Tetrahedron Letters No.28, pp. 3341-3345, 1966. Pergamon Press Ltd.
Printed in Great Britain.

# THE INTRAMOLECULAR PHOTOCHEMICAL CYCLIZATION OF 2-HALOPYRIDINIUM SALTS

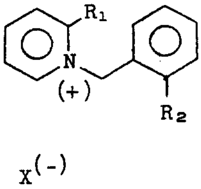
Alan Fozard and C. K. Bradsher
Department of Chemistry, Duke University, Durham, North Carolina

(Received 23 April 1966; in revised form 16 May 1966)

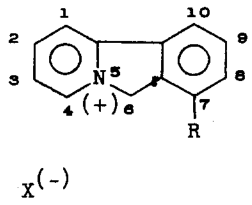
Although N-methyl-2-pyridones and N-methyl-2-aminopyridine derivatives are known[1,2] to dimerize when irradiated with ultraviolet light to give 1,4-dimers, no other 2-substituted pyridine derivatives[3] have been reported to undergo photochemical reactions. In the 2-halo-substituted pyridinium salts the non-bonding electrons of the halogen atoms evidently participate to some extent[4] in resonance interactions with the $\pi$-electrons of the pyridine ring, and it might be expected that, on irradiation, these salts would undergo photochemical reaction. We have found no evidence of dimerisation or halogen replacement when an aqueous solution of 2-bromo-1-methylpyridinium bromide was irradiated with ultraviolet light. However, we have irradiated a number of N-benzyl- and N-phenacyl-2-halopyridinium salts and found that intramolecular cyclizations occur readily with the loss of hydrogen bromide.

When an aqueous solution of 2-bromo-N-benzylpyridinium bromide (I, $R_1$ = Br, $R_2$ = H, X = Br) was irradiated with a water-cooled

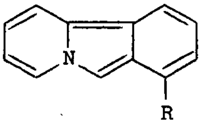
Hanovia 450w. ultraviolet lamp having either a Corex or Pyrex filter, the ultraviolet spectrum of the solution was changed over a period of 4 hrs. From this solution was isolated a salt, mp 207.5-209.5°, which had the elemental analysis required for 6-H-benzo[a]indolizinium bromide (II, R = H, X = Br). The ultraviolet spectrum of this compound ($\lambda_{max}^{H_2O}$ 256, 313 mμ $\log_{10}\epsilon$ 4.14, 4.02) is somewhat similar to that of fluorene[5]. The N.M.R. spectrum showed a singlet peak at δ 6.05 ppm (attributed to the methylene protons), a doublet at δ 9.14 ($C_4$ proton), a series of peaks between δ 8.06-δ 8.86 ($C_1$, $C_2$, $C_3$ protons), and a sharp peak at δ 7.92 ($C_7$, $C_8$, $C_9$, $C_{10}$ protons). When the indolizinium salt (II, R = H, X = Br) was treated with aqueous sodium carbonate, a yellow insoluble compound was obtained, mp 225° (decomposition), the elemental analysis of which suggested that it was the previously unknown heterocyclic system III (R = H). The N.M.R. spectrum of this compound showed peaks in the δ 8.07 - δ 9.86 range only. The ultraviolet spectrum of the system (III, R = H) ($\lambda_{max}^{95\%\ EtOH}$ 255, 308, 321sh, 334, 394, $\log_{10}\epsilon$ 4.61, 3.65, 3.62, 3.76, 3.85) showed longer wavelength maxima than did that of the salt (II, R = H, X = Br), indicating increased conjugation. The new system (III, R = H) was obtained in 65% yield by direct basification of the irradiated solution.



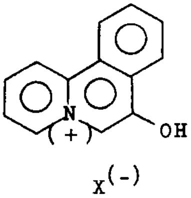
(I)



(II)



(III)



(IV)

The chlorine analog of the benzylpyridinium salt (I, $R_1$ = Cl, $R_2$ = H, X = Br) also cyclized on irradiation to give the same indolizinium salt (II, R = H, X = Br). No significant difference in the rate of reaction or the yield was noted. N-(2'-Bromo) benzyl-pyridinium bromide (I, $R_1$ = H, $R_2$ = Br, X = Br) was also found to cyclize on irradiation, though in this case the rate of cyclization was considerably slower; 24 hrs. irradiation giving a 38% yield of the indolizine (III, R = H). Irradiation of the dibromo-quaternary salt (I, $R_1$ = Br, $R_2$ = Br, X = Br) resulted in exclusive photolysis of the bromine atom on the pyridinium ring to form compound II (R = Br, X = Br). Confirmation of the structure was given by the characteristic doublet of the α pyridinium proton ($C_4$) at $\delta = 9.31$ in the N.M.R. spectrum and by the ultraviolet spectrum ($\lambda_{max}^{H_2O}$ 209, 258, 312 $\log_{10}\epsilon$ 4.59, 4.07, 4.10). N-Benzylpyridinium bromide (I, $R_1 = R_2$ = H, X = Br) failed to undergo cyclization even after prolonged irradiation.

Also N-phenacyl-2-bromopyridinium salts on irradiation with ultraviolet light have given 7-hydroxybenzo[a]quinolizinium salts (IV) in good yield. The unsubstituted N-phenacylpyridinium salts did not cyclize under the same conditions. Several derivatives, including benzologues, of the indolizinium system (II) have been synthesized but attempted cyclization of salts containing a nitro substituent in the phenyl ring was unsuccessful. The mechanism of this reaction is, as yet, unknown but any mechanistic formulation must account for the failure of 2-bromo-1-methylpyridinium bromide and N-4'-nitrobenzyl-2-bromopyridinium salts to undergo any detectable photolysis under the conditions used[6]. This suggests that the reaction may not proceed by simple homolytic cleavage of the pyridinium carbon-halogen bond followed by free radical substitution into the phenyl group, as is the case in the free-radical synthesis of phenanthrenes from bromo-stilbenes[7] and, presumably, photochemically from iodo-stilbenes[8].

## Acknowledgement

This investigation was supported by Public Health Service Research Grant No. CA-05509 of the National Cancer Institute.

## REFERENCES

(1) G. Slomp, F. A. MacKellar and L. A. Paquette, J. Amer. Chem. Soc., **83**, 4472 (1961), and also L. A. Paquette and G. Slomp ibid., **85**, 765 (1963).

(2) E. C. Taylor and R. O. Kan, J. Amer. Chem. Soc., **85**, 776 (1963).

(3) R. E. Doolittle and C. K. Bradsher, Chem. and Ind., 1631 (1965) have however, prepared benzo[a]quinolizinium (phenanthridizinium) salts by irradiation of N-styrylpyridinium salts.

(4) 2-Bromopyridine methiodide ($\lambda_{max}^{H_2O}$ 225, 295) shows a shift of 36 mμ to longer wavelengths of the $\pi \longrightarrow \pi^*$ $\alpha$ band compared with pyridine methiodide.

(5) R. A. Friedel and M. Orchin, "Ultraviolet Spectra of Aromatic Compounds", John Wiley and Sons, Inc., New York, 1951, no. 311.

(6) o-Bromobiphenylmethane also fails to cyclize on irradiation (hexane solution) though in this case halogen abstraction occurs. P. W. Jeffs and J. F. Hansen, personal communication.

(7) M. Tiecco, Chem. Comm., 555 (1965).

(8) S. M. Kupchan and H. C. Wormser, J. Org. Chem., **30**, 3792 (1965).