The Primary Process of the Photochemical Isomerization of Azanaphthalene *N*-Oxides

Norisuke HATA and Isao ONO

Department of Chemistry, College of Science and Engineering, Aoyama Gakuin University, Chitosedai, Setagaya, Tokyo 157

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The quantum yields for the photochemical isomerization of azanaphthalene *N*-oxides, such as quinoline *N*-oxide and isoquinoline *N*-oxide, into lactam (Process I) or oxazepine (Process II) were determined in benzene (or carbon tetrachloride), in methanol, and in mixtures of the two solvents. Consequently, the reaction was revealed to be closely related to whether or not the *N*-oxide oxygen atom forms a hydrogen bond with the solvent molecule; that is, a strong hydrogen-bonding interaction between the excited singlet *N*-oxide and alcohol is essential for Process I, but not for Process II. It was further demonstrated that Process II occurred with the formation of powerful oxidants (probably oxaziridines) from the excited singlet *N*-oxide, whereas such an oxidizing species was not involved in Process I. The reaction mechanisms of Processes I and II were also discussed on the basis of the present experimental results.

It has been well established that the photochemical isomerization of quinoline *N*-oxide or isoquinoline *N*-oxide into lactam (Process I) or oxazepine (Process II)[1] occurs from the lowest excited singlet state (S_1).[2,3] In order to account for such a photoisomerization, oxaziridines have been customarily postulated as the primary photoproduct from which all the products were derived.[4] However, several experimental data conflicting with this idea have recently been documented in the literature. Lohse has concluded from the results of his laser photolysis and quantum-yield measurements of isoquinoline *N*-oxides that there was no common intermediate leading to both Processes I and II.[2] In view of the photochemical behavior of isoquinoline *N*-oxide in water at different pH values, we have also indicated that the intervention of an oxaziridine intermediate is extremely doubtful in Process I.[3]

In the present paper, we wish to report some new observations and interpretations of the primary process of the photochemical isomerization of azanaphthalene *N*-oxides, such as quinoline *N*-oxide and isoquinoline *N*-oxide.

Experimental

2-Phenyl-, 3-phenyl-, and 2-cyano-quinoline *N*-oxides, and isoquinoline *N*-oxide were synthesized and purified according to the method given in the literature.[5,6] In the irradiation experiments, reagent-grade benzene, methanol, and ethanol of Wako Pure Chemical Industries Co. and also spectro-grade carbon tetrachloride (Dojindo Co.) were used without further purification. The photolytic procedure was quite similar to that described in a previous paper.[3] Small-scale photolyses for the determination of the quantum yield were performed in a quartz cylindrical cell (5-cm in diameter and 1-cm in length), using a 250 W high-pressure mercury lamp (USH-250D) equipped with a filter combination of a nickel sulfate solution with UV-31 and UVD-25 Toshiba filters, while the light intensity was determined by means of a potassium tris-(oxalato)ferrate(III) actinometer. Large-scale photolyses were carried out in a Pyrex vessel (70 ml) using a 100 W high-pressure immersion mercury lamp (Riko Kagaku Sangyo Co.). All the photolytic experiments were undertaken in a nitrogen atmosphere. The UV absorption spectra were measured with a Hitachi recording spectrophotometer EPS-3T.

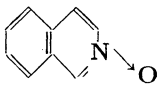
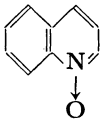
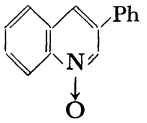
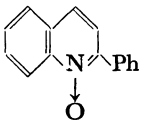
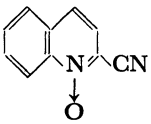
Results and Discussion

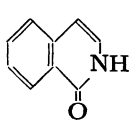
The photochemical isomerization of azanaphthalene *N*-oxides in solution is well known to be very sensitive to the nature of the solvent or substituent group.[4] That is, isoquinoline *N*-oxide **1**, quinoline *N*-oxide **2**, or 3-phenylquinoline *N*-oxide **3** isomerizes predominantly to the corresponding lactam, **1a**, **2a**, or **3a**, in a hydroxylic solvent, such as alcohol and water (Process I), whereas in a nonhydroxylic solvent, such as benzene and acetone, these *N*-oxides are primarily converted into the corresponding oxazepines **1b**, **2b**, and **3b** (Process II). In the case of 2-phenylquinoline *N*-oxide **4** or 2-cyanoquinoline *N*-oxide **5**, having an electron-withdrawing group at the 2-position of a quinoline nucleus, however, Process II occurs preferentially to give rise to a stable oxazepine, **4b** or **5b**, irrespective of the nature of the solvent, whether hydroxylic or nonhydroxylic. Table 1 lists the chemical yields of the main products of the photolyses of **1**—**5** in various solvents. Meanwhile, the intermolecular hydrogen-bonding in heterocyclic *N*-oxides has been investigated spectroscopically in detail.[12] It has been thus proved that the oxygen atom of the $N\rightarrow O$ group in **1**, **2**, or **3** formed a strong hydrogen bond to alcohol or water, whereas such a hydrogen-bonding interaction was negligibly small in the case of **4** or **5** because of the electron-withdrawing group at the 2-position of a quinoline nucleus.

It is inferred from the foregoing that the remarkable dependence of the photochemical isomerization of azanaphthalene *N*-oxides on the nature of the solvent or substituent is closely related to whether or not the *N*-oxide oxygen atom can form a hydrogen bond with a hydroxylic solvent. In order to clarify this point, we determined the qunatum yield of both the disappearance of *N*-oxide (Φ_{dis}) and the formation of lactam or oxazepine (Φ_{lac} or Φ_{oxa}) for **1**, **3**, and **4** in benzene (or carbon tetrachloride), in methanol, and in mixtures of the two solvents at room temperature.

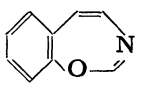
Figure 1 shows the results when the quantum yield for the disappearance of **1** or **4** was plotted against the concentration of methanol in a carbon tetrachloride

TABLE 1. PRODUCT DISTRIBUTION IN PHOTOLYSES OF AZANAPHTHALENE *N*-OXIDES

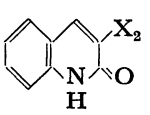
N-Oxide	Solvent	Product (Yield, %)		Ref.
 **1**	Ethanol	**1a** (67)		2
	Acetone	**1a** (8)	**1b** (unstable)	2
	Benzene	**1a** (10)	**1b** (unstable)	Present work
 **2**	Ethanol	**2a** (49)	**2b** (unstable)	7
	Acetone	**2a** (15)	**2b** (unstable)	8
 **3**	Ethanol	**3a** (98)		9
	Acetone	**3a** (20)	**3b** (unstable)	9
	Benzene	**3a** (21)	**3b** (unstable)	Present work
 **4**	Ethanol	**4a** (8)	**4b** (80)	6, 10, 11
	Benzene		**4b** (95)	Present work
 **5**	Ethanol		**5b** (84)	Present work
	Acetone		**5b** (90)	11
	Benzene		**5b** (88)	Present work



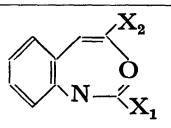
1a



1b



2a (X_2=H)
3a and **4a** (X_2=Ph)



2b (X_1=H, X_2=H)
3b (X_1=H, X_2=Ph)
4b (X_1=Ph, X_2=H)
5b (X_1=CN, X_2=H)

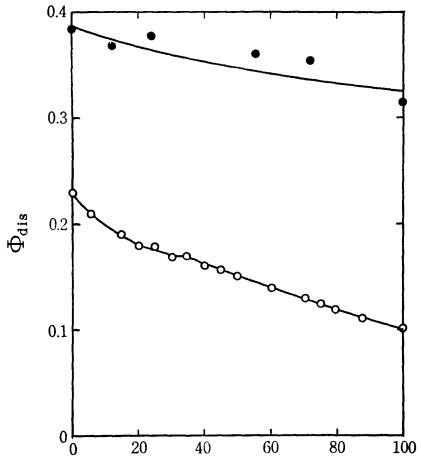


Fig. 1. Quantum yield of the disappearance of **1** or **4** in methanol–CCl_4 or methanol–benzene.
—○—: Isoquinoline *N*-oxide **1** in methanol–CCl_4 ([**1**]; 4.0×10^{-5} M), —●—: 2-Phenylquinoline *N*-oxide **4** in methanol–benzene ([**4**]; 1.0×10^{-4} M).

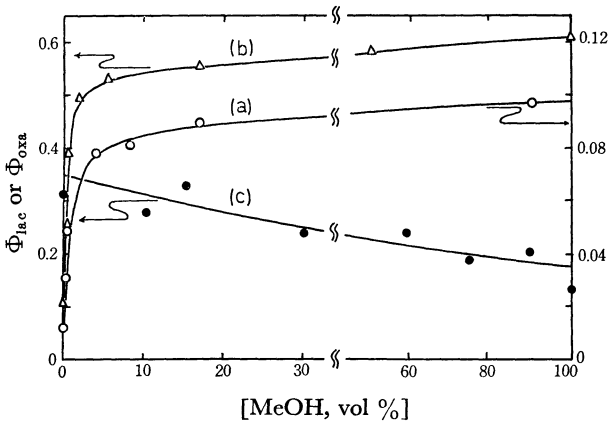


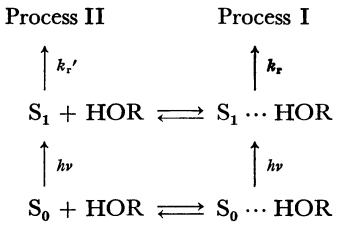
Fig. 2. Quantum yield of the formation of **1a**, **3a**, or **4b** in methanol–benzene ([*N*-oxide]; 2.0×10^{-3} M).
(a) —○—: **1a**, (b) —△—: **3a**, (c) —●—: **4b**.

or benzene solution, from which the quantum yield was noticed to decrease with an increase in the concentration of methanol.

Figure 2 shows the quantum yield of the formation of lactam or oxazepine determined as a function of the concentration of methanol in a benzene solution. As can be seen from Curve (a) or (b) in the figure, the value of Φ_{lac} in a benzene solution of **1** or **3** increased steeply upon the addition of a small amount of methanol until it became approximately a constant value at a concentration of methanol greater than 5 vol%. On the other hand, **4** showed a continuous decrease in Φ_{oxa} as the concentration of methanol increased (Curve (c) in Fig. 2).

As is shown in Scheme 1, such a dependence of the quantum yield on the concentration of the alcohol could be interpreted in terms of a hydrogen-bonding equilibrium between the *N*-oxide and alcohol;[13,14] in

this scheme it was assumed that Process I proceeds from the excited singlet *N*-oxide hydrogen-bonded to alcohol ($S_1 \cdots HOR$), while the nonhydrogen-bonded excited singlet *N*-oxide (S_1) undergoes Process II.



Scheme 1.

Assuming photostationary state conditions, the quantum yield for the formation of oxazepine or lactam is given by Eq. 1 or 2;

$$1/\Phi_{oxa} = K_e(k_r+k_d)[ROH]/k_{r'} + (k_{r'}+k_{d'})/k_{r'} \quad (1)$$

$$1/\Phi_{lac} = (k_{r'}+k_{d'})/K_e k_r[ROH] + (k_r+k_d)/k_r \quad (2)$$

where k_d or $k_{d'}$ is the sum of the rate constants of the deactivation of $S_1 \cdots HOR$ or S_1 other than the reaction, k_r or $k_{r'}$ is the rate constant of the reaction of $S_1 \cdots HOR$ or S_1 to give products responsible for Process I or Process II, and K_e is the equilibrium constant between $S_1 \cdots HOR$ and S_1. Accordingly, if this scheme is correct, the reciprocal of Φ_{oxa} or Φ_{lac} should be directly proportional to the alcohol concentration or its reciprocal. In fact, as is shown in Figs. 3 and 4, the plot of Φ_{oxa} or Φ_{lac} against [MeOH] or its reciprocal was found to be linear, which was consistent with Eq. 1 or 2. This means that Process I proceeds through the S_1-species hydrogen-bonded to methanol, while the nonhydrogen-bonded S_1-species is responsible for Process II.

The first step in the photochemical isomerization of heterocyclic *N*-oxides has been supposed to be the formation of an oxaziridine intermediate common to both Processes I and II. However, all attempts to observe oxaziridine intermediates have been unsuccessful, except for the case of 9-cyano- or 9-chloroacridine *N*-oxide, where the isolation of oxaziridine has been effected in the form of the valence-tautomer.[15] If the photochemical isomerization of quinoline *N*-oxide or isoquinoline *N*-oxide proceeds *via* an oxaziridine intermediate, irradiations of the *N*-oxides in the presence of the iodide ion would have to bring about the liberation of iodine and the formation of parent amine at the same

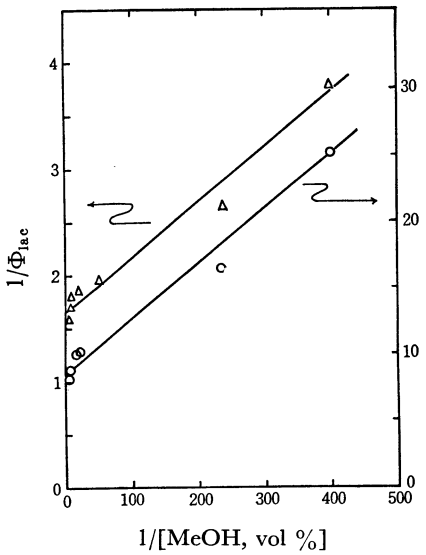


Fig. 3. Quantum yield of the formation of **1a** or **3a** *vs.* concentration of methanol.
—○—: **1a**, —△—: **3a**.

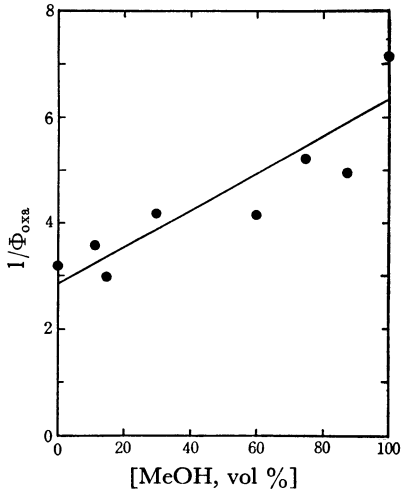


Fig. 4. Quamtum yield of the formation of **4b** *vs.* concentration of methanol.

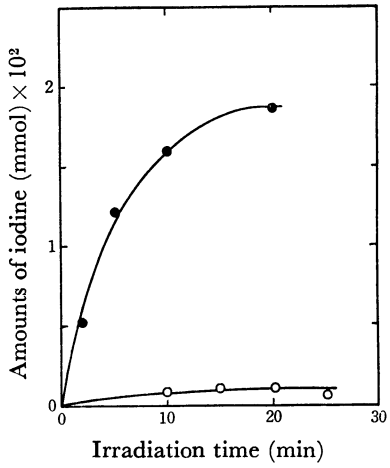


Fig. 5. Amounts of iodine liberated *vs.* irradiation time.
—○—: Isoquinoline *N*-oxide **1**, —●—: 2-Cyanoquinoline *N*-oxide **5**. [*N*-oxide]: 2.0×10^{-3} M, [KI]: 1.0 M, Solvent: 20 ml of ethanol–water (1: 1).

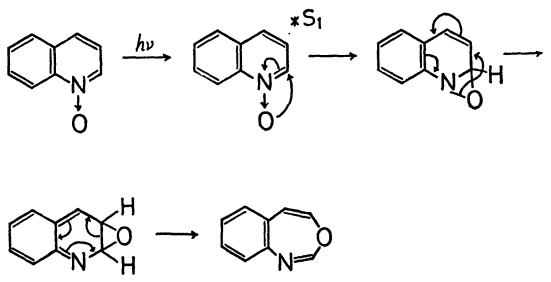
TABLE 2. THE EFFECT OF IODIDE ION ON PHOTOLYSES OF *N*-OXIDES **1** AND **5**

N-Oxide	Concentration of KI	Product (Yield, %)
1	0 M	**1a** (66), Isoquinoline (trace)
	1.0 M	**1a** (52), Isoquinoline (trace)
5	0 M	**5b** (73), 2-Quinolinecarbonitrile (trace)
	1.0 M	2-Quinolinecarbonitrile (68)

Concentration of *N*-oxide; 5×10^{-3}M. Solvent; 40 ml of ethanol–water (1: 1). Irradiation Time; 20 min.

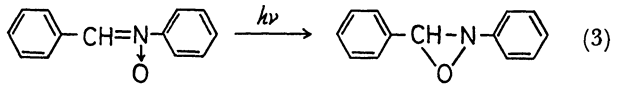
time, for oxaziridines are normally powerful oxidants. Figure 5 and Table 2 show the results when the photolysis of **1** or **5** was performed in aqueous ethanol containing potassium iodide in a nitrogen atmosphere, where iodine release was followed iodometrically as a function of the irradiation time. As may be seen from Fig. 5, iodine was detected in quantity in the case of **5**, but not in the case of **1**. In addition, in the case of **5** there was observed a complete quenching of the photoisomerization and a marked increase in the yield of the deoxygenation product (2-quinolinecarbonitrile), whereas the photochemical reaction of **1** was scarcely affected by iodide ions (Table 2). These results suggest that Process II takes place with the formation of a powerful oxidant (probably oxaziridine) from the excited singlet *N*-oxide, whereas such an oxidizing intermediate is not involved in Process I.

From the experimental results presented above, the following conclusions can be obtained regarding the primary process of the photochemical isomerization of azanaphthalene *N*-oxides: (i) When the *N*-oxide oxygen atom does not form a hydrogen bond with solvent molecules, the azanaphthalene *N*-oxide excited into the S_1 state may be initially converted into the oxaziridine and thereafter transformed into the oxazepine (Process II). This is quite consistent with the mechanism given by earlier investigators (Scheme 2).[4] (ii) When there



Scheme 2.

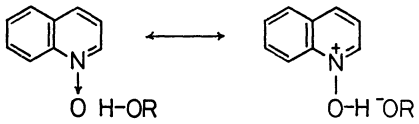
is a strong hydrogen-bonding interaction between the *N*-oxide oxygen atom and the solvent molecule, the azanaphthalene *N*-oxide may undergo photochemical rearrangement to the lactam without the formation of an oxaziridine intermediate (Process I), as we have deduced in a previous paper.[3] These conclusions also imply that the formation of oxaziridine from the excited singlet *N*-oxide is greatly diminished by the hydrogen-bonding interaction between the *N*-oxide oxygen atom and the hydroxylic solvent. A very similar conclusion has also been obtained by Tanaka *et al.* in the case of the photochemical isomerization of α,*N*-diphenylnitrone to oxaziridine (singlet reactions) in solution



(3)

(Eq. 3),[16] where the drop in the quantum yield of the reaction has been shown to be produced either by changing the solvent from cyclohexane to ethanol or by introducing a hydroxyl group to the *ortho*-position of an α-phenyl ring.

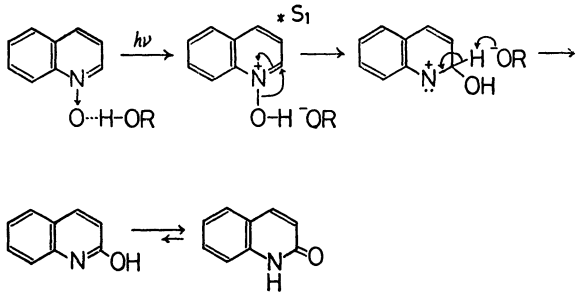
As to the mechanism of Process I, Kaneko and Buchardt have independently presented the idea that the primary photoproduct was an oxaziridine which can be postulated to undergo a heterolytic cleavage to give a carbonium ion or a zwitterion[4] (*cf.* Schemes 1 and 2 in Ref. 3), but such a mechanism evidently conflicts with the conclusion described above. Therefore, we propose the following mechanism to account for Process I (Scheme 3): According to the concept of electron donor-acceptor interaction, hydrogen bond formation is generally accepted to be due to the stabilization caused by resonance interaction between the no-bond structure and the CT structure, *e.g.*, Eq. 4, which is shown for quinoline *N*-oxide, and the contribution of the CT structure may be important in strong



(4)

no-bond structure CT structure

hydrogen-bonding.[12c] Therefore, as is shown in Scheme 3, the photoexcitation of such a hydrogen-bonded *N*-oxide is presumed to cause a protonation of the N→O group to give ion-pairs, through which a conversion to the lactam could occur.[17]



Scheme 3.

In conclusion, the authors wish to thank Professor Oyo Mitsunobu for his kind discussion and Miss Michiko Maniwa for her assistance.

References

1) According to the convention in the previous paper,[3] the photochemical isomerization to a lactam is referred to as Process I, and the photochemical conversion to an oxazepine is termed Process II.

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