# Synthesis of 2-Pyridinylbenzoxazole: Mechanism for the Intramolecular Photosubstitution of the Haloarene with the Carbonyl Oxygen of the Amide Bond in Basic Medium

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*Received June 11, 1999*

2-Pyridinylbenzoxazole derivatives have been synthesized by the intramolecular photosubstitution reaction of *N*-(2-halophenyl)pyridinecarboxamide (**1** and **2**) with its amide bond in basic medium. In neutral medium both intramolecular photosubstitution and photoreduction reactions occurred. In the photosubstitution reaction a singlet state of the *o*-haloarene is involved, whereas in the photoreduction a triplet state of the *o*-haloarene is involved; oxygen inhibited the photoreduction but not the photosubstitution. The relative rate studies showed that a base accelerates the photosubstitution reaction but decelerates the photoreduction. *o*-Iodoarenecarboxamide is more reactive than *o*-bromoarenecarboxamide, which in turn is more reacitive than *o*-chloroarenecarboxamide. UV−vis absorption change in the presence of a base showed that an imidol and/or imidolate anion is involved in the reaction. Several transient species, such as charge-transfer excited states and a cyclohexadienyl anion radical, have been identified from the photolysis of **1** and **2** in basic medium by laser flash photolysis. In neutral medium dibromide anion radical and a phenyl $\sigma$ radical were identified in addition to the above intermediates. On the basis of the photokinetic and laser flash photolysis studies, an intramolecular photosubstitution of *N*-(*o*-halophenyl)-pyridinecarboxamide with its amide bond occurs via an intramolecular $S_N(ET)Ar^*$ mechanism to afford 2-pyridinylbenzoxazole derivative, and the photoreduction proceeds via a free radical mechanism to give *N*-phenylpyridinecarboxamide.

## Introduction

In an attempt to develop a photochemical ring formation of *o*-haloarene tethered to arene,[1,2] we recently found that a photoreaction of *N*-(2-halophenyl)pyridinecarboxamide gave a 2-pyridinylbenzoaxole, a photosubstitution product of the *o*-haloarene with the carbonyl oxygen of the amide bond within the molecule. The intramolecular photosubstitution reaction is valuable and simple for the benzoxazole ring formation and virtually unknown.

There are few literature reports[3−5] on the intramolecular photosubstitution reaction of *o*-haloarene with carbonyl oxygen and thiocarbonyl sulfur of amide and thioamide, even though there are several reports[6−8] on the intramolecular aromatic substitution reaction of ground-state *o*-haloarene with thiocarbonyl sulfur nucleophile of thioamide and analogues.

Ramakrishnan and co-workers[3a] reported that 2-methylbenzothiazoles were synthesized via intramolecular photosubstitution of *o*-halothioacetanilides. Recently they[3b] proposed a reasonable intramolecular electron-transfer mechanism for the formation of benzothiazole. Bowman and co-workers[4] reported that 2-phenyl- and 2-methylbenzothiazole were prepared in high yield from the photoinduced intramolecular aromatic substitution of *o*-iodothioacetanilide and *o*-iodothiobenzanilide in the presence of potassium *t*-buthoxide and acetone. Arad-Yellin and co-workers[5] reported that on UV irradiation, 2,6-dichlorocinnamic acid and its ester underwent photosubstitution to yield 5-chlorocoumarin; amide derivative yielded the corresponding imino analogues. For imino analogue formation (*N*-methyl-5-chloro-2*H*-benzopyran-2-imine), an intermediate formed from an addition of carbonyl oxygen of the amide bond to the *o*-phenyl carbon bearing chlorine in the 2,6-dichlorophenyl group was assumed.

However, the intramolecular photosubstitution of *o*-haloarene with the carbonyl oxygen of the amide bond is rare and has not been explored mechanistically. This paper describes the result of our investigations for the synthesis of benzoxazole derivative and this reaction mechanism.

## Results and Discussion

*N*-(2-Halophenyl)pyridinecarboxamides and *N*-(phenyl)pyridinecarboxamide (**1** and **2** in Chart 1) were

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(3) (a) Paramasivam, R.; Palaniappan, R.; Ramakrishnan, V. T. *J. Chem. Soc., Chem. Commun.* **1979**, 260. (b) Jayanthi, G.; Muthusamy, S.; Paramasivam, R.; Ramakrishnan, V. T.; Ramasamt, N. K.; Ramamurthy, P. *J. Org. Chem.* **1997**, *62*, 5766.
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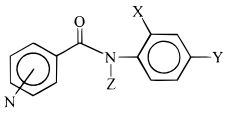
10.1021/jo9909498 CCC: $18.00 
Published on Web 11/12/1999

**Table 1. Products and Their Yield in the Photoreaction of *N*-(2-Halophenyl)pyridinecarboxamide**

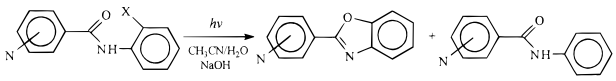
| starting compd | reaction medium | reaction time (h) | recovered starting compd (%) | product | product yield (%) |
|---|---|---|---|---|---|
| **1a** | $CH_3CN$ (210 mL)/2 M aq NaOH (30 mL) | 30.0 | 38.2 | **3** | 25.3 |
| **1b** | $CH_3CN$ (210 mL)/2 M aq NaOH (30 mL) | 8.0 | 23.3 | **3** | 34.4 |
| **2a** | $CH_3CN$ (210 mL)/2 M aq NaOH (30 mL) | 21.0 | 11.4 | **4** | 37.3 |
| **2b** | $CH_3CN$ (210 mL)/2 M aq NaOH (30 mL) | 3.5 | 27.7 | **4** | 43.1 |
| **1b** | $CH_3CN$ (140 mL)/0.2 M aq NaOH (100 mL) | 6.0 | 4.6 | **3** | 29.2 |
| | | | | **1d** | 7.6 |
| **2b** | $CH_3CN$ (220 mL)/0.02 M aq $Na_2CO_3$ (20 mL) | 6.5 | 11.1 | **4** | 19.5 |
| | | | | **5** | 27.3 |

**Chart 1**



**1a**: N; 4-N (4-pyridinyl), X = Cl, Z = H, Y = H
**1b**: N; 4-N (4-pyridinyl), X = Br, Z = H, Y = H
**1c**: N; 4-N (4-pyridinyl), X = I, Z = H, Y = H
**1d**: N; 4-N (4-pyridinyl), X = H, Z = H, Y = H
**1e**: N; 4-N (4-pyridinyl), X = Br, Z = $CH_3$, Y = H
**2a**: N; 3-N (3-pyridinyl), X = Cl, Z = H, Y = H
**2b**: N; 3-N (3-pyridinyl), X = Br, Z = H, Y = H

**Scheme 1**



**1a**: N; 4-N(4-pyridinyl), X= Cl
**1b**: N; 4-N(4-pyridinyl), X= Br
**2a**: N; 3-N(3-pyridinyl), X= Cl
**2b**: N; 3-N(3-pyridinyl), X= Br
**3**: N; 4-N(4-pyridinyl)
**4**: N; 3-N(3-pyridinyl)
**1d**: N; 4-N(4-pyridinyl)
**5**: N; 3-N(3-pyridinyl)

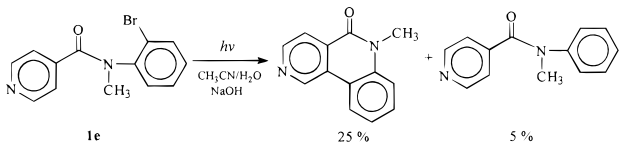
prepared by reacting pyridinecarboxylic acids with the appropriate 2-haloanilines and aniline. The preparation details of these pyridinecarboxamides will be described in the Experimental Section.

**Preparative Reaction.** When an acetonitrile solution (240 mL) of *N*-(2-chlorophenyl)-4-pyridinecarboxamide (**1a**, 1 mmol) containing 30 mL of aqueous 2 M NaOH was irradiated by a Hg lamp (150 W, high pressure) under nitrogen for 30 h, a photosubstituted product, 2-(4-pyridinyl)benzoxazole (**3**), was obtained in 25% yield (Scheme 1). This compound (mp, 130−131; lit. value, 130−131[9]) was identified by its spectral properties (NMR, IR, MS) and elemental analysis. The photosubstitution reaction is novel and involves replacement of the chlorine of the chlorophenyl moiety by the carbonyl oxygen of the amide bond within the molecule.

When bromo analogue **1b** was irradiated under the above conditions for 8 h, the same product, 2-(4-pyridinyl)benzoxazole (**3**), was obtained in 34% yield. The reaction was extended to *N*-(2-halophenyl)-3-pyridinecarboxamide (**2**). The pertinent results of the synthetic reactions are shown in Table 1 and Scheme 1. The photosubstitution reaction yields in the table range from a value of 20% for **2b** in acetonitrile containing $Na_2CO_3$ to 43% for **2b** in acetonitrile with NaOH. This reaction is valuable and simple for the synthesis of arylbenzoxazole derivative.

In weak bases such as acetonitrile containing $Na_2CO_3$ or dillute NaOH (last two entries in Table 1), a photoreduced product, *N*-(phenyl)pyridinecarboxamide (**1d**, **5**), was formed in addition to the photosubstitution products. The photoreduction of haloarene is well known in neutral medium.[10]

**Scheme 2**



**1e** 25 % 5 %

**Table 2. Quantum Yield on the Photosubstitution of *N*-(2-Halophenyl)pyridinecarboxamide (1) with and without Oxygen[a]**

| substrate | quantum yield ($\phi$) with Ar | quantum yield ($\phi$) with $O_2$ |
|---|---|---|
| **1a** | 0.002 | 0.002 |
| **1b** | 0.025 | 0.025 |
| **1c** | 0.060 | 0.055 |

[a] In $CH_3CN$ containing 0.1 N aq NaOH (50/1) with monochromatic light (266 ± 3 nm, Xe lamp, 450 W).

*N*-(2-Bromophenyl)-*N*-methyl-4-pyridinecarboxamide (**1e**) did not give the expected photosubstituted product but produced photocyclized (25%) and photoreduced (5%) products (Scheme 2). This abnormal bahavior of **1e** suggests an important imidol structure for the photosubstitution of **1a**, **1b**, and **2**.

A blank test for the photoreaction was performed. The thermal reaction of **1a** and **1b** under the above conditions for 2 days did not produce a cyclized and reduced product but a small amount of a hydrolyzed product. Thus the reactions that produced 2-arylbenzoxazole and *N*-(phenyl)pyridinecarboxamide are not the thermal reactions but the photoinduced subsititution and reduction reactions.

**Kinetics.** To elucidate the reaction mechanism, the quantum yields of the photosubstitution reactions and the relative rates of the reaction on several conditions have been studied.

The quantum yields of the photosubstitution in several conditions have been measured and are shown in Table 2. The quantum yield in Table 2 ranges from a value of 0.002 for **1a** to 0.06 for **1c**. The iodoarene **1c** is about 2 times more reactive than bromoarene **1b**, which in turn is about 10 times more reactive than chloroarene **1a**. The quantum yield of **1a** and **1b** was not changed in the presence of oxygen as a triplet quencher, although that of iodoarene **1c** was reduced a little (8%). These results imply that the singlet excited state of the haloarene may be mainly involved in the photosubstitution reaction for iodoarene **1c**, a small portion of a triplet being involved in addition to the singlet excited-state reaction.

As an example for the relative rate of the haloarene, bromo analogue **1b** (17 mg) was dissolved in acetonitrile

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(10) Bunce, N. J. In *CRC Handbook of Organic Photochemistry and Photobiology*; Horspool, W. H., Song, P.-S., Eds.; CRC Press: New York, 1995; p 1181.

**Table 3. Relative Rates of the Formations of 2-Pyridinylbenzoxazole and *N*-Phenylpyridinecarboxamide in the Photoreaction of *N*-(2-Halophenyl)pyridinecarboxamide with a Broad Spectrum of Light from a Hg Lamp (150 W)**

| | | | | relative rate | |
|---|---|---|---|---|---|
| entry | substr[a] | solvent | atm | photosub | photored[b] |
| 1 | **1b** | $CH_3CN$ | $N_2$ | 2.2 | 3.8 |
| 2 | **1b** | $CH_3CN$ | $O_2$ | 2.2 | <0.01 |
| 3 | **1b** | $CH_3CN$/2 M NaOH[b] | $N_2$ | 5.1 | 1.2, (nd)[d] |
| 4 | **1b** | $CH_3CN$/2 M NaOH[b] | $O_2$ | 5.1 | <0.01 |
| 5 | **1c** | $CH_3CN$/2 M NaOH[b] | $N_2$ | 15.0 | 12.5 |
| 6 | **1b** | benzene | $N_2$ | 1.0 | 0.4 |
| 7 | **1b** | cyclohexane | $N_2$ | 0.3 | 0.7 |
| 8 | **1b** | MeOH | $N_2$ | <0.01 | 0.7 |
| 9 | **2a** | $CH_3CN$ | $N_2$ | 0.1 | 0.05 |
| 10 | **2a** | $CH_3CN$ | $O_2$ | 0.1 | <0.01 |
| 11 | **2a** | $CH_3CN$/2 M NaOH[b] | $N_2$ | 1.6 | 0.06 |
| 12 | **2b** | $CH_3CN$/2 M NaOH[b] | $N_2$ | 6.0 | 0.06 |
| 13 | **1b** | $CH_3CN/NEt_3$ (2.1 mM) | $N_2$ | 1.8 | 4.2 |
| 14 | **1b** | $CH_3CN$/MMA[c] (5.6 mM) | $N_2$ | 2.1 | 2.9 |
| 15 | **1b** | $CH_3CN$/2 M NaOH $5.0 \times 10^{-4}$ M isoprene | $N_2$ | 4.6 | nd |
| 16 | **1b** | $CH_3CN$/2 M NaOH 0.05 M $K_2S_2O_8$ | $N_2$ | 1.5 | nd |

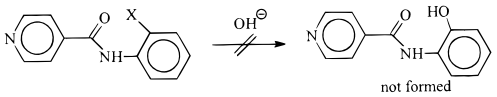
[a] The concentration of the substrates used is $4.1 \times 10^{-3}$ M. [b] $CH_3CN$/2 M NaOH = 13/2. [c] Methyl methacrylate. [d] Not detected when methanol solution filter is used before the cuvette.

(15 mL), and the solution was purged with nitrogen (or oxygen) for 10 min and irradiated with a Hg lamp (150 W, high pressure) for 1.5 h. The reaction mixture was analyzed by GC (FID), and formation of the substituted products and the reduced product was monitored (Table 3).

In acetonitrile the rate of photoreduction of **1b** is faster than that for photosubstitution (entry 1 in Table 3). In the presence of oxygen the substitution reaction rate of **1b** was again not affected, whereas the reduction rate was reduced extensively (entries 1 and 2). This held true for the photoreactions of **2a** in acetonitrile and of **1b** in acetonitrile containing NaOH (entries 9, 10, 3, and 4). These results are in line with the oxygen effect on the quantum yield as described above. Thus, in the photosubstitution reaction a singlet excited state of the haloarene is involved, whereas in the photoreduction a triplet state is involved.

The presence of a base such as NaOH led to an acceleration for the photosubstitution by more than twice and to a deceleration for the photoreduction by more than 3 times (entries 1 and 3). Similar trends were observed for the photosubstitution (entries 9 and 11) of **2a** and **2b**. One possible explanation is that an anionic nucleophile of carbonyl oxygen of the amide bond in basic medium intramolecularly displaces the halogen of the haloarene in the singlet excited state ($S_N2Ar^*$).[11] Another possibility is that an anionic radical species photoinduced from anionic carbonyl oxygen of the imidol in basic medium (vide infra) intramolecularly substitutes the halogen of the haloarene ($S_N(ET)Ar^*$).[11]

When the photosubstitution reactivities of the iodoarenecarboxamide and bromoarenecarboxamide are compared, the iodo analogue, which has a better leaving group, is 3 times more reactive than the bromo analogue (entries 3 and 5). A similar trend was observed for the photosubstitution rate of **2a** and **2b** (entries 11 and 12). This effect of the leaving halide anions on the subsititution rate is consistent with the quantum yields of **1** as described above. It seems likely that the substitution reaction is governed by the leaving trend of the halide anion from a reaction intermediate. In other words the rate-determining step of the reaction is the leaving step of the halide anion of an intermediate. Moreover, if the $S_N2Ar^*$ mechanism is operative, a phenolic-type product, which could be formed from the intermolecular substitution reaction of the haloarene with hydroxide ion, could not be detected in the reaction condition. Thus these results suggest that the intramolecular $S_N(ET)Ar^*$ mechanism is more favorable than $S_N2Ar^*$.




The reactivities of the haloarene toward the photoreduction were not very clear because of the low reaction rates in basic medium (entries 11 and 12), although iodo analogue **1c** was somewhat reactive (entry 5). Probably the heavy atom effect of the iodo group increases the population of the triplet state, which is involved in the reduction, by enhancing intersystem crossing. The phenyl $\sigma$ radical is possible by a homolytic cleavage of the phenyl-iodine bond from the triplet state even in basic medium and may then cause an increasing photoreduction reaction rate.

In nonpolar solvents such as benzene and cyclohexane, the substitution rates of **1b** were quite lower than that in acetonitrile, and the reduction rate was moderately lower than that in acetonitrile (entries 6 and 7). Probably an imidolate anion and/or imidol is not efficiently populated in this medium for the substitution and reduction. In the protic solvent methanol, the substitution reaction of **1b** sparingly occurred, and its reduction reaction occurred weakly (entry 8). Methanol probably inhibits the substitution by blocking the formation of the imidolate anion of **1b** by its protonation.

It is noteworthy that the reduction product was not detected when a methanol solution filter was used before the window of the reaction cuvette (entry 3). This suggests that the reduction path is blocked by filtering out the shorter wavelength from the broad spectrum of light. In other words, a locally excited state of the pyridinecarboxamide, probably the excited state of the halo phenyl moiety produced by the excitiation by the shorter wavelength, undergoes reduction reaction via a homolytic cleavage of phenyl-halogen bond (vide infra).

3-Pyridinylcarboxamide **2b** is more reactive than 4-pyridinylcarboxamide **1b** (entries 3 and 12) for the photosubstitution, indicating the importance of the electronic effect of nitrogen position in the pyridine moiety; the nitrogen on the 3-pyridine moiety of **2b** withdraws electrons more effectively to give a more acidic imidol, to provide a more anionic form of the imidol, and eventually to produce more substitution product compared to the reaction of **1b**.

In the presence of triethylamine, which is known as a good electron donor for stimulated $S_{R^-N}1Ar$ reactions,[12] the photosubstitution rate is reduced a little, whereas

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(12) Beugelmans, R. In *CRC Handbook of Organic Photochemistry and Photobiology*; Horspool, W. H.; Song, P.-S., Eds.; CRC Press: New York, 1995; p 1200.

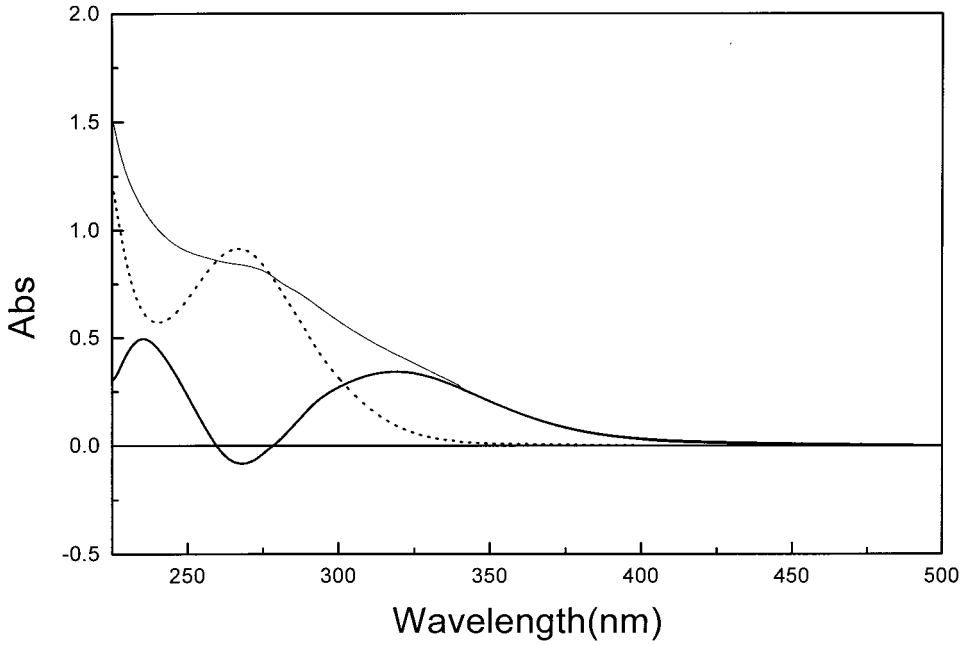


**Figure 1.** UV−vis absorption spectra of **1b** in acetonitrile ($1.2 \times 10^{-4}$ M **1b**, 2 mL, dotted line) and in acetonitrile containing NaOH ($1.2 \times 10^{-4}$ M **1b**, 2 mL; 1.0 M NaOH, 0.1 mL; thin solid line). The thick solid line was obtained by subtraction of the dotted line from the thin solid line.

the photoreduction rate is enhanced somehow (entry 13). This result implies that the $S_R^-{}_N1Ar$ mechanism is not present in the photosubstitution reaction but may partially be in the reduction reaction.

In the presence of radical scavengers such as methyl methacrylate or isoprene, the photosubstitution reaction is retarded a little, whereas the photoreduction reaction is retarded extensively (entry 14 and 15). This implies that photoreduction obviously proceeds via a radical-mediated reaction.

The presence of $K_2S_2O_8$, which is known as a solvated electron acceptor for a stimulated $S_R^+{}_N1Ar^*$ reaction,[13] did not improve the photoreactions, indicating that the mechanism is other than $S_R^+{}_N1Ar^*$ (entry 16).

**Laser Flash Photolysis.** Before the laser flash photolysis study, the UV−vis absorption behavior of the halophenylpyridinecarboxamide was studied. The $\lambda_{max}$ values of all *N*-(2-halophenyl)pyridinecarboxamides in acetonitrile are from 264 to 267 nm, whereas that of *N*-phenylpyridinecarboxamide (**1d**, no *o*-substituent) is 270 nm and that of *N*-(2-bromophenyl)-*N*-methylpyridinecarboxamide (**1e**) is 254 (sh) nm. Thus, the energy state of the singlet excited state of an arene with an *o*-halogen substituent is higher than that of an arene without an *o*-substituent (see Experimental Section for data).

The absorption spectra of **1b** in acetonitrile (dotted line) and acetonitrile containing NaOH (thin solid line) are shown in Figure 1. The prototype absorption spectra of **1b** in acetonitrile ($\lambda_{max}$ = 267 nm) changed to a structureless type of absorption spectra by the addition of NaOH. If the prototype absorption was subtracted from the structureless absorption, two new peaks around 242 and 325 nm were obtained (thick solid line). The species at about 325 and 242 nm is believed to be an intramolecular charge-transfer excited state from the imidolate anion of **1b** formed from the amide by action of the base and/or light absorption, because the species was not seen in the UV−vis absorption of **1b** in methanol containing NaOH and the similar species was not seen in the UV−vis absorption of **1e** in acetonitrile containing NaOH (see the Supporting Information). Moreover, the species with $\lambda_{max}$ at 242 and 325 nm was not seen in the above conditions in the UV−vis absorption of **1e**, which has a methyl group on the nitrogen of the amide bond and thus is not possible for the formation of the imidol structurally in acetonitrile containing NaOH (not shown). The same UV−vis absorption behavior of **1a** in the basic medium as that of **1b** was observed ($\lambda_{max}$ 266 nm, not shown). The lifetime of the imidol form from **1a** by irradiation by a Xe lamp was measured. The lifetime was 2.84 h (Table 4). In fact, an imidol formation from the photoinduced proton-transfer tautomerization of benzanilide has been reported.[14]

The fluorescence spectra of **2b** in acetonitrile with and without NaOH were obtained at 200 ns delay after laser flash (power 30 mJ) and are shown in Figure 2. The luminescence spectra consists of two bands around 337 and 400 nm, with onset at 319 and 350 nm, respectively (solid line; the sharp line at 532 nm is from the laser source). In the presence of NaOH a new broad fluorescence spectra around 475 nm (dotted line) appeared in addition to the two peaks in acetonitrile only. The inset of Figure 2 showed the fluorescence spectra of **2b** measured 50 ns after the laser flash (80 mJ). The thick solid line (lowest one) in the inset shows a diffused fluorescence spectra in these conditions. It seems that the efficient formation of a band around 400 nm by high power laser (80 mJ) blocks the observation of the band at about 337 nm (vide infra). The thin solid line exhibits that just the scanning (irradiation) increased the fluorescence intensity around 400 nm. The dotted lines show that the addition of NaOH increased the fluorescence

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(14) Tang, G.-Q.; MacInnis, J.; Kasha, M. *J. Am. Chem. Soc.* **1987**, *109*, 2531.

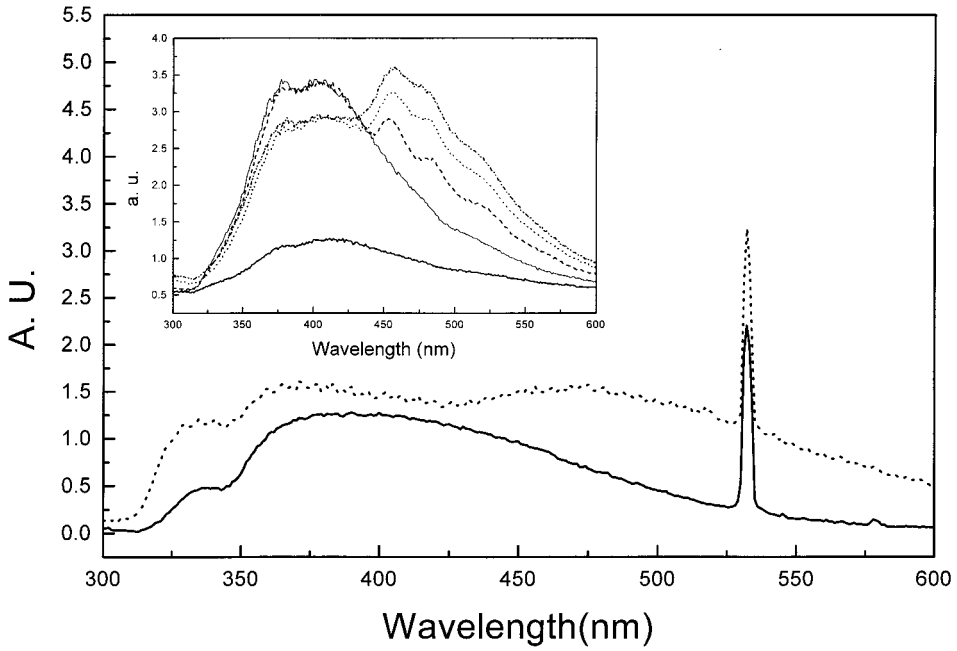
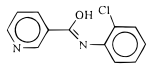
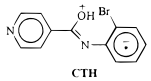
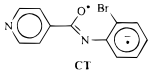
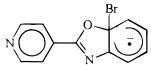
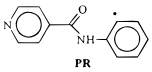


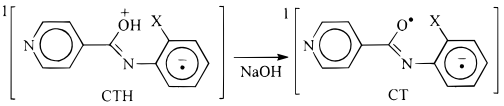

**Figure 2.** Fluorescence spectra of **2b** 200 ns after laser flash (30 mJ) in acetonitrile without NaOH (solid curve) and with NaOH (dotted line). Inset: fluorescence spectra of **2b** (36 mg/500 mL AN) 50 ns after laser flash (80 mJ) on several conditions: — first scan; — second scan; – – – with 0.5 mL of 4 M NaOH; - - - - - with 1.0 mL of 4 M NaOH; – · · –, with 1.5 mL of 4 M NaOH.

**Table 4. Transient Species from the Photolysis of 1 and 2**

| transient | $\lambda_{max}$ nm | lifetime | detecting method | starting material (medium) |
|---|---|---|---|---|
|  | 325 | 2.84 hr | uv absorption | **2** (base) |
|  CTH | 415 | | fluorescence | **1b** (base) |
|  CT | 451 | < 200 ns | fluorescence | **1b** (base) |
|  CHAR | 393 | 39 μs<br>21 μs | transient absorption | **1b** (base)<br>(neutral) |
|  PR | 280-310 | 4 ms | transient absorption | **1b** (neutral) |
| $Br_2^{\bullet -}$ | 360 | 33 μs | transient absorption | **1b** (neutral) |
| $I_2^{\bullet -}$ | 370 | 1.8 ms | transient absorption | **1c** (base) |

intensity around 475 nm with an isosbestic point at about 440 nm. It seems likely that the fluorescence intensity around 475 nm increases by simultaneous expenditure of the band around 400 nm in the basic medium, even though the irradiation (scanning) disrupts the intensity around 400 nm. Figure 3 shows the fluorescence spectra of **1b** in acetonitrile with and without NaOH (at 50 ns delay, laser power 80 mJ). Again a scan (irradiation of laser) increased the intensity of the luminescence at about 410 nm, the addition of NaOH shifted the $\lambda_{max}$ of the fluorescence (415 nm) to that of fluorescence at 451 nm with an isosbestic point at 434 nm, and the band around 475 nm increased by expenditure of the band around 375 nm. It is assumed that, in Figure 2, in acetonitrile the small luminescence peak around 337 nm and the strong luminescence peak around 400 nm arise from the locally singlet excited state of the keto amide (LE) and the intramolecular charge-transfer excited state of the imidol (CTH), respectively, and in the base the diffused luminescence peak around 475 nm originated from the intramolecular charge-transfer excited state of the enolate ion (CT).

It should be noted that the variation of the fluorescence intensity on the basicity of the medium could be seen at 50 ns delay after laser flash but not at 200 ns delay (Figure 3, Table 4). Thus the lifetime of the charge transfer species is around 50 ns, less than 200 ns. It seems likely that in high laser intensity (80 mJ) the process of the strong luminescence species (CTH) to a deprotonated species (CT) by deprotonation with NaOH was the major one. Thus, with the deprotonation process of the excited state, the p$K_a$ value of the charge-transfer excited state from the imidol could be measured. The p$K_a$




pKa ~ 10

values for the excited imidol **2b** and **1b** were roughly estimated to be 9 and 10, respectively, by measuring the fluorescence change in several pH ranges (Figures 2 and 3). The excited state is extremely acidic compared with that of the ground state of benzanilide (p$K_a$ = 16.5)[15] and thus probably provides the intramolecular charge-transfer species (CT), which undergoes an intramolecular photosubsitution reaction via an anionic radical intermediate [$S_N$(ET)Ar* reaction].

Transient absorption spectra were obtained from the laser flash photolysis of **1b** in argon-saturated acetonitrile containing NaOH as shown in Figure 4. There is a transient absorption peak at about 393 nm at 10 μs delay

(15) Homer, R. B.; Johnson, C. D. In *The Chemistry of Amides*; Patai, S., Ed.; Interscience: London, 1970; p 187.

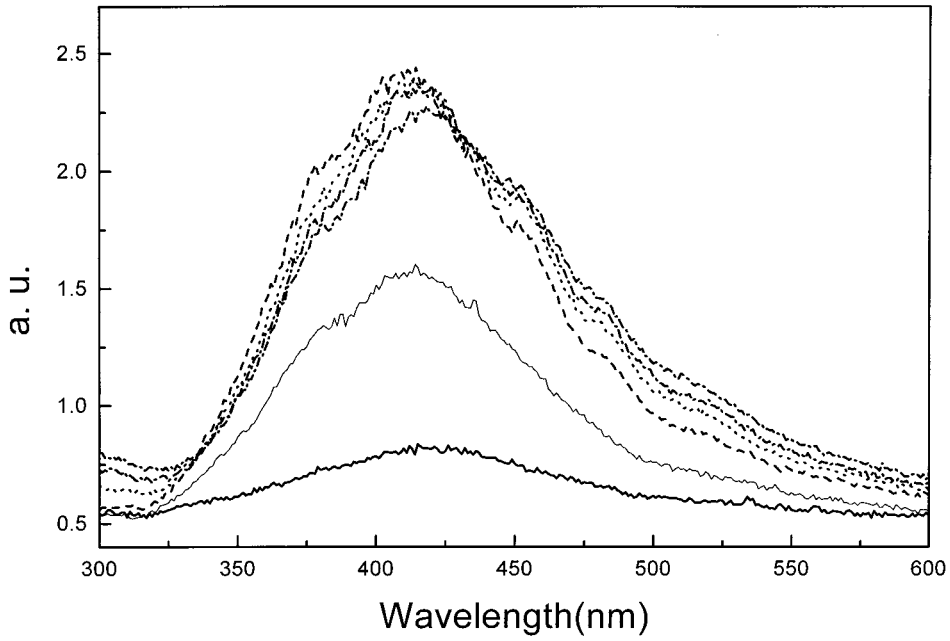



**Figure 3.** Fluorescence of **1b** 50 ns after laser flash (80 mJ) in acetonitrile (36 mg/500 mL AN): — first scan; ⎯ second scan; – – – with 0.5 mL of 4 M NaOH; - - - - - with 1.0 mL of 4 M NaOH; —· – · —with 1.5 mL of 4 M NaOH; – · · – · · with 2.5 mL of 4 M NaOH.

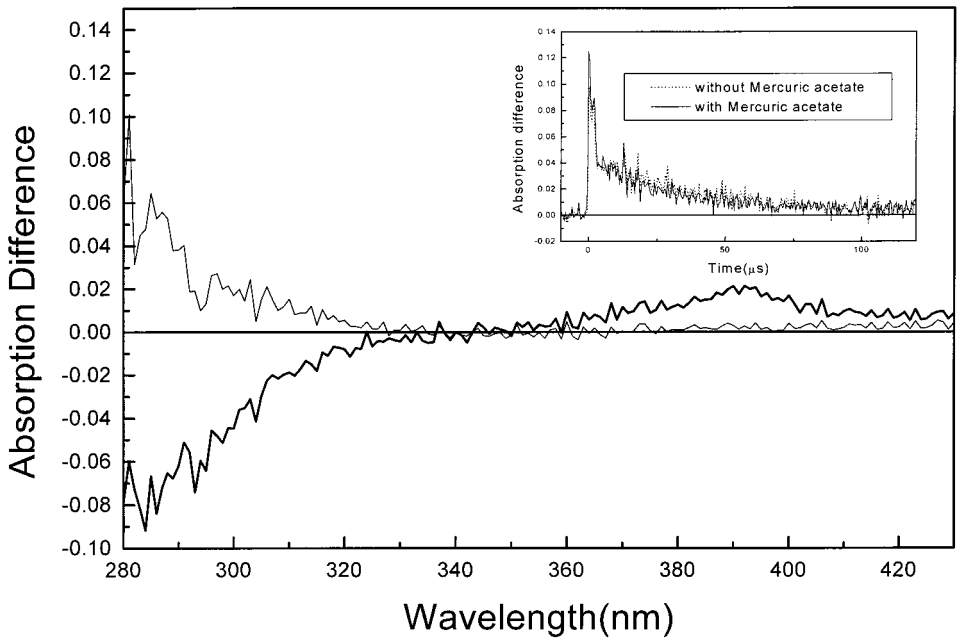
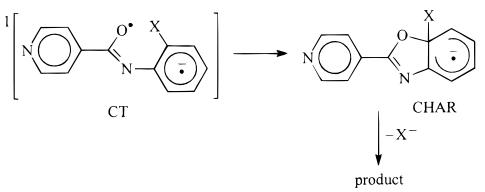



**Figure 4.** Transient absorption spectra obtained upon 266 nm excitation of **1b** in acetonitrile (1 L) containing 1 mL of 4 M NaOH 10 $\mu$s (—) and 1 ms (⎯) after laser pulse. Inset: temporal profile of 393 nm transient (- - - -) and with mercuric acetate (⎯).

after laser flash. The region between 280 and 320 nm is governed by the luminescence of **1b**. At 1 ms delay after laser flash the absorption band at about 393 nm disappeared, whereas a new band at about 285 nm appeared. The temporal profile of the transient at about 393 nm from the photolysis of **1b** is shown in the inset of Figure 4. The species decays in a first-order process, and its lifetime is 39 $\mu$s. The species was not quenched by radical scavengers isoprene or oxygen but was quenched weakly by the presence of mercuric acetate ($\tau = 27$ $\mu$s), indicating an anionic radical species (thin curve in inset of Figure 4). Thus, the transient species that has a lifetime of 39 $\mu$s is assigned to a cyclohexadienyl anion radical (CHAR), which produces the pyridinylbenzoxazole (Table 4). This




assignment was strengthened by the observation that dibromide anion radical could not be seen in the laser flash photolysis of **1b** in acetonitrile containing NaOH. Furthermore, the 393-transient was not seen in the laser flash photolysis of the unsubstituted *N*-phenyl-4-pyridinecarboxamide (**1d**) and *N*-(2-bromophenyl)-*N*-methyl-

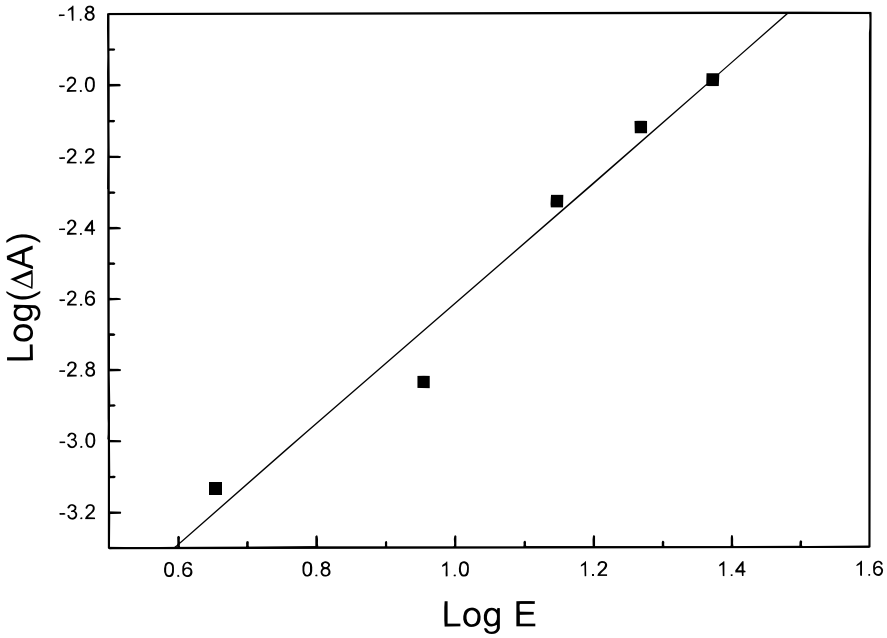



**Figure 5.** Dependence of the 393 nm transient concentration (10 $\mu$s after laser pulse) on the laser pulse energy in the photolysis of acetonitrile of **1b** ($1.4 \times 10^{-4}$ M) under argon; the slope in the log−log plot is 1.8.

4-pyridinecarboxamide (**1e**), which do not afford the photosubstituted product (both transient absorption spectra shown as Supporting Information).

Figure 5 shows the dependence of the cyclohexadienyl anion radical intermediate (CHAR, 393-nm transient species) from **1b** in the basic medium on the photolysis laser pulse energy. The slope of the log−log plot for the intermediate versus laser pulse energy was obtained to be 1.8. This result indicates that the intermediate (CHAR) was formed mainly by a biphotonic process.

The band from 285 to 315 nm in Figure 4 is quenched by the presence of a radical scavenger, *N*-*tert*-butyl-α-phenylnitrone. Thus it is assigned to phenyl $\sigma$ radical from **1b**. It is believed that this is related with reduction product (vide infra).

Similar transient absorption spectra were obtained from the laser flash photolysis studies of **1a** and **1c** under basic conditions (shown as Supporting Information). However, for iodo analogue **1c**, there was an additional transient absorption band around 370 nm whose lifetime was 1.8 ms. The transient was not formed at all in the presence of *N*-*tert*-butyl-α-phenylnitrone, probably a precursor for the transient formation being quenched completely. The transient formation was lowered in the presence of oxygen, probably because the precursor, the triplet state of **1c**, for the transient formation was quenched by oxygen (shown as Supporting Information). The transient was quenched by addition of *o*-xylene to yield a complex between an iodine atom and *o*-xylene ($\lambda_{max} = 580$ nm, $\tau_{580} = 43$ $\mu$s) which is known.[16] It seems likely that the transient at 370 nm corresponds to diiodide anion radical, which could be formed by reaction of iodine radical with iodide ion: the iodine radical was formed by the homolytic cleavage of the phenyl-iodine bond from the excited state, and the iodide ion was formed from the preceding photoreaction (Table 4). The identification of diiodide anion radical and its kinetics were reported by Grossweiner and Matheson;[17] $\lambda_{max}$ of the diiodide anion radical is 370 nm in aqueous solution.

In acetonitrile only, transient absorption spectra from the photolysis of **1b** were obtained and are shown in Figure 6. At 10 $\mu$s delay after laser flash the weak diffused absorption band in the region between 340 and 420 nm was seen, whereas a luminescence disturbed the region between 280 and 320 nm. It seems likely that the diffused band consists of two bands peaking at 360 and 393 nm. At 1 ms delay a certain band in the region between 280 and 320 nm (the same band in the basic medium) was observed.

A temporal profile of the band at 360 nm decayed in the first order with a lifetime of 33 $\mu$s. Although the lifetime (33 $\mu$s) in acetonitrile is longer than that of dibromide anion radical in water (10 $\mu$s),[1] the band is assigned to dibromide anion radical because its formation increased in the presence of tetraethylammonium bromide and its lifetime remained (33 $\mu$s, right inset of Figure 6, Table 4).

The behavior of the 393-nm band from this neutral solvent is the same as that observed in acetonitrile containing NaOH. The lifetime is somewhat shorter (21 $\mu$s) than that in the base.

The lifetime of the band from 280 to 320 nm was 4 ms. Oscilloscope traces show (left inset of Figure 6) a matching decay of the band (300 nm) and a band formation of *N*-*tert*-butyl-α-phenylnitrone adduct (300 nm), indicating the band at 300 nm to be radical species. The property of the band of the 300-nm transient is similar to the phenyl $\sigma$ radical from the photolysis of *N*-(*o*-halophenyl)-pyridinium salt.[1] On the basis of the above observations of its radical property and of the presence of dibromide anion radical in the medium, the band between 280 and 320 is assigned to phenyl $\sigma$ radical formed from homolytic cleavage of the phenyl-bromine bond in the triplet state, probably a locally excited state of the amide. This phenyl

(16) Strong, R. L.; Rand, S. J.; Britt, J. A. *J. Am. Chem. Soc.* **1960**, *82*, 5053.

(17) Grossweiner, L. I.; Matheson, M. S. *J. Phys. Chem.* **1957**, *61*, 1089.

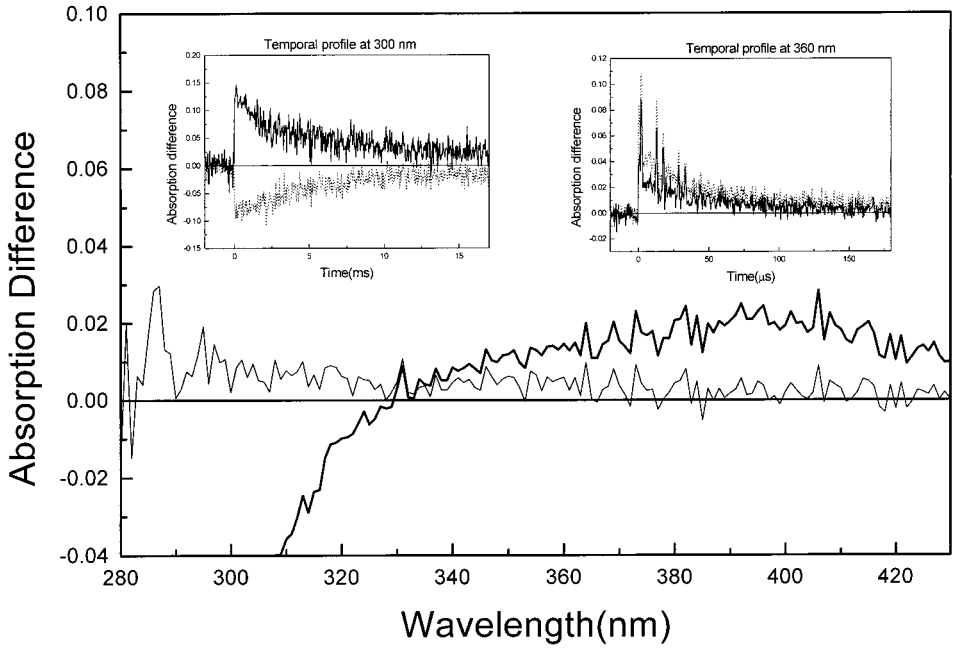
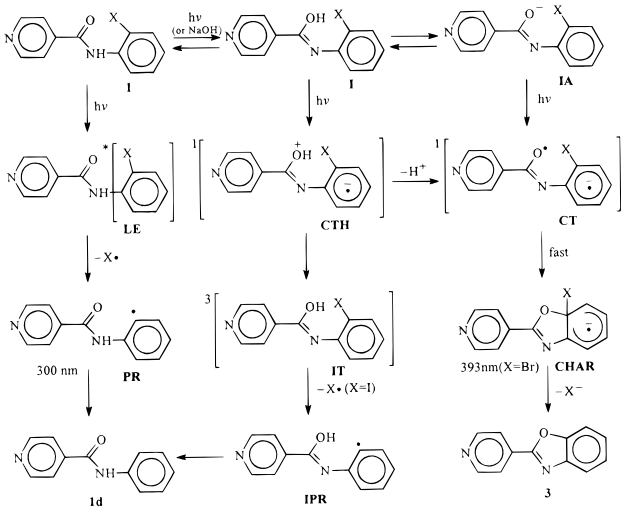



**Figure 6.** Transient absorption spectra obtained upon 266 nm excitation of **1b** in acetonitrile ($1.4 \times 10^{-4}$ M) 10 $\mu$s (—) and 1 ms (—) after laser pulse. Left inset: solid line, decay curve of 300 nm transient; dotted line, the formation of an adduct of *N*-*tert*-butyl-α-phenylnitrone. Right inset: solid line, decay curve of 360 nm-transient; dotted line, the same decay curve in the presence of tetraethylammonium bromide.

**Scheme 3**




$\sigma$ radical from **1b** is a reaction intermediate for the photoreduction, whereas a cyclohexadienyl anion radical is a reaction intermediate for the photosubstitution.

**Mechanism.** Steady state and laser flash studies indicate that the intramolecular $S_N$(ET)Ar* mechanism is involved in the photosubstitution, whereas a free phenyl $\sigma$ radical is involved in the photoreduction (Scheme 3). The keto form of the amide **1** is in equilibrium with the imidol **I** and the imidolate anion (**IA**) by its (their) absorption of light and/or the action of the base NaOH. In the presence of NaOH the imidolate anion and/or the imidol is excited by absorption of light to populate the intramolecular charge-transfer excited state (CT and/or CTH), which produces a cyclohexadienyl anion radical (CHAR) by the intramolecular addition of the oxygen radical of the imidol to the very close anionic halophenyl moiety in the charge-transfer excited state (with deprotonation step in case of CTH) and, in turn, yields the 2-(pyridinyl)benzoxazole (**3**) by ejection of the halide anion (right path in the Scheme 3). This mechanism also explains why no intermolecular hydroxide anion-substitution product is observed in the haloarene and why radical savengers cannot quench the anion radical. A similar intramolecular electron-transfer mechanism has been proposed for the benzothiazole formation in the photoreaction of *o*-halothioacetanilide.[3b]

In neutral conditions the intramolecular charge-transfer excited state of imidol (CTH) is involved in the substitution. Deprotonation of CTH produces charge-transfer excited state (CT), which in turn eventually yields the 2-pyridinylbenzoxazole (middle path in Scheme 3). Either the locally excited state or the triplet imidol is involved in the reduction reaction via a homolytic cleavage of the phenyl-halogen bond of the haloarene to produce a halogen radical (eventually dihalide anion radical) and a phenyl $\sigma$ radical, and the subsequent hydrogen atom abstraction of the phenyl radical from the environment affords the reduced product (left path in Scheme 3).

If the intramolecular $S_N$(ET)Ar* mechanism is involved in the substitution, deuterium-exchanged product can be seen in 2-pyridinylbenzoxazole when the reaction is performed in deuterium oxide. A small amount (deuterium content 5%) of deuterated 2-(4-pyridinyl)benzoxazole was indeed observed in the GC−MS spectra. If the proposed mechanisms are operated in the photoreaction of the *o*-halophenylpyridinecarboxamide in the basic medium, a triplet photosensitizer such as benzophenone will accelerate the reduction reaction but not the substitution. Indeed, the experiment showed that photoreduction of **1b** occurred in the presence of benzophenone, but photosubstitution of **1b** did not occur upon only excitation of benzophenone by a monochromatic light (360 nm). These results confirmed the proposed $S_N$(ET)Ar* mechanism and free radical mechanism for the photosubstitution and photoreduction reactions, respectively.

## Experimental Section

**Materials.** All reagents (nicotinic acid, isonicotinic acid, 2-chloroaniline, 2-bromoaniline, 2-iodoaniline, methyl iodide, deuterium oxide, methyl methacrylate, benzophenone, acetophenone, and isoprene) and solvents used were obtained from Aldrich.

Melting points were measured on a capillary melting point apparatus, Thomas Hoover, or digital scanning calorimeter (DSC). UV−vis absorption spectra were recorded on a Varian Cary 3E spectrophotometer or a Hewlett-Packard 8452A diode array spectrophotometer. Infrared spectra were recorded on a Nicolet Magna 550 FT−IR (Mattson Galax series 7020) spectrophotometer or a Hewlett-Packard IRD equipped 5890 series II gas chromatograph. A gas chromatograph with NPD (6890 series Hewlett-Packard) was used. NMR spectra were recorded on a Brucker Ac 200 (200 MHz) operating at 200 MHz for proton studies. The $^1$H NMR spectra were referenced with respect to TMS. The mass spectra were obtained from a Hewlett-Packard 5989A mass spectrometer with a Hewlett-Packard 5890 series II gas chromatograph. Elemental analysis was performed on an elemental analyzer, Carlo Erba CHNS-O E.A. 1180.

**General Procedure for the Preparation of *N*-(2-Halophenyl)pyridinecarboxamide (1 and 2).** The mixture of isonicotinic acid (2.46 g, 0.02 mole) and thionyl chloride (20 mL) was refluxed for 2 h. After the excess thionyl chloride was stripped off, pyridine (20 mL) was added to the mixture. After 2-chloroaniline (3.18 g, 0.025 mole) was added to the above mixture in an ice−water bath, the reaction mixture was stirred in the ice−water bath for 30 min and then at room temperature for 1 night. When water (200 mL) was added to the reaction mixture at 0 °C, a white solid appeared. The solid was dried at 50−55 °C and recrystallized from diethyl ether/*n*-hexane.

***N*-(2-Chlorophenyl)-4-pyridinecarboxamide (1a):** yield 1.47 g (63%); mp 134 °C; UV ($\lambda_{max}$ in acetonitrile) 266 nm ($\epsilon = 8.9 \times 10^3$ L/mol cm); IR (gas phase) 3438, 3079, 1715 cm$^{-1}$;$^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 8.80 (dd, $J$ = 4.4, 1.6 Hz, 2H), 8.55 (br s, 1H), 8.45 (dd, $J$ = 8.2, 1.5 Hz, 1H), 7.74 (dd, $J$ = 4.4, 1.6 Hz, 2H), 7.42 (dd, $J$ = 7.9, 1.5 Hz, 1H), 7.33 (dt, $J$ = 7.9, 1.5 Hz, 1H), 7.12 (dd, $J$ = 7.8, 1.5 Hz, 1H); MS (EI) *m*/*z* (rel intensity) 234 (3, $M^+ + 2$), 232 (9, $M^+$), 197 (84, $M^+ - Cl$), 106 (100). Anal. Calcd for $C_{12}H_9ON_2Cl$: C, 61.95; H, 3.90; N, 12.04. Found: C, 61.68; H, 3.65; N, 12.15.

***N*-(2-Bromophenyl)-4-pyridinecarboxamide (1b):** yield 2.20 g (79%); mp 132 °C; UV ($\lambda_{max}$ in acetonitrile), 266 nm ($\epsilon = 8.6 \times 10^3$ L/mol cm); IR (gas phase) 3425, 3079, 1715 cm$^{-1}$;$^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 8.81 (dd, $J$ = 4.4, 1.7 Hz, 2H), 8.56 (br s, 1H), 8.44 (dd, $J$ = 8.2, 1.5 Hz, 1H), 7.75 (dd, $J$ = 4.4, 1.7 Hz, 2H), 7.58 (dd, $J$ = 8.0, 1.5 Hz, 1H), 7.37 (dt, $J$ = 7.8, 1.5 Hz, 1H), 7.05 (dt, $J$ = 7.8, 1.5 Hz, 1H); MS (EI) *m*/*z* (rel intensity) 278 (5, $M^+ + 2$), 276 (5, $M^+$), 197 (100, $M^+ - Br$). Anal. Calcd for $C_{12}H_9ON_2Br$: C, 52.01; H, 3.27; N, 10.11. Found: C, 52.07; H, 2.92; N, 10.36.

***N*-(2-Iodophenyl)-4-pyridinecarboxamide (1c):** yield 4.99 g (77%); mp 122−123 °C; UV ($\lambda_{max}$ in acetonitrile), 267 nm ($\epsilon = 9.5 \times 10^3$ L/mol cm); IR (KBr) 3252, 3028, 1653 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 8.84 (d, $J$ = 6.0 Hz, 2H), 8.41 (dd, $J$ = 8.2, 1.5 Hz, 1H), 8.30 (br s, 1H), 7.82 (dd, $J$ = 8.1, 1.5 Hz, 1H), 7.78 (dd, $J$ = 4.4, 1.5 Hz, 2H), 7.41 (dt, $J$ = 8.1, 1.5 Hz, 1H), 6.92 (dt, $J$ = 7.5, 1.5 Hz, 1H); MS (EI) *m*/*z* (rel intensity) 324 (4, $M^+$), 197 (68, $M^+ - I$). Anal. Calcd for $C_{12}H_9ON_2I$: C, 44.47; H, 2.80; N, 8.64. Found: C, 44.39; H, 2.83; N, 8.59.

***N*-Phenyl-4-pyridinecarboxamide (1d):** yield 3.16 g (80%); mp 165 °C; UV ($\lambda_{max}$ in acetonitrile), 270 nm ($\epsilon = 1.0 \times 10^4$ L/mol cm); IR (KBr) 3340, 3043, 1655 cm$^{-1}$; $^1$H NMR (200 MHz, $CD_3OD$) $\delta$ 8.71 (dd, $J$ = 4.5, 1.7 Hz, 2H), 7.87 (dd, $J$ = 4.5, 1.7 Hz, 2H), 7.69 (dt, $J$ = 7.2, 1.4 Hz, 2H), 7.41−7.31 (m, 2H), 7.16 (tt, $J$ = 7.4, 1.4 Hz, 1H); MS (EI) *m*/*z* (rel intensity) 198 (54, $M^+$), 106 (100). Anal. Calcd for $C_{12}H_{10}ON_2$: C, 72.71; H, 5.08; N, 14.13. Found: C, 72.77; H, 4.82; N, 14.16.

***N*-(2-Bromophenyl)-*N*-methyl-4-pyridinecarboxamide (1e).** *N*-Methylation of *N*-(2-bromophenyl)-4-pyridinecarboxamide was performed by using the Johnstone method.[18] *N*-(2-Bromophenyl)-4-pyridinecarboxamide (1.39 g, 5 mmol) was dissolved in acetone (30 mL). To the above solution at 50 °C were added potassium hydroxide (1.12 g) and methyl iodide (1.13 g, 8 mmol). The reaction mixture was refluxed for 5 min, and then the excess methyl iodide and acetone were stripped off. The reaction mixture was analyzed on silica gel column (70−230 mesh) with acetone/*n*-hexane (2/5) as eluent. The solid ($R_f$ = 0.25) was recrystallized from *n*-hexane/diethyl ether: yield 1.10 g (73%); mp 101 °C; UV ($\lambda_{max}$ in acetonitrile), 250 nm (sh) ($\epsilon = 7.0 \times 10^3$ L/mol cm); IR (gas phase) 3075, 2943, 1690 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 8.40 (d, $J$ = 5.6 Hz, 2H), 7.50 (d, $J$ = 7.9 Hz, 1H), 7.17−7.02 (m, 5H), 3.35 (s, 3H); MS (EI) *m*/*z* (rel intensity) 292 (0.2, $M^+ + 2$), 290 (0.2, $M^+$), 211 (100). Anal. Calcd for $C_{13}H_{11}ON_2Br$: C, 53.65; H, 3.81; N, 9.62. Found: C, 53.47; H, 3.88; N, 9.62.

***N*-(2-Chlorophenyl)-3-pyridinecarboxamide (2a):** yield 1.36 g (66%); mp 82 °C; UV ($\lambda_{max}$ in acetonitrile), 264 nm ($\epsilon = 1.0 \times 10^4$ L/mol cm); IR (gas phase) 3440, 3084, 1712 cm$^{-1}$; IR (KBr) 1653 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 9.16 (d, $J$ = 2.1 Hz, 1H), 8.80 (dd, $J$ = 4.8, 1.5 Hz, 1H), 8.51−8.46 (m, 2H), 8.24 (dt, $J$ = 8.0, 2.0 Hz, 1H), 7.50−7.28 (m, 3H), 7.12 (dt, $J$ = 7.8, 1.5 Hz, 1H); MS (EI) *m*/*z* (rel intensity) 234 (4, $M^+ + 2$), 232 (11, $M^+$), 197 (74), 106 (100). Anal. Calcd for $C_{12}H_9ON_2Cl$: C, 61.95; H, 3.90; N, 12.04. Found: C, 61.63; H, 3.60; N, 12.22.

***N*-(2-Bromophenyl)-3-pyridinecarboxamide (2b):** yield 2.15 g (78%); mp 90.5 °C; UV ($\lambda_{max}$ in acetonitrile), 264 nm ($\epsilon = 9.6 \times 10^3$ L/mol cm); IR (gas phase) 3427, 3083, 1712 cm$^{-1}$; IR (KBr) 1663 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 9.17 (d, $J$ = 1.9 Hz, 1H), 8.78 (dd, $J$ = 4.8, 1.6 Hz, 1H), 8.53 (br s, 1H), 8.43 (dd, $J$ = 8.2, 1.6 Hz, 1H), 8.23 (dt, $J$ = 2.0, 8.0 Hz, 1H), 7.57 (dd, $J$ = 7.9, 1.5 Hz, 1H), 7.48−7.31 (m, 2H), 7.03 (dt, $J$ = 7.8, 1.5 Hz, 1H); MS (EI) *m*/*z* (rel intensity) 278 (7, $M^+ + 2$), 276 (7, $M^+$), 197 (93), 106 (100). Anal. Calcd for $C_{12}H_9ON_2Br$: C, 52.01; H, 3.27; N, 10.11; Found: C, 51.96; H, 2.93; N, 10.23.

**Preparative Photoreaction. Photoreaction of *N*-2-(Chlorophenyl)-4-pyridinecarboxamide (1a). General Procedure.** To a large (300 mL) quartz immersion well photolysis unit with provision for circulation of nitrogen were added 210 mL of acetonitrile, 30 mL of 2 N aqueous NaOH, and 1 mmol of *N*-2-(chlorophenyl)-4-pyridinecarboxamide (**1a**). With nitrogen circulation, the solution was irradiated with a 150 W mercury lamp (high pressure) at 100 V at 4 °C for 30 h. From time to time solids (products) precipitated on the sleeve of the photocell were removed for better passage of light. The resulting two-phase mixture was separated, and the water layer was extracted with ethyl acetate. The acetonitrile and ethyl acetate portion were together evaporated and analyzed by column chromatography (2.523 cm, silica gel 70−230/230−400 mesh = 3/1, THF/cyclohexane = 1/9). The eluents, THF/*n*-hexane = 15/135, 40/160, and 75/175 (v/v), were used in the order given. The column fractions corresponding to $R_f$ 0.26 and 0.49 on TLC were collected and identified as the starting material (38%) and 2-(4-pyridinyl)benzoxazole (**3**, 25%), respectively. This compound (mp 130−131; lit. value[9] 130−131 °C) was identified by its spectral properties (NMR, IR, MS) as well as elemental analysis.

**2-(4-Pyridinyl)benzoxazole (3)**: UV ($\lambda_{max}$ in acetonitrile), 299.6 nm, 312 (sh); IR (gas phase) 3049, 1669 cm$^{-1}$; IR (KBr) 3045, 1613 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 8.81 (dd, $J$ = 4.5, 1.6 Hz, 2H), 8.07 (dd, $J$ = 4.5, 1.6 Hz, 2H), 7.84−7.80 (m, 1H), 7.64−7.60 (m, 1H), 7.46−7.36 (m, 2H); MS (EI) *m*/*z* (rel intensity) 196 (100, $M^+$). Anal. Calcd for $C_{12}H_8ON$: C, 73.46; H, 4.11; N, 14.28. Found: C, 73.51; H, 4.08; N, 14.33.

**Photoreaction of *N*-(2-Bromophenyl)-4-pyridinecarboxamide (1b).** The photoreaction of **1b** was carried out for 8 h as in the case of **1a**. The reaction mixture was separated on silica gel column with THF/*n*-hexane = 1/7. The product was the same as the product from **1a**.

**Photoreaction of *N*-(2-Chlorophenyl)-3-pyridinecarboxamide (2a).** The photoreaction of **2a** was carried out for

(18) Johnstone, R. A. W.; Payling, D. W.; Thomas, C. *J. Chem. Soc. (C).* **1969**, 2223.

21 h as in the case of **1a**. The product separated by using column chromatograph was 2-(3-pyridinyl)benzoxazole (**4**): yield 37%; mp 110 (lit.[19] 108 °C); UV ($\lambda_{max}$ in acetonitrile), 299.4 nm, 311 (sh); IR (gas phase) 3087, 1619 $cm^{-1}$; IR (KBr) 3058, 1613 $cm^{-1}$;$^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 9.47 (dd, $J$ = 2.1, 0.6 Hz, 1H), 8.75 (dd, $J$ = 4.8, 1.7 Hz, 1H), 8.49 (dt, $J$ = 8.0, 2.0 Hz, 1H), 7.83−7.74 (m, 1H), 7.65−7.55 (m, 1H), 7.49−7.33 (m, 3H); MS (EI) *m*/*z* (rel intensity) 196 (100, $M^+$). Anal. Calcd for $C_{12}H_8ON$: C, 73.46; H, 4.11; N, 14.28; Found. C, 73.38; H, 4.07; N, 14.40.

**Photoreaction of *N*-(2-Bromophenyl)-3-pyridinecarboxamide (2b).** The photoreaction was performed for 3.5 h as in the case of **1a**. The same product as that from **2a**, 2-(3-pyridinyl)benzoxazole, was obtained in 43% yield.

**Photoreaction of *N*-(2-Bromophenyl)-4-pyridinecarboxamide (1b) in Dilute NaOH.** The procedure is the same as for **1a**. The separation of the reaction mixture gave 2-pyridinylbenzoxazole (**3**, 29%) and *N*-phenyl-4-pyridinecarboxamide (**1d**, 8%). The idendification of **1d** has been done by comparison with the authentic sample.

**Photoreaction of *N*-(2-Bromophenyl)-3-pyridinecarboxamide (2b) in Weak Base.** The acetonitrile solution of **2b** (**2b,** 278 mg; acetonitrile, 220 mL) containing 20 mL of aqueous $Na_2CO_3$ (55 mg) solution was irradiated for 6.5 h as in the case of **1a**. The resulting mixture was analyzed on the silica column with *n*-pentane/ethyl acetate [150/30, 80/20, 90/30, 250/100, 140/160, 50/50, 0/200 (v/v) in the order given] as eluents to yield 2-(3-pyridinyl)benzoxazole (**4**, 20%), *N*-phenyl-3-pyridinecarboxamide (**5**, 27%), and starting material (11%).

**2-(3-Pyridinyl)benzoxazole (4)**: yield 54 mg (20%); mp 110 °C (lit.[19] 108 °C).

***N*-Phenyl-3-pyridinecarboxamide (5)**: yield 54 mg (27%); mp 118.5−119 (lit. 119−120 °C[20] and 116.8−117.2 °C[21]); IR (gas phase) 3462, 3071, 1712 $cm^{-1}$; IR (KBr) 3351, 3055, 1653 $cm^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 9.03 (d, $J$ = 2.1 Hz, 1H), 8.96 (br s. 1H), 8.65 (dd, $J$ = 4.8, 1.4 Hz, 1H), 8.14 (dt, $J$ = 1.9, 7.9 Hz, 1H), 7.61 (d, $J$ = 7.7, 2H), 7.35−7.27 (m, 3H), 7.14 (dt, $J$ = 0.8, 7.3 Hz, 1H); MS (EI) *m*/*z* (rel intensity) 198 (44, $M^+$), 197 (11, $M^+ - H$), 106 (100). Anal. Calcd for $C_{12}H_{10}ON_2$: C, 72.71; H, 5.08; N, 14.13. Found: C, 72.86; H, 5.15; N, 14.32.

**Photoreaction of *N*-(2-Bromophenyl)-*N*-methyl-4-pyridinecarboxamide (1e).** An acetonitrile solution of **1e** (278 mg) was irradiated for 10 h as in the case of **1a**. A separation of the resulting reaction mixture on column chromatograph with THF/*n*-hexane (70/280, 60/140) gave two products, 6-(methyl)benzo[*c*][2,6]naphthyridin-5-(6*H*)-one (50 mg, 25%) and *N*-methyl-*N*-phenyl-4-pyridinecarboxamide (5%).

**6-(Methyl)benzo[*c*][2,6]naphthyridin-5-(*6H*)-one**: mp 89.5 °C; IR (gas phase) 3074, 2954, 1683 $cm^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 9.64 (s, 1H), 8.79 (d, $J$ = 5.2 Hz, 1H), 8.35 (dd, $J$ = 8.0, 1.1 Hz, 1H), 8.25 (d, $J$ = 5.2 Hz, 1H), 7.60 (dt, $J$ = 1.3, 7.9, 1H), 7.45−7.33 (m, 2H), 3.79 (s, 3H); MS (EI) *m*/*z* (rel intensity) 211 (16, $M^+$+H), 210 (100, $M^+$). Anal. Calcd for $C_{13}H_{10}ON_2$: C, 74.28; H, 4.79; N, 13.32. Found: C, 73.95; H, 4.81; N, 13.15.

**Measurement of Quantum Yield.** The procedure of light intensity measurement was described in the preceding paper.[2] An acetonitrile solution of *N*-(2-halophenyl)-4-pyridinecarboxamide (**1**) ($1.0 \times 10^{-3}$ M, 2.5 mL) containing 0.1 M NaOH (50/1, v/v) was deaerated with nitrogen or oxygen for 30 min and irradiated for 30 min with monochromatic light (266 ± 3 nm, Xe lamp, 450 W). The reaction mixture was analyzed by GC. There were two peaks whose retention times were 7.3 and 11.8 min (in the case of **1b**). The peak with retention time 7.3 was the 2-(4-pyridinyl)benzoxazole, and the peak with retention time 11.8 was the starting material. The quantitative measurement was determined by standard curve of authentic sample.

**Relative Rate. General Procedure.** *N*-(2-Bromophenyl)-4-pyridinecarboxamide (**1b**, 17 mg) was dissolved in acetonitrile/2 M NaOH (15 mL; 13/12, v/v), purged with nitrogen (or oxygen), and irradiated with a Hg lamp (150 W, high pressure) for 1.5 h. The reaction mixtures were analyzed by GC (FID). The relative area of the peak (retention time, 7.3 min) on several conditions such as the presence of inhibitors were compared and are shown in Table 3.

**UV Absorption.** An acetonitrile solution of **1b** ($1.2 \times 10^{-4}$ M, 2 mL) was placed in a UV cuvette, and the absorption spectrum was taken by the UV spectrometer (dotted line in Figure 1). The $\lambda_{max}$ of the absorption was 266 nm. Then, an acetonitrile solution of **1b** ($1.2 \times 10^{-4}$ M, 2 mL) containing NaOH ($1.2 \times 10^{-4}$ M, 2 mL) was placed in the UV cuvette, and the absorption spectrum was taken (thin solid line). The spectrum was diffused into longer wavelength. When the prototype absorption (dotted line) was subtracted from the diffused absorption spectra, two bands peaking at 245 and 325 nm appeared. This behavior was not seen for **1b** in methanol containing NaOH. Furthermore, this behavior was not observed for **1e**, which has a methyl group on the nitrogen of the amide bond in acetonitrile containing NaOH.

**Laser Flash Photolysis.** A detailed description of the experimental setup can be found elsewhere.[1] The fourth harmonic (266 nm) output from a Q-switched Nd:YAG laser (Spectron SL852G-30) was used as an excitation source. The time duration of the excitation pulse was ca. 6 ns, and the pulse energy was typically 30 or 80 mJ. A cw Xe lamp (Oriel model 6259, 300 W) was used as a probe light source for transient absorption measurement. The spectral resolution was obtained by using a SP-275l monochromator (JAMS 27 model 82-49702) after the probe light passed through the sample solution. A boxcar signal averager (Standard Research system SR 250) was used in recording the transient signals. The temporal profile of the transient absorption signal was monitored by a 500 MHz digital storage oscilloscope (DSO, Tektronix TDS620B). Sample solutions were prepared by dissolving the reactants in acetonitrile with or without tetramethylammonium chloride, and the concentration of the solution was adjusted to be 0.5-1.5 in the absorbance at 266 nm. The experiment of the temporal profile with DSO was performed in the same concentration of **1b** in acetonitrile. The sample solution was circulated from a bottle (3 L in volume) to the fluorometer quartz cuvette of 10 mm in pathlength (flow type, Helma QS 1.0) to reduce the effect of the accumulation of the product and dissociation of the reactant in the photolysis cell.

**Fluorescence Measurement. General Procedure.** The fluorescence spectrum was obtained from the laser flash photolysis of an acetonitrile solution of the pyridinecarboxamide **2b**; the flow-type UV cuvette, which is connected to the 1 L reservoir of the acetonitrile solution of **2b**, was illuminated by 266 nm laser light (30 or 80 mJ), and the fluorescence produced from the UV cuvette after 200 ns delay after the laser flash was detected with a photomultiplier tube and quantified with the appropriate electronic devices (thick solid line in Figure 2). To study the effect of base on the excited states of the pyridinecarboxamides, the fluorescences of **1** and **2** were also measured in the presence of NaOH (thin solid line) or in different concentrations of NaOH (Figures 2 and 3).

**Laser Intensity Dependence.** From the argon-saturated acetonitrile solution of **1b** (40 mg in 1 L of acetonitrile) containing 10 mL of 0.5 N NaOH, the absorption intensity at 393 nm, where a transient appeared, was monitored with the boxcar averager at 10 $\mu$s delay after laser flash (266 nm). The absorption intensity of the 393-nm transient versus laser power were plotted and are shown in Figure 5.

**Transient Absorption.** The concentration (absorbance 1) of the pyridinecarboxamide **1b** (**1d** or **1e)** was prepared by dissolving the amide **1b**, **1d**, or **1e** (about 40 mg) in acetonitrile (1 L) containing 1 mL of 4 M NaOH. The solution was circulated through a flow-type UV cuvette, which was connected to a 2 L reservoir, and deaerated with argon. Transient absorption spectra and their temporal profiles were obtained at 10 $\mu$s and 1 ms delay after the laser flash (80 mJ) of the

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solution (Figures 4 and 6), with the appropriate electronic devices such as the boxcar averager and a 500 MHz digital storage oscilloscope.[2]

**Deuteriation and Photosensitization.** *N*-(2-Bromophenyl)pyridinecarboxamide (**1b**) was dissolved in $CD_3CN$ (2 mL, $1.8 \times 10^{-3}$ M) containing 0.1 mL of $D_2O$ and irradiated with a Xe lamp (450 W, 10 cm path of MeOH solution filter) for 40 min. The reaction mixture was analyzed by GC−MS. Deuteriation content in the product was calculated by examining the increment in mass of the molecular ion.[22] Deuterium was incorporated in 5% yield in 2-pyridinylbenzoxazole (spectra not shown).

An acetonitrile solution (10 mL) of **1b** ($1.2 \times 10^{-4}$ M) and benzophenone ($1.7 \times 10^{-3}$ M) containing 0.1 mL of 1.0 M NaOH was placed in a quartz cell (volume 10 mL), deaerated with nitrogen, and irradiated with a monochromatic light (360 ± 3 nm) from a Xe lamp (450 W) for 15 min. The substituted and reduced product formation was analyzed by GC (FID) as described in relative rate studies. The reduced product was produced, but the substituted product not formed (spectra not shown).

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**Acknowledgment.** This research was supported by the Basic Science Research Program, Ministry of Education, 1999 (Project 1998-015-D00174, Y.-T.P.) and the Research Project of Korea Research Institute of Standards and Science, 1999 (Project 8).

**Supporting Information Available:** Copies of UV absorption spectra of **1b** in methanol and **1e** in acetonitrile, transient absorption spectra from the laser flash photolysis of **1a**, **1c**, **1d**, and **1e** in acetonirile containing NaOH, and temporal profile of a 370-nm transient from **1c** in the presence of oxygen. This material is available free of charge via the Internet at http://pubs.acs.org.

JO9909498