Effects of Additives on Photo-methoxylation of Methyl 2-Pyridinecarboxylate in Acidic Methanolic Solutions. Promotion by 4-Substituted Pyridines

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The rate of photo-methoxylation of methyl 2-pyridinecarboxylate(**1**) in acidic methanol is accelerated by 4-substituted pyridines and their analogs, 4,4'-bipyridine and pyrazine. The photo-methoxylation of **1** is not promoted by triplet sensitizers, electron donors, or electron acceptors. Detailed analyses on the **1**–4-pyridinecarbonitrile(**3**) system including wavelength dependence lead to a mechanism for the promotion *via* an excited complex formed from an excited **1** and **3** in the ground state.

The promotion and inhibition of photoreactions are an important theme in the studies of photochemistry from the viewpoints of both mechanistic and synthetic organic photochemistry. The promotion and inhibition *via* energy transfer[1] and electron transfer[2] have been investigated extensively.

The field of photosensitization is, however, wide and studies from new aspects are needed. Increasing interest has been paid to the sensitization *via* excited complexes. For the apparently peculiar "quencher-sensitized" photo-dimerization of anthracene derivatives,[3,4] the participation of an exciplex has been proposed.[3] The selectivity and specificity due to complex formation are important. Photochemical formation of optically active *trans*-cyclooctene and 1,5-cyclooctadiene induced by chiral sensitizers has been explained in terms of the exciplex formation.[5,6]

We describe here the specific promotion of photo-methoxylation of methyl 2-pyridinecarboxylate by 4-substituted pyridines and propose a mechanism for the promotion *via* an exciplex.[7] Concerning the photo-methoxylation of methyl 2-pyridinecarboxylate in the absence of sensitizers, we have observed remarkable concentration dependence and proposed a mechanism *via* an excimer.[8]

Results and Discussion

Indices Describing (Promoting or Inhibiting) Effects of Additives, Y- and A-Value. In the case where the additive and the substrate absorb the incident light competitively, the effects of addititives should be analyzed by taking the distribution of light absorption between the substrate and the additive into consideration.

In a system where the incident light is completely absorbed by the substrate even in the absence of the additive, an index, A, defined below can be used for describing the promoting or inhibiting effect by the additive:

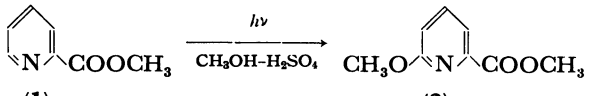
$$A = Y/L$$

$$Y = \frac{\text{Yield in the presence of additive}}{\text{Yield in the absence of additive}}$$

$$L = \frac{\text{Light absorbed by substrate (1)}}{\text{Light absorbed both by substrate (1) and by additive (S)}} = \frac{c_1\varepsilon_1}{c_1\varepsilon_1 + c_S\varepsilon_S},$$

where c_1 and c_S represent the concentrations of **1** and additive, and ε_1 and ε_S are the molar absorption coefficients of **1** and of additive at the wavelength of the photolyzing light, respectively. $A>1$ indicates promotion by the additive and $A<1$ means inhibition.

Effects of Triplet Sensitizer, Triplet Quencher, Electron Donor, and Electron Acceptor. UV-irradiation of methyl 2-pyridinecarboxylate (**1**) in methanol acidified with sulfuric acid gives methyl 6-methoxy-2-pyridinecarboxylate (**2**).



(**1**) (**2**)

TABLE 1. EFFECTS OF TRIPLET SENSITIZER, ELECTRON DONOR, AND ELECTRON ACCEPTOR ON PHOTO-METHOXYLATION OF METHYL 2-PYRIDINECARBOXYLATE (**1**) $[H_2SO_4]=5\times10^{-2}$ mol dm^{-3}; Irradiated with 254 nm light.

Additive	10^3 [**1**] / mol dm^{-3}	10^3 [Additive] / mol dm^{-3}	L	Y	A
Benzene	1.0	1.0	0.96	0.83	0.86
	1.0	10	0.68	0.62	0.91
Naphthalene	1.0	6.0	0.16	0.055	0.34
Acetophenone	1.0	1.0	0.45	0.44	1.0
	1.0	3.0	0.21	0.21	1.0
Anisole	1.0	1.0	0.74	0.72	0.97
Ferrocene	1.0	1.0	0.64	0.0	0.0
1, 2, 4, 5-Tetracyanobenzene	0.25	1.0	0.17	0.0	0.0
Nitrobenzene	0.25	1.0	0.27	0.0	0.0

As reported earlier,[8] the photo-methoxylation has a remarkable concentration dependence on **1**: at 32 °C, quantum yields for **2** at $[\mathbf{1}]=5\times10^{-4}$, 1.0×10^{-3}, 2.0×10^{-3}, 5.0×10^{-3}, and 2.0×10^{-2} mol dm^{-3} are 0.009, 0.02, 0.025, 0.051, and 0.17, respectively.

We studied the effects of additives on photo-methoxylation of **1** at $[\mathbf{1}]=1.0\times10^{-3}$ mol dm^{-3}, where the photo-methoxylation is not so efficient. In Table 1 are listed the effects of several typical sensitizers, electron donors, and electron acceptors. The photo-methoxylation of **1** is not promoted by acetophenone, benzene, and naphthalene, and is not inhibited by 1,3-pentadiene (Fig. 1). These results indicate that the photo-methoxylation proceeds *via* a singlet excited state. Anisole, naphthalene, ferrocene, nitrobenzene, and 1,2,4,5-tetracyanobenzene, which can be expected to undergo electron transfer type interactions, have no promoting effect.

Effects of Pyridine Derivatives on Photo-methoxylation of ***1****.* The results of a systematic survey of effects of pyridine derivatives on photo-methoxylation of **1** are shown in Table 2. It should be noted that 4-substituted pyridines

Table 2. Effects of substituted pyridines and related compounds on photo-methoxylation of methyl 2-pyridinecarboxylate (**1**) $[H_2SO_4]=5\times10^{-2}$ mol dm^{-3}; Irradiated with 254 nm light.

Additive	10^3 [**1**] / mol dm^{-3}	10^3 [Additive] / mol dm^{-3}	*L*	*Y*	*A*
2-Methylpyridine	1.0	0.1	0.89	0.92	1.03
	1.0	1.0	0.46	0.59	1.28
2-Pyridinol	1.0	0.2	0.92	0.86	0.93
	1.0	1.0	0.70	0.38	0.55
2-Pyridinamine	1.0	0.2	0.98	1.1	1.1
	1.0	1.0	0.90	0.97	1.1
2-Pyridinecarboxamide	1.0	0.2	0.85	0.77	0.91
	1.0	1.0	0.53	0.44	0.83
2-Pyridinecarbonitrile	1.0	1.0	0.62	0.56	0.90
2-Acetylpyridine	1.0	1.0	0.38	0.19	0.50
3-Methylpyridine	0.25	1.0	0.23	0.0	0.0
3-Pyridinol	1.0	0.2	0.98	0.64	0.65
	1.0	1.0	0.90	0.58	0.64
3-Pyridinamine	1.0	0.2	0.67	0.58	0.87
	1.0	1.0	0.29	0.26	0.89
3-Pyridinecarboxamide	0.25	1.0	0.22	0.0	0.0
3-Pyridinecarbonitrile	1.0	1.0	0.61	0.59	0.97
4-Methylpyridine	0.4	0.2	0.50	0.75	1.5
	0.4	1.0	0.17	0.75	4.4
4-*t*-Butylpyridine	1.0	0.2	0.82	0.67	0.82
	1.0	1.0	0.48	0.37	0.77
4-Phenylpyridine	1.0	1.0	0.44	1.00	2.3
4-Benzylpyridine	1.0	1.0	0.43	0.50	1.2
4-Pyridinol	1.0	1.0	0.87	2.8	3.2
4-Pyridinamine	1.0	0.1	0.76	0.93	1.2
Methyl 4-pyirdinecarboxylate	1.0	0.1	0.93	4.2	4.5
	1.0	0.3	0.81	4.0	4.9
4-Pyridinecarboxamide	1.0	0.2	0.83	1.6	1.9
	1.0	1.0	0.49	1.2	2.4
4-Pyridinecarbonitrile	1.0	0.1	0.96	3.0	3.1
	1.0	1.0	0.71	7.4	10.4
4-Acetylpyridine	0.4	0.2	0.69	0.91	1.3
2, 2′-Bipyridine	1.0	0.1	0.89	0.58	0.65
4, 4′-Bipyridine	1.0	0.2	0.56	1.15	2.1
	1.0	1.0	0.21	2.21	10.5
Dimethyl 2, 4-pyridinedicarboxylate	1.0	0.1	0.97	1.8	1.9
	1.0	1.0	0.74	5.0	6.7
Dimethyl 2, 5-pyridiendicarboxylate	1.0	0.2	0.88	2.9	3.3
	1.0	1.0	0.60	3.1	5.2
Pyridazine	1.0	0.2	0.97	1.5	1.5
	1.0	1.0	0.85	2.1	2.4
Pyrimidine	1.0	0.2	0.94	0.99	1.1
	1.0	1.0	0.77	0.81	1.1
Pyrazine	1.0	0.1	0.91	1.1	1.2
	1.0	1.0	0.49	1.3	2.7

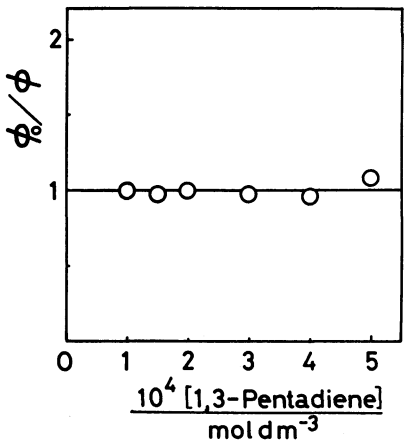


Fig. 1. Stern-Volmer plot for quenching of photo-methoxylation of methyl 2-p ridinecarboxylate (**1**) by 1,3-pentadiene. $[\mathbf{1}]=1.0\times10^{-3}$ mol dm^{-3}; $[H_2SO_4]=5\times10^{-2}$ mol dm^{-3}.

show remarkable promoting effects independently of the electron-accepting or electron-donating character of the substituents. Pyrazine and 4,4'-bipyridine, which can be regarded as analogs of 4-substituted pyridines, show high promoting effects.

Some 2-substituted pyridines accelerate the photo-methoxylation of **1**, but less effectively than 4-substituted pyridines. 3-Substituted pyridines have no promoting effects.

*Characteristics of Promotion by 4-Pyridinecarbonitrile (**3**).* Among 4-substituted pyridines, 4-pyridinecarbonitrile has a large promoting effect. In the methyl 2-pyridine-carboxylate (**1**)-4-pyridinecarbonitrile (**3**) system, the characteristics of the promotion was studied in detail. In Table 3, are shown the data of photosensitization by **3** at $[\mathbf{1}]=1.0\times10^{-3}$ mol dm^{-3} at various concentrations of **3** in the irradiation with 254 nm light. From Table 3 the following points should be noted.

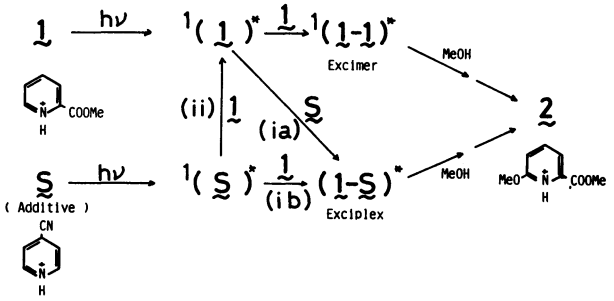
1) The additive, **3**, was recovered almost quantitatively. This means that **3** works as a "true catalyst" (not sacrificially). For example, we analyze the data of line 2 in Table 3. By the irradiation of the solution containing 10^{-3} mol dm^{-3} of **1** and 10^{-4} mol dm^{-3} of **3**, 2.5×10^{-5} mol dm^{-3} of **2** are formed and 5×10^{-7} mol dm^{-3} of **3** are consumed. The formation of **2** is 50 times greater than the consumption of **3**.

2) Both *A*-values, which are indices of promotion normalized on the basis of the light absorbed by **1**, and also *Y*-values, which are indices of promotion without the correction of light absorption are larger than 1.

3) The presence of **3** increases both the consumption of **1** and the selectivity for **3** (selectivity=[**2** formed]/[**1** reacted]). The combination of these two effects results in the large *A*- and *Y*-values.

The promotion by **3** is greater than that *via* self-catalysis by **1**: the addition of 10^{-3} mol dm^{-3} of **3** to 10^{-3} mol dm^{-3} of **1** increased the yield of **2** 7.4 times (in *Y*-value), while the yield of **2** at $[\mathbf{1}]=2\times10^{-3}$ mol dm^{-3} is only 1.23 times of the yield at $[\mathbf{1}]=1\times10^{-3}$ mol dm^{-3} at 32 °C.

Mechanism for Promotion by 4-Pyridinecarbonitrile. For the promotion of photo-methoxylation of **1** by additives, the following mechanisms are conceivable (Scheme 1).



Scheme 1.

(i) Mechanism *via* exciplex formation
It is subdivided into three categories:
(ia) Mechanism *via* an exciplex formed from an excited **1** and a ground state-additive
(ib) Mechanism *via* an exciplex formed from an excited additive and a ground state- **1**.
(ic) Mechanism in which (ia) and (ib) operate simultaneously.

(ii) Singlet energy transfer mechanism

As stated in the previous section, the photo-methoxylation is neither promoted by triplet sensitizer nor inhibited by triplet quencher. A triplet energy transfer mechanism is thus excluded.

The above postulated mechanisms were further examined in the **1**—**3** system.

Table 3. Dependence of promotion of photo-methoxylation of methyl 2-pyridinecarboxylate (**1**) on concentration of added 4-pyridinecarbonitrile (**3**) in irradiation with 254 nm light

Irradiation time, 2 min; $[\mathbf{1}]=1.0\times10^{-3}$ mol dm^{-3}; $[H_2SO_4]=5\times10^{-2}$ mol dm^{-3}.

10^4 [**3**] / mol dm^{-3}	*L*	10^5 [**2**] / mol dm^{-3}	10^5 [**1** reacted] / mol dm^{-3}	*Y*	*A*	[**2** formed] / [**1** reacted]	Recovery of **3** / %
0.0	1.00	0.84	2.3			0.36	
1.0	0.96	2.5	6.2	3.0	3.1	0.40	99.5
3.0	0.89	3.2	7.5	3.9	4.4	0.42	100
5.0	0.83	3.7	7.4	4.7	5.6	0.51	100
6.0	0.80	3.9	6.1	4.8	6.0	0.65	100
7.0	0.78	5.4	7.3	6.7	8.6	0.74	100
8.0	0.75	5.6	6.9	7.0	9.4	0.83	100
10.0	0.71	6.0	7.3	7.4	10.4	0.83	100

A singlet energy transfer mechanism (ii) can be excluded on the basis of the data in Table 3. *Y*-values in the **1**—**3** system are greater than 1. If Mechanism (ii) operates, *Y* can not exceed 1, because in the system, where all the incident light are completely absorbed by **1** and **3**, the sum of singlet excited states of **1** and **3** is constant and the number of the excited **1** in the presence of additive can not exceed the number of the excited **1** in the absence of additive, even if the efficiency of the singlet energy transfer is 100%.

In order to answer the question whether (ia), (ib), or (ic) is more plausible, the wavelength dependence of the promotion is studied. The spectra of **1** differ from those of **3**: 254 nm light is absorbed more efficiently by **1** (ε=4350) than by **3** (ε=1800), while 280 nm light is absorbed more efficiently by **3** (ε=4330) than by **1** (ε=1200).

If the promotion is effected *via* an exciplex from an excited **1** and a ground state- **3** (Mechanism (ia)), *A*-values at the different wavelengths should be the same. In Mechanism (ia), the fate of the excited **1** (to form an excimer (**1**—**1**)* or to form an exciplex (**1**—**3**)*) is determined by the concentrations of **1** and **3**. Therefore, *A*-value, which is the relative yield on the basis of the quantity of the excited **1**, should not change by varying the distribution of light absorption, as long as the concentrations of **1** and **3** remain the same. In Mechanism (ia), the *A*-value, however, should be dependent on the concentrations of **1** and **3**.

In Mechanism (ib) the *A*-value should depend on the wavelength and a higher *A*-value should be expected in the irradiation with light of a wavelength at which **3** absorbs more than **1**.

If the process (ia) and (ib) occur in parallel, the *A*-value for the wavelength at which light is absorbed less by **1** than **3** should be greater than that for the wavelength at which light is absorbed more by **1** than by **3**, because the light absorbed by **3** should be effective for the formation of **2**.

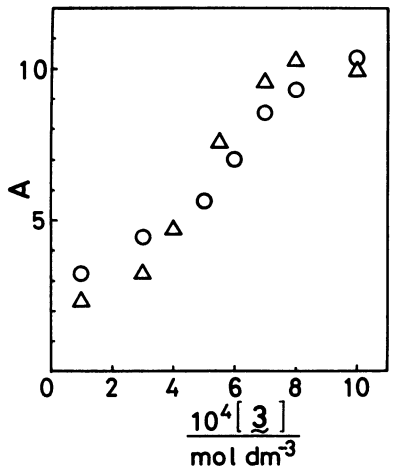


Fig. 2. Wavelength dependence of promotion of photo-methoxylation of methyl 2-pyridinecarboxylate (**1**) by 4-pyridinecarbonitrile (**3**).
Promoting effect is expressed in *A*-value. [**1**]=1.0×10^{-3} mol dm^{-3}. ○, Irradiated with 254 nm light. △, Irradiated with 280 nm light.

Figure 2 shows the wavelength dependence of the promotion of photo-methoxylation of **1** by **3**. The *A*-values in the irradiation at 254 nm light agree with those in the irradiation at 280 nm light in the region of 10^{-4}—10^{-3} mol dm^{-3} of [**3**]. This indicates that Mechanism (ia) should operate in the promotion of photo-methoxylation by **3**.

A question why an exciplex between **1** and **3** has higher reactivity for methoxylation than an excimer of **1** is difficult to answer. However, the higher reactivity of an exciplex could be partially ascribed to the greater polarity of an exciplex than an excimer: The polarity generated in a complex formed between different species should be greater than that in a complex formed from the same species. The greater polarity should result in the increase in the higher reactivity for ionic reaction.

Experimental

Materials. Commercial methyl 2-pyridinecarboxylate (GR grade reagent of Tokyo Kasei Co.) was purified by vacuum distillation (bp, 130—131 °C/27 mmHg, 1 mmHg ≈133.322 Pa). 4-Pyridinecarbonitrile (GR grade of Wako Junyaku Co.) was recrystallized from ether (mp, 82—83 °C). The other reagents used were commercial GR or EP grade reagents.

Preparation of Solution for Irradiation. Solutions (20 cm^3) containing **1** (normally [**1**]=1.0×10^{-3} mol dm^{-3}), sulfuric acid (normally [H_2SO_4]=5×10^{-2} mol dm^{-3}), and additive in methanol were deaerated by bubbling nitrogen through them for at least 45 min.

UV-Irradiation. For the irradiation with 254 nm light, a merry-go-round irradiation apparatus equipped with a 17 W low-pressure mercury lamp was employed. The merry-go-round apparatus was set up in a thermostat and the temperature was maintained at 25.5 °C. For 280 nm light irradiation, a monochrometer (made by Shimadzu-Bausch-Lomb Co.) equipped with a super-high-pressure mercury lamp was used. The resolution in our experimental condition was ±10.5 nm.

Quantitative Analyses. The quantities of **2** formed were determined either by spectrophotometric or by gas-chromatographic method.

i) For the spectrophotometric determination of **2**, its characteristic absorption at 287 nm was used. By means of the spectral method the following systems were analyzed: **1**–benzene, anisole, ferrocene, 1,2,4,5-tetracyanobenzene, nitrobenzene, 2-methylpyridine, 2-pyridinecarboxamide, 3-methylpyridine, 3-pyridinol, 3-pyridinecarboxamide, 3-pyridinecarbonitrile, 4-methylpyridine, 4-*t*-butylpyridine, 4-phenylpyridine, 4-benzylpyridine, 4-pyridinamine, 4-pyridinecarboxamide, 4-acetylpyridine, 2,2′-bipyridine, or pyrimidine.

ii) Gas-chromatographic method was applied for the analyses of the following systems: **1**–naphthalene, acetophenone, 2-pyridinol, 2-pyridinamine, 2-pyridinecarbonitrile, 3-pyridinamine, 4-pyridinol, methyl 4-pyridinecarboxylate, 4-pyridinecarbonitrile, 4,4′-bipyridine, dimethyl 2,4-pyridinedicarboxylate, dimethyl 2,5-pyridinedicarboxylate, or pyrazine.

A typical example applied for the analysis of the **1**—**3** system was done in the following way. After the irradiation, methanol was evaporated under reduced pressure. The solution was neutralized with aqueous $NaHCO_3$ solution and was extracted repeatedly with dichloromethane. The dichloromethane extract was analyzed gas-chromatographically in the following conditions: apparatus, Shimadzu GC-6A; column, 2 m column

of Triton QS-15 (15%) on Uniport B (60/80 mesh); column temperature, 160 °C; internal standard, 3-acetylpyridine.

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