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Photochemical Magnetic-Field Effects of Isoquinoline *N*-Oxide in Various Alcohols

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A pronounced solvent dependence of the magnetic-field effect due to the HFI-J mechanism was found for the first time in the case of a photochemical isomerization of isoquinoline *N*-oxide into lactam (1-isoquinolone). The chemical yield of the lactam showed a minimum at a higher magnetic field as one changes the reaction medium from *t*-butyl alcohol to 2-propanol (or ethanol) and then to methanol, which was the same order as the pK_a value (*t*-butyl alcohol>2-propanol≈ethanol>methanol). Such a solvent dependence provides corroborating evidence that the photoisomerization proceeds via the S_1-born singlet radical-ion-pair intermediate, which is linked by a hydrogen bond between the N→O group in the cation radical of *N*-oxide and the OH group in the anion radical of alcohol. Another interesting finding was that, in the case of the photochemical isomerization in *t*-butyl alcohol, the chemical yield of the lactam showed distinct maxima at approximately 0.9T and 1.35T in addition to a minimum at about 0.72T. The anomalous magnetic-field effect in a high field region (>0.8T) could reasonably be explained in terms of an HFI-J mechanism by assuming the T_1-born triplet hydrogen-bonded radical-ion pair to have an electron-exchange interaction larger than that in the S_1-born singlet hydrogen-bonded radical-ion pair.

As has been described in a previous paper,[1] the photochemical isomerization of isoquinoline *N*-oxide in ethanol was found to show a new type of magnetic-field effect in 1976, the chemical yield of the product (1-isoquinolone) having a minimum at approximately 1T. This phenomenon was successfully interpreted in terms of a hyperfine-interaction mechanism including an electron-exchange interaction (HFI-J mechanism) in the S_1-born singlet hydrogen-bonded radical ion-pair, assumed to be a transient intermediate of this reaction. In 1979 the photochemical magnetic-field effect was found to depend greatly on the pK_a of the alcohol (methanol, ethanol, 2-propanol, or *t*-butyl alcohol) used as a reaction medium; further, in the case of a *t*-butyl alcoholic solution, an anomalous field dependence of the chemical yield was observed at a magnetic field higher than 0.8T.[2] These findings were partly reported in a preliminary form.[2] The present paper will present further details of these phenomena, together with an interpretation.

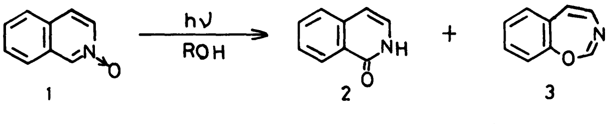
Experimental

The isoquinoline *N*-oxide **1** used as a sample was prepared and purified according to the method described in a previous paper;[1] mp 103—105 °C. The 1,3-cyclohexadiene used as a triplet quencher was a reagent-grade product of the Tokyo Kasei Kogyo Co., which was further purified by distillation; bp 80—81 °C. The methanol, 2-propanol, and *t*-butyl alcohol used as the photoreaction medium were reagent-grade products of Wako Pure Chemical Industries.

The experimental procedure was quite similar to that described proviously;[1] a 50-cm^3 portion of an alcoholic solution (methanol, 2-propanol or *t*-butyl alcohol) containing 35 mg of isoquinoline *N*-oxide in a quartz vessel (44×45×25 mm) was irradiated with a 500W Ushio super-high-pressure Mercury Lamp (USH-500D) equipped with a Toshiba filter UV-31 for 15 min in the cases of methanolic and 2-propanolic solutions (or 10 min in the case of a *t*-butyl alcoholic solution), while nitrogen was being bubbled in, in a magnetic field of 0—1.65T at room temperature. A similar experiment was also performed on a *t*-butyl alcoholic solution containing the *N*-oxide (35 mg) and 1,3-cyclohexadiene (4.80×10^{-1} mol dm^{-3}). In the case of a methanolic or 2-propanolic solution, unreacted *N*-oxide **1** and a photoproduct (lactam) **2** were separated by means of silica-gel TLC (Merck silica-gel plate 60F_{254}; layer thickness, 2 mm; the eluent, benzene–ethanol–diethyl ether (5:1:2)). In the case of a *t*-butyl alcoholic solution, the irradiated solution was chromatographed on an alumina column (Wako activated aluminium oxide, about 300 mesh) by elution with chloroform–diethyl ether (1:3), chloroform–ethanol (40:1), and then chloroform–ethanol (20:1) to separate some decomposition products, unreacted *N*-oxide **1** and then lactam **2**. The amounts of the unreacted *N*-oxide **1** and the product **2** were determined spectrophotometrically. The UV absorption spectra were taken with a Shimadzu recording spectrophotometer, UV-220.

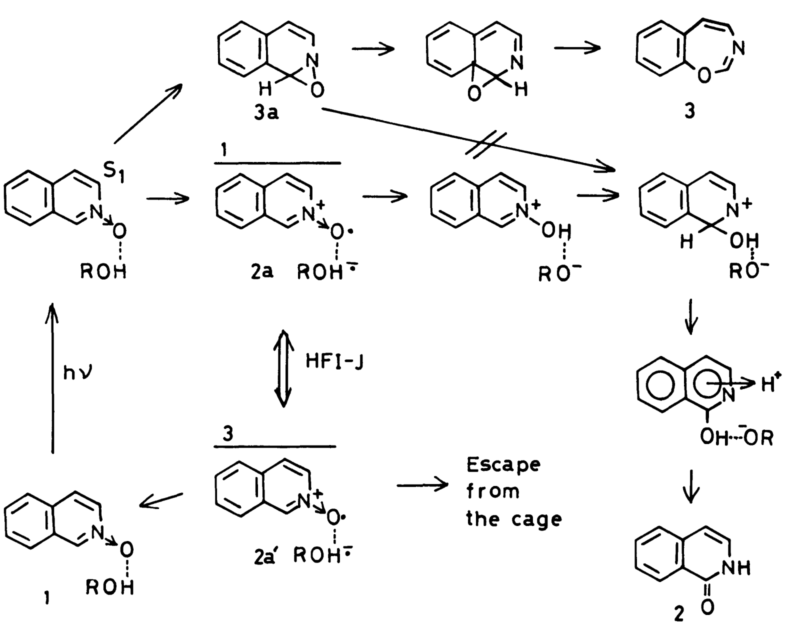
Results and Discussion

The irradiation of isoquinoline *N*-oxide **1** in hydroxylic solvent (ROH) leads to the isomerization into lactam **2** (1-isoquinolone) and 1,3-benzoxazepine **3** (Eq. 1), but the latter product **3** is quite unstable and can not be isolated.[1,3]

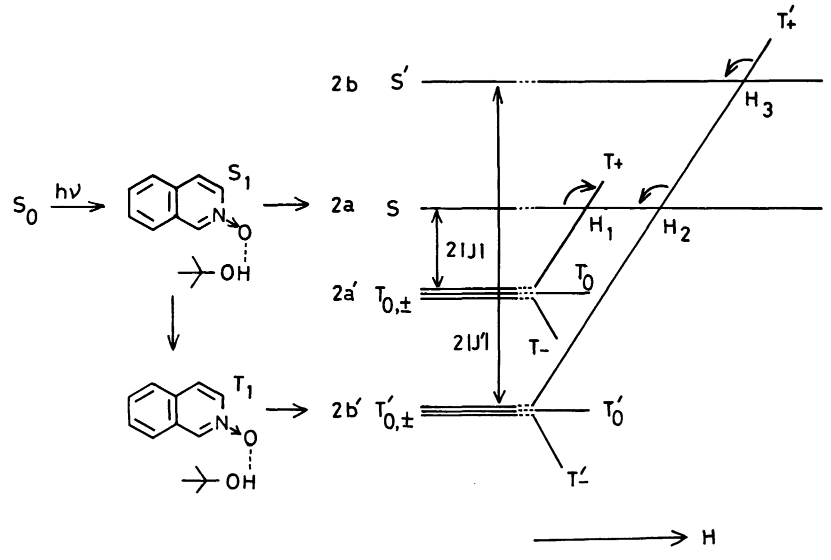
 (1)

As has been reported previously,[1] when the photochemical isomerization of isoquinoline *N*-oxide **1** in ethanol was carried out in the presence of a magnetic field, the chemical yield of lactam **2** showed a minimum at approximately 1T (Fig. 2). In order to interpret this phenomenon, "the radical-ion-pair mechanism" (as shown in Scheme 1) has been proposed for the photoisomerization of isoquinoline

N-oxide **1** into lactam **2** in hydroxylic solvents (ROH).[1] In this scheme, the field-sensitive singlet radical-ion-pair intermediate **2a** responsible for the formation of lactam **2** was reasonably assumed to be formed by the transfer of an electron (πO:) from the excited singlet *N*-oxide (S_1) to the hydrogen-bonded alcohol (ROH). The exchange interaction between the unpaired electrons in the pair **2a** is thought to be larger than the electron-nuclear hyperfine interaction, for the radical centers are in close proximity as a result of hydrogen-bonding interaction between the radical ions. This means that, as is shown in Scheme 2, the singlet (S) and triplet ($T_{0,\pm}$) levels of the S_1-born radical-ion pair (**2a** and **2a'**) are nondegenerate, having an energy gap of $2|J|$, where J denotes the electron-exchange integral. Therefore, the hyperfine-induced intersystem crossing ($S \leftrightarrow T_{0,\pm}$) of the pair does not occur at the zero field. As can be seen from Scheme 2, however, the application of the magnetic field to this system causes a crossing of the levels of S and T_+ at a particular magnetic field, H_1. Consequently, the chemical yield of the lactam **2** as an S_1-born cage product comes to show a minimum at this field strength, H_1 (ca. 1T in Fig. 2), i.e., the magnetic-field dependence of the chemical yield of the S_1-born cage product due to the HFI-J mechanism.[4]



Scheme 1.



Scheme 2.

If this interpretation is valid, the magnetic field, H_1, should be progressively shifted to a higher field as the electron-exchange interaction in the radical-ion pair **2a** increases, because the electron-exchange interaction determines the singlet-triplet splitting $(2|J|)$ of the pair.[6] The exchange integral, $J(r)$, depends exponentially on the interradical distance, r, according to:

$$J(r) = J_0\exp(-\alpha r) \qquad (2)$$

where α is a parameter.[6a] In the photochemical system under consideration, the distance between the radical centers of the pair **2a** can be assumed to vary with the pK_a of the reaction medium (ROH) which is linked by hydrogen bond to the oxygen atom of the *N*-oxide. This, in turn, leads to the idea that the electron-exchange interaction is dependent on the pK_a of the alcohol used as a reaction medium. The values of pK_a of some conventional aliphatic alcohols are known to be in the following order:[7] *t*-butyl alcohol>2-propanol≈ethanol>methanol. Accordingly, the magnetic field, H_1, responsible for the minimal yield of lactam **2** can be expected to be shifted to a progressively higher field as the reaction medium is changed from *t*-butyl alcohol to 2-propanol (or ethanol) and then methanol. In order to determine whether or not this presumption is correct, therefore, the photochemical isomerizations of isoquinoline *N*-oxide in the various alcohols were examined in either the absence or presence of a magnetic field.

In the absence of a magnetic field, the chemical yield of lactam **2** was dependent on the nature of the alcohol used as a reaction medium, decreasing in this order: methanol (ca. 74%), ethanol (ca. 67%), 2-propanol (ca. 55%) and *t*-butyl alcohol (ca. 43%), where the values in parentheses are the chemical yields.

Figures 1 to 4 show the results when the chemical yield of lactam **2** in various alcohol is plotted as a function of the magnetic-field strength. In the case of a 2-propanolic solution (Fig. 3), the minimal yield (ca. 44%) was observed at approximately 1T, just as in the case of an ethanolic solution (Fig. 2) reported previously.[1] In the case of a methanolic solution (Fig. 1), the chemical yield of lactam **2** was ca. 74% at a magnetic field below 1.4T, but it decreased steeply with an increase in the field strength reaching ca. 68% at 1.62T. It may safely be concluded from this finding that a minimal yield would appear in the vicinity of

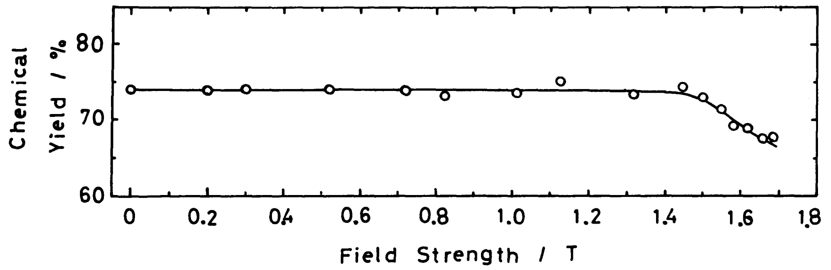


Fig. 1. Photochemical magnetic field effect of isoquinoline *N*-oxide **1** in methanol. Chemical yield of lactam **2** vs. magnetic field strength. $[\mathbf{1}]=4.81\times10^{-3}$ mol dm^{-3}. Irradiation time: 15 min. Conversion: ca.18%.

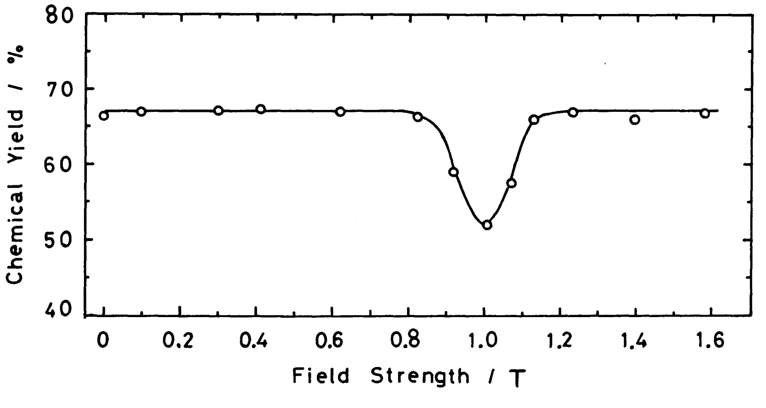


Fig. 2. Photochemical magnetic field effect of isoquinoline *N*-oxide **1** in ethanol. Chemical yield of lactam **2** vs. magnetic field strength.[1] $[\mathbf{1}]=4.82\times10^{-3}$ mol dm^{-3}. Irradiation time: 10 min. Conversion: ca. 17%.

1.7T, although the measurement was not performed at a magnetic field above 1.65T because of the limited capability of the electromagnet employed in the experiment. In the case of a *t*-butyl alcoholic solution, unexpectedly, the complicating magnetic-field effect shown by Curve (a) in Fig. 4 was observed; the chemical yield of lactam **2** showed two maxima (ca. 50 and 55%), at approximately 0.9 and 1.35T, as well as a minimum (ca. 34%) at about 0.72T. The anomalous magnetic-field effect in the high-field region (>0.8T) disappeared completely upon the addition of 1,3-cyclohexadiene, C_6H_8, (triplet quencher)8) to the reaction system, while a minimum of the chemical yield was still observed at approximately 0.75T (Curve (b) in Fig. 4). The results indicate clearly that the quencher-insensitive-field effect around 0.7T should be assigned to the HFI-J magnetic-field effect, which can itself be ascribed to the S_1-born singlet hydrogen-bonded radical-ion pair **2a**. The anomalous and quencher-sensitive magnetic-field effect will be discussed later.

The experimental results described above are, surprisingly, in fair agreement with the presumption that a minimum in the chemical yield of lactam **2** may appear at a higher magnetic field as one changes the reaction medium in the order: *t*-butyl alcohol, 2-propanol (or ethanol) and methanol. Hence, the observed solvent dependence can be taken as corroborating evidence that, as is shown in Scheme 1, the photochemical isomerization of isoquinoline *N*-oxide **1** into lactam **2** in hydroxylic solvents (ROH) occurs with the intervention of the S_1-born singlet hydrogen-bonded radical-ion pair **2a**, but it does not proceed via the S_1-born oxaziridine **3a** previously postulated as an intermediate of this reaction (cf. Ref. 1).

Next, let us discuss the anomalous field dependence of the chemical yield that is observed only in the case of *t*-butyl alcoholic solution in a magnetic field above 0.8T. As can be seen from Fig. 4, the chemical yield of lactam **2** showed distinct maxima at approximately 0.9 and 1.35T, but this effect disappeared upon the

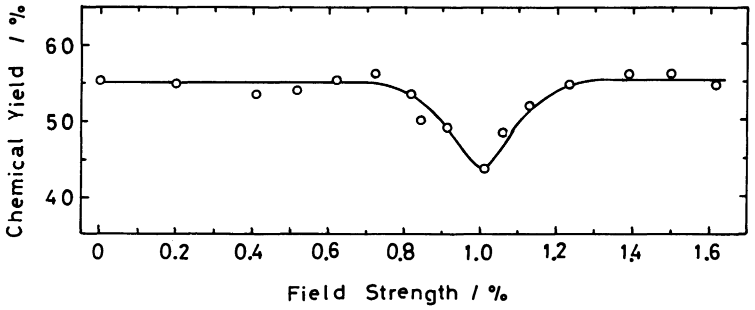


Fig. 3. Photochemical magnetic field effect of isoquinoline *N*-oxide **1** in 2-propanol. Chemical yield of lactam **2** vs. magnetic field strength. [**1**]=4.82 × 10^{-3} mol dm^{-3}. Irradiation time: 15 min. Conversion: ca. 16%.

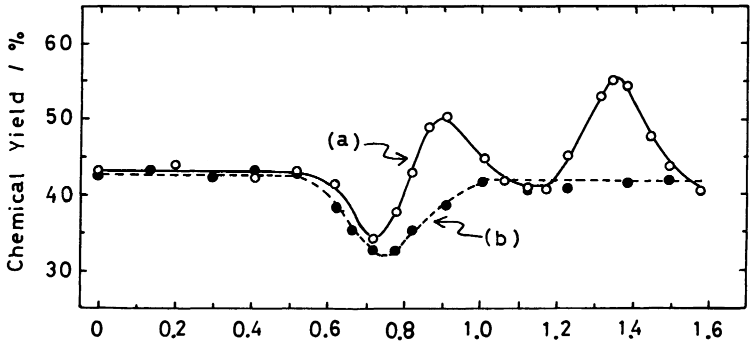


Fig. 4. Photochemical magnetic field effect of isoquinoline *N*-oxide **1** in *t*-butyl alcohol. Chemical yield of lactam **2** vs. magnetic field strnegth. [**1**]=4.81 × 10^{-3} mol dm^{-3}.
(a) —○—: [C_6H_8]=0. Irradiation time: 10 min. Conversion: ca. 17%.
(b) --●--: [C_6H_8]=4.80 × 10^{-1} mol dm^{-3}. Irradiation time: 10 min. Conversion: ca. 12%.

addition of the triplet quencher. The quencher-sensitive magnetic-field effect showed, of course, the same pattern as that for the field dependence of the chemical yield of the T_1-born cage product due to the HFI-J mechanism (cf. Fig. 6 in Ref. 5).[4] This strongly suggests that the transfer of an electron (πO:) from the *N*-oxide to the hydrogen-bonded alcohol occurs not only in the S_1 state, but also in the T_1 state, to produce two kinds of field-sensitive radical-ion-pair intermediates (**2a** and **2b′**) quite similar to each other (Scheme 2). The only difference between the two pairs is the magnitude of the electron-exchange interaction. The exchange interaction in the T_1-born radical ion pair, **2b′**, should be much larger than that in the S_1-born radical ion pair, **2a**, since the maximal yields of the lactam **2** as a T_1-born cage product appear in a higher-field region compared to the minimal yield of the lactam **2** as an S_1-born cage product. For the formation of such radical-ion pairs, a hydrogen-bonding interaction between the oxygen atom of the *N*-oxide and the alcoholic solvent has to be much stronger in the T_1 state than in the S_1 state.

Kubota et al.[9] have demonstrated clearly, prior to 1972, from solvent-effect studies of the absorption (singlet–singlet and singlet–triplet) and fluorescence spectra of some heterocyclic *N*-oxides, that the hydrogen-bonding ability of the oxygen atom of the N→O group is much larger in the S_0 and T_1 states than in the S_1 state; this is in conformity with the result of molecular-orbital consideration that the charge transfer from the oxygen atom of the N→O group to the ring π-electron system is much larger in the S_1 state than in the S_0 and T_1 states. The results strongly support the idea that the T_1-born triplet hydrogen-bonded radical-ion pair **2b′** has an electron-exchange interaction (J') much larger than that (J) in the S_1-born singlet hydrogen-bonded radical-ion pair **2a**.

One may construct a schematic energy-level diagram (as is shown in Scheme 2) for the hydrogen-bonded radical-ion pairs produced from the S_1 and T_1 states, by considering that the singlet-triplet splitting ($2|J'|$) in the T_1-born radical-ion pair is greater than that ($2|J|$) in the S_1-born radical-ion pair. On the basis of this diagram, the observed photochemical magnetic-field effect of isoquinoline *N*-oxide in *t*-butyl alcohol can be reasonably interpreted in terms of an HFI-J mechanism as follows.

In the absence of an external magnetic field, the hyperfine-induced intersystem crossing ($S \rightarrow T_{0,\pm}$ or $T'_{0,\pm} \rightarrow S'$) from the S_1-born singlet or T_1-born triplet radical-ion pair (**2a** or **2b′**) does not occur at the zero field because of the large electron-exchange interaction. As a result, the S_1-born singlet hydrogen-bonded radical-ion pair **2a** mostly undergoes a geminate reaction within a solvent cage to give rise to lactam **2** as an S_1-born cage product, whereas the T_1-born triplet hydrogen-bonded radical-ion pair **2b′** undergoes a diffusive separation into the solvent bulk. However, the application of the magnetic field to this system resolves the triplet level $T_{0,\pm}$ (or $T'_{0,\pm}$) into three sublevels, T_0, T_+, and T_- (or T'_0, T'_+, and T'_-), and the T_+ (or T'_+) level approaches the S and S′ levels as the field strength increases. Consequently, a crossing of the levels of S and T_+ occurs first at the magnetic field of H_1 and the chemical yield of the lactam **2** as an S_1-born cage product becomes minimal, corresponding to a minimal yield around 0.7T (Fig. 4). A further increase in the field strength causes an intersystem crossing of $T'_+ \rightarrow S$ at the magnetic field H_2,[10] followed by a crossing from the T'_+ to S′ levels at the magnetic field H_3. As a result, the chemical yield of the lactam **2** as a T_1-born cage product comes to show maxima at the magnetic fields of H_2 and H_3, corresponding probably to maximal yields at approximately 0.9 and 1.35T (Curve (a) in Fig. 4).

In the case of a methanolic, ethanolic or 2-propanolic solution, no such anomalous field effect was observed at all at any magnetic field below 1.65T (Figs. 1 to 3). This is probably because a hyperfine-induced intersystem crossing between the T'_+ and S (or S′) levels can not occur in this field region because of a large electron-exchange interaction in the hydrogen-bonded radical-ion-pair intermediate.

Conclusion

Remarkable solvent dependences of the magnetic-field effect attributable to the HFI-J mechanism were found for the first time in the case of a photochemical isomerization of isoquinoline *N*-oxide **1** into lactam **2** in alcoholic solvents. First, the chemical yield of the lactam **2** as an S_1-born cage product showed a minimum at a particular magnetic field, which was progressively shifted to a higher field as the reaction medium (ROH) was changed from *t*-butyl alcohol to 2-propanol (or ethanol) and then methanol. Such a solvent dependence was attributable to the influence of an electron-exchange interaction on the hyperfine-induced intersystem crossing of the S_1-born singlet hydrogen-bonded radical-ion pair **2a**, assumed to be a transient intermediate of this reaction. Second, in the case of a *t*-butyl alcoholic solution, the chemical yield of lactam **2** showed two maxima in the field region of 0.8—1.4T, in addition to a minimum at ca. 0.7T. This phenomenon was also reasonably explained in terms of an HFI-J mechanism by assuming the formation of the triplet hydrogen-bonded radical-ion pair **2b′** from the T_1 state (Scheme 2). The present studies demonstrate definitely that the photochemical isomerization of isoquinoline *N*-oxide in hydroxylic solvent proceeds according to the mechanism shown in Scheme 1.

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3) As to the photochemistry of aromatic amine *N*-oxides, see, for example, G. G. Spence, E. C. Taylor, and O. Buchardt, *Chem. Rev.*, **70**, 231 (1970); F. Bellamy and J. Streith, *Heterocycles*, **4**, 1391 (1976); A. Albini and M. Alpegiani, *Chem. Rev.*, **84**, 43 (1984).

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10) The fact that the chemical yield of lactam **2** shows a maximum at the magnetic field of H_2 (ca. 0.9T in Fig. 2) indicates explicitly that the intersystem crossing $T'_+ \rightarrow S$ occurs, while the $S \rightarrow T'_+$ does not. This is probably because a geminate reaction (**2a**→**2b**) of the singlet hydrogen-bonded radical-ion pair **2a** takes place much faster than the intersystem crossing $S \rightarrow T'_+$.