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Oxygen-Dependent Photoreactions of 3-Substituted *N*-Methylpyridinium in Methanol

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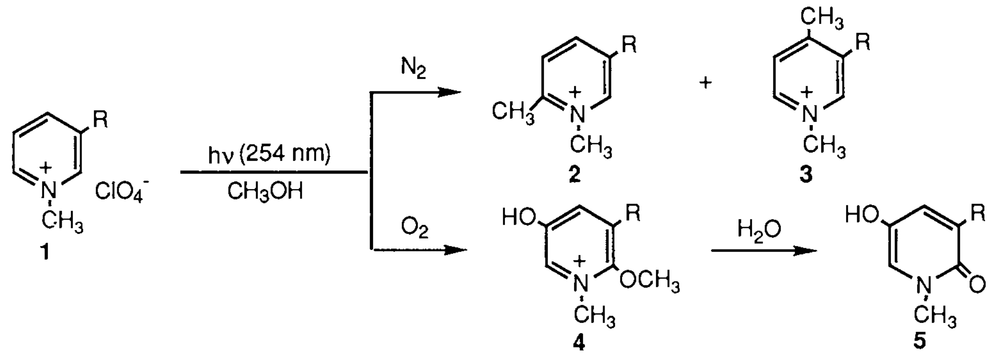
The photoreactions of 3-methoxycarbonyl-*N*-methylpyridinium perchlorate (**1a**) and 3-carbamoyl-*N*-methylpyridinium perchlorate (**1b**) under N_2 give the products methylated at the 6- and 4-positions in methanol. Under O_2, the photoreaction of **1a** is drastically changed to give a product methoxylated at the 2-position and hydroxylated at the 5-position simultaneously. This compound is unstable and changes to 5-hydroxy-3-methoxycarbonyl-*N*-methyl-2-pyridone (**5a**). Only one atom of O_2 is incorporated in **5a**. The photoreaction of **1b** is completely inhibited by O_2.

We previously reported that the photoreactions of methyl 4-pyridinecarboxylate in alcohol in the presence of sulfuric acid are affected drastically by O_2. Under N_2, methoxylation or hydroxymethylation occurs at the 2-position, while under O_2, methoxylation selectively occurs at the 3-position.[1] Several photochemical studies of 3-substituted-*N*-alkylpyridinium salts as NAD^+ models have been reported. Matsuura *et al.* showed that the UV-irradiation of 3-carbamoyl-*N*-benzylpyridinium chloride in aqueous ammonia in the presence of ascorbic acid gives the corresponding 1,4-dihydronicotinamide as the major product.[2] It is also known that the UV-irradiation of 3-carbamoyl-*N*-methylpyridinium in an aqueous solution gives 3-carbamoyl-*N*-methyl-2-pyridone.[3] We reported that the irradiation of 3-pyridinecarboxamide and methyl 3-pyridinecarboxylate in alcohol in the presence of sulfuric acid brings about alkylation and alkoxylation simultaneously under N_2.[4,5] However, the effects of oxygen on the photoreactions of these 3-substituted pyridines have not been taken into account. We report here that O_2 causes drastic changes of the photoreactions of 3-methoxycarbonyl-*N*-methylpyridinium perchlorate (**1a**), 3-carbamoyl-*N*-methylpyridinium perchlorate (**1b**), and methyl 3-pyridinecarboxylate (**1c**) in methanol.

The compound **1a** ([**1a**] = 2×10^{-2} mol dm^{-3}) was irradiated in methanol with a low pressure mercury lamp under N_2 or O_2. Under N_2, methylation occurred effectively at the 6- and 4-positions (formation of **2a** and **3a**)[6] in 55 and 40% yields, respectively. The experiment using CD_3OD indicated that the incorporated methyl group derived from methanol. Under O_2, the photoreaction of **1a** is drastically changed to give 5-hydroxy-3-methoxycarbonyl-*N*-methyl-2-pyridone (**5a**)[7] as the final product in 44% yield. However, the ^1H and ^{13}C NMR and FABMS of the sample observed immediately after the irradiation suggested the intermediary formation of 5-hydroxy-2-methoxy-3-methoxycarbonyl-*N*-methylpyridinium (**4a**) (Eq.1).[8] The yield of **4a** was estimated to be 42% on the basis of ^1H NMR. This value is similar to that of **5a** (44%). It was also found that the UV-irradiation of **1c** in methanol in the presence of sulfuric acid gave 5-hydroxy-2-methoxy-3-methoxycarbonyl-pyridine (**4c**)[9] as a stable product in 19% yield. These results support the conclusion that **4a** is the primary photoproduct of **1a**. The experiment using CD_3OD indicated that the incorporated methoxy group derived from methanol. UV-irradiation of the amide **1b** under N_2 gave methylated products at the 6- and 4-positions (formation of **2b** and **3b**)[10] in 18 and 14% yields, respectively (Table 1). But under O_2, no photoreaction occurred.



(1)

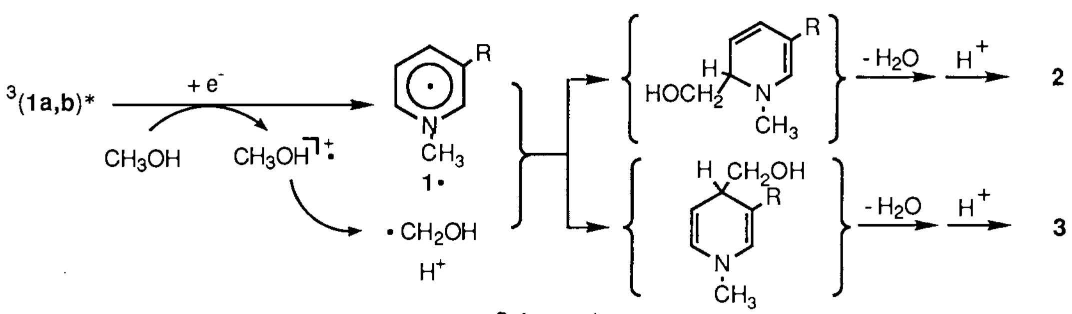
Table 1. Photoreaction of **1** in methanol

R	10^2[1] mol dm^{-3}	Atmosphere	Irrad.time min	Conversion %	Yield /%[a)] 2	3	4
1a:CO_2CH_3	2.0	N_2	60	11.4	55	40	0
1a:CO_2CH_3	2.0	O_2	60	22.4	0	0	42
1b:$CONH_2$	0.8	N_2	120	29.4	18	14	0
1b:$CONH_2$	0.8	O_2	120	5.8	0	0	0

a) Yields were determined on the basis of **1** consumed.

Broad emissions from **1a**, **1b**, and **1c** were observed at 77 K in methanol with the peak around 400 nm. These spectra are very similar to the phosphorescences from the triplet π-π* state of pyridinium cations which were reported by Motten and Kwiram.[11] Therefore, we assign the emissions to the phosphorescence from the triplet π-π* state of **1**. No fluorescence from **1a**-**1c** was observed. After UV-irradiation of **1a-c** in methanol at 77 K, the ESR signals of hydroxymethyl radical[12] (g=2.003, hfsc=1.8 mT, 1: 2: 1) were observed.

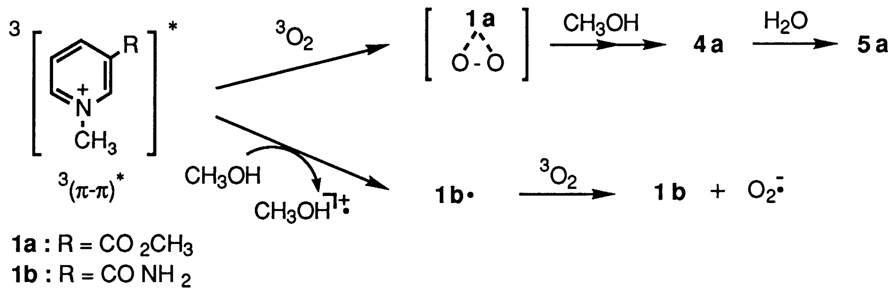
A possible mechanism of methylation under N_2 is as follows. The electron transfer occurs from methanol to the excited triplet π-π* state of **1a** or **1b** to generate 3-methoxycarbonyl-*N*-methylpyridinyl radical (**1a·**) or 3-carbamoyl-*N*-methylpyridinyl radical (**1b·**) and hydroxymethyl radical. Pyridinyl radicals and hydroxymethyl radical combine to form the photoproducts **2** and **3** *via* dehydration (Scheme 1).



Scheme 1.

Concerning the photoreaction of **1a** under O_2, the incorporation of oxygen is important. We carried out a label experiment by the use of labeled O_2; its ^{18}O abundance $[^{18}O/(^{16}O+^{18}O)]$ is 54%. The peak at M+4 (*m/z* =187) in the MS of **5a** was not detected and the M+2 peak was detected. The ratio of the intensity of the M+2 peak (*m/z* =185) to the sum of intensities of the M+2 peak and the M peak (*m/z* =183) was 0.54. This indicates that one atom of O_2 is incorporated in the photoproduct **5a**. Interestingly, the participation of O_2 in the photoreaction of **1a** is quite different from that of methyl 4-pyridinecarboxylate in alcohol in the presence of sulfuric acid.[1] In the latter case, the bubbled oxygen was not incorporated in the photoproduct. The photooxygenation of **1a** was not initiated by the singlet oxygen ($^1O_2$) or by the superoxide radical anion ($O_2^{\cdot-}$); the irradiation of methylene blue and rose bengal did not induce any reaction in this system.[13]

In the photoreaction of **1a**, the ground-state oxygen ($^3O_2$) may trap the excited triplet π-π^* state of **1a** which has a biradical character, before the electron transfer occurs from methanol to the excited **1a**. Then the formed peroxide of **1a** is attacked by methanol to generate **4a** and water. Therefore, one atom of O_2 is incorporated in the photoproduct **4a** and the other oxygen atom is eliminated as water. Compound **4a** undergoes hydrolysis to give **5a**. In contrast, amide **1b** undergoes no photoreaction under O_2. This may be due to the difference in the reactivities of excited triplet state of **1a** and excited triplet state of **1b**. In the photoreaction of **1b**, $^3O_2$ does not trap the excited triplet π-π^* state of **1b** for some as yet unknown reason. So the electron transfer would occur from methanol to the excited triplet π-π^* state of **1b** to generate **1b**·. The radical **1b**· is a relatively strong reducing agent and reacts with O_2 to generate the parent compound **1b** and $O_2^{\cdot-}$,[14] the latter of which is unreactive towards **1b** (Scheme 2). The detailed analyses of the reactions under O_2 are in progress.



Scheme 2.

References

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4) A. Sugimori, E. Tobita, Y. Kumagai, and G. P. Sato, *Bull. Chem. Soc. Jpn.*, **54**, 1761 (1981).
5) A. Sugimori, H. Itoh, M. Kanai, and N. Itoh, *Bull. Chem. Soc. Jpn.*, **61**, 2832 (1988).
6) 6-Methyl-3-methoxycarbonyl-*N*-methylpyridinium (**2a**) : ^{1}H NMR (CD_3OD) δ =2.90 (3H, s, CH_3), 4.02 (3H, s, $COOCH_3$), 4.36 (3H, s, *N*-CH_3), 8.09 (1H, d), 8.83 (1H, d), 9.37 (1H, s). 4-Methyl-3-methoxycarbonyl-*N*-methylpyridinium (**3a**) : ^{1}H NMR (CD_3OD) δ =2.88 (3H, s, CH_3), 4.00 (3H, s, $COOCH_3$), 4.40 (3H, s, *N*-CH_3), 8.00 (1H, d), 8.79 (1H, d), 9.27 (1H, s).

7) 5-Hydroxy-3-methoxycarbonyl-*N*-methyl-2-pyridone (**5a**) : mp 92 °C; UV (CH_3OD) 287 nm (ε, 6800 cm^{-1} mol^{-1} dm^3); IR (KBr disk) 1716, 1654, 1614, 1325, 1244, and 1090 cm^{-1}; ^1H NMR (CD_3OD) δ =3.68 (3H, s, $COOCH_3$), 3.87 (3H, s, *N*-CH_3), 6.92 (1H, s, OH), 7.31 (1H, d, *J*=2.3 Hz, H at the 4-position), 7.79 (1H, d, *J*=2.3 Hz, H at the 6-position); ^{13}C NMR ($CDCl_3$) δ =38.0, 52.2, 110.6, 112.4, 133.3, 145.3, 159.5, and 164.9; MS (70 eV) *m/z* (rel intensity) 183 (M^+; 84), 152 (100), 124 (23), and 68 (35). Found: C, 52.33; H, 4.87; N, 7.30%; M^+,183. Calcd for $C_8H_9NO_4$: C, 52.46; H, 4.95; N, 7.65%; M, 183.

8) Compound **4a** could not be isolated, but its ^1H and ^{13}C NMR and FABMS could be selected in the spectra of the reaction mixture. The spectra which are ascribed to **4a** are as follows: ^1H NMR (CD_3OD) δ =3.97 (3H, s, $COOCH_3$), 4.09 (3H, s, *N*-CH_3), 4.61 (3H, s, OCH_3), 8.12 (1H, d, *J*=1.9 Hz, H at the 4-position), and 8.61 (1H, d, *J*=1.9 Hz, H at the 6-position); FABMS *m/z* 198 (M^+), 183, 152, and 139.

9) Methyl 5-hydroxy-2-methoxypyridinecarboxylate (**4c**), a photoproduct from protonated methyl 3-pyridinecarboxylate was isolated and was identified on the bases of the spectra and elemental analysis. mp 143 °C; IR (KBr disk) 1722, 1608, 1450, 1419, 1311, and 1269 cm^{-1}; ^1H NMR (CD_3CN) δ = 3.84 (3H, s, $COOCH_3$), 4.01 (3H, s, OCH_3), 7.08 (1H, br-s, OH), 7.54 (1H, d, *J*=2.0 Hz, H at the 4-position), and 8.30 (1H, d, *J*=2.0 Hz, H at the 6-position); MS (70 eV), *m/z* (rel intensity) 183 (M^+;100), 152 (57) and 124 (19). Found: C, 52.22; H, 5.04; N, 7.72%; M^+,183. Calcd for $C_8H_9NO_4$: C, 52.46; H, 4.95; N, 7.65%; M, 183.

10) 6-Methyl-3-carbamoyl-*N*-methylpyridinium (**2b**) : ^1H NMR (CD_3OD) δ =2.72 (3H, s, CH_3), 4.36 (3H, s, *N*-CH_3), 7.98 (1H, d), 8.97 (1H, d), 8.94 (1H, s). 4-Methyl-3-carbamoyl-*N*-methylpyridinium(**3b**): ^1H NMR (CD_3OD) δ =2.89 (3H, s, CH_3), 4.33 (3H, s, *N*-CH_3), 8.07 (1H, d), 8.79 (1H, d), 9.28 (1H, s).

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13) P. C. Lee and M. A. J. Rodgers, *Photochem. Photobiol.*, **45**, 79 (1987): they showed that the irradiation of methylene blue and rose bengal in solution produces not only $^1O_2$ but also $O_2^{\cdot-}$.

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