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Change of Orientation in Photoreaction by Oxygen. Effect of Oxygen on Photo-methoxylation of Dimethyl Esters of 2,4- and 3,4-Pyridinedicarboxylic Acid

Toru Sugiyama,* Mitsuharu Kanai, Setsuko Takenaka, and Akira Sugimori*
Department of Chemistry, Faculty of Science and Technology, Sophia University, Kioi-cho 7-1, Chiyoda-ku, Tokyo 102
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Synopsis. The UV-irradiation of dimethyl 2,4- and 3,4-pyridinedicarboxylates in methanol in the presence of H_2SO_4 under O_2 brings about methoxylation at the β- position of the pyridine ring, while under N_2 methoxylation occurs at the α-position.

In a preceding paper,[1] we described a remarkable effect of oxygen on the photoreaction of methyl 4-pyridinecarboxylate in methanol: Even a small amount of oxygen causes a change of orientation in the photomethoxylation. The role of oxygen cannot be explained by any generally accepted effect (the acceleration of intersystem crossing or charge-transfer interaction). To survey the scope of this novel types of effect, we have studied the effect of oxygen on the photoreactions of dimethyl pyridinedicarboxylates in acidic methanolic solutions.

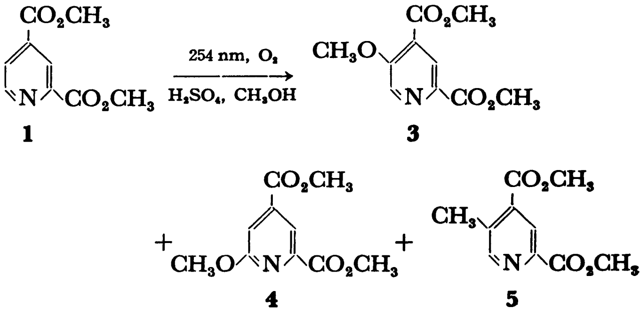
Results and Discussion

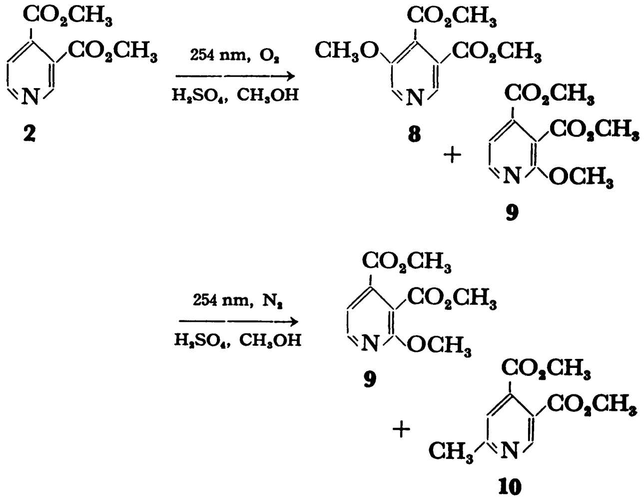
Photoreactions in the Presence or in the Absence of O_2. Similar to the photoreaction of 4-pyridinecarboxylic ester, the photoreactions of dimethyl pyridinedicarboxylates show a remarkable oxygen effect: Oxygen causes the change of the position of methoxylation at the α-position of the pyridine ring into that at the β-position.

UV-irradiation of dimethyl 2,4-pyridinedicarboxylate (**1**) under N_2 in methanol in the presence of H_2SO_4 brings about methoxylation mainly at the 6-position of the pyridine ring (**4**), accompanied by the methylation at the 5- and 6-positions (**5**),(**6**) and hydroxymethylation at the 6-position (**7**) in low yields (Table 1).[2]

On the other hand, under O_2 these reactions are supperssed and the methoxylation at the 5-position (**3**) predominates (Table 1).

Dimethyl 3,4-pyridinedicarboxylate (**2**) undergoes photo-methoxylation at the 5-position (**8**) under O_2, while under N_2 the methoxylation occurs only at the 2-position (**9**), accompanied by methylation at the 6-position (**10**) (Table 1).





Role of Oxygen for the Methoxylation at the β-Position. Similar to the case of 4-pyridinecarboxylic ester in the photo-methoxylation at the β-position,[1] oxygen does not serve as an oxidant in the methoxylation at the β-position of pyridinedicarboxylic esters because after the irradiation of **1** under N_2 the addition of $K_3[Fe(CN)_6]$ or bubbling oxygen has no effect on the formation of the methoxylated product at the 5-position (Table 1).

Table 1. Photoreactions of **1** and **2** in methanol in the presence of H_2SO_4[a]

Diester	Atmosphere	Conversion %	Additive	Yield of product/%[b] 3	4	5	6	7	8	9	10
1	O_2	16	—	9	4	0.4	0	0	—	—	—
1	N_2	20	—	0	12	4	0.7	4	—	—	—
1	N_2	20	O_2(bubbled)[c]	0	12	4	0.3	4	—	—	—
1	N_2	20	$K_3[Fe(CN)_6]$[d]	0	12	4	0.2	4	—	—	—
1	N_2	2	Ph_2CO(365 nm)[e]	0	0	0	0	0	—	—	—
2	O_2	23	—	—	—	—	—	—	3	5	0
2	N_2	24	—	—	—	—	—	—	0	11	1

a) [**1**]=[**2**]=0.01 mol dm^{-3}; [H_2SO_4]=1.0 mol dm^{-3}; Irradiation time, 1 h; Temp., 30 °C. b) Yields are based on the amount of **1** and **2** consumed. c) O_2 was bubbled after the irradiation. d) $K_3[Fe(CN)_6]$ was added after the irradiation. e) [Ph_2CO]=0.05 mol dm^{-3}; irradiated for 2.5 h with a 100 W high pressure mercury lamp through 365 nm filter.

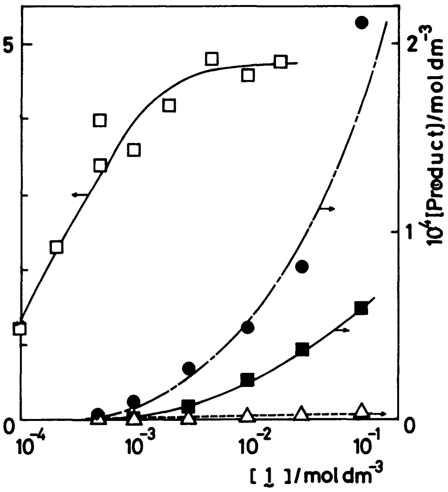


Fig. 1. Dependences of the photoreactions of **1** under O_2 and under N_2 on the concentration of **1**.
-●---: **3**; -■—: **4**; --△---: **5** (under O_2); -□—: **4** (under N_2).

When the irradiation of **1** with 365 nm light was carried out in the presence of benzophenone under N_2, the methoxylation at the 5-position was not observed as is shown in Table 1. *trans*-1,3-Pentadiene, a triplet quencher, does not quench the reaction. These facts indicate that the methoxylation at the β-position occurs from an excited singlet state of the pyridinium form of **1** and thus oxygen does not accelerate the intersystem crossing from the excited singlet state to the triplet excited state.

Because the UV-absorption spectra of **1** in acetonitrile were not markdly affected by oxygen, it is concluded that under these conditions the contribution of a ground state contact charge-transfer complex between the protonated **1** and O_2 is very improbable. Similar oxygen effects were also observed in the photomethoxylation at the β-position of 4-pyridinecarboxylic ester.[1]

Since the methoxylation at the 6-position of **1** under N_2 shows the dependence on the concentration of the substrate, the reaction may proceed *via* an excimer.[2] The methoxylation of **1** at the 6- and 5-positions under O_2 are also more dependent on the concentration of the substrate over the range of higher concentration than that under N_2 as are shown in Fig. 1. It is noteworthy that the concentration dependence curves of the methoxylations are not reduced by oxygen but are shifted to the region of higher concentrations in the presence of oxygen. These results indicate that the decrease of the methoxylation at the 6-position is not due to the quenching of the excimer by oxygen. The participation of another excited complex in the reaction can be presumed. It may be an excited terplex which consists of two molecules of protonated **1** and one molecule of oxygen.

Experimental

Materials. Dimethyl pyridinedicarboxylates (**1**, **2**) were synthesized by the esterification of pyridinedicarboxylic acids with methanol in the presence of hydrogen chloride.

UV-irradiation. Through the solutions of **1** or **2** (0.01 mol dm^{-3}) containing 1.0 mol dm^{-3} of H_2SO_4, O_2, or N_2 were bubbled for 45 min before irradiation. The solutions were irradiated with a 17 W low pressure mercury lamp at 30 °C.

Isolation and Identification of Photo-products. After the irradiation, the solutions were concentrated under reduced pressure, were neutralized with sodium carbonate, and were extracted with ethyl acetate. The products were separated by means of TLC (plate, GF_{254} (Type 60) of E. Merck Co.; developing solvent, ethyl acetate–dichloromethane 1:4) or by means of GLC (column, PEG 20 M 2%, 2 m on Celite 545 (60/80 mesh); Temp., 200 °C) with a Ohkura gas chromatograph model GC 103.

Dimethyl 5-methoxy-2,4-pyridinedicarboxylate (**3**), mp 142—144 °C; ^{1}H NMR ($CDCl_3$) δ=8.52 (1H, s, H at 6-position), 8.42 (1H, s, H at 3-position), 4.09 (3H, s, OCH_3), 3.99 and 3.94 (6H, s, CO_2CH_3); IR (KBr) 1726 and 1714 (ester C=O) and 1255 cm^{-1} (C–O–C); MS (70 eV), *m/z* (rel intensity), 225 (M^+; 11), 195 (14), 194 (18), 167 (100), and 166 (18). Found: *m/z* 225.0649. Calcd for $C_{10}H_{11}NO_5$: M, 225.0636; Found: C, 53.01; H, 5.02; N, 6.38%. Calcd for $C_{10}H_{11}NO_5$: C, 53.33; H, 4.92; N, 6.22%.

Other photo-products of **1** (**4**—**7**) see Ref. 2.

Dimethyl 5-methoxy-3,4-pyridinedicarboxylate (**8**), mp 67—68 °C (lit,[3] 78—80 °C); ^{1}H NMR ($CDCl_3$) δ=8.82 (1H, s, H at 2-position), 8.48 (1H, s, H at 6-position), 3.93 (3H, s, OCH_3), 3.90 and 3.88 (6H, s, CO_2CH_3); IR (KBr), 1750 and 1730(ester C=O) and 1245 cm (C–O–C); MS (70 eV), *m/z* (rel intensity), 225 (M^+; 37), 194 (100), 193 (21), 166 (24), and 135 (20). Found: *m/z* 225.0637.

Dimethyl 2-methoxy-3,4-pyridinedicarboxylate (**9**), mp 48—51 °C; ^{1}H NMR ($CDCl_3$) δ=8.24 (1H, d, *J*=5 Hz, H at 6-position), 7.32 (1H, d, *J*=5 Hz, H at 5-position), 3.96 (3H,s,OCH_3), 3.90 and 3.87 (6H, s, CO_2CH_3); IR (KBr), 1730 (ester C=O) and 1270 cm^{-1}(C–O–C); MS (70 eV), *m/z* (rel intensity), 225 (M^+; 43), 195 (11), 194 (100), 193 (31), 180 (39), and 135 (31). Found: *m/z* 225.0637. Calcd for $C_{10}H_{11}NO_5$: M, 225.0636; Found: C, 53.23; H, 5.04; N, 6.18%. Calcd for $C_{10}H_{11}NO_5$: C, 53.33; H, 4.92; N, 6.22%.

Dimethyl 6-methyl-3,4-pyridinedicarboxylate (**10**), mp 63—64 °C; ^{1}H NMR ($CDCl_3$) δ=8.96 (1H, s, H at 2-position), 7.30 (1H, s, H at 5-position), 3.93 and 3.90 (6H, s, CO_2CH_3), and 2.65 (3H, s, CH_3); IR (KBr), 1742 and 1720 cm^{-1} (ester C=O); MS (70 eV), *m/z* (rel intensity), 209 (M^+; 19), 208 (12), 179 (24), 178 (100), and 150 (11). Found: *m/z* 209.0691.

Qunatitative Analysis of Photo-products. The yields of the products were determined by means of HPLC (column, 4.0 mm×25 cm column of Lichrosorb RP-18, 7 μm: eluent, H_2O–CH_3CN 8:2 or 81:19 v/v) with a Shimadzu liquid chromatograph model LC 3A or with a Hitachi model 655 and/or by means of GLC (column, PEG 20 M 5%, 1 m on Celite 545 (60/80 mesh)) with a Shimadzu gas chromatograph model GC 6A.

Spectral Measurements. ^{1}H NMR spectra were recorded on a Hitachi R 22 NMR spectrometer (90 MHz) with tetramethylsilane as an internal standard and IR spectra were measured on a Hitachi 260—50 spectrometer. Mass spectra were determined with a JEOL D-300 spectrometer. UV spectra were recorded on a Hitachi 228 spectrophotometer.

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