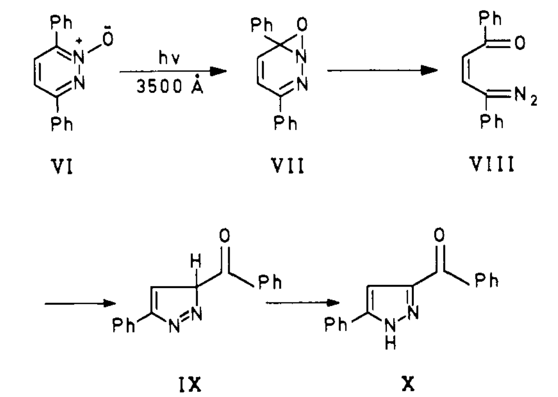
(4) The light-induced reactions of five pyridazine N-oxides in methanol solution were recently reported.[5] The major products isolated from these photolyses were the parent pyridazines. Trace amounts (0.2%) of acylpyrazoles, analogous to X, were isolated in two of the experiments. A poor material balance (<35%) was realized in all cases.

expected to result in formation of 2,5-diphenylfuran, by analogy with the behavior of the phthalazine N-oxide I.

Photolysis[6] of the pyridazine N-oxide in acetone, followed by preparative layer chromatography of the reaction mixture on silica gel, resulted in the isolation of 3-benzoyl-5-phenylpyrazole (X) in 75% yield. The substance was identical (melting point, mixture melting point, infrared spectrum) with an authentic sample of 3-benzoyl-5-phenylpyrazole.[7] Other products were formed during the irradiation, but only one, a colorless crystalline solid containing nitrogen, mp 221–222°, has been isolated in sufficient yield (~10%) for investigation.

A tentative mechanism to account for the formation of the benzoylpyrazole X from the pyridazine N-oxide VI is presented in Scheme II.

Scheme II



We believe that photolysis of the amine oxide leads initially to the oxaziridine VII[8] which is converted, in either a photochemical or a thermal process, to the diazo compound VIII. Conversion of the oxaziridine to the diazo compound is analogous to the formation of phenylnitrene from 2,3,3-triphenyloxaziridine observed by Splitter and Calvin.[9] Isomerization of the diazo compound VIII to 3-benzoyl-5-phenylpyrazole (X) *via* the tautomeric 3H-pyrazole IX, involving an intramolecular 1,3-dipolar cycloaddition that should be faster than the long-known isomerization of vinyldiazomethane to pyrazole,[10] seems wholly reasonable.

The intermediacy of the diazo compound VIII was suggested by the appearance during irradiation of a persistent, intense yellow color ($\lambda_{max}^{CH_3OH}$ 410 mμ) which faded in the dark and by the appearance of absorption at 2070 cm^{-1} in the infrared spectrum of 10% chloroform solutions of the pyridazine N-oxide immediately after irradiation. This absorption, which disappeared along with the yellow color when solutions were kept in the dark, is in the region 2040–2120 cm^{-1} where diazo compounds absorb.[11]

(5) (a) M. Ogata and K. Kano, *Chem. Commun.*, 1176 (1967); (b) H. Igeta, T. Tsuchiya, M. Yamada, and H. Arai, *Chem. Pharm. Bull.* (Tokyo), **16**, 767 (1968).

(6) The light source for all photolyses was the RUL-3500 lamps of a Rayonet reactor, Type RPR-208.

(7) D. G. Farnum and P. Yates, *J. Am. Chem. Soc.*, **84**, 1399 (1962). We thank Dr. Yates for a sample.

(8) For discussion of the photochemical formation of oxaziridines from aromatic amine N-oxides see earlier papers in this series.

(9) J. S. Splitter and M. Calvin, *Tetrahedron Letters*, 1445 (1968).

(10) (a) C. D. Hurd and S. C. Lui, *J. Am. Chem. Soc.*, 57, 2656 (1935); (b) D. W. Adamson and J. Kenner, *J. Chem. Soc.*, 286 (1935).

It seems reasonable to assume that loss of nitrogen occurs from the diazo compound III because the thermal cyclization (analogous to the process VIII → IX) is energetically very unfavorable. It is possible that some of the minor products observed in the photolysis of 3,6-diphenylpyridazine N-oxide arise by loss of nitrogen from the diazo compound or the 3H-pyrazole derivative IX.[12]

Further attempts to elucidate the detailed mechanisms operating in the photolyses of aromatic 1,2-diazine N-oxides are currently in progress. Such experiments are primarily directed toward detection of the diazo compound III or the carbene IV during photolysis of 1,4-diphenylphthalazine N-oxide (I). These results, together with the photochemical behavior of other aromatic 1,2-diazine N-oxides, will be reported in the full paper.

Acknowledgment. We wish to acknowledge the financial support of the Carlsberg Foundation (purchase of the Rayonet reactor) and the North Atlantic Treaty Organization (NATO postdoctoral fellowship to P. L. K.).

(11) A. Foffani, C. Pecile, and S. Ghersetti, *Tetrahedron*, **11**, 285 (1960).

(12) The thermal loss of nitrogen from diazo compounds and pyrazolines is well documented. It is also known that 3H-pyrazoles can lose nitrogen in a photochemical reaction,[13] with ring opening preceding nitrogen elimination. In some cases transient diazoalkenes have been detected.[13c]

(13) (a) G. L. Closs and W. Böll, *Angew. Chem.*, **75**, 640 (1963); (b) G. L. Closs and W. A. Böll, *J. Am. Chem. Soc.*, **85**, 3904 (1963); (c) G. L. Closs, W. A. Böll, H. Heyn, and V. Dev, *ibid.*, **90**, 173 (1968).

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Received July 1, 1968

Total Synthesis of Anthramycin

Sir:

Recently we reported on the isolation and characterization of anthramycin,[1] a new antitumor antibiotic to which we assigned structure **1** primarily on spectroscopic evidence.[2,3] We now wish to record the total synthesis of anthramycin by methods which confirm this unique structure.

We have shown previously that anthramycin (**1**) can be obtained by partial synthesis from anthramycin methyl ether (**2**) *via* anhydroanthramycin (**5**).[1] The problem of the total synthesis was therefore reduced to the task of synthesizing anthramycin methyl ether (**2**), a comparatively stable and well-characterized derivative which had been obtained in the course of our isolation work by crystallization of the antibiotic from methanol–water.[1]

We selected as our first synthetic objective compound **17**, the structure of which differs from that of anthramycin only by the absence of two hydrogen atoms. It appeared particularly attractive to attempt the synthesis of this compound from a naturally occurring amino acid.

(1) W. Leimgruber, V. Stefanović, F. Schenker, A. Karr, and J. Berger, *J. Am. Chem. Soc.*, 87, 5791 (1965).

(2) W. Leimgruber, A. D. Batcho, and F. Schenker, *ibid.*, **87**, 5793 (1965).

(3) W. Leimgruber, A. D. Batcho, and F. Schenker, 4th International Symposium on the Chemistry of Natural Products, IUPAC Congress, Stockholm, 1966, Abstracts, p 106.