REACTIONS OF 2-ACYLPYRIDINE 1-OXIDES WITH ACID ANHYDRIDES

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Abstract——Treatment of 2-acetyl- and 2-propionyl-pyridine 1-oxides (**1a** and **1b**) with hot acetic, propionic and benzoic anhydrides initially gives the respective enol acylates (**A**), which further undergo deoxygenative β-acyloxylation to give enediol diacylates (**E**) and ketol esters (**F**).

We recently reported on 2-acylation of nicotinic acid and N-acetyl-N-methylnicotinamide 1-oxides (**I** and **II**) with hot acetic or propionic anhydride, and showed that, while the 2-acetylation product of **I** (**III**) was isolated as such, the 2-propionylation product of **I** (**IV**) and the 2-acetylation product of **II** (**V**) further reacted with the acid anhydride to give deoxygenative β-acyloxylation products (**VI** and, **VII** and **VIII**, respectively) as shown in Chart 1.[1,2]

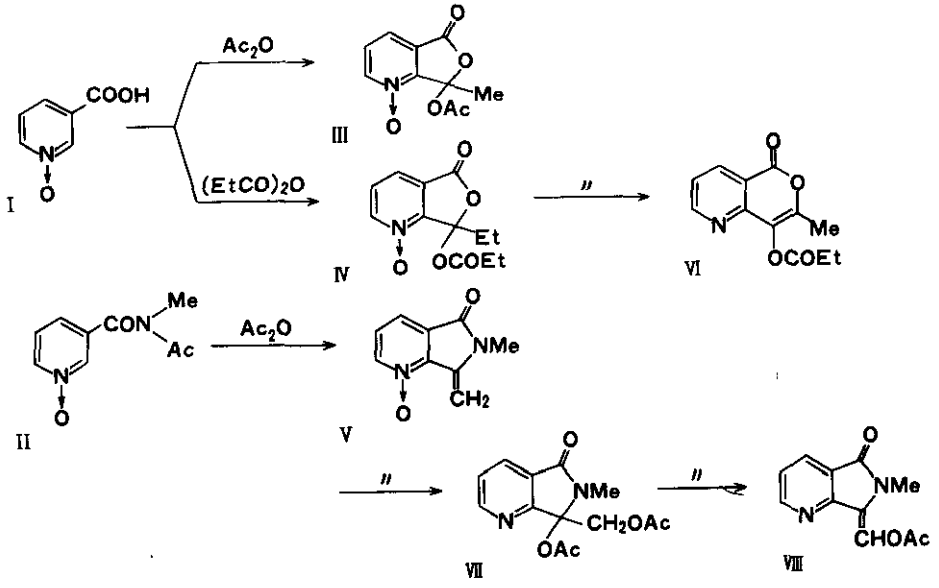
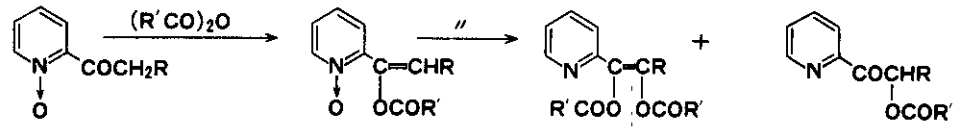


Chart 1

The mechanistic cosiderations[1,2] of these reactions suggest the possibility that enol derivatives of 2-acylpyridine 1-oxides or the N-oxides themselves might undergo the reaction of the same pattern when heated with acid anhydrides. In order to explore this possibility, we investigated reactions of 2-acetylpyridine 1-oxide[3] (**1a**) and 2-propionylpyridine 1-oxide (**1b**) with acid anhydrides, and found that the anticipated reactions took place as summarized in Table.

Table. Reactions of 2-Acylpyridine 1-Oxides with $(R'CO)_2O$



1a: R=H
1b: R=Me

A **E** **F**

No.	N-Oxide[a] (R)	$(R'CO)_2O$ R' (ml)	Reaction Temp.(°C)	Time(h)	Product(%) A	E	F
1[b]	**1a**(H)	Me (15)	70 100-110	0.5 1.0	**2a**, 19.7	**3a**, 4.8	**4a**, 8.6
2	**1a**(H)	Me (20)	140	2.0	**2a**[c]	**3a**, 11.7	**4a**, 35.9
3	**1a**(H)	Et (20)	120-125	1.5	**5a**[d]	**6a**, 6.8	**7a**, 7.5
4[e]	**1a**(H)	Et (20)	140	2.0	——	**6a**, 5.4	**7a**, 16.5
5	**1a**(H)	Ph (15 g)	125	5.0	——	**9a**, 16.5	**10a**, 28.8
6	**1b**(Me)	Me (5)	130	2.0	**2b**, 26.6	——	**4b**, 36.1
7	**1b**(Me)	Et (8)	115-125	3.0	**5b**, 34.1	**6b**[f]	**7b**, >21.6

a) Reactions were carried out using 1.37 g(10 mmol) of **1a** (No.1-5) or using 453 mg (3 mmol) of **1b**. b) With a 53.5% recovery of **1a**. c) A minute amount. d) It was obtained as a mixture with **1a**, but its isolation failed. e) With a 22.8% recovery of **1a**. f) A mixture of **6b** and **7b** was obtained in addition to **5b** and **7b**, and it was converted into **7b** (15.1%) by heating with water.

Preparation of **1a** and **1b** was achieved in reasonable yields (51.5 and 39.5%, respectively) by treatment of the corresponding 2-acylpyridines with m-chloroperbenzoic acid (m-CPBA) in chloroform at room temperature for 0.5 h and then under reflux for 0.5 h.[4] These N-oxides are fairly unstable under basic conditions; thus, heating of **1a** in 20% sodium hydroxide for 10 min caused deacetylation to give pyridine 1-oxide in a high yield of 80%.

Heating of **1a** with excess acetic anhydride (Ac_2O) at 70°C for 0.5 h and then at

100-110°C for 1 h gave the enol acetate of **1a** (**2a**), 2-(1,2-diacetoxyvinyl)pyridine (**3a**) and acetoxymethyl 2-pyridyl ketone (**4a**) in the respective yields of 19.7, 4.8 and 8.6%, accompanied by a 53.5% recovery of **1a** (No.1). The reaction at 140°C for 2 h gave **3a** and **4a** in 11.7 and 35.9% yields, respectively, with minute amounts of **1a** and **2a** (No.2).

The reaction of the enol acetate **2a** with Ac_2O proceeded more smoothly and gave **3a** and **4a** in 18.1 and 50.3% yields, respectively, upon heating at 140°C for 1.5 h. The enol acetate **2a** was readily hydrolyzed to **1a** in hot water, whereas its formation from **1a** was effected rather with difficulty. Thus, treatment of **1a** with acetyl chloride in the presence of triethylamine in dichloromethane at -5—0°C for 0.5 h gave **2a** only in 10% yield; a higher temperature caused red coloration and gave an untractable mixture. Only a trace of **2a** was detected by TLC when **1a** was treated with Ac_2O in boiling chloroform. The enediol diacetate **3a** was easily transformed to **4a** (60%) upon heating in methanol-water (1:1) on a steam bath for 0.5 h (Chart2).

When **1a** was heated with propionic anhydride at 120-125°C for 1.5 h, the enediol dipropionate (**6a**; 6.8%) and the ketol ester (**7a**; 7.5%) were obtained together with a mixture (ca. 30%) of **1a** and the enol propionate (**5a**), the isolation of **5a** being unsuccessful because of its high instability (No.3). The reaction at 140°C for 2 h gave **6a** (5.4%) and **7a** (16.5%) with a 22.8% recovery of **1a** (No.4). The reaction of **1a** with benzoic anhydride proceeded in a similar way, and the enediol dibenzoate (**9a**) and the ketol ester (**10a**) were formed in 16.5 and 28.8% yeilds, respectively, when conducted at 125°C for 5 h (No.5). However, the reaction of **1a** with phenylacetic anhydride led to a complicated and untractable mixture.

As a part of exploration of the mechanism, the reaction of the enol benzoate of **1a** (**8a**) with Ac_2O was examined. As in the case of **2a**, **8a** was prepared in a low yield of 19.5% by treatment of **1a** with benzoyl chloride-triethylamine in dichloromethane at -5—0°C for 0.5 h and then at room temperature for 0.5 h. Heating of **8a** with Ac_2O at 130-135°C for 4 h resulted in the formation of 2-(2-acetoxy-1-benzoyloxyvinyl)pyridine (**11**), the enediol diacetate **3a** and the ketol ester **4a** in 20, 15 and 19.3% yields, respectively. Product **11** is a pale yellow oil, and its structure was deduced from the nmr spectrum ($CDCl_3$) which showed a three-proton singlet at δ 2.12 and ten-proton multiplet in the aromatic region, and from its conversion into **4a** upon refluxing in 50% acetic acid for 3 h (Chart 2).

Similar reactions occurred also with 2-propionylpyridine 1-oxide (**1b**). The reac-

tion with Ac_2O at 130°C for 2 h gave the enol acetate (**2b**; 26.6%) and the ketol ester (**4b**; 36.1%), the corresponding enediol diacetate (**E**: R=Me, R'=Me) being not detected (No. 6). The reaction with propionic anhydride at 115-125°C for 3 h gave the enol propionate (**5b**; 34.1%), the ketol ester (**7b**; 21.6%) and a mixture of the enediol dipropionate (**6b**) and **7b**, which was converted to **7b** (15.1%) by heating with water (No.7).

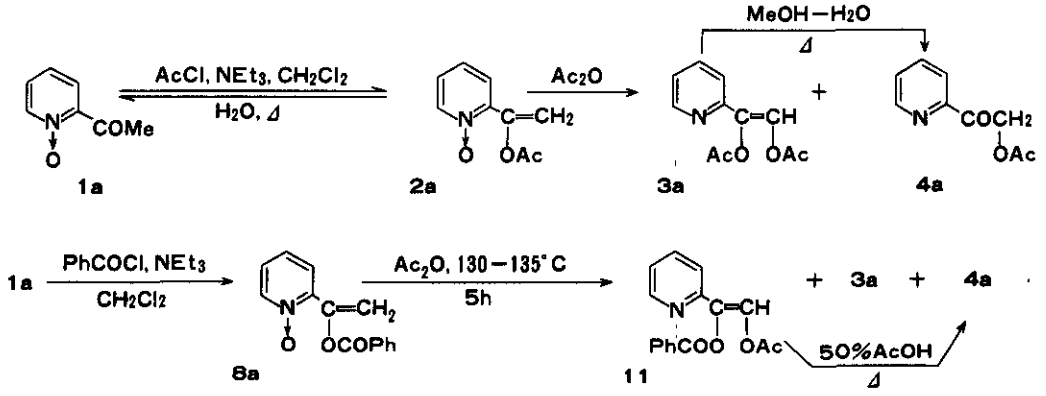


Chart 2

The structures of these products were assigned on the basis of the analytical and spectral data in the usual way. However, the configurations of the enol acylates of **1b** (**2b**, **5b**) and the enediol diacylates (**3a**, **6a**, **9a**, **11**) were not determined.

The reaction can be rationalized by deoxygenative β-acyloxylation as formulated in Chart 3. The initially formed enol acylate **A** undergoes conjugate addition of an acid anhydride (A_2O) to give an anhydro base **C** through an acyl-adduct **B**, and **C** rearranges to **D**. Elimination of acid (AOH) from **D** yields enediol diacylate **E**, and loss of acid anhydride (A_2O) leads to ketol ester **F**. This reaction pattern is evidently the same as that of the reactions of 2-styrylpyridine 1-oxide[5] and 4-styrylquinoline 1-oxide[6] with Ac_2O. However, an alternative path may be formally conceivable for the transformation of **C** to **E** as shown in Eq.(1) in Chart 4; this is a deoxygenative α-acyloxylation type reaction, and Eq.(1) corresponds to the elimination of acetic acid from 1,2-diacetoxy-1,2-dihydropyridine [Eq.(2)], and product **E** can be regarded as a deoxygenative γ-acyloxylation product of **A**. Nevertheless, we conclud that this deoxygenative α-acyloxylation process should be denied on the basis of the following three points. 1) 2-Acetylation product of **II**, **V**, reacts with Ac_2O to give not only **VIII** but also **VII** corresponding to **D**. 2) The formation of **3a** and **11** from **8a** and Ac_2O (Chart 2) may be well visualized by intermediacy of **D'** (Chart 3), although the acyl-exchange during the reaction can-

not be ruled out. 3) The β-acetoxystyryl-pyridine (G in Chart 4) or -quinoline was not noticed at all in reactions of 2-styrylpyridine and 4-styrylquinoline 1-oxides with Ac_2O.[5,6] As for the formation of F, the extrusion of acid anhydride from D seems preferable to hydrolysis of E during the reaction or work-up, in view of the intermediacy of D.

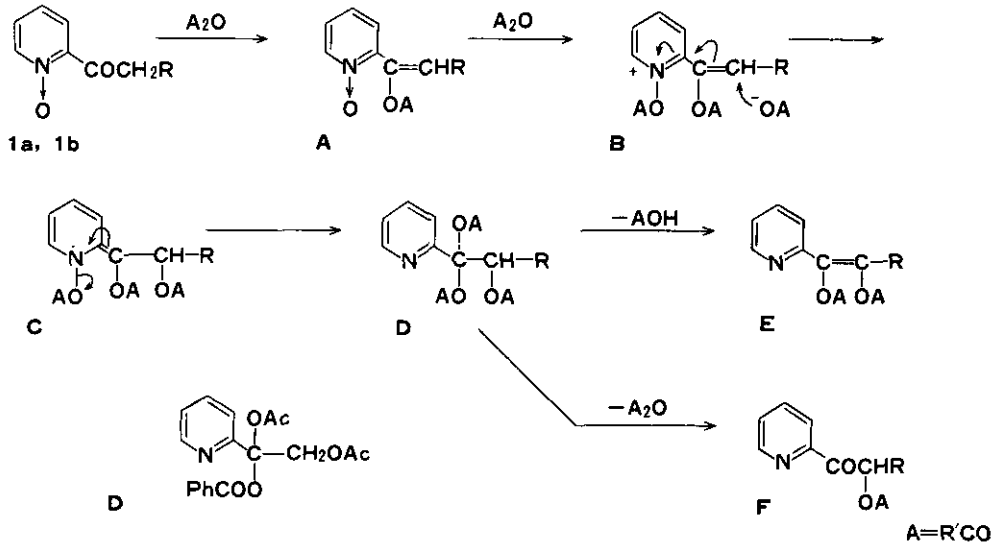


Chart 3

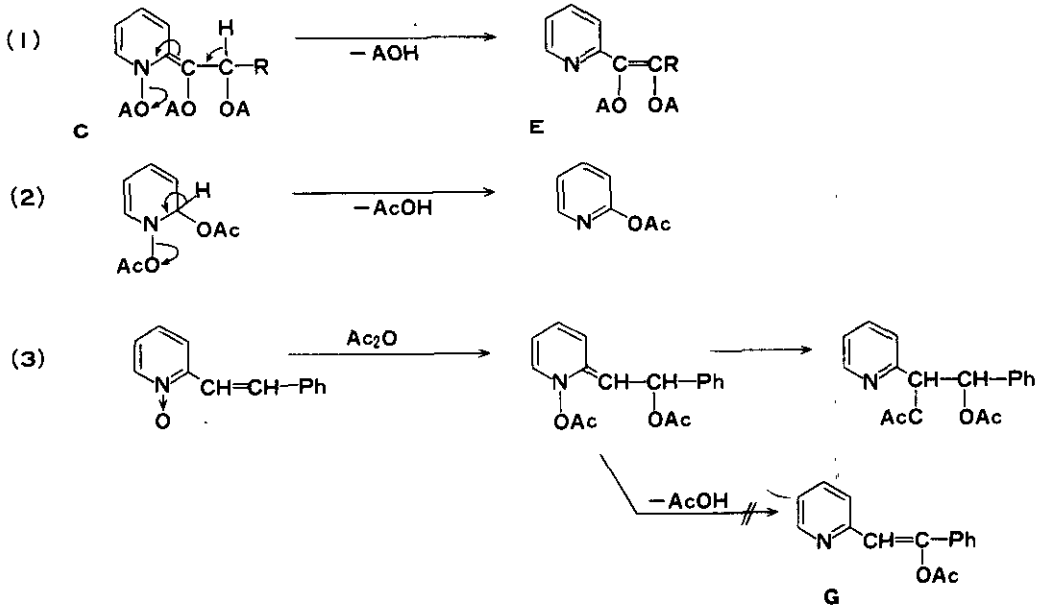


Chart 4

EXPERIMENTAL

Melting points were measured with a Yanagimoto micromelting point apparatus and a Mettler FP61 apparatus, and are uncorrected. Spectral data were recorded on the following instruments. Ir, Hitachi 260-30 infrared spectrophotometer; Ms, Shimadzu LKB 9000; Pmr and Cmr, JEOL FX-200. Column chromatography was carried out on Wako-gel C-200 (100-200 mesh).

2-Acetylpyridine 1-Oxide (**1a**) —— 1) A solution of 2-acetylpyridine (6.05 g) and m-CPBA (11 g) in $CHCl_3$ (50 ml) was stirred at room temperature for 0.5 h then refluxed for 0.5 h. The solvent was evaporated in vacuo, and the residue was shaken with ether (50 ml) and H_2O (50 ml). The separated ether layer was washed twice with H_2O, and the combined H_2O solutions were concentrated in vacuo, and the residue was purified by chromatography on silica gel with $CHCl_3$-MeOH to give 3.53 g (51.5%) of **1a**, a pale yellow oil. Ms m/z: 137 (M^+), 121 (M^+-16). Ir (neat): 1695 (C=O) cm^{-1}. Pmr ($CDCl_3$) δ: 2.76 (3H, s, CH_3), 7.19-8.31 (4H, m, Py-H). Cmr ($CDCl_3$) δ: 30.5 (q, CH_3), 125.6 (d), 126.6 (d), 128.2 (d), 140.5 (d), 146.8 (s, C_2), 194.9 (s, CO).

2) A mixture of **1a** (1.37 g) and 20% NaOH (15 ml) was heated on a steam bath for 10 min, then neutralized with 2N HCl, concentrated in vcuo and the residue was chromatographed on silica gel with $CHCl_3$-MeOH to give 0.76 g (80%) of pyridine 1-oxide.

2-Propionylpyridine 1-Oxide (**1b**) —— A solution of 2-propionylpyridine (4.05 g) and m-CPBA (6.5 g) in $CHCl_3$ (50 ml) was treated as mentioned above to give 1.79 g (39.5 %) of **1b**, a pale yellow oil. Ms m/z: 151 (M^+). Ir (neat): 1690 (C=O) cm^{-1}. Pmr ($CDCl_3$) δ : 1.19 (3H, t, J=7.2 Hz, CH_3), 3.21 (2H, q, J=7.2 Hz, CH_2), 7.13-8.23 (4H, m, Py-H). Cmr ($CDCl_3$) δ : 8.0 (q, CH_3), 36.3 (t, CH_2), 125.6 (d), 126.7 (d), 127.7 (d), 140.6 (d), 146.7 (s, C_2), 198.6 (s, CO).

General Procedure for Reaction of **1a** or **1b** with Acid Anhydrides —— A solution of **1a** (1.37 g, 10 mmol) or **1b** (453 mg, 3 mmol) in excess acid anhydride was heated under the conditions shown in Table. The reaction mixture was concentrated in vacuo and the residue was chromatographed on silica gel with $CHCl_3$-MeOH to give products.

2a (**A**: R=H, R'=Me): An oil. Anal. Calcd for $C_9H_9NO_3$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.18; H, 5.21; N, 7.79. Ms m/z: 179 (M^+), 163 (M^+-16). Ir (neat): 1760 (C=O) cm^{-1}. Pmr ($CDCl_3$) δ : 2.23 (3H, s, CH_3), 5.44 (1H, s, =CH), 6.36 (1H, s, =CH), 7.0-7.7 (3H, m, Py-H), 8.0-8.3 (1H, Py-H). Cmr ($CDCl_3$) δ : 20.6 (q, CH_3), 111.5 (t, $=CH_2$), 124.9 (d), 125.2 (d), 125.5 (d), 140.8 (d), 143.2 (s), 145.1 (s), 168.5 (s, CO).

3a (**E**: R=H, R'=Me): An oil. Anal. Calcd for $C_{11}H_{11}NO_4$: C, 59.73; H, 5.01; N, 6.33.

Found: C, 60.07; H, 5.09; N, 6.62. Ms m/z: 221 (M^+). Ir (neat): 1760 (C=O) cm^{-1}. Pmr ($CDCl_3$) δ : 2.22 (3H, s, CH_3), 2.36 (3H, s, CH_3), 6.98-8.78 (4H, m, Py-H), 8.29 (1H, s, CH). Cmr ($CDCl_3$) δ : 20.5 (q, CH_3), 20.6 (q, CH_3), 118.3 (d), 122.9 (d), 128.1 (d), 134.1 (s, $=\overset{1}{C}-O$), 136.6 (d), 149.6 (d), 150.9 (s, C_2), 166.6 (s, CO), 167.8 (s, CO).

4a (**F**: R=H, R'=Me): An oil. Anal. Calcd for $C_9H_9NO_3$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.59; H, 5.10; N, 7.81. Ir (neat): 1725, 1750 (C=O) cm^{-1}. Pmr ($CDCl_3$) δ : 2.18 (3H, s, CH_3), 5.57 (2H, s, CH_2), 7.29-8.78 (4H, m, Py-H). Cmr ($CDCl_3$) δ : 20.6 (q, CH_3), 66.9 (t, CH_2), 121.9 (d), 128.0 (d), 137.1 (d), 149.1 (d), 151.6 (s, C_2), 170.5 (s, COMe), 193.4 (s, CO).

6a (**E**: R=H, R'=Et): A pale yellow oil. Ms m/z: 249 (M^+). Ir (neat): 1760 (C=O) cm^{-1}. Pmr ($CDCl_3$) δ: 0.97-1.50 (6H, m, 2xCH_3), 2.26-2.88 (4H, m, 2xCH_2), 6.98-7.84 (3H, m, Py-H), 8.28 (1H, s, CH), 8.39-8.68 (1H, m, Py-H). Cmr ($CDCl_3$) δ : 8.8 (q, CH_3), 9.3 (q, CH_3), 27.4 (t, CH_2), 28.1 (t, CH_2), 118.2 (d), 122.8 (d), 128.1 (d), 134.2 (s), 136.6 (d), 149.5 (d), 151.1 (s, C_2), 170.1 (s, CO), 171.2 (s, CO).

7a (**F**; R=H, R'=Et): A pale yellow oil. Ms m/z: 193 (M^+). Ir (neat): 1720, 1745 (C=O) cm^{-1}. Pmr ($CDCl_3$) δ : 1.22 (3H, t, J=7.4 Hz, CH_3), 2.52 (2H, q, J=7.4 Hz, CH_2), 5.58 (2H, s, CH_2), 7.23-8.20 (3H, m, Py-H), 8.53-8.80 (1H, m, Py-H). Cmr ($CDCl_3$) δ: 9.1 (q, CH_3), 27.3 (t, CH_2), 66.7 (t, CH_2), 121.8 (d), 127.8 (d), 137.0 (d), 149.1 (d), 151.7 (s, C_2), 173.9 (s, CO), 193.6 (s, CO).

9a (**E**: R=H, R'=Ph): Colorless needles, mp 121-122°C (ether-hexane). Anal. Calcd for $C_{21}H_{15}NO_4$: C, 73.04; H, 4.38; N, 4.06. Found: C, 73.15; H, 4.37; N, 4.05. Ms m/z: 345 (M^+). Ir (KBr): 1730 (C=O) cm^{-1}. Pmr ($CDCl_3$) δ: 7.0-8.73 (15H, m, Ar-H, CH). Cmr ($CDCl_3$) δ: 118.5 (d), 123.0 (d), 128.4, 128.5, 128.6, 128.8, 128.9, 130.0, 133.8 (d), 133.9 (d), 135.1 (s), 136.7 (d), 149.6 (d), 151.0 (s), 162.2 (s, CO), 163.7 (s, CO).

10a (**F**: R=H, R'=Ph): Colorless needles, mp 106.4°C (iso-PrOH-hexane). Anal. Calcd for $C_{14}H_{11}NO_3$: C, 69.70; H, 4.60; N, 5.81. Found: C, 69.71; H, 4.54; N, 5.80. Ms m/z: 241 (M^+). Ir (KBr): 1730, 1720 (C=O) cm^{-1}. Pmr ($CDCl_3$) δ : 5.84 (2H, s, CH_2), 7.20-8.80 (9H, m, Ar-H). Cmr ($CDCl_3$) δ : 67.3 (t, CH_2), 121.9 (d), 127.9 (d), 128.4 (d), 129.7 (d), 133.2 (d), 137.0 (d), 149.1 (d), 151.6 (s), 166.1 (s, CO), 193.3 (s, CO).

2b (**A**: R=Me, R'=Me): An oil. Ms m/z: 193 (M^+). Ir (neat): 1750 (C=O) cm^{-1}. Pmr ($CDCl_3$) δ: 1.78 (3H, d, J=7.0 Hz, CH_3), 2.27 (3H, s, CH_3), 6.89 (1H, q, J=7.0 Hz, CH), 7.05-7.50 (3H, m, Py-H), 8.03-8.33 (1H, m, Py-H). Cmr ($CDCl_3$) δ : 11.9 (q, CH_3), 20.3 (q, CH_3), 122.8, 124.2, 125.1, 125.3, 139.8, 140.6, 143.9 (s), 168.0 (s, CO).

4b (**F**: R=Me, R'=Me): An oil. Ms m/z: 193 (M^+). Ir (neat): 1735, 1750 (C=O) cm^{-1}. Pmr ($CDCl_3$) δ : 1.57 (3H, d, J=7.0 Hz, CH_3), 2.12 (3H, s, CH_3), 6.37 (1H, q, J=7.0 Hz,

CH), 7.21-8.20 (3H,m,Py-H),8.53-8.80 (1H, m,Py-H). Cmr ($CDCl_3$) δ: 16.9 (q, CH_3), 20.7 (q, CH_3), 71.8 (d, CH), 122.7 (d), 127.5 (d), 137.0 (d), 149.0 (d), 151.5 (s, C_2), 170.4 (s, CO), 197.4 (s, CO).

5b (**A**: R=Me, R'=Et): An oil. Ms m/z: 207 (M^+), 191 (M^+-16). Ir (neat): 1755 (C=O) cm^{-1}. Pmr ($CDCl_3$) δ: 1.22 (3H, t, J=7.2 Hz, CH_3), 1.76 (3H, d, J=7.2 Hz, CH_3), 2.58 (2H, q, J=7.2 Hz, CH_2), 6.77 (1H, q, J=7.2 Hz, CH), 7.0-7.5 (3H, m, Py-H), 8.0-8.3 (1H, m, Py-H). Cmr ($CDCl_3$) δ: 9.1 (q, CH_3), 11.9 (q, CH_3), 27.0 (t, CH_2), 122.8, 124.2, 125.3, 125.4, 139.8, 140.7, 144.1 (s, C_2), 171.8 (s, CO).

7b (**F**: R=Me, R'=Et): An oil. Ms m/z: 207 (M^+). Ir (neat): 1715, 1735 (C=O) cm^{-1}. Pmr ($CDCl_3$) δ: 1.27 (3H, t, J=7.2 Hz, CH_3), 1.59 (3H, d, J=7.2 Hz, CH_3), 2.45 (2H, q, J=7.2 Hz, CH_2), 6.38 (1H, q, J=7.2 Hz, CH), 7.3-8.2 (3H, m, H_3,H_4,H_5), 8.68 (1H, dd, $J_{4,6}$= 1.8 Hz, $J_{5,6}$=5.0 Hz, H_6). Cmr ($CDCl_3$)δ: 9.0 (q, CH_3), 16.9 (q, CH_3), 27.3 (t, CH_2), 71.5 (d, CH), 122.7 (d), 127.5 (d), 137.0 (d), 149.0 (d), 151.6 (s, C_2), 173.9 (s, CO), 197.6 (s, CO).

2-(1-Acetoxyvinyl)pyridine 1-Oxide (2a) ——1) A solution of AcCl (0.9 g) in CH_2Cl_2 (10 ml) was added dropwise at -5—0°C to a solution of **1a** (1.37 g) and NEt_3 (3 ml) in CH_2Cl_2 (20 ml), and the reactants were stirred at the same temperature for 0.5 h. The solvent was evaporated in vacuo, and the residue was shaken with aq. NaCl and THF. The separated THF layer was concentrated in vacuo, and the residue was chromatographed on silica gel with $CHCl_3$-MeOH to give 180 mg (10%) of **2a**.

2) A mixture of **2a** (179 mg) and H_2O (5 ml) was heated on a steam bath for 1 h to give 89 mg (65%) of **1a** after chromatographic purification (SiO_2, $CHCl_3$-ether).

Reaction of **2a** with Ac_2O ——A solution of **2a** (179 mg) in Ac_2O (5 ml) was heated at 140°C for 1.5 h to give 40 mg (18.1%) of **3a** and 90 mg (50.3%) of **4a**.

Conversion of **3a** to **4a** ——A solution of **3a** (221 mg) in MeOH (5 ml)-H_2O (5 ml) was heated on a steam bath for 0.5 h. The solvent was evaporated in vacuo, and the residue was chromatographed on silica gel with $CHCl_3$-ether to give 107 mg (60%) of **4a**. Treatment of **3a** or **4a** with alkaline solution gave an untractable mixture.

2-(1-Benzoyloxyvinyl)pyridine 1-Oxide (**8a**) ——1) A solution of PhCOCl (1.54 mg) in CH_2Cl_2 (10 ml) was added dropwise at -5—0°C to a solution of **1a** (1.37 g) and NEt_3 (3 ml) in CH_2Cl_2 (15 ml), and the reactants were stirred as the same temperature for 0.5 h and then at room temperature for 0.5 h. The solvent was evaporated in vacuo, and the residue was shaken with ether and aq. NaCl. The residue from the ether solution was chromatographed on silica gel with $CHCl_3$-MeOH to give 1.17 g of a mixture of **1a** and its enol benzoate (**8a**). Upon shaking this mixture with ether

(100 ml) and H_2O (100 ml), **8a** was taken up in ether and **1a** remained in aq. layer. The ether solution gave 471 mg (19.5%) of **8a** as an oil. Ms m/z: 241 (M^+), 225 (M^+-16). Pmr ($CDCl_3$) δ: 5.22 (1H, d, $J_{a,b}$=1.8 Hz, C=CH_aH_b), 6.24 (1H, d, $J_{a,b}$=1.8 Hz, C=CH_aH_b), 7.06-7.72 (6H, m, Ar-H), 8.06-8.34 (3H, m, Ar-H). Cmr ($CDCl_3$) δ: 112.4 (dd, CH_2), 124.8 (d), 125.0 (d), 125.2 (s), 128.7, 128.9, 130.3, 133.8, 140.9, 143.2, 145.0 (s), 164.4 (s, CO).

2) A mixture of **8a** (241 mg) and H_2O (5 ml) was heated on a steam bath for 0.5 h to give 110 mg (80%) of **1a**.

Reaction of **8a** with Ac_2O ——A mixture of **8a** (482 mg) and Ac_2O (5 ml) was heated at 130-135°C for 4 h. The reaction mixture was concentrated *in vacuo*, and the residue was chromatographed on silica gel with $CHCl_3$-MeOH to give successively **4a** (66 mg, 19.3%), 2-(2-acetoxy-1-benzoyloxyvinyl)pyridine (**11**) (113 mg, 20%) and **3a** (66 mg, 15.0%). **11**: An oil. Ir (neat): 1765, 1745 (C=O) cm^{-1}. Pmr ($CDCl_3$) δ: 2.12 (3H, s, CH_3), 7.0-8.43 (6H, m, Ar-H), 8.0-8.74 (4H, m, Ar-H, CH).

Conversion of **11** into **4a** ——A solution of **11** (142 mg) in AcOH (5 ml)-H_2O (5 ml) was refluxed for 3 h. The solvent was evaporated *in vacuo*, and the residue was chromatographed on silica gel with $CHCl_3$-ether to give 40 mg (44.5%) of **4a**.

REFERENCES AND NOTE

1. H. Nagano, Y. Nawata, and M. Hamana, Chem. Pharm. Bull., 1987, **35**, 4068.
2. H. Nagano, Y. Nawata, and M. Hamana, Chem. Pharm. Bull., 1987, **35**, 4093.
3. A.R. Katritzky, A.M. Monro, J.A.T. Beard, D.P. Dearnaley, and N.J. Earl, J. Chem. Soc., 1958, 2182.
4. Attepted reactiions of 2-pyridinecarbonitrile 1-oxide with Grignard reagents failed, the starting materials being recovered.
5. S. Furukawa, Yakugaku Zasshi, 1959, **79**, 487.
6. M. Hamana and H. Noda, Yakugaku Zasshi, 1963, **83**, 342.

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