  Bull. Chem. Soc. Jpn., 61, 2837—2846 (1988)

Photochemical Alkylation, Hydroxyalkylation, and Alkoxylation of Pyridinecarboxamides in Alcohol

Akira SUGIMORI,* Hiroshi ITOH, (the late) Mitsuharu KANAI,
Nobuko ITOH, and Toru SUGIYAMA
Department of Chemistry, Faculty of Science and Technology, Sophia University,
Kioi-cho 7-1, Chiyoda-ku, Tokyo 102
(Received August 7, 1987)

The UV-irradiation of 2- and 4-pyridinecarboxamides in alcohol brings about alkylation and/or hydroxyalkylation in the pyridine ring. In the irradiation of 3-pyridinecarboxamide in the presence of sulfuric acid, ionic reaction (alkoxylation at the 2- and 6-position) and radical reaction (alkylation at the 4- and 6-position) occur in parallel. The effects of quenchers indicate that two alkylation products originate from one excited triplet state which is quenched by energy-transfer mechanism and that two alkoxylation products originate from the excited singlet state.

In the preceding papers,[1-8] we have reported the remarkable photoreactivities of pyridinecarboxylic esters: parallel occurrence of ionic and radical reactions and simultaneous participation of several excited states of the same multiplicity. The most characteristic example is the photoreaction of methyl 3-pyridinecarboxylate in methanol in the presence of sulfuric acid.[2,3] It has been concluded that an excited singlet state, the n-π* triplet state, and the π-π* triplet state coexist and that the excited singlet state gives the products methoxylated at the 2- and 6-positions, while the π-π* and the n-π* triplet states give the methylation products at the 4- and 6-positions. The parallel occurrence of ionic and radical reactions has been observed in the photoreactions of 2-pyridinecarbonitrile in alcohol.[9]

In the present paper, we report the photoreactions of pyridinecarboxamides in alcohol, in order to compare their photochemical behavior with that of the esters.[10]

Results and Discussion

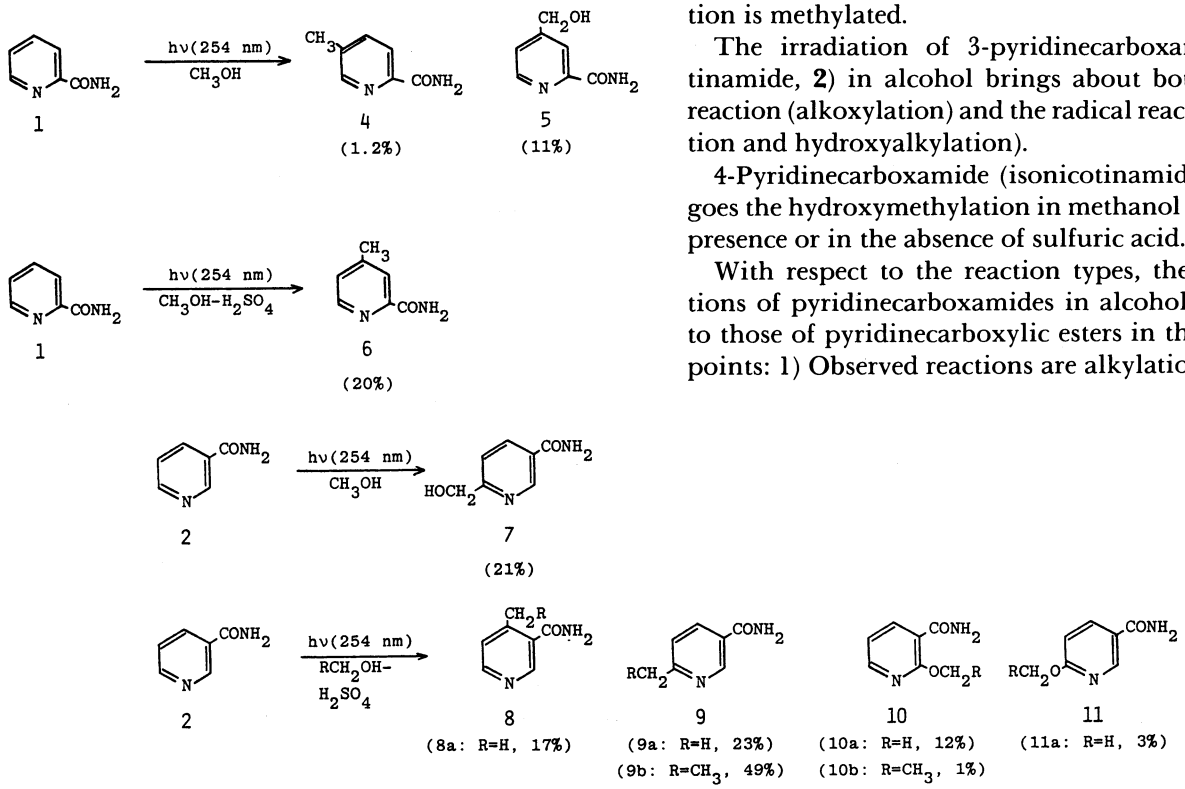
Types of Photoreactions of Pyridinecarboxamides. In the UV-irradiation of 2-pyridinecarboxamide (picolinamide, **1**) in methanol in the absence of added acid, methylation and hydroxymethylation occur in parallel. Irradiation in the presence of sulfuric acid gives a methylation product.

The position of the methylation depends on the presence and the absence of sulfuric acid. In the absence of the acid, the 5-position is methylated, whereas in the presence of sulfuric acid the 4-position is methylated.

The irradiation of 3-pyridinecarboxamide (nicotinamide, **2**) in alcohol brings about both the ionic reaction (alkoxylation) and the radical reaction (alkylation and hydroxyalkylation).

4-Pyridinecarboxamide (isonicotinamide, **3**) undergoes the hydroxymethylation in methanol either in the presence or in the absence of sulfuric acid.

With respect to the reaction types, the photoreactions of pyridinecarboxamides in alcohol are similar to those of pyridinecarboxylic esters in the following points: 1) Observed reactions are alkylation, hydroxy-

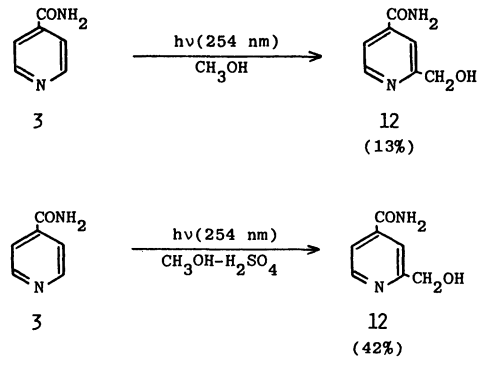


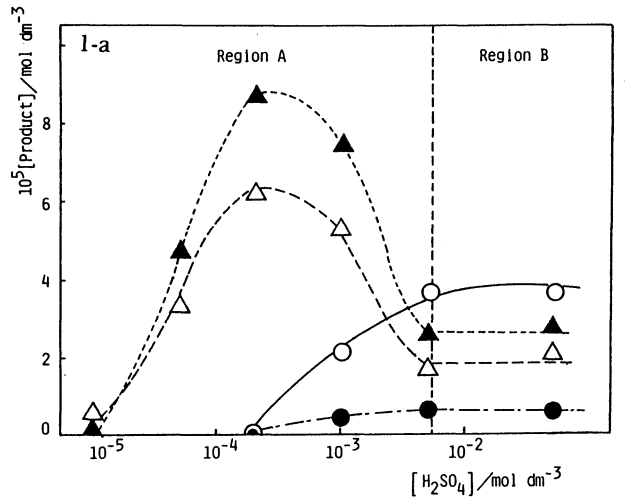
1 → 4 (1.2%), 5 (11%)

1 → 6 (20%)

2 → 7 (21%)

2 → 8 (8a: R=H, 17%), 9 (9a: R=H, 23%; 9b: R=CH3, 49%), 10 (10a: R=H, 12%; 10b: R=CH3, 1%), 11 (11a: R=H, 3%)





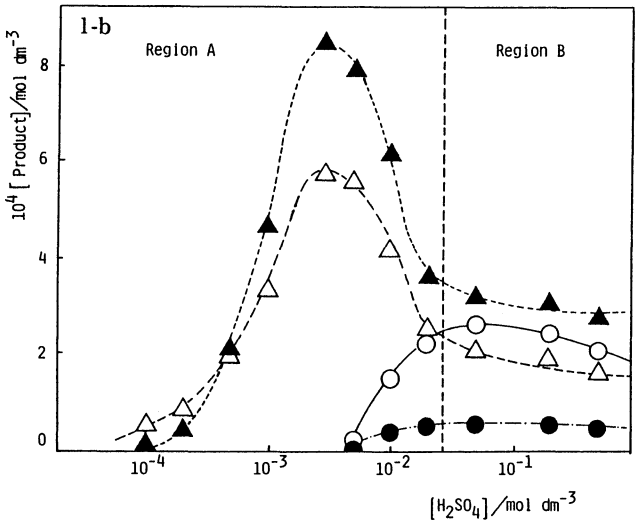


Fig. 1. Dependence of photoreactions of 3-pyridinecarboxamide (**2**) in methanol on the concentration of H_2SO_4. 1-a: [**2**]=1.0×10^{-2} mol dm^{-3}; 30 °C; irradiation time, 3 h. 1-b: [**2**]=1.0×10^{-3} mol dm^{-3}; 30 °C; irradiation time, 20 min. --△--, **8a**; ----▲----, **9a**; —○—, **10a**; -·-●-·-, **11a**.

alkylation, and alkoxylation. In particular, the photoreactions of 3-pyridinecarboxamide (**2**) are very similar to those of the corresponding ester[2,3] (in the reaction type as well as in the positions of the reaction). 2) The change of alcohol from methanol to

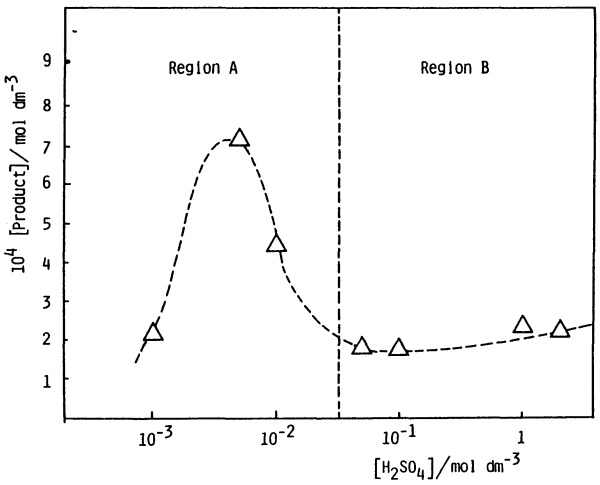


Fig. 2. Dependence of the photomethylation of 2-pyridinecarboxamide (**1**) at the 4-position on the concentration of H_2SO_4. [**1**]=1.0×10^{-2} mol dm^{-3}; irradiation time, 4 h.

ethanol causes the change in the product distribution in the photoreaction of 3-pyridinecarboxamide. In ethanol alkoxylation decreases, while alkylation increases. In ethanol alkoxylation occurs selectively at the 4-position. 3) Similar to methyl 2-pyridinecarboxylate,[4] 2-pyridinecarboxamide (**1**) undergoes the methylation at the 5-position in the absence of sulfuric acid but at the 4-position in its presence. Although the similarities should be stressed as a whole, the details of the photoreactivities of the amides are different from those of the esters: UV-irradiation of 2- and 4-pyridinecarboxamides gives only the products from radical reactions (alkylation or hydroxyalkylation), whereas the corresponding esters give alkoxylation products in addition to the alkylation and hydroxyalkylation products.[4,5]

Photoreactivity and Form of Substrate in Solution. The photoreactions of pyridinecarboxamides are controlled by an added acid. The photoreactions of 2- and 3-pyridinecarboxamide in the presence of sulfuric acid are different from those in its absence. The remarkable dependences of the photoreactions on the concentrations of added sulfuric acid are observed in cases of 2- and 3-pyridinecarboxamides (Figs. 1 and 2).

In UV-irradiation of 3-pyridinecarboxamide in methanol (Figs. 1-a and 1-b), the methylation occurs effectively at lower concentrations of sulfuric acid (Region A), while the methylation and methoxylation occur in parallel at higher concentrations of sulfuric acid (Region B). This type of acidity dependence is similar to that of methyl 3-pyridinecarboxylate.[3]

In Fig. 3 are shown the correlations between the molar absorption coefficient of **2** and the concentration of added sulfuric acid. The change in the molar absorption coefficient shows the change in the form of **2**. Figures 1 and 3 indicate that **2** exists in the pyridinium form in Region B and that the pyridinium form

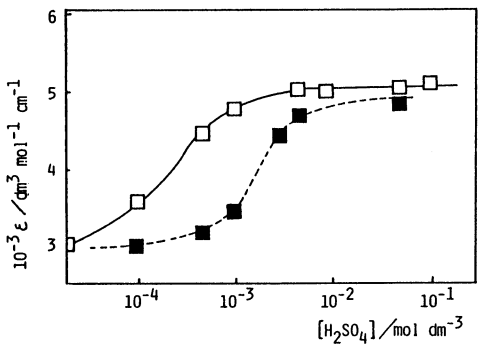


Fig. 3. Relation between molar absorption coefficient of 3-pyridinecarboxamide (**2**) at 262 nm and concentration of added sulfuric acid. —□—: [**2**]=1.0×10^{-3} mol dm^{-3}; ----■----: [**2**]=3.0×10^{-3} mol dm^{-3}.

and the free base form of **2** coexist in Region A. The correlation between the photoreactivity and the forms of **2** in solution is also similar to that for methyl 3-pyridinecarboxylate. However, there exists a remarkable difference between the amide and the ester: In methyl 3-pyridinecarboxylate the peak for the methylation in Region A becomes lower as the concentration of the substrate is lowered,[3] whereas in 3-pyridinecarboxamide such a dependence of the methylation on the concentration of the substrate was not observed.

Mechanism of Photoreactions of Pyridinecarboxamides. A significant feature of the photoreactions of pyridinecarboxylic esters is the simultaneous participation of various kinds of excited states. Do pyridinecarboxamides show the similar photochemical fea-

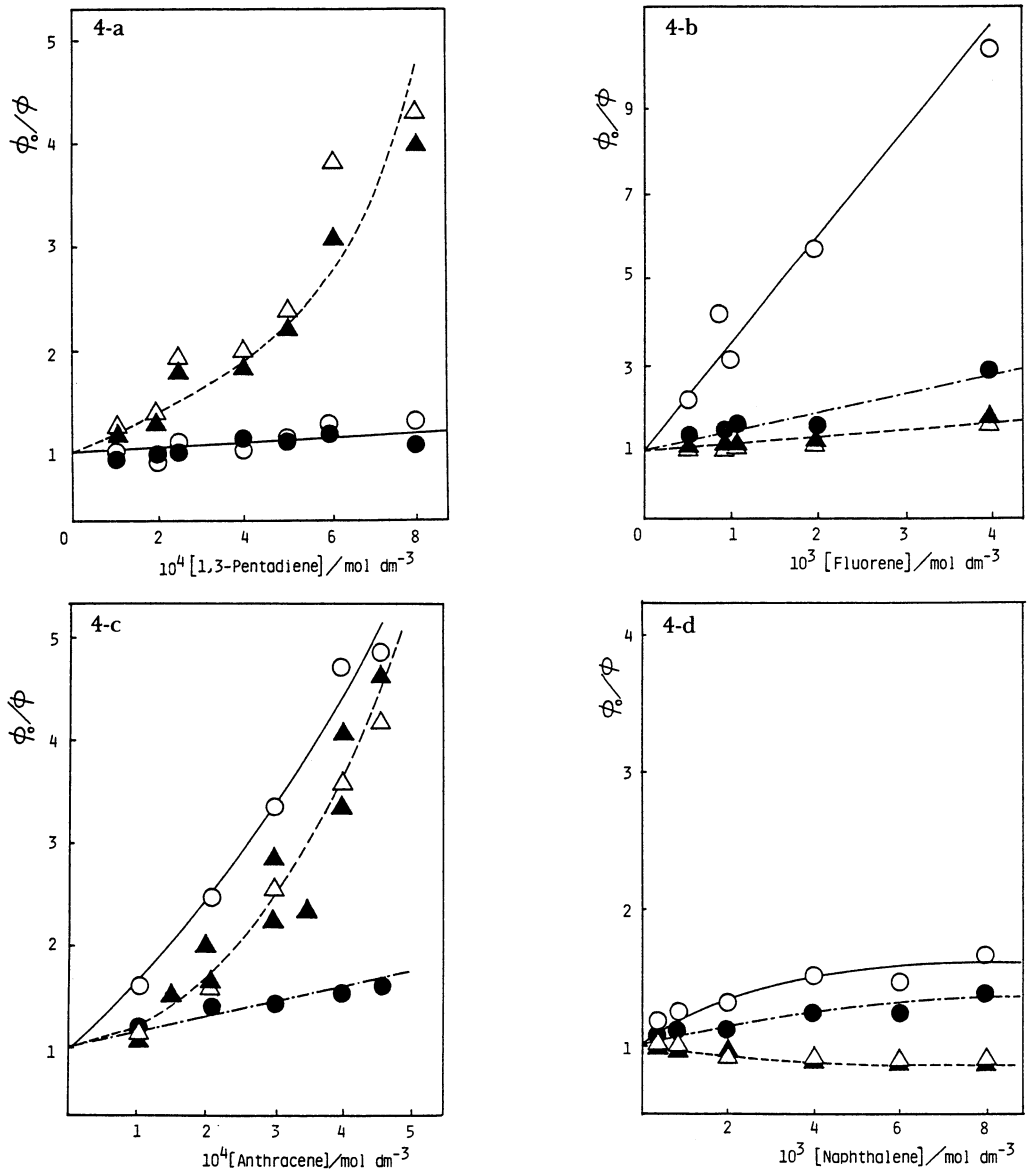


Fig. 4. Stern-Volmer plots for quenching of the photoreactions of 3-pyridinecarboxamide(**2**) in methanol by 1,3-pentadiene (4-a), fluorene (4-b), anthracene (4-c), and naphthalene (4-d). [**2**]=1.0×10^{-2} mol dm^{-3}; [H_2SO_2]=5×10^{-2} mol dm^{-3}; irradiation time, 3 h; 30 °C. ----△----, methylation at the 4-position; ----▲----, methylation at the 6-position; —○—, methoxylation at the 2-position; -·-●-·-, methoxylation at the 6-position.

ture? We analyze the photoreactions by means of the effects of quenchers in order to identify the excited states which may participate in the photoreactions.

For the Stern-Volmer analysis of the effects of additives, the quantum yields are calculated on the basis of the light quanta which are absorbed by the substrate.[11] The values Y and L are defined as,

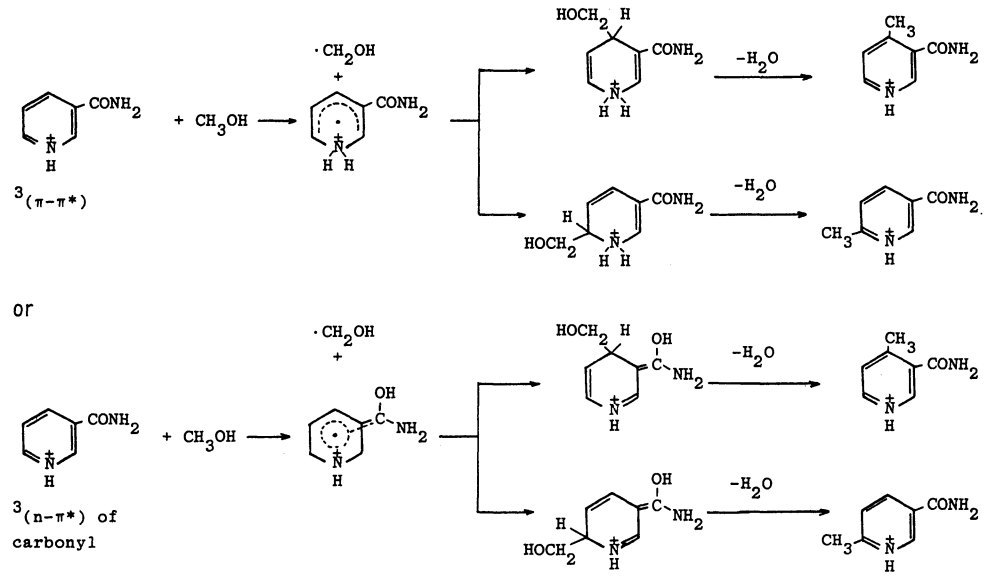
$$Y = \frac{\text{Yield of product in the presence of quencher}}{\text{Yield of product in the absence of quencher}},$$

$$L = \frac{\text{Light absorbed by substrate}}{\text{Light absorbed by substrate and quencher}}.$$

Thus, $\phi_0/\phi = L/Y$.

Photoreaction of 3-Pyridinecarboxamide in Strongly Acidic Alcoholic Solution (Reaction in Region B in Fig. 1-a). The Stern-Volmer plots for the effects of 1,3-pentadiene, fluorene, naphthalene, and anthracene on the photoreactions of **2** in methanol in the presence of sulfuric acid ($[H_2SO_4]=5\times10^{-2}$ mol dm^{-3}; $[2]=1.0\times10^{-2}$ mol dm^{-3}) are shown in Figs. 4-a—4-d.

With respect to the effects of the additives, the photoreactions of 3-pyridinecarboxamide in strongly acidic methanolic solutions can be classified into 3 groups: the two methylation reactions (the formation of **8a** and **9a**), the methoxylation at the 2-position (the formation of **10a**), and the methoxylation at the 6-position (the formation of **11a**). The formation of **8a**



Scheme 1.

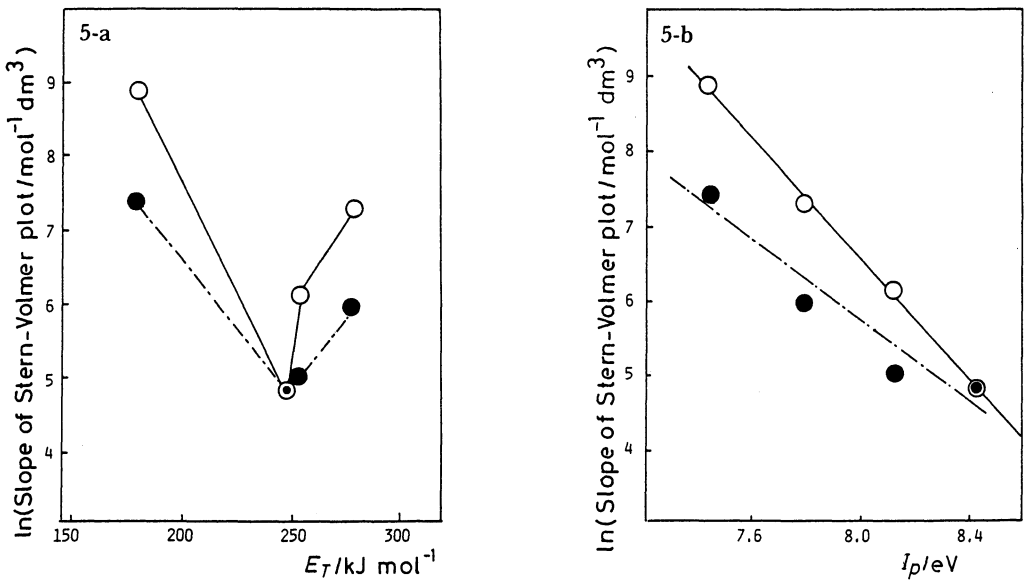


Fig. 5. Relations between the slope of Stern-Volmer plot and triplet energy (5-a) as well as between the slope of Stern-Volmer plot and ionization potential (5-b) of the additives in the quenching of the photomethoxylation of 3-pyridinecarboxamide in methanol. —○—, methoxylation at the 2-position; ···●···, methoxylation at the 6-position.

and **9a** is affected by the additives always to the same extent. The effects of quenchers on the methoxylation differ from those on the methylation and, furthermore, the effects of additives on the formation of **10a** and **11a** are different from each other.

The photomethylation reactions are quenched[12] by the additives with low triplet energies (anthracene: E_T=176 kJ mol^{-1}; 1,3-pentadiene: E_T=248 kJ mol^{-1})[13] but are slightly affected or even promoted by the additives with higher triplet energies (fluorene: E_T=285 kJ mol^{-1}; naphthalene: E_T=255 kJ mol^{-1}). These facts suggest that the methylation reactions originate from an excited triplet state. The photomethylation reactions at the 4- and 6-positions can be explained either by $^3(\pi\text{-}\pi^*)$ or by $^3(n\text{-}\pi^*)$ of carbonyl (Scheme 1).

The slopes of Stern-Volmer plots for photomethoxylation are plotted against the triplet energy values[13] (Fig. 5-a) and the ionization potential values[14] (Fig. 5-b) of the additives. The slopes correlate well with the I_p values of the quenchers, while those have no correlation with the E_T values of the quenchers.

The photomethoxylation reactions should originate from the excited singlet state(s), because the inhibition of the photomethoxylation is not correlated with the triplet energies of the quenchers.

The methoxylation is inhibited by the electron transfer from the electron-rich aromatic hydrocarbons to the excited states or precursors for the methoxylation products. The inhibition would not be due to the direct attack of the quencher to the excited singlet state of 3-pyridinecarboxamide, because the lifetime of the species to be quenched would be too long for an excited singlet state. The lifetime of the reactive species is in the order of 10^{-6} s, when we calculate it from the $k_q\tau$=2.6×10^3 mol^{-1} dm^3 (in the inhibition by fluorene) and the assumed k_q value of 10^9 mol^{-1} dm^3 s^{-1}. The inhibition of the photomethoxylation would occur in the attack of the quenchers to the certain intermediates which are formed from the excited singlet state of **2**.

The following fact also supports the above conclusion. In the presence of fluorene the methoxylation at the 2-position is inhibited but the both methylation reactions (via the excited triplet state) are not inhibited. If the singlet state itself is quenched, the yield of the excited triplet state, which is formed from the excited singlet state, should be decreased. Therefore, if we assume that the inhibition of the methoxylation is due to the quenching of the excited singlet state of the substate, the methylation reactions which originate from an excited triplet state should be inhibited by fluorene to the similar or greater extent than the methoxylation (the reaction from the excited singlet state). This type of phenomena was not observed in

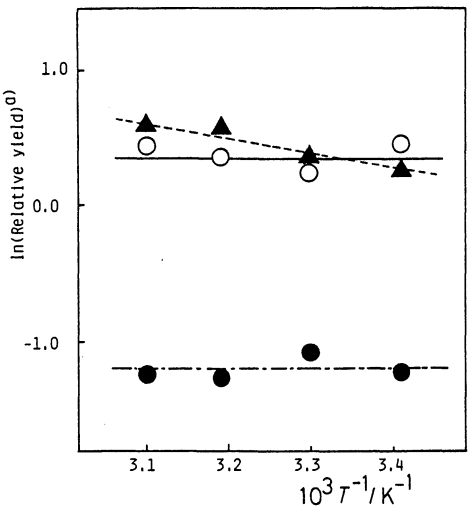
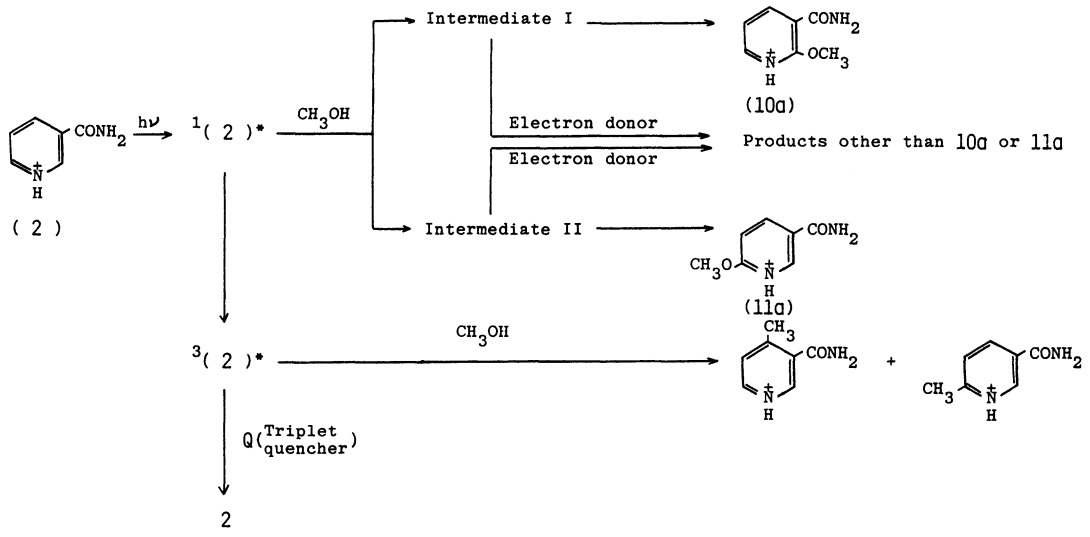


Fig. 6. Temperature dependence of the relative yields of the products from the photoreaction of 3-pyridinecarboxamide in methanol. ----▲----, yield of **9a**/yield of **8a**; —○—, yield of **10a**/yield of **8a**; -·-●-·-, yield of **11a**/yield of **8a**.



Scheme 2.

the quenching of the photoreaction of 3-pyridinecarboxamide by fluorene. The photoreaction of 3-pyridinecarboxamide shows no remarkable temperature dependence unlike that of the ester (Fig. 6).

The photoreactions of 3-pyridinecarboxamide in methanol acidified with sulfuric acid are summarized in Scheme 2.

Photoreaction of 3-Pyridinecarboxamide in the Presence of Chloride Ion. The UV-irradiation of 3-pyridinecarboxamide in alcohol in the presence of HCl resulted in the increase in the yields of the alkylation products and in the decrease in the yields of the alkoxylation products as shown in Table 1. This observation is similar to that in the photoreaction of methyl 3-pyridinecarboxylate.

More detailed studies by means of Stern-Volmer analysis by using LiCl as an additive in the photoreactions of 3-pyridinecarboxamide in the presence of sulfuric acid (Fig. 7) reveals that chloride ion inhibits the two types of photomethoxylation and, furthermore, to different extents. On the other hand, chloride ion promotes the methylation reactions at the 4- and 6-position to the same extent.

As the roles of chloride ions, we can consider two possibilities: 1) chloride ion accelerates the intersystem crossing of the excited 3-pyridinecarboxamide and 2) chloride ion donates an electron to the excited state(s) of 3-pyridinecarboxamide to give chlorine atom which would bring about the methylation in a radical process (Scheme 3).

We can not determine which process occurs actually. The fact that the isomeric ratio of the photomethylation products is not affected by chloride ion supports

Table 1. Difference in Effect of H_2SO_4 and HCl on Photoreaction of 3-Pyridinecarboxamide (**2**) in Alcohol[a)]

Alcohol	Acid	Irr. time	[Product]/10^{-4} mol dm^{-3}			
		h	**8**	**9**	**10**	**11**
MeOH[b)]	H_2SO_4	6	4.5	6.8	4.1	1.1
	HCl	1.5	4.9	6.9	0.4	0.0
EtOH[c)]	H_2SO_4	3		24	0.3	
	HCl	2		57		

a) [**2**]=1.0×10^{-2} mol dm^{-3}; [H_2SO_4]=5×10^{-2} mol dm^{-3} or [HCl]=5×10^{-1} mol dm^{-3}; temperature, 30 °C. b) Irradiated with a "merry-go-round" type irradiation apparatus. c) Irradiated separately at the center of a spiral type low pressure mercury lamp.

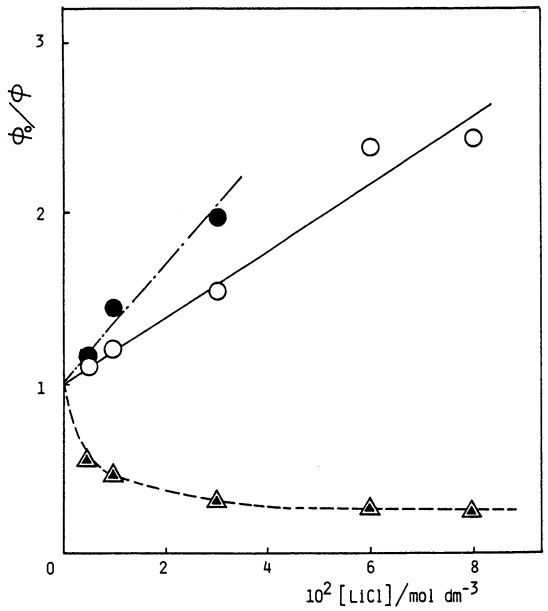
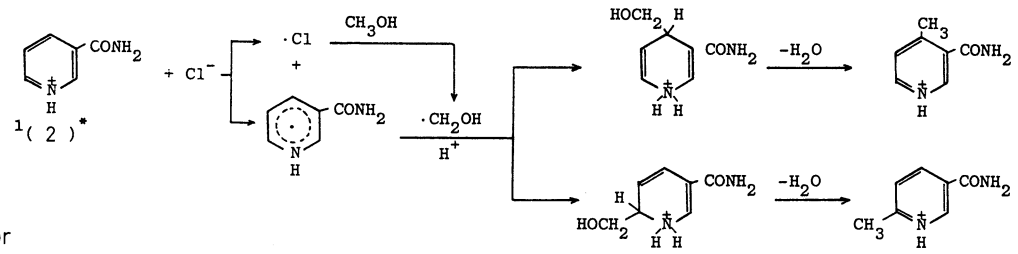


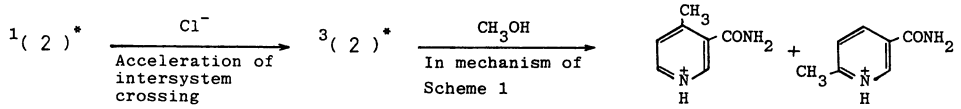
Fig. 7. Effect of LiCl on the photoreaction of 3-pyridinecarboxamide (**2**) in methanol.
[**2**]=1.0×10^{-2} mol dm^{-3}; [H_2SO_4]=5×10^{-2} mol dm^{-3}; irradiation time, 3 h. ----△----, methylation at the 4-position; ----▲----, methylation at the 6-position; —○—, methoxylation at the 2-position; -·-●-·-, methoxylation at the 6-position.

Mechanism via electron transfer



or

Mechanism via acceleration of intersystem crossing



Scheme 3.

Table 2. Dependence of Yields of Products on Concentration of 3-Pyridinecarboxamide (**2**) in Photoreaction in Methanol in the Presence of Sulfuric Acid[a)]

[2]	[Product]/10^{-5} mol dm^{-3}			
mol dm^{-3}	**8a**	**9a**	**10a**	**11a**
2×10^{-4}	2.1	2.9	3.3	0.4
1×10^{-3}	1.6	2.4	3.4	0.5
1×10^{-2}	1.4	2.0	2.8	0.7

a) $[H_2SO_4]=5\times10^{-2}$ mol dm^{-3}; irradiation time, 18 min; temperature, 30 °C.

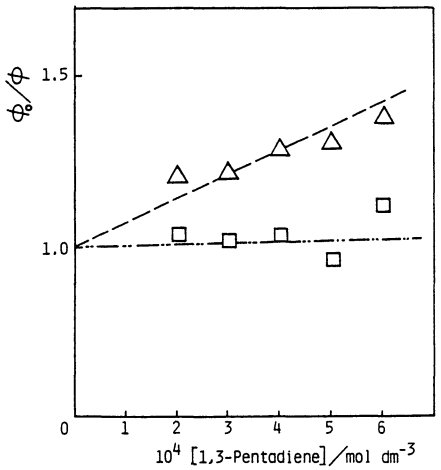


Fig. 8. Stern-Volmer plots for quenching of the photoreactions of 2-pyridinecarboxamide (**1**) by 1,3-pentadiene in the absence of sulfuric acid. [**1**]=9.9×10^{-3} mol dm^{-3}; irradiation time, 10 h. ----△----, methylation at the 5-position; ---□---, hydroxymethylation at the 4-position.

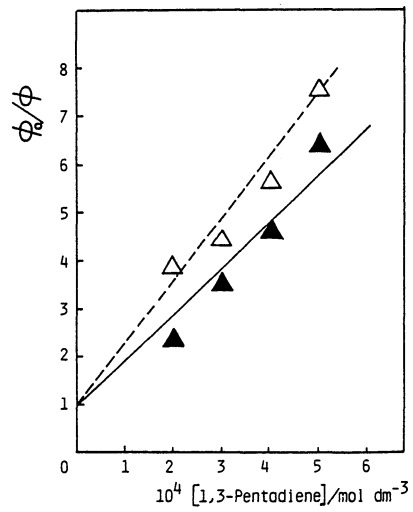


Fig. 9. Stern-Volmer plots for quenching of the photomethylation at the 4-position of 2-pyridinecarboxamide (**1**) by 1,3-pentadiene in the presence of sulfuric acid. [**1**]=1.0×10^{-2} mol dm^{-3}; irradiation time, 4 h. —▲—, $[H_2SO_4]=5\times10^{-3}$ mol dm^{-3}; --△--, $[H_2SO_2]=2\times10^{-1}$ mol dm^{-3}.

the mechanism of the acceleration of the intersystem crossing. However, the different quenchings of chloride ion on the two methoxylation reactions can not be explained by the acceleration of the intersystem crossing, but can be explained more easily by the electron transfer from the intermediates to chloride ion.

Dependence of Photoreaction on Concentration of 3-Pyridinecarboxamide. The photoalkoxylation reactions of 2-pyridinecarboxylic acid,[15] 2-pyridinecarboxylic ester,[4] and 2-pyridinecarbonitrile[9] are characterized by the dependences on the concentration. The reaction occurs effectively at the higher concentrations of the substrate. The alkoxylation reactions of these compounds have been explained by a mechanism via an excimer. The photoreactions of 3-pyridinecarboxamide, however, show only a small concentration dependence as shown in Table 2. It is suggested that an excimer plays no important role in the photoreactions of 3-pyridinecarboxamide in strongly acidic methanolic solutions.

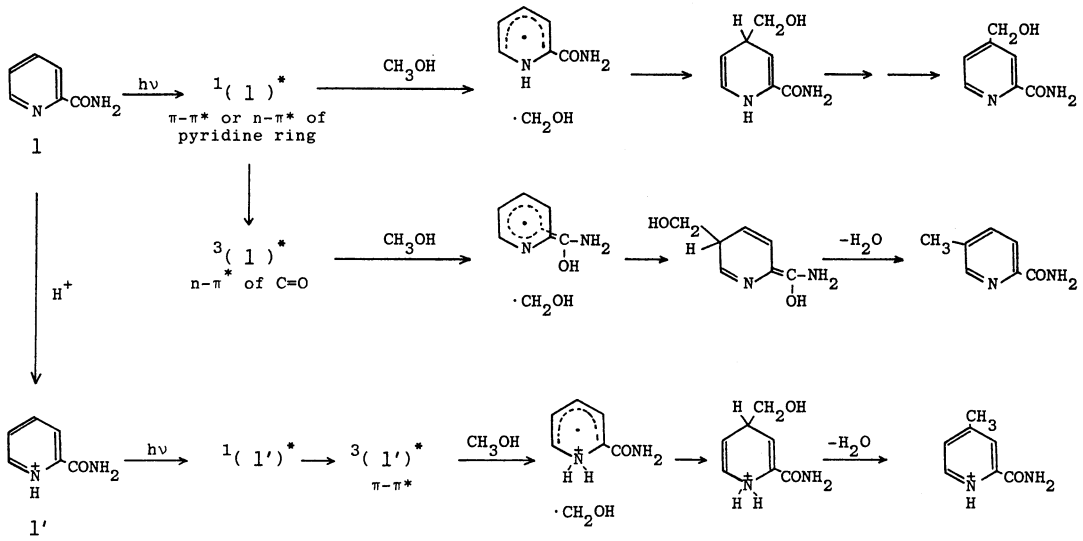
Photoreaction of 2-Pyridinecarboxamide in Methanol. In contrast to methyl 2-pyridinecarboxylate, 2-pyridinecarboxamide (**1**) gives no methoxylation product (the products in ionic reaction). However, the radical type photoreactions of **1** are similar to those of the ester: the methylation at the 5-position in the absence of added acid and the methylation at the 4-position in the presence of H_2SO_4.

The effects of 1,3-pentadiene on the photoreactions of 2-pyridinecarboxamide in the absence of sulfuric acid (Fig. 8) suggest that the methylation at the 5-position and the hydroxymethylation at the 4-position occur from the different kinds of excited species: The formation of **4** is inhibited by a triplet quencher, 1,3-pentadiene, while that of **5** is not affected by 1,3-pentadiene. Therefore, the photoreaction of **1** in the absence of acid might occur via the triplet n-π^* state of amide carbonyl to give **4** but via the singlet n-π^* or π-π^* state of the pyridine ring to give **5**.

The photomethylation at the 4-position in the presence of sulfuric acid is quenched by 1,3-pentadiene (Fig. 9). Anthracene ([anthracene]=4×10^{-4} mol dm^{-3} for [**1**]=1.0×10^{-2} mol dm^{-3} and $[H_2SO_4]=0.2$ mol dm^{-3}) inhibits the formation of **6** completely. These facts suggest that the photomethylation at the 4-position originates from an excited triplet state.

The photomethylations at the 4- and 5-positions are explained by the hydrogen abstractions by the n-π^* of the amide carbonyl and π-π^* of the pyridinium, respectively (Scheme 4).

Photoreaction of 4-Pyridinecarboxamide. The photoreaction of 4-pyridinecarboxamide (**3**) is simpler than those of 2- and 3-pyridinecarboxamide. The UV-irradiation of **3** in methanol gives 2-hydroxymethyl-4-pyridinecarboxamide (**12**) either in the presence or in the absence of an added acid. The photohydroxymethylation was not inhibited by 1,3-pentadiene either



Scheme 4.

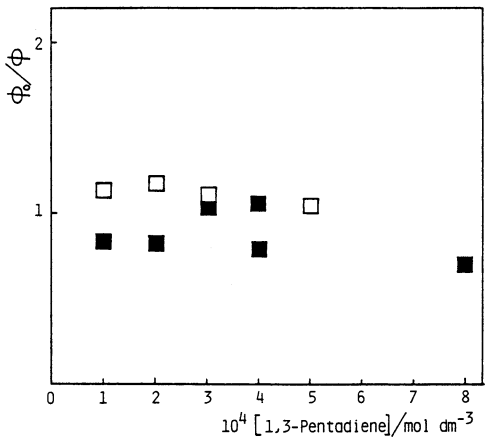


Fig. 10. Stern-Volmer plots for quenching of the photohydroxymethylation of 4-pyridinecarboxamide (**3**) in methanol by 1,3-pentadiene. [**3**]= 1.0×10^{-3} mol dm^{-3}. □, in the absence of sulfuric acid (irradiation time, 30 min); ■, in the presence of sulfuric acid ([H_2SO_2]=5×10^{-2} mol dm^{-3}; irradiation time, 90 min).

in the presence or in the absence of sulfuric acid (Fig. 10). The excited singlet states of protonated and non-protonated **3** might be responsible for the formation of **12**.

Experimental

Materials. Commercial 2- and 4-pyridinecarboxamide (GR-grade of Tokyo Kasei Co.) were purified by recrystallization from benzene and from benzene-ethanol, respectively. 3-Pyridinecarboxamide supplied by Yuki Gosei Yakuhin Co. was recrystallyzed from benzene-ethanol. 2-Pyridinecarboxamide, mp 106 °C; 3-pyridinecarboxamide, mp 126—127 °C; 4-pyridinecarboxamide, mp 152—153 °C.

1,3-Pentadiene (GR-grade of Wako Junyaku Co.), anthracene (analytical standard reagent of BDH Chemical Co.), naphthalene (Reagent for scintillator made by Dojindo Laboratories), and fluorene (zone-refined U.P. grade reagent of Tokyo Kasei Co.) were used without further purification.

UV-Irradiation. Methanolic or ethanolic solutions containing pyridinecarboxamide (in most cases, 1.0×10^{-2} mol dm^{-3}), sulfuric acid, and additives were deaerated by bubbling nitrogen or argon through for 40 min before irradiation.

In the quenching experiment with 1,3-pentadiene, the quencher was added after the deaeration of the substrate solutions in order to avoid the evaporation of the quencher during the bubbling of an inert gas.

For the quenching expeiment, a "merry-go-round" irradiation apparatus was employed, and the solutions (each 20 cm^3) were irradiated with a low-pressure mercury lamp at about 30 °C.

Isolation of Photoproducts. After the irradiation, the solvent was evaporated under reduced pressure. The solution was neutralized with sodium hydrogencarbonate (when the photoreaction has been carried out in the presence of sulfuric acid) and the products were extracted with ethyl acetate. The products were separated by means of TLC (plate, GF_{254} (Type 60) of E. Merck Co.; the developing solvent was ethyl acetate-methanol (9:1) for the products from 2- and 3-pyridinecarboxamides and ethyl acetate-methanol-NH_3 (9:1:small amount) for the products from 4-pyridinecarboxamide.). The separation of the photoproducts from 2- and 3-pyridinecarboxamides was carried out by HPLC (column, RP-18 of E. Merck Co.; eluent, methanol-water (2:8) for the products from 3-pyridinecarboxamide and methanol-water (35:65) for the products from 2-pyridinecarboxamide).

Identification of Photoproducts. The identification of 4-methyl-2-pyridinecarboxamide (**6**), 4-methyl-3-pyridinecarboxamide (**8a**), 6-methyl-3-pyridinecarboxamide (**9a**), and 2-hydroxymethyl-4-pyridinecarboxamide (**12**) was described in our earlier paper.[16]

2-Methoxy-3-pyridinecarboxamide (10a): Mp 131—133 °C; lit,[17] 130—131 °C); IR(KBr disk) 3460, 1670, and 1650 cm^{-1}; ^{1}H NMR (D_2O) δ=4.01 (3H, s), 7.12 (1H, t, J=6.2 Hz, H at the 5-position), and 8.20 (2H, d, J=6.2 Hz, H at the 4-and 6-positions).

2-Ethoxy-3-pyridinecarboxamide (10b) was identified by

the similarity of its spectra to those of **10a**. ^{1}H NMR (D_2O) δ=1.49 (3H, t, J=7.0 Hz), 4.51 (2H, q, J=7.0 Hz), 7.18 (1H, t, J=6.4 Hz, H at the 5-position), and 8.27 (2H, d, J=6.4 Hz, H at the 4- and 6-positions).

6-Methoxy-3-pyridinecarboxamide (11a): Mp 167—168 °C; IR(KBr disk) 3420, 3170, 1670, and 1625 cm^{-1}; ^{1}H NMR (D_2O) δ=4.03 (3H, s), 7.01 (1H, d, J=9.4 Hz, H at the 5-position), 8.16 (1H, dd, J=9.4 and 3.0 Hz, H at the 4-position), and 8.60 (1H, d, J=3.0 Hz, H at the 2-position). Found: C, 54.6; H, 5.3; N, 18.1%. Calcd for $C_7H_8N_2O_2$: C, 55.2; H, 5.3; N, 18.4%.

6-Ethyl-3-pyridinecarboxamide (9b): Mp 161—163 °C; IR(KBr disk) 3220 and 1655 cm^{-1}; ^{1}H NMR (D_2O) δ=1.30 (3H, t, J=7.2 Hz), 2.88 (2H, q, J=7.2 Hz), 7.40 (1H, d, J=8.0 Hz, H at the 5-position), 8.09 (1H, dd, J=8.0 and 2.0 Hz, H at the 4-position), and 8.84 (1H, d, J=2.0 Hz, H at the 2-position); Found: C, 63.7; H, 6.7; N, 18.9%. Calcd for $C_8H_{10}N_2O$: C, 64.0; H, 6.7; N, 18.7%.

5-Methyl-2-pyridinecarboxamide (4) was identified by the similarity of its spectra to those of methyl 5-methyl-2-pyridinecarboxylate. ^{1}H NMR ($CDCl_3$) δ=2.41 (3H, s), 7.62 (1H, dd, J=8.0 and 2.0 Hz, H at the 4-position), 8.08 (1H, d, J=8.0 Hz, H at the 3-position), and 8.37 (1H, d, J=2.0 Hz, H at the 6-position); MS (70 eV) m/z (rel intensity) 137 ($(M+1)^+$; 4), 136 (M^+; 51), 118 ($(M-NH_2)^+$; 8), 94 (7), 93 ($(M-CONH_2)^+$; 100), 92 (46), 66 (25), and 64 (30).

4-Hydroxymethyl-2-pyridinecarboxamide (5) was not obtained in pure form and was identified spectroscopically. ^{1}H NMR (CD_3COCD_3) δ=4.75 (2H, s), 7.50 (1H, dd, J=5.0 and 1.5 Hz, H at the 5-position), 8.08 (1H, d, J=1.5 Hz, H at the 3-position), and 8.49 (1H, d, J=5.0 Hz, H at the 6-position); MS (70 eV) m/z (rel intensity) 153 (5), 152 (M^+; 43), 109 (100), 108 ($(M-CONH_2)^+$; 23), 80 (21), and 78 (14).

Found: m/z 152.0562. Calcd for $C_7H_8N_2O_2$: M, 152.0584.

Quantitative Analysis of Photoproducts. The quantitative analyses of the photoproducts in the quenching experiments were carried out by means of gas chromatography for 4- and 5-methyl-2-pyridinecarboxamides (column, 1 m column of PEG 5%; column temperature, 160 °C). Analyses with HPLC were applied for 4-hydroxymethyl-2-pyridinecarboxamide and for the photoproducts from 3-pyridinecarboxamide (column, 25 cm column of Zorbax ODS of DuPont Co.; eluent, acetonitrile-water (1 : 9) buffered at pH=6.7—7.1 with phosphate buffer) and for the photoproducts from 4-pyridinecarboxamide (column, 25 cm column of Zorbax-ODS; eluent, methanol-water (2 : 8)).

The present work was partially supported by a Grant-in-Aid for Scientific Research No. 60470028 from the Ministry of Education, Science and Culture.

References

1) A review; A. Sugimori, *Yuki Gosei Kagaku Kyokai Shi*, **39**, 712 (1981).

2) T. Sugiyama, E. Tobita, K. Takagi, M. Sato, Y. Kumagai, G. P. Sato, and A. Sugimori, *Chem. Lett.*, **1980**, 131.

3) A. Sugimori, E. Tobita, Y. Kumagai, and G. P. Sato, *Bull. Chem. Soc. Jpn.*, **54**, 1761 (1981).

4) T. Sugiyama, T. Furihata, K. Takagi, M. Sato, S. Akiyama, G. P. Sato, and A. Sugimori, *Bull. Chem. Soc. Jpn.*, **54**, 3585 (1981).

5) T. Sugiyama, K. Yagi, Y. Ito, and A. Sugimori, *Chem. Lett.*, **1982**, 917; T. Sugiyama, Y. Kusano, K. Yagi, Y. Ito, and A. Sugimori, *Bull. Chem. Soc. Jpn.*, **57**, 1882 (1984).

6) A. Sugimori and M. Kanai, *Nippon Kagaku Kaishi*, **1984**, 37.

7) T. Sugiyama, M. Kanai, S. Takenaka, and A. Sugimori, *Bull. Chem. Soc. Jpn.*, **58**, 1331 (1985).

8) A. Sugimori, T. Ogishima, Y. Miyazawa, R. Hasegawa, and Y. Suzuki, *Bull. Chem. Soc. Jpn.*, **56**, 1817 (1983).

9) A. Sugimori, T. Furihata, S. Mikayama, M. Yoshida, and Y. Nakanishi, *Bull. Chem. Soc. Jpn.*, **55**, 2906 (1982).

10) Preliminary report on the photoreactions of 3-pyridinecarboxamide: A. Sugimori and H. Itoh, *Chem. Lett.*, **1986**, 209. The mechanism of the photoreaction of 3-pyridinecarboxamide was reinvestigated.

11) When the quencher absorbs the light, the effective concentration of the quencher might be smaller than the charged concentration, because a part of the quencher is in the excited state. However, the decrease in the effective concentrations of the quencher is negligible under our reaction conditions, where the stationary irradiation with a "merry-go-round" irradiation apparatus equipped with a 17 W low pressure mercury lamp was employed. The measured light quanta absorbed by 20 cm^3 of the solution was 4×10^{16} s^{-1} (3×10^{-6} mol dm^{-3} s^{-1}). If we consider the reported triplet lifetimes of the quenchers (for anthracene in ethanol: 3000+2000 μs (D. N. Dempstor, T. Morrow, and M. F. Quinn, *J. Photochem.*, **2**, 399 (1974) and 150±45 μs (G. Porter and M. W. Windsor, *Discuss. Faraday Soc.*, **17**, 178 (1954); for fluorene in hexane at 300 K: 150 μs (W. Heinzelmann and H. Laphart, *Chem. Phys. Lett.*, **4**, 20 (1969)) the stationary concentration of these quenchers in their excited states should be much lower than the charged concentration of the quenchers (ca. 10^{-4} mol dm^{-3}).

12) We observed the upward-curved Stern-Volmer plots for the quenching of the photomethylation reactions. It indicates that the inhibition of the photomethylation does not occur in a simple triplet energy transfer mechanism.

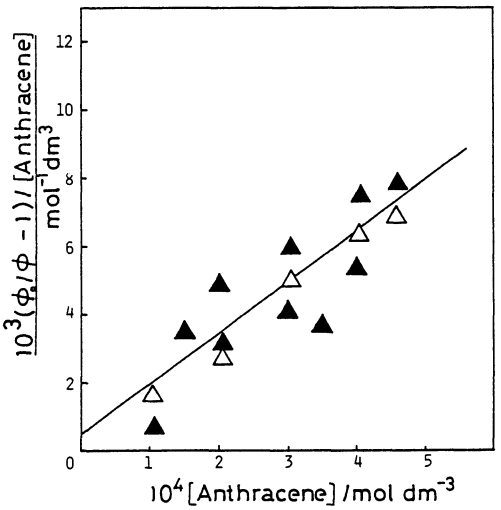


Fig. 11. Plot of $(\phi_0/\phi-1)$/[anthracene] vs. [anthracene] in the quenching of photomethylation reactions of **2** by anthracene. Reaction conditions are the same for Fig. 4-c. —△—, methylation at the 4-position; —▲—, methylation at the 6-position.

The Stern-Volmer plots curved upward are observed (1) in the case of the participation of the static quenching and (2) in the case of the participation of two excited states ((2.1) in the case where each of two states, whether in equilibrium or not, is quenched and the lower one is reactive and (2.2) in the case where two reactive states which are quenched react in parallel) (P. J. Wagner, "Energy Transfer Kinetics in Solution," in "Creation and Detection of the Excited State" ed by A. A. Lamola, Marcel Dekker, Inc. New York (1971), Vol. 1, part A, Chap. 4, pp. 173—212). The concentrations of 1,3-pentadiene in our reaction conditions for quenching (10^{-4}—10^{-3} mol dm^{-3}) are much lower than those which are required for the simple statistical chance that the reactant and the quencher will be nearest neighbors (it occurs under the conditions of [quencher]$>$0.1 mol dm^{-3}). The evidence for the formation of "a complex" between **2** and 1,3-pentadiene which will cause the static quenching at lower concentrations of the quencher has not been obtained in the careful examination of UV-vis. spectra of their mixtures. The Stern-Volmer plots curved upward can be explained by the mechanism (2.1) which involves two states (R_1^* and R_2^*) both of which are quenched and one of which is reactive.

$$R_1^* + Q \xrightarrow{k_{t1}} R_0 + Q_1^* \text{ (Q: Quencher)}$$

$$R_1^* \xrightarrow{k_i} R_0$$

$$R_1^* \xrightarrow{k_{12}} R_2^*$$

$$R_2^* + Q \xrightarrow{k_{t2}} R_0 + Q_2^*$$

$$R_2^* \xrightarrow{k_d} R_0$$

$$R_2^* \xrightarrow{k_{r2}} I \longrightarrow P \text{ (I: Intermediate; P: product)}$$

When R_1^* and R_2^* are in equilibrium, we add,

$$R_2^* \xrightarrow{k_{21}} R_1^*$$

In this mechanism the Stern-Volmer plots should be parabolic and a linear relationship between $(\phi_0/\phi-1)/$[quencher] and [quencher] should be expected.

In the case where R_1^* and R_2^* are not in equilibrium,

$$\frac{(\phi_0/\phi-1)}{[Q]} = (k_{t1}\tau_1 + k_{t2}\tau_2) + k_{t1}\tau_1 k_{t2}\tau_2[Q].$$

In the case where R_1^* and R_2^* are in equilibrium,

$$\frac{(\phi_0/\phi-1)}{[Q]} = (X_2 k_{t2} + X_1 k_{t1})\tau_e + \frac{k_{t1}k_{t2}}{k_{12}+k_{21}}[Q].$$

In the equation, we define as $X_1=k_{21}/(k_{12}+k_{21})$ and $X_2=k_{12}/(k_{12}+k_{21})$, The apparent lifetime is expressed as τ_e.

The plot for the quenching of photomethylation by anthracene fits this kinetics (Fig. 11).

The participation of two excited triplet states in the photomethylation of 3-pyridinecarboxamide can be conceivable, because $^3(\pi\text{-}\pi^*)$ and $^3(n\text{-}\pi^*$ of carbonyl) states could contribute to the photomethylation. The photomethylation reactions at the 4- and 6-positions can be explained either by $^3(\pi\text{-}\pi^*)$ or by $^3(n\text{-}\pi^*$ of carbonyl) (Scheme 1). The fact that the ratio of the two photomethylation products is not affected by the quenchers supports that the reactive state to undergo methylation would be one of them (the lower excited triplet state). Therefore, the mechanism (2.2) which involve two reactive states is less probable.

We have not yet determine which of the excited triplet states, $^3(\pi\text{-}\pi^*)$ or $^3(n\text{-}\pi^*$ of carbonyl) undergoes the photomethylation reactions.

13) Triplet energy values of quenchers: S. L. Murov, "Handbook of Photochemistry," Marcel Dekker, NY (1973), pp. 3—7.

14) Inization potential values of quenchers: S. L. Murov, "Handbook of Photochemistry," Marcel Dekker, NY (1973), pp. 198—199.

15) H. Kurokawa, T. Furihata, F. Takeuchi, and A. Sugimori, *Tetrahedron Lett.*, **1973**, 2623.

16) A. Sugimori, M. Nishijima, and H. Itoh, *Bull. Chem. Soc. Jpn.*, **55**, 3055 (1982).

17) E. C. Taylor and A. J. Crovetti, *J. Am. Chem. Soc.*, **78**, 214 (1956).