HETEROCYCLES, Vol. 4, No. 6, 1976

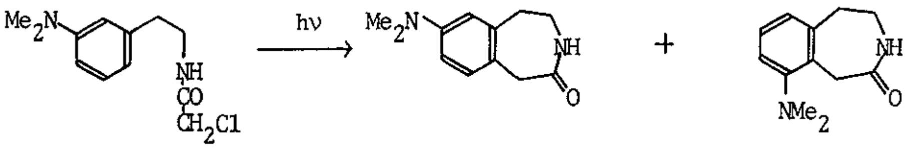
INTRA- AND INTER-MOLECULAR PHOTOREACTIONS OF N-CHLOROACETYL DERIVATIVES OF DIMETHYLAMINOPHENETHYLAMINES AND DIMETHYLAMINOBENZYLAMINES IN BOTH ACIDIC AND BASIC SOLUTIONS

Naganori Numao and Osamu Yonemitsu*
Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo 060, Japan

Photocyclization of N-chloroacetyl derivatives of dimethylaminophenethylamines and dimethylaminobenzylamines were examined. Intramolecular photoreactions little affected by acid gave azepinones (V, VI) and a cage compound (VIII), while novel diazametacyclophanes (IX, XII) were obtained intermolecularly, which was strongly depressed by acid. These results suggest that the photoreactions involve the singlet excited state of the dimethylaniline moiety.

The mechanism of the photocyclizations of N-chloroacetylphenethylamines having an electron-donating group on aromatic rings has been proposed to include an electron transfer from the electron-rich aromatic rings to the electron-deficient chloroacetyl group *via* an intramolecular exciplex.[1] The intermolecular reactions of electron-rich aromatics such as phenol, anisole and indole with chloroacetamide also proceeded smoothly,[2] but aromatics without electron-donating groups such as benzene and benzoic acid were recovered unchanged under the same conditions. In this communication, these photoreactions have been extended to N-chloroacetyl derivatives of dimethylaminophenethylamines and dimethylaminobenzylamines, which were expected to cyclize more effectively, because the dimethylamino group having more negative Hammett σ^3 is usually more electron-donative than the hydroxy and methoxy groups.

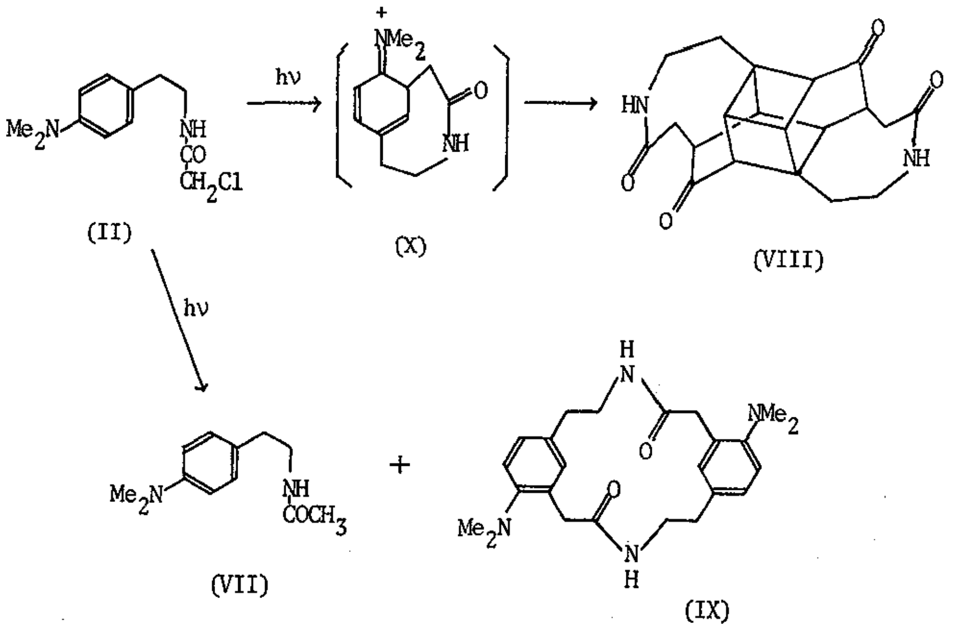
When a 10 mM solution of N-chloroacetyl-m-dimethylaminophenethylamine (I) in 50% aqueous acetonitrile containing excess $NaHCO_3$ was irradiated with a 100 W high pressure mercury lamp for 2 hr, both ortho and para cyclizations with reference to the dimethylamino group proceeded smoothly, and 7-dimethylamino-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (V) [40%; mp 166-168° (EtOAc)] and 9-dimethylamino analogue (VI) [32%; mp 158-160° (EtOAc)] were isolated after silica gel chromatography. The structures of V and VI were easily assigned on the basis of coupling patterns of the aromatic protons in their nmr spectra.[4]



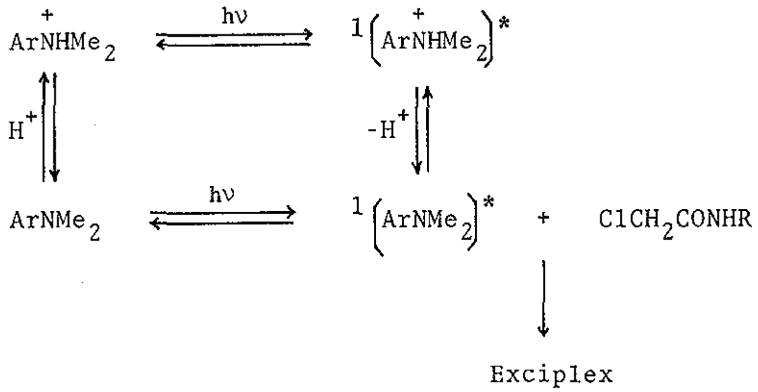
(I) (V) (VI)

On irradiation under the same conditions, N-chloroacetyl-p-dimethylaminophenethylamine (II) gave a complex mixture of photoproducts containing an N-acetyl derivative (VII) [9.7%; mp 113-114° (benzene-hexane)] and two interesting dimeric compounds, a cage compound (VIII)[5] (11.7%) and a novel diaza[5,5]metacyclophane (IX) [13%; mp 277-280° (dec, EtOH-H_2O); m/e 408 (M^+, 94), 204 (96), 188 (83), 187 (100), 160 (85), 146 (75), 132 (61); ν^{Nujol} 3260, 1645, 1550 cm^{-1}; $\lambda_{\text{max}}^{\text{MeOH}}$ 251 nm (ε 9590)]. The intramolecular ortho cyclization to form a reactive intermediate (X) must have led to the formation of VIII, while the intermolecular photoreaction gave IX.

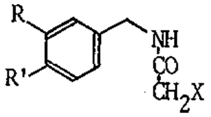
Since the pK_a of dimethylaniline is 5.21,[6] the dimethylamino group is no longer electron-donative in a strong acid solution. The photocyclizations of I, however, were interestingly little affected by acid even in a 0.5% HCl solution (pH 0.9), and two azepinones, V and VI, were isolated in 65% yield. In the photolysis of II, the intermolecular reactions forming IX and a polymeric mixture were clearly depressed, while the cage compound (VIII) became the main product and was isolated in 55% yield.



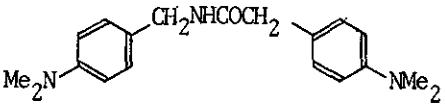
If these photoreactions involve the singlet excited states of I and II, the exciplex formation in acidic solutions must have occurred after deprotonation from the singlet excited anilinium cation moiety.[7] Therefore, the intermolecular reactions, which cannot exceed the diffusion controlled limit, were depressed, while the rapid intramolecular reactions were little affected. A detailed mechanistic discussion based on absorption and emission spectra and quantum yields will be reported soon.



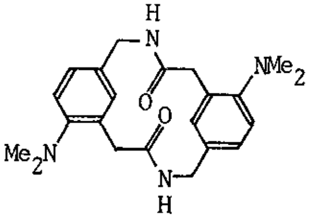
Next, the photolysis of N-chloroacetyl-m-dimethylaminobenzylamine (III) was examined. Attempts to yield cyclization products in both acidic and basic solutions were unsuccessful and an N-acetyl derivative (XI) [mp 59.5-60.5° (ether-petroleum ether)] was the only isolable product. On irradiation in the presence of $NaHCO_3$, N-chloroacetyl-p-dimethylaminobenzylamine (IV) gave two intermolecular photoproducts, a novel diaza[4,4]metacyclophane (XII) [8.8%; mp > 305° ($EtOH-H_2O$); m/e 380 (M^+, 82), 191 (49), 175 (64), 173 (63), 160 (100), 148 (51), 132 (78); ν^{Nujol} 3280, 1650, 1550 cm^{-1}] and XIII [4.3%; mp 154-156° (dec, benzene-hexane); m/e 311 (M^+, 14),



(III): $R=NMe_2;R'=H;X=Cl$
(IV) : $R=H;R'=NMe_2;X=Cl$
(XI) : $R=NMe_2;R'=X=H$



(XIII)



(XII)

190 (14), 189 (12), 135 (14), 134 (100); ν^{Nujol} 3275, 1640, 1550 cm^{-1}]. In higher concentration of IV, the yield of XII increased to 17%.

The data presented here may provide an example of photoreactions using the characteristics of excited state pK's.[9]

REFERENCES

1 S. Naruto, O. Yonemitsu, N. Kanamaru and K. Kimura, *J. Am. Chem. Soc.*, 1971, **93**, 4053; O. Yonemitsu, H. Nakai, Y. Okuno, S. Naruto, K. Hemmi and B. Witkop, *Photochem. Photobiol.*, 1972, **15**, 509; S. Naruto and O. Yonemitsu, *Tetrahedron Lett.*, 1975, 3399; Y. Okuno and O. Yonemitsu, *Chem. Pharm. Bull.* (Tokyo), 1975, **23**, 1039.

2 O. Yonemitsu and S. Naruto, *Chem. Pharm. Bull.* (Tokyo), 1971, **19**, 1158; S. Naruto and O. Yonemitsu, *ibid.*, 1972, **20**, 2163.

3 D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, **23**, 420; H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, 1958, **80**, 4979.

4 *Cf.* Y. Okuno, K. Hemmi and O. Yonemitsu, *Chem. Pharm. Bull.* (Tokyo), 1972, **20**, 1164.

5 T. Iwakuma, H. Nakai, O. Yonemitsu and B. Witkop, *J. Am. Chem. Soc.*, 1974, **96**, 2564; T. Iwakuma, K. Hirao and O. Yonemitsu, *ibid.*, 1974, **96**, 2570.

6 J. A. Dean, ed., "Lange's Handbook of Chemistry," McGraw-Hill, New York, N. Y., 1973, p 5-24.

7 The pK_a values of the S_1 and T_1 states of dimethylaniline are estimated to be *ca.* -2 and *ca.* 3, respectively, from the values of 2-naphthylamine.[8]

8 G. Jackson and G. Porter, *Proc. Roy. Soc.* (London), 1961, **A**, **260**, 13.

9 *Cf.* I. Tabushi, T. Nakajima and Z. Yoshida, *Chem. Pharm. Bull.* (Tokyo), 1975, **23**, 2929; F. Saeva and G. R. Olin, *J. Am. Chem. Soc.*, 1975, **97**, 5631.

Received, 15th March, 1976