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PHOTOCHEMICAL REARRANGEMENT OF PYRIDINE AND QUINOLINE 1-OXIDES HAVING STERICALLY HINDERED 4-NITRO GROUP*[1,2]

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Some recent investigations on solvent and oxygen effects in the previously reported photochemical reactions of 4-nitropyridine 1-oxide[1,2] have led to a discovery of a photochemical isomerization of 3,5-dimethyl-4-nitropyridine 1-oxide[3] (I) to 3,5-dimethyl-4-hydroxypyridine 1-oxide (II).

As reported in the previous paper of this series[2], irradiation of 4-nitropyridine 1-oxide in ethanol or in isopropanol in the presence of oxygen resulted in the formation of the nitrate of 4-hydroxypyridine 1-oxide, while, under exactly the same condition, if nitrogen was passed into the solution during the irradiation, the product obtained was 4-hydroxyaminopyridine 1-oxide.[1] The fact that these photochemical reactions of 4-nitropyridine 1-oxide did not proceed in aqueous solution, either in the presence or absence of oxygen, indicated that the use of these alcoholic solvents is a prerequisite in the above-mentioned photochemical reactions.*[3] However, the photochemical isomerization of I to II occurs very rapidly in these alcoholic solvents as well as in water, either in the presence or absence of oxygen, and in any conditions examined, there was no formation of the corresponding 4-hydroxyamino

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*1 Studies on N-Oxides of π-Deficient N-Heteroaromatics. VIII. For previous paper, see ref. (2).

*2 This paper was reported at the symposium on photochemistry (Osaka, Oct. 17, 1966: Abstract of papers; page 51).

*3 An example currently available for these photo-isomerizations of 4-nitropyridine 1-oxide suggests that the solvents should be capable of acting not only as a hydrogen donor, or in other wards, as a reducing agent, but also form hydrogen bonding to the N-O group. For example, irradiation of 4-nitropyridine 1-oxide in dioxan induced an entirely different photochemical reaction.

compound.*4

In one of the several experiments, a solution of I (1.0 g) in ethanol (550 ml) was irradiated in nitrogen atmosphere for 1.5 hr by a Hanovia 450-watt high-pressure mercury arc lamp placed inside a water-cooled Pyrex immersion well. After evaporation of the solvent, the residue was recrystallized from methanol-acetone mixture (1:10 v/v) to a compound (250 mg) of m.p. 184°, which was found to be 3,5-dimethyl-4-hydroxypyridine 1-oxide (II) (30% yield). Analytical data indicated the formula of $C_7H_9O_2N$ (mol. wt. 142 by osmotic pressure method), and the molecular structure was deduced from its UV and NMR spectral data (see below).

The UV spectra of II in various solvents (λ_{max}^{EtOH} mμ (log ε); 274 (4.18), $\lambda_{max}^{5\%K_2CO_3}$; 282 (4.14), $\lambda_{max}^{5\%H_2SO_4}$; 249 (3.89)) were quite similar to those of 4-hydroxypyridine 1-oxide available from earlier work.[2)] The NMR spectrum (CF_3COOH), which was determined with tetramethylsilane as an internal standard, showed a singlet at 7.59 τ (6 protons), assigned to the methyl groups, and a singlet at 1.71 τ (2 protons), assigned to the ring-protons. As a further confirmatory evidence for the structure of the photo-product, 3,5-dimethyl-4-hydroxypyridine 1-oxide was separately prepared from 3,5-dimethyl-4-nitropyridine 1-oxide by the procedure described by Hertog et al.[4)] in the synthesis of 4-hydroxypyridine 1-oxide from 4-nitropyridine 1-oxide. The identity of this compound with the photo-product was assured by the mixed melting point determination as well as from their superimposable IR spectra.

In view of the sterically hindered nature of 4-nitro group in I, it seems reasonable to assume that the formation of II should be facilitated by steric features of the molecule (I), which tend to hold the nitro group out of the plane of the pyridine-ring.*5 Recent reports of several photo-induced Nef-type

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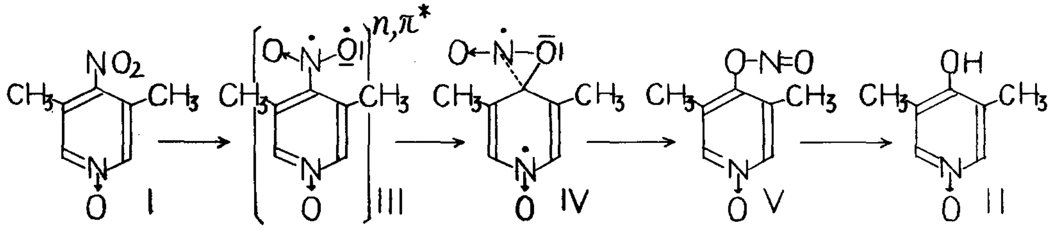
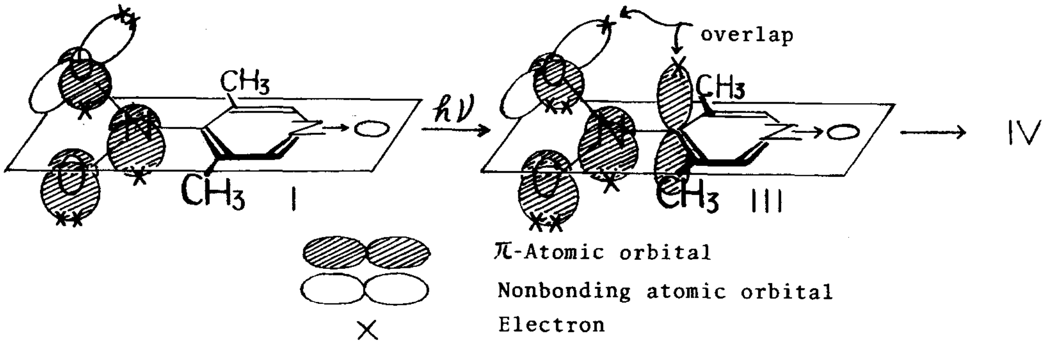
*4 In aprotic solvents, i.e., dioxane, an entirely different photochemistry of I has been observed. This indicates that the hydrogen bonding between I and the solvents plays an important role in this reaction.

*5 Steric inhibition of resonance in I is assured by the UV spectroscopy. The longest wavelength absorption maxima (in mμ) of I and its related compounds in ethanol are: I, 280; 4-nitropyridine 1-oxide, 332; 4-nitro-2-picoline 1-oxide, 334; 4-nitro-3-picoline 1-oxide, 327; 4-nitro-2,6-lutidine 1-oxide, 334.

reactions of nitro-olefins[5,6] are of particular interest in this connection, and the following mechanistic pathwav, I → III → IV → V → II, involving nitro-nitrite rearrangement as a key step, is tentatively suggested to account for the present reaction. The formation of IV-type intermediate from n,π* excited species*6 of I should be facilitated by the steric features as depicted in the stereo-formula.





In the photolysis of I in an ethanol or isopropanol, the steric hindrance to the nitro group by two ortho-methyl groups in I may also be preventing the hydrogen abstraction of its excited species from the solvents, which is a key step to form the corresponding 4-hydroxyamino compound.

Extension of this reaction to quinoline derivatives was then carried out. Under the same condition, though 4-nitroquinoline 1-oxide (VI) gave rise to 2,4-dihydroxyquinoline[7] (VII), $C_9H_7O_2N$, m.p. >300°, as an only detectable product (7%), 3-methyl-4-nitroquinoline 1-oxide[8] (VIII) gave somewhat higher yield (30%) of the corresponding 2,4-dihydroxy derivative[9] (IX), $C_{10}H_9O_2N$,

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6 As oxygen has no effect on this reaction, this rearrangement may involve the n,π singlet, and not the triplet.

m.p. 264-265° (monoacetate, $C_{12}H_{11}O_3N$, m.p. 241-243°). The structures of these photo-products*7 (VII and IX) were assured by the direct comparison with the authentic samples prepared separetely. Contrary to the photolysis[1,2] of 4-nitro derivatives of pyridine, 2-picoline, 3-picoline, and 2,6-lutidine 1-oxides, the oxygen did not affect the formation of these products but the yields of the corresponding 4-hydroxy derivatives were somewhat lower.

Further experiments towards elucidation of the mechanism of these reactions are in hand, and the scope of this reaction is also being investigated.

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*7 Many examples have been reported on the photochemical rearrangement of 2-unsubstituted quinoline 1-oxides to the corresponding 2-hydroxyquinolines. See references (10) and (11).