

PHOTOCHEMICAL FORMATION OF PYRROLOINDOLE SKELETON
FROM N-CHLOROACETYL-2,5-DIMETHOXYPHENETHYLAMINE

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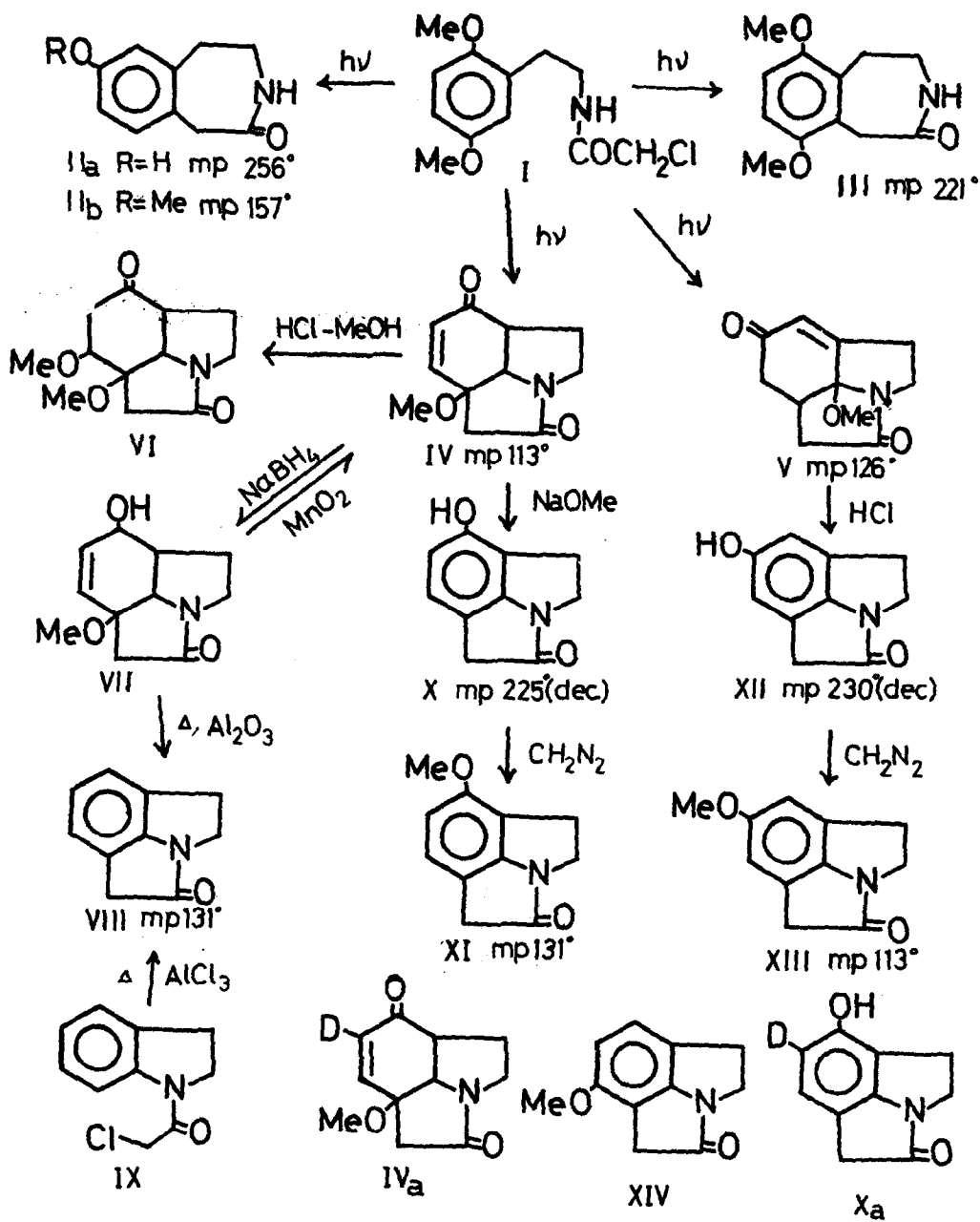
The photocyclizations of N-chloroacetylphenethylamines,² which afforded novel heterocycles, have now been extended to N-chloroacetyl-2,5-dimethoxyphenethylamine (I) to give novel tricyclic enones with pyrrolo(3,2,1-hi) indole skeleton.

When 10 mM solution of I in 20 % aqueous ethanol was irradiated with a 100 W high pressure mercury lamp under nitrogen for 1.5 hr, two benzazepinones and two tricyclic enones were isolated.

7-Hydroxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (IIa, 2.2 %) isolated by recrystallization of the methylene chloride insoluble fraction from methanol, and its methylated compound IIb were identical with the authentic samples,³ respectively.

The structure of another benzazepinone, 6,9-dimethoxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (III, 8.3 %), isolated by chromatography on silicagel, was confirmed by analogy with the 6,7-dimethoxy compound⁴ by its spectral data: mass m/e 221 (M⁺); nmr (CDCl₃) δ 2.98 (t, 2H, J = 7 Hz), 3.50 (t, 2H, J = 7 Hz), 3.74 (s, 6H), 6.65 (broad s, 1H) and 6.68 (s, 2H).

The chromatography was continued to isolate two enones, IV (12.4 %) and V (3 %). The composition of IV was determined by mass spectrometry as C₁₁H₁₃NO₃, which differs from the starting material by the loss of hydrogen chloride and a methylene group. In the ir spectrum two carbonyl groups of enone and lactam happen to be in the same position at 1685 cm⁻¹, and two vinyl protons appear at δ 6.28 and 6.53 ppm in the nmr spectrum. Compound IV has a n- π^* absorption band at 333 nm (ϵ 43) in ethanol or at 340 nm (ϵ 36) in methylene chloride, however a π - π^* absorption appears surprisingly not at the usual position (calculated value by the Woodward rule; 227 nm),⁵ but at 198 nm (ϵ 14000 in water), probably superposed upon a π - π^* absorption of the lactam group.



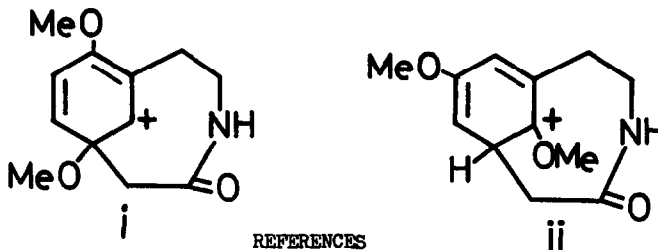
The structure of IV was confirmed by the following chemical evidence: i) The treatment with 1 N hydrogen chloride in anhydrous methanol at room temperature gave a methanol addition product VI [mass m/e 239 (M^+); nmr δ , two methoxy groups at 3.32 and 3.38 ppm and no vinyl protons]. ii) The reduction with sodium borohydride gave an alcohol VII, though in 22 % yield, which was reverted easily to IV by the treatment with manganese dioxide. Upon heating with alumina in toluene,⁴ VII aromatized with the loss of methanol and water to 2-oxo-1,2,4,5-tetrahydropyrrolo[3,2,1-hi]indole (VIII), which is identical with the authentic sample synthesized from N-chloroacetylindoline (IX) by Friedel-Crafts reaction.⁶ iii) The treatment with 1.5 equivalents of sodium methoxide in methanol at room temperature for 2 hr, IV rearranged with the loss of methanol to a phenol X [mass m/e 175 (M^+)], which was treated with diazomethane overnight to give a methoxy compound XI. The mass (m/e 189 (M^+), 161, 146, 130 and 118) and nmr spectra [δ 3.52 (t, 2H, $J = 7$ Hz), 3.67 (s, 2H), 3.82 (s, 3H), 4.00 (t, 2H, $J = 7$ Hz), 6.36 (d, 1H, $J = 8$ Hz) and 6.87 (d, 1H, $J = 8$ Hz)] are almost identical with those of the known isomer XIV,⁴ however XI and XIV differ from one another in melting point, ir and uv spectra. iv) A brief treatment (6 min) with 1 equivalent of sodium methoxide in deuterio-methanol gave a deuterium exchanged product IVa,⁷ in whose nmr spectrum an unchanged vinyl proton appears at δ 6.35 ppm as a singlet. An overnight treatment gave a monodeutero-phenol Xa with an aromatic proton at 6.80 ppm as a singlet.

Another enone V has the composition $C_{11}H_{13}NO_3$, isomeric with IV, two carbonyl groups (ir 1705 (lactam) and 1670 cm^{-1} (enone)), one methoxy group [nmr δ 3.33 ppm (s, 3H)] and one vinyl proton [δ 5.85 ppm (s, 1H)]. In the uv spectrum $\pi-\pi^*$ and $n-\pi^*$ absorption peaks appear at 240 nm (ϵ 5100 in cyclohexane) (calcd. 244 nm)⁵ and at 324 nm (ϵ 39 in ethanol) respectively. By the treatment with hydrochloric acid in ethanol, V aromatized easily to a phenol XII [m/e 175 (M^+)], which was treated with diazomethane to give a methoxy compound XIII, isomeric with XI and XIV. The mass and nmr spectra are almost the same with those of XI and XIV, only except a signal of aromatic protons at δ 6.64 ppm (s, 2H).

The quite large blue shift (ca. 30 nm) in the $\pi-\pi^*$ absorption of the enone IV, which may be caused by the nonplanarity of the enone group in the fused tricyclic system, still require further clarification.⁸ This unusual evidence in uv spectroscopy of enone may be without precedents.

As reported already in the case of other N-chloroacetylphenethylamines,⁹ the formation of

IV and V may be initiated with an electron transfer from the excited singlet state of the aromatic moiety to the chlorinated amide group to cleave the carbon-chlorine bond, followed by a radical coupling reaction to yield cationic intermediates, i and ii, which convert readily to IV and V, respectively.



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2. T. Iwakuma, H. Nakai, O. Yonemitsu, D. S. Jones, I. L. Karle and B. Witkop, J. Amer. Chem. Soc., 94, 5136 (1972), and references cited therein.
3. Y. Okuno, K. Hemmi and O. Yonemitsu, Chem. Pharm. Bull. (Tokyo), 20, 1164 (1972).
4. O. Yonemitsu, Y. Okuno, Y. Kanaoka and B. Witkop, J. Amer. Chem. Soc., 92, 5686 (1970).
5. H. H. Jaffe and M. Orchin, "Theory and Application of Ultraviolet Spectroscopy," Wiley, New York, N. Y., 1962, p 215.
6. S. Naruto and O. Yonemitsu, Chem. Pharm. Bull. (Tokyo), 20, 2163 (1972).
7. Without sodium methoxide no deuterium exchange was observed. Cf. M. F. Rockett, T. M. Harris and C. R. Hauser, J. Amer. Chem. Soc., 85, 3491 (1963); M. F. Zinn, T. M. Harris, D. R. Hill and C. R. Hauser, ibid., 85, 71 (1963).
8. Only the nonplanarity is not necessarily the reason for the large blue shift. G. L. Buchanan, A. F. Cameron and G. Jamieson, Chem. Commun., 1145 (1969).
9. O. Yonemitsu, H. Nakai, Y. Okuno, S. Naruto, K. Hemmi and B. Witkop, Photochem. Photobiol., 15, 509 (1972); S. Naruto and O. Yonemitsu, Chem. Pharm. Bull. (Tokyo), 21, 629 (1973).