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PHOTOLYSIS OF 2,6-DICYANOPYRIDINE 1-OXIDES*

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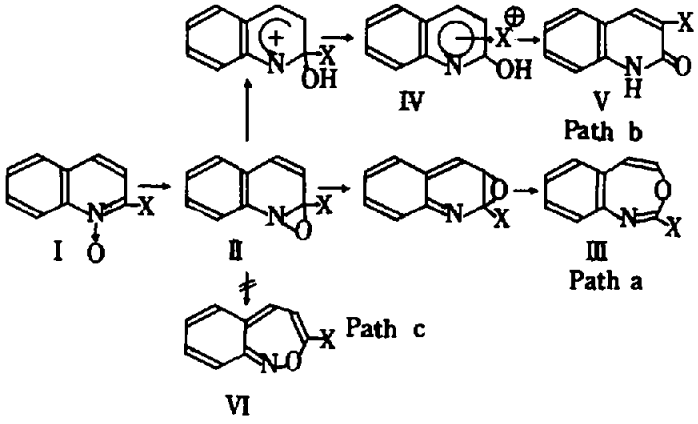
Abstract—Irradiation of 2,6-dicyanopyridine 1-oxide (VIIa) in dichloromethane with >290 mμ rays gave rise to 2,6-dicyanopyridine (VIIIa; 20%), 5-cyano-2-pyrrolecarbonyl cyanide (IXa) (20%), and an oxazepine (Xa) tentatively assigned as 2,4-dicyano-1,3-oxazepine (Aa; 35%). 4-Methyl-2,6-dicyanopyridine 1-oxide (VIIb) gave similar photo-products. The mechanism implied in these photochemical reactions has been discussed.

RECENTLY we reported the photochemical isomerization of aza- and diazanaphthalene N-oxides to benzoxazepines and benzoxadiazepines.[1–3] In view of the current interest in these irradiation reactions of aza- and diazabenzene N-oxides,[4–6] we investigated the photochemical reaction of pyridine 1-oxide derivatives.

In the photochemical isomerization of quinoline 1-oxides (I) to benz[*d*] 1,3-oxazepines (III), the following reaction pathway (path **a**) has been accepted and the intermediary formation of the oxaziridine species (II) has been strongly suggested by a recent trapping experiment.[7] If the substituent (X) has a low affinity for electrons,



such as hydrogen, alkyl, and phenyl, irradiation of these N-oxides (I) in a protic solvent in most cases results in the formation of 2-oxo compounds[8] (V) *via* the carbonium ion rearrangement of the substituent as indicated by path **b**.[9]

In a similar photochemical reaction of pyridine 1-oxides, if intermediates having the 1,2-epoxypyridine structure are formed, they may valence-tautomerize to 1,2-oxazepines. The formation of the corresponding benz[*c*] 1,2-oxazepines (VI) has

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not been detected in the photolysis of quinoline 1-oxides examined, and this as suggested[10] may be due to the loss of a stable benzenoid system in the valence-tautomerization (step **c**). Competing with the above step, there may be an analogous route to step **a** leading to 1,3-oxazepines.

In order to obtain the unknown 1,2- or 1,3-oxazepines, 2,6-dicyanopyridine 1-oxides (VIIa, b) were chosen as starting materials. The reasons for this choice were: (i) the symmetrical arrangement of the substituents to the N–O axis may minimize the product distribution and simplify the structure elucidation; (ii) the expected oxazepines should be stable due to the direct attachment of the cyano group to the C=N function in the oxazepine structure;[9-11] (iii) the presence of cyano groups next to the N-oxide group may protect the undesirable carbonium ion rearrangement (cf. path **b**) leading to 2-pyridone derivatives due to their high affinity for electrons and thus the high energy requirement of the transition state[9] (cf. IV).

2,6-Dicyanopyridine 1-oxide (VIIa) and its 4-Me derivative (VIIb) were successfully synthesized in high yield from the corresponding pyridines[12] (VIIIa, b) by oxidation with hydrogen peroxide in trifluoroacetic acid.

Irradiation of VIIa in dichloromethane by high-pressure mercury lamp with Corex filter afforded three products after repeated fractionation and recrystallization from pentane. The pentane-soluble part gave Xa in 30% yield as yellow needles, m.p. 61–63° (dec), with elemental composition identical with that of the starting N-oxide (VIIa). The ether-soluble part afforded 12% of 2,6-dicyanopyridine (VIIIa). The ether insoluble portion was recrystallized from carbon tetrachloride to afford 40% of pale yellow needles (IXa), m.p. 130° (dec), also isomeric with the starting N-oxide. Irradiation of this N-oxide in benzene gave similar results, although, in this case, formation of a small amount (less than 5% to the consumed N-oxide) of phenol was detected. The formation of phenol under similar conditions was recently reported by two groups.[13, 14] IR, UV and NMR spectra indicate that the structure of IXa is 5-cyano-2-pyrrolecarbonyl cyanide. The mass spectrum contains peaks of strong intensity at *m/e* 118, 91, and 64, and these peaks are all observed in the spectrum of methyl 5-cyano-2-pyrrolecarboxylate[15] (XIa). The structure of IXa was finally confirmed by its quantitaitve conversion to the above ester* (XIa) by boiling in methanol. Treatment of IXa with ethanol as above gave the corresponding ethyl ester (XIIa). Similarly, 5-cyano-N,N-diethyl-2-pyrrolecarboxamide (XIIIa) was obtained from IXa by the action of diethylamine.

Irradiation of VIIb with >290 mμ rays afforded 16% of yellow needles (Xb), m.p. 66–68°, from the pentane-soluble fraction. The portion insoluble to pentane was boiled in methanol and the residual mixture was separated by silica gel chromatography into 36% of VIIIb and 29% of XIb.† From its similarity in UV and IR spectra with those of XIa together with its NMR and mass spectra, XIb was identified as methyl 5-cyano-3-methyl-2-pyrrolecarboxylate. The isolation of XIb clearly indicates the photochemical formation of 5-cyano-3-methyl-2-pyrrolecarbonyl cyanide (IXb) from VIIb.‡

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† The yields are calculated from the N-oxide (VIIb).

‡ Column chromatography using silica gel or alumina for purification of the photo-products (IX, X) from VIIa, b was unsuccessful, since these compounds are unstable in these adsorbents.

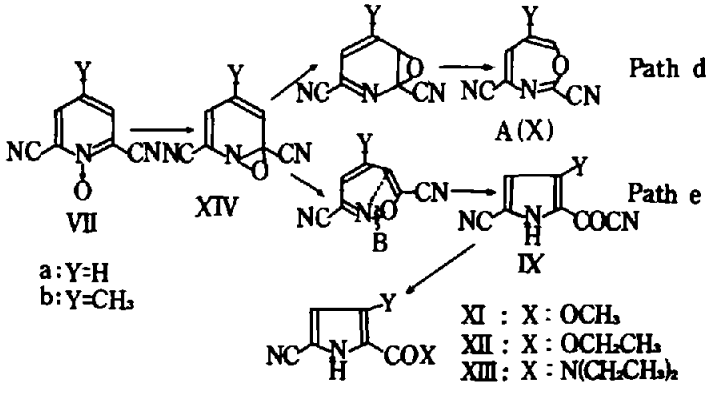
TABLE 1. SPECTRAL DATA OF THE OXAZEPINES (Xa AND Xb)

	UV, $\lambda_{max}^{CH_2Cl_2}$		IR, ν_{max}^{KBr}	NMR, τ-value	Mass spectra *m/e* (relative abundance)			
	mμ	log ε	cm^{-1}	($CDCl_3$)				
Xa	331	3·38	2227 m 1653 w 1626 s	ABC multiplet (3H) 3·05–3·95	145 129 117	(35%) (40%) (18%)	93 64	(100%) (67%)
Xb	334	3·37	2225 m 1625 s	8·09 (3H, d) 4·05 (1H, q) $J = 1·5$ c/s 3·16 (1H, s)	159 143 131	(24%) (100%) (35%)	130 116 105	(55%) (42%) (34%)

The spectroscopic properties of the pentane-soluble photoproducts (Xa, b) are summarized in Table 1.

The similarity of the UV and NMR spectra with those of oxepine,[16] indicates that the ring system of these photo-products must be either 1,3-oxazepine (A) or 1,2-oxazepine (B). We prefer A structure for X for the following two reasons. (i) The mass spectra of compounds Xa, b are consistent with their assigned structures. Xa exhibits peaks at *m/e* 145 (M^+), 129, 93 ($M - [CN]_2^+$) and Xb at *m/e* 159 (M^+), 143, 105 ($M-COCN^+$). Though these facts do not exclude the alternative structure (B) for these compounds, the presence of M-CO ions at *m/e* 117 and 131 as a strong intensity in both spectra supports A structure rather than B structure, since the mass spectrum of 2-cyanobenz[*d*] 1,3-oxazepine (III, X = CN) has been known to show the M-CO ion as a significant peak.[17] (ii) Irradiation of these photo-products (X) under the conditions used in the photolysis of VIIa, b shows the stability of these compounds and therefore, Xa, b are not precursors of IXa, b. The photostability of these compounds also indicates the inadequacy of B structure for these compounds, since 5-membered heteroaromatics having a weak hetero-hetero linkage such as isoxazoles and pyrazoles are usually photolabile and are known to isomerize to the compounds having no hetero-hetero linkage (oxazoles or indazoles).[18]

Finally, the preference of A structure for these photo-products is also supported by the mechanistic considerations. At present, we propose the following pathway for these photochemical reactions.



The initially formed 1,2-epoxypyridines (XIV) valence-tautomerize partly to 1,2-oxazepines (B) which by further irradiation yield IX *via* N—O bond cleavage and recombination processes (path **e**). The above process competes with step **d** which gives 1,3-oxazepines (A) and is essentially similar to the photoisomerization of quinoline 1-oxides to benz[*d*] 1,3-oxazepines (path **a**).

The mechanism proposed is not only in accord with that proposed in the photochemistry of azanaphthalene N-oxides[1-3] but also with the reported photochemical behavior of pyridine and pyrazine N-oxides. Thus, step **e** is essentially similar to the photochemical isomerization of 2-picoline 1-oxide to 5-formyl-2-methylpyrrole reported by Streith *et al.*,[4] and step **d** agrees with the mechanism proposed by Ikekawa and Honma[5] for the photochemical formation of 1-acetamido-2-formamido-1-propene from 2,5-dimethylpyrazine 1-oxide, in which the formation of 1,3,6-oxadiazepine intermediate was postulated.

The reactions and further confirmation of these novel oxazepines and photolysis of the related N-oxides are in progress.

EXPERIMENTAL

M.ps are not corrected. The UV spectra were determined in 95% EtOH, unless otherwise specified, and the IR spectra as KBr pellets. Unless otherwise noted, NMR spectra were taken in $CDCl_3$ containing a small amount of D_2O with TMS as an internal reference.* The mass spectra were determined with a Hitachi RMU-6E double-focussing mass spectrometer with all-glass heated inlet system.

Pyridines. 2,6-Dicyanopyridine (VIIIa) was prepared according to Ref. 12. 4-Methyl-2,6-dicyanopyridine (VIIIb) was prepared from 2-cyano-4-picoline 1-oxide by the method described[12] in 60% yield, m.p. 135–136°. (Found: C, 67·18; H, 3·58; N, 29·57. $C_8H_5N_3$ requires: C, 67·12; H, 3·52; N, 29·36%).

Pyridine 1-oxides. Compound VIIa was prepared as follows: To a mixture of VIIIa (6 g) and 30 ml CF_3COOH, 6 ml 90% H_2O_2 was added and the mixture was kept at 50° for 3 hr. After addition of 6 ml of the peroxide soln, the mixture was again kept at 50° for further 4 hr. The solvent was removed under reduced press and addition of 40 ml water to the residue afforded a crude N-oxide which was recrystallized from acetone as colorless prisms, m.p. 182–183°; yield, 5·6 g (83%); UV, λ_{max}: 243·5, 292 and 357 mμ (log ε: 4·57, 3·94 and 3·13). (Found: C, 58·15; H, 2·17; N, 28·57. $C_7H_3ON_3$ requires: C, 57·93; H, 2·08; N, 28·96%).

Compound VIIb was prepared from VIIIb in 80–85% yield by a similar method, m.p. 189–191°; UV, λ_{max}: 243·5, 298, and 365 mμ (log ε: 4·53, 4·02 and 3·20). (Found: C, 60·73; H, 3·23; N, 25·97. $C_8H_5ON_3$ requires: C, 60·37; H, 3·17; N, 26·41%).

Irradiation of 2,6-dicyanopyridine 1-oxide† (VIIa). A soln of VIIa (500 mg) in CH_2Cl_2 (500 ml) was irradiated for 10 hr with a high-press Hg lamp (Hanovia, 450 W) with a Corex filter. The solvent was removed under a reduced press and the brown oily residue was extracted several times with pentane. Concentration and repeated recrystallization from pentane afforded Xa as yellow needles, m.p. 61–63° (dec), yield, 150 mg (30%). [Found: C, 58·26, H, 2·20; N, 28·75. $C_7H_3ON_3$: required: C, 57·93; H, 2·08; N, 28·96%].

The insoluble residue was extracted several times with boiling ether, and concentration and recrystallization from ether afforded VIIIa as colourless prisms, m.p. 127°, yield, 60 mg (12%). (Found: C, 65·04; H, 2·40; N, 32·30. $C_7H_3N_3$ requires: C, 65·11; H, 2·34; N, 32·55%).

The more insoluble portion of the irradiation products was recrystallized from CCl_4 to yield brownish yellow needles, m.p. 129–130° (dec), yield, 200 mg (40%); UV, $\lambda_{max}^{CH_2Cl_2}$: 321 mμ (log ε: 4·24). IR, ν_{max}: 3286, 2240, and 1656 cm^{-1}. (Found: C, 57·04; H, 2·14; N, 28·10. $C_7H_3ON_3$ requires: C, 57·93; H, 2·08; N, 28·96%). The NMR spectrum in CD_3SOCD_3 exhibited a set of two doublets at 2·53 τ (1H) and 2·75 τ (1H) with J = 4·8 c/s, and a broad singlet (1H) at 1·6 τ.

* The NMR spectra measured in pure $CDCl_3$ gave more complex ring proton signals due to the coupling of these protons with N—H in the pyrrole ring.

† See footnote ‡ on page 296.

Reactions of IXa *with alcohols and amines.* A soln of 500 mg of IXa dissolved in 50 ml MeOH was refluxed for 5 hr. Evaporation of the solvent and recrystallization of the residue from ether–hexane afforded XIa as colourless needles, m.p. 170–171°. Mixed m.p. and IR comparison with the authentic sample[15,*] confirmed the structure, yield, 480 mg (95%); UV, λ_{max}: 266 and 273·5 (sh.) mμ (log ε: 4·58 and 4·50); IR, ν_{max}: 3255, 2232, and 1695 cm^{-1}. (Found: C, 55·80; H, 3·97; N, 18·15. $C_7H_6O_2N_2$ requires: C, 56·02; H, 4·03; N, 18·66%). The NMR spectrum exhibited a singlet at 6·0 τ (3H) and a set of two doublets centred at 3·08 and 3·0 τ (1H each) with J = 4·1 c/s.

Similarly, XIIa was obtained from IXa by boiling with EtOH, yield, 90%, m.p. 121–122°; UV, λ_{max}: 268 and 275 (sh.) mμ (log ε: 4·50 and 4·38); IR, ν_{max}: 3235, 2240, and 1700 cm^{-1}. (Found: C, 58·33; H, 4·76; N, 17·22. $C_8H_8O_2N_2$ requires: C, 58·53; H, 4·91; N, 17·07%). The NMR spectrum showed the signals due to an Et group (a triplet at 8·58 τ (3H) and a quartet at 5·50 τ (2H) with J = 7·2 c/s), and a set of two doublets at 3·11 and 3·02 τ (1H each) with J = 4·0 c/s.

Compound XIIIa was obtained from IXa (500 mg) by keeping a soln in dioxan (30 ml) containing 1 ml diethylamine for 24 hr at room temperature, yield, 420 mg (80%), m.p. 141–142° (recrystallized from MeOH); UV, λ_{max}: 268 mμ (log ε: 4·30); IR, ν_{max}: 3150, 2240, and 1607 cm^{-1}. (Found: C, 62·72; H, 6·96; N, 21·84. $C_{10}H_{13}ON_3$ requires: C, 62·80; H, 6·85; N, 21·98%). The NMR spectrum exhibited a triplet at 8·68 τ (6H, J = 7·2 c/s), a quartet at 6·30 τ (4H, J = 7·2 c/s), and a pair of doublets at 3·48 and 3·21 τ (1H each) with J = 4·0 c/s.

Irradiation of 4-*methyl*-2,6-*dicyanopyridine* 1-*oxide* (VIIb). Irradiation of VIIb (500 mg) was carried out under the conditions given. The pentane-soluble portion (Xb) was purified by recrystallization from pentane as yellow needles, m.p. 66–68°, yield, 80 mg (16%). (Found: C, 61·00; H, 3·29; N, 25·93. $C_8H_5ON_3$ requires: C, 60·37; H, 3·17; N, 26·41%).

Further purification of the portion insoluble in pentane did not succeed either by fractionation or chromatography† and therefore the whole fraction was dissolved in 20 ml of MeOH and the soln was refluxed for 12 hr. Evaporation of the solvent followed by silica gel chromatography of the residue with hexane–ether afforded XIb and VIIIb in respective yield of 150 mg (29%) and 160 mg (35·5%).‡ The former product was recrystallized from ether–hexane as colorless needles, m.p. 184–185·5°; UV, λ_{max}: 269·5 mμ (log ε: 4·36); IR, ν_{max}: 3240, 2240, and 1700 cm^{-1}. (Found: C, 58·74; H, 4·93; N, 16·94. $C_8H_8O_2N_2$ requires: C, 58·53; H, 4·91; N, 17·07%). The NMR spectrum exhibited a singlet at 7·63 τ (3H), a singlet at 6·02 τ (3H), and a signlet at 3·32 τ (1H).

Similarly, XIIb was obtained from the portion insoluble in pentane by refluxing in EtOH in a comparative yield, m.p. 120–122°. (Found: C, 60·83; H, 5·59; N, 6·68. $C_9H_{10}O_2N_2$ requires: C, 60·66; H, 5·66; N, 6·33%).

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* See footnote * on page 296.
† See footnote ‡ on page 296.
‡ See footnote † on page 296.

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