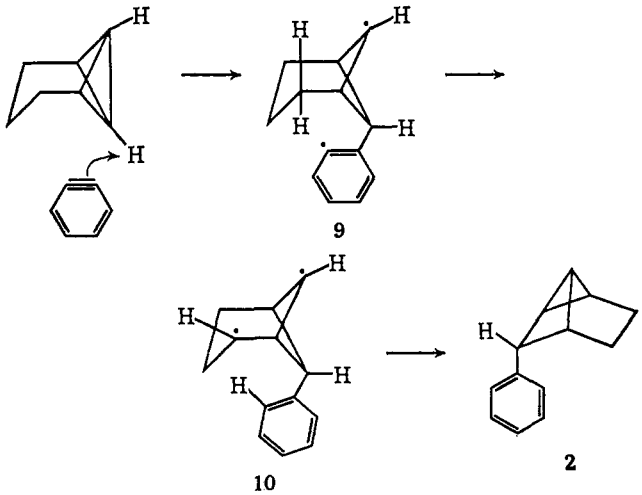

9

10 2

most probably mechanistic path involves initial formation of **9** followed by hydrogen transfer to give **10** and subsequent closure of the diradical to yield **2**.[12]

The addition of benzyne to **1** from inside the sterically hindered "flap" formed by the fused rings of the bicyclo[1.1.0]butane portion of **1** indicates the overwhelming preference for "backside" attack on the bent C_1–C_7 bond. Studies designed to further elucidate the steric and strain requirements of this reaction are in progress.

Acknowledgment. We are indebted to the National Science Foundation for Grant GP 7063 which partially supported this investigation.

(12) An alternate mechanism which cannot be ruled out on the basis of the evidence presently available would be a thermal 2 + 2 + 2 concerted reaction. For a discussion of symmetry considerations in relation to 2 + 2 + 2 reactions see R. Hoffmann and R. B. Woodward, *J. Am. Chem. Soc.*, 87, 2046 (1965).

(13) Alfred P. Sloan Research Fellow, 1967–1969.

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Elimination Reactions under High Pressure. Reactions of Alkyl Iodides with 2,6,N,N-Tetramethylaniline

Sir:

It is well established that a highly sterically hindered amine, 2,6,N,N-tetramethylaniline (I), does not react with methyl iodide under conventional methods.[1]

We wish now to report that I reacted with methyl iodide under high pressure to yield 2,6,N,N-tetramethylanilinium iodide (II) instead of 2,6,N,N,N-pentamethylanilinium iodide. The reaction was carried out with an excess of methyl iodide (mole ratio 1:4) under 5000–5500 atm at 120–130° for 15 hr.[2] II could result from the α elimination of hydrogen iodide from methyl iodide with the base. Thus, the reaction was carried out in the presence of excess cyclohexene as a carbene acceptor. In the liquid products of the reaction, norcarane (3–5%) (III), 3-methylcyclohexene (15–20%) (IV), 1-methylcyclohexene (6–8%) (V),[3] and a tar material were isolated.

The presence of III among the reaction products is interpreted as evidence for the formation of carbene.[4] The mechanisms of the formation of IV and V need further study, although these products have a tendency to isomerize and polymerize under the present reported reaction condition.[5]

I did not react significantly with ethyl iodide by refluxing the mixture for a long period. However, I reacted with ethyl iodide (using five to six times excess) under 4000–5000 atm at 100–110° for 16–18 hr. The reaction gave ethylene and 2,6,N-trimethyl-N-ethylanilinium iodide (75–80%) yield) (VI).[6] The formation of VI may be due to an exchange reaction of the ethyl moiety of ethyl iodide with the N-methyl of II, which is the first product from I with ethyl iodide by the elimination reaction.[7] Under similar conditions, I also reacted with isopropyl iodide to yield II and propylene.

The reaction of simple alkyl halides with amines gave, in general, the substituted product and very little of the elimination product. However, one would expect the elimination reaction to proceed preferentially over the substitution on increasing the steric requirement of the amines. Thus, the above-reported reactions are *extreme examples* of those reactions which produce quantitatively elimination products and none of the substituted compounds.

(1) H. C. Brown and M. Grayson, *J. Am. Chem. Soc.*, **75**, 20 (1953). The failure of the reaction was attributed to the large strain energy of the expected product, 2,6,N,N,N-pentamethylanilinium iodide (strain energy was estimated as 17 kcal).

(2) The detailed procedure of a high-pressure reaction was reported in a previous paper: Y. Okamoto and H. Shimizu, *J. Am. Chem. Soc.*, in press.

(3) Products were characterized and identified by gas chromatographic and infrared comparisons with authentic samples. The yields were calculated based on the amount of compound I added.

(4) W. Kirmse, "Carbene Chemistry," Academic Press, New York, N. Y., 1964, p 40.

(5) The reaction of benzyl chloride with *n*-butyllithium in the presence of cyclohexene also produced a considerable amount of 3-benzylcyclohexene: G. L. Closs and L. E. Closs, *Tetrahedron Letters*, No. 24, 26 (1960).

(6) II: yield 65–60%; mp 160° dec; nmr (D_2O, internal TMS), δ 2.58 (singlet, six *o,o'*-dimethyl protons), 3.42 (singlet, six N-dimethyl protons), 7.27 (three aromatic protons). VI: mp 133–135°; nmr (D_2O, internal TMS), δ 1.12 (triplets, three methyl protons, N–C_2H_5), 2.58 (singlet, six *o,o'*-dimethyl protons), 3.42 (singlet, three N-methyl protons), 3.85 (multiplets, two methylene protons, N–C_2H_5).

(7) A similar exchange reaction was reported in a previous paper.[2]

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Slaframine. Absolute Stereochemistry and a Revised Structure

Sir:

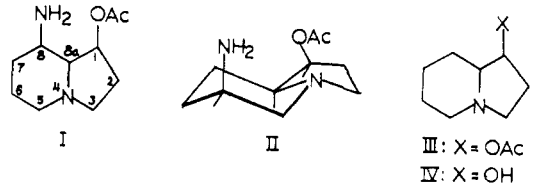
We recently assigned structure I to the parasympathomimetic fungal alkaloid slaframine;[1,2] we now revise this structure to II,[3] (1*S*,6*S*,8a*S*)-1-acetoxy-6-aminooctahydroindolizine.

Spin-decoupling experiments performed on N-acetylslaframine hydrochloride (100 MHz, D_2O solution) reveal that H-8a (3.41 ppm), coupled to H-1 (5.49 ppm,

(1) S. D. Aust, H. P. Broquist, and K. L. Rinehart, Jr., *J. Am. Chem. Soc.*, 88, 2879 (1966).

(2) After our earlier publication appeared, another group [B. J. Whitlock, D. P. Rainey, N. V. Riggs, and F. M. Strong, *Tetrahedron Letters*, 3819 (1966)] employed arguments much like ours to assign the same structure (I) to slaframine.

(3) The key mass spectral peak at M − 43 earlier attributed[1] to loss of C_3H_7 has been shown in a high-resolution mass spectrum (determined at the Purdue Mass Spectrometry Center) to be a doublet in the spectrum of slaframine, arising from loss of C_2H_5N (major ion) and C_2H_3O (minor ion); in deacetylslaframine the M − 43 peak is also due to loss of C_2H_5N (major) and C_2H_3O (minor).

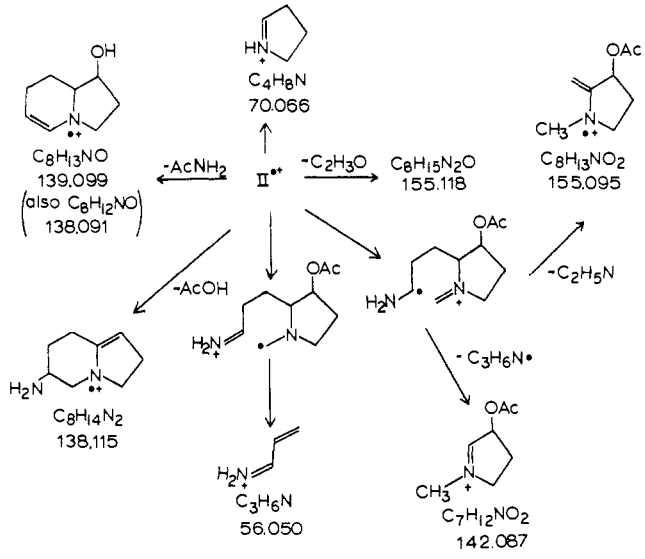


J = 6.5 Hz), is also coupled to one or more protons at 2.1 ppm (H-8) rather than to the –CHNAc proton. That proton (H-6, multiplet, 4.15 ppm) is coupled to H-5_{axial} (quartet, 3.21 ppm, $J_{5a,6}$ = 2.8 Hz), which in turn is coupled only to H-$5_{equatorial}$ (doublet, 3.90 ppm, $J_{5a,5e}$ = 13.0 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.

(7) Public Health Service Predoctoral Fellow and Allied Chemical Co. Fellow.

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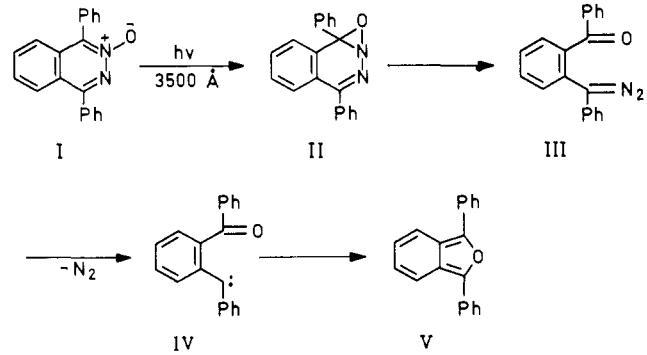
The Photolysis of 3,6-Diphenylpyridazine N-Oxide.[1] Detection of a Transient Diazo Compound

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.