SYNTHESIS OF PYRIDO[2,3-*b*]PYRAZINES FROM PYRIDO[2,3-*c*]FUROXAN

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Abstract - The synthesis of substituted pyrido[2,3-*b*]pyrazines was carried out. Pyrido[2,3-*b*]pyrazine 1,4-dioxides (**3**) and pyrido[2,3-*b*]pyrazine 1-oxides (**4**) were obtained from pyrido[2,3-*c*]furoxan (**1**) and 1,3-diketones or ß-keto esters catalyzed by silica gel, alumina, or molecular sieves.

INTRODUCTION

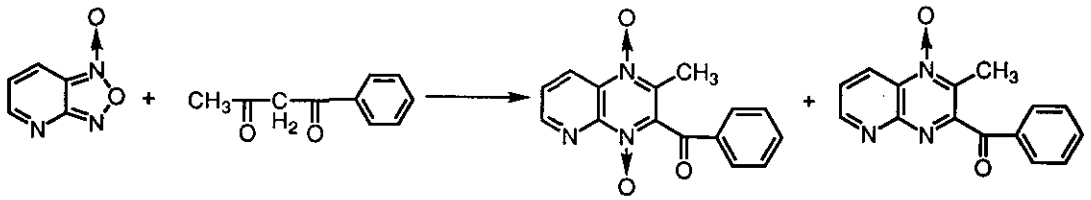
Reactions of pyrido[2,3-*c*]furoxan (**1**) with 1,3-diketones in a basic medium give the corresponding pyrido[2,3-*b*]pyrazine 1,4-dioxides.[1,2] In an aromatic furazan study, quinoxaline *N*, *N*-dioxides were synthesized from benzofuroxan catalyzed by silica gel[3] or molecular sieves; [4,5] their antibacterial activity[6] was determined and the photoreactions of **1** were examined using a high or low pressure mercury lamp.[7] This paper presents the synthesis of pyridopyrazines from **1** and 1,3-diketones or ß-keto esters catalyzed by silica gel, alumina, or molecular sieves.

RESULTS AND DISCUSSION

Pyrido[2,3-*b*]pyrazines were synthesized as follows: A solution of compound (**1**) and carbonyl compound (**2**) in dichloromethane was evaporated in the presence of silica gel, alumina, or molecular sieves; both reagents were adsorbed on silica gel, alumina, or molecular sieves followed by standing at 90° or room temperature. The mixture was chromatographed on silica gel to give the corresponding pyrido[2,3-*b*]pyrazine 1,4-dioxides (**3**) and pyrido[2,3-*b*]pyrazine 1-oxides (**4**).

Various catalysts in reaction of compound (**1**) with benzoylacetone were examined (Table 1). In the method using catalysts, reaction efficacy varied considerably depending on the catalyst used. Silica gel B (Merck, Silica gel 60, Art. 7754) as the catalyst gave the best results.

Table 1



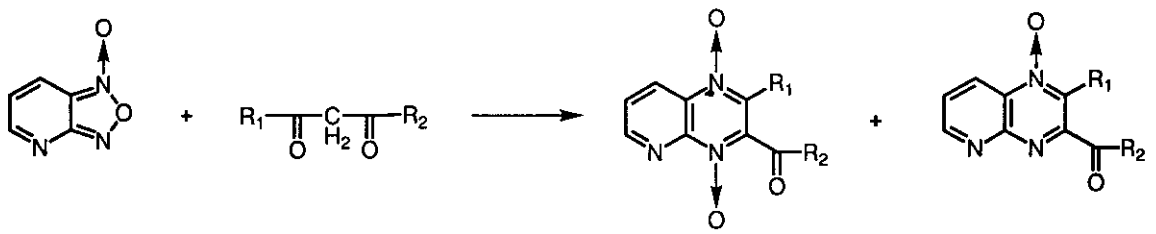
1 **2d** **3d** **4d**

Catalysts		Reaction Condition	Yield (%) 3d	4d
Silica gel	A (Poresize 40Å)	90 °C, 2 h	24	0
	B 60	90 °C, 2 h	57	0
			65[a)]	1
	C 80	90 °C, 2 h	41	4
	D 100	90 °C, 2 h	40	3
Molecular sieves	3A	90 °C, 2 h	27	3
	4A	90 °C, 2 h	47	3
	5A	90 °C, 2 h	42	4
	13X	90 °C, 2 h	14	0
Aluminum oxide	basic	room temperture, 0 min	49	0
	acidic	room temperture, 0 min	42	0
	neutral	room temperture, 0 min	20	0

a) **1** : **2d** = 1 : 1.5, the other **1** : **2d** = 1 : 1.1.

1,3-Diketones (**2a-e**) in reaction with compound (**1**) were examined (see Table 2). A comparison of the yields of compound (**3**) with enol content of the carbonyl compound, it showed the yield is proportioned to the reactivity of the enol form with compound (**1**). It seemed likely that the enol form of carbonyl compounds was necessary to the formation of pyridopyrazine 1,4-dioxides. We are thoroughly investigating the reaction mechanism.

Table 2

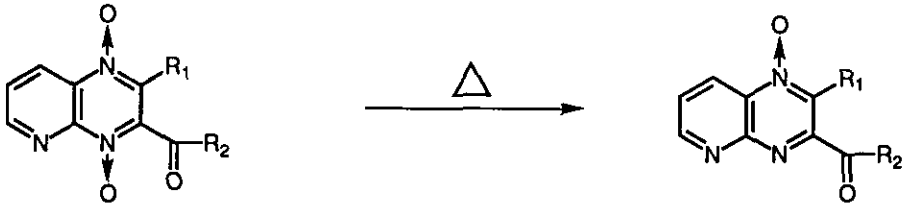


1 **2** **3** **4**

Compound No.	R_1	R_2	Yield (%) 3	Yield (%) 4	Enol Content of **2** (%) (in Ethanol)
2a	CH_3	OCH_3	10	0.1	12.6 [8]
2b	CH_3	OC_2H_5	10	1	12 [9]
2c	CH_3	CH_3	52	2	84 [8]
2d	CH_3		65	1	94 [8]
2e			49	3	90-100 [8]

When pyridopyrazine 1,4-dioxides were synthesized from **1** and 1,3-diketones or ß-keto esters catalyzed by using adsorbents, pyrido[2,3-*b*]pyrazine monooxides were also obtained. The thermal reactions of pyrido[2,3-*b*]pyrazine 1,4-dioxide with the adsorbents were thus examined. Pyrido[2,3-*b*]pyrazine 1,4-dioxides were adsorbed on silica gel, alumina, or molecular sieves, followed by standing at 90° or 110°. These reactions produced the monooxides (Table 3). 4-Oxide of pyridopyrazine 1,4-dioxides with the adsorbents was deoxidized. It was likely that monooxides were obtained by thermal deoxidization of *N*-oxide from the dioxides.

Table 3

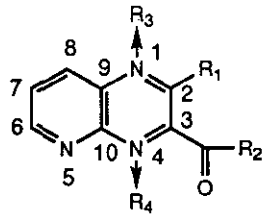


3 **4**

Compound No.	R_1	R_2	Catalyst	Reaction Conditions	**4** Yield (%)	**3** (recovery)
3b	CH_3	OC_2H_5	Silica gel C	110°, 2 h	7	81
3c	CH_3	CH_3	Silica gel C	110°, 2 h	2	79
3d	CH_3		Silica gel C	90°, 2 h	1	96
3d	CH_3		Silica gel B	90°, 2 h	1	97
3d	CH_3		Molecular sieves 4A	90°, 2 h	2	97
3d	CH_3		Aluminum oxide (basic)	90°, 2 h	3	68

Pyrido[2,3-*b*]pyrazine dioxides and monooxides assignments were made based on the following; Assignment was based primarily on which of the two ring nitrogens (*N*-1 and *N*-4) was *N*-oxide. By comparing ^{13}C nmr spectra of the present products with data on quinoxaline monoxides as reported by Kluge *et al.*,[10] we could assign the absorptions of C-8 and the methyl group (R1) as key carbons. By comparing 3-acetyl-2-methylpyrido[2,3-*b*]pyrazine (**5**) with 3-acetyl-2-methylpyrido[2,3-*b*]pyrazine 1-oxide (**4c**) (See Table 4), the methyl ^{13}C chemical shifts of **4c** and **3c** were each shown to be 10.59 - 10.39 ppm upfield from **5** based on the shielding effects of the ortho-oxygen

Table 4. ^{13}C-Nmr Spectra of Pyridopyrazines



Compound	R_1	R_2	R_3	R_4	R_1 (CH_3)	C (2)	C (3)	C (6)	C (7)	C (8)	C (9)	C (10)	C=O
3a	CH_3	OCH_3	O	O	14.36	140.00	137.81	153.06	127.62	130.60	134.70	145.65	160.01
3b	CH_3	OC_2H_5	O	O	13.94	139.93	137.97	153.01	127.55	130.58	134.61	145.67	159.64
3c	CH_3	CH_3	O	O	13.76	140.00	141.96	153.10	127.60	130.62	134.52	145.42	193.71
3d	CH_3	Ph	O	O	14.02	140.51	141.17	152.99	127.57	130.60	134.64	145.62	186.12
3e	Ph	Ph	O	O	-	139.97	140.94	153.23	128.05	130.74	135.77	146.03	186.21
4a	CH_3	OCH_3	O	-	13.96	141.23	149.42	155.13	126.16	128.43	133.66	150.76	164.60
4b	CH_3	OC_2H_5	O	-	13.94	140.84	150.04	154.98	126.01	128.39	133.51	150.83	164.18
4c	CH_3	CH_3	O	-	13.56	141.14	152.59	154.87	126.18	128.57	133.57	150.19	199.62
4d	CH_3	Ph	O	-	13.94	140.22	155.82	154.85	125.74	128.48	133.24	150.74	191.32
4e	Ph	Ph	O	-	-	140.37	157.07	155.50	125.96	129.23	128.03	151.46	190.84
5	CH_3	CH_3	-	-	24.15	154.54	149.02	154.10	126.67	137.41	138.36	148.49	200.96

ppm

while those of C-8 of **4c** and **3c** were each 8.84 - 6.79 ppm upfield from **5** due to the same effects. Assignments of the mono *N*-oxide and substituents were determined from Heteronuclear chemical shift correlation spectroscopy (^{13}C-^{1}H-COSY) and correlation spectroscopy *via* long range coupling (COLOC) and analogy with pyrido[2,3-*b*]pyrazine.[11] *N*-1 of pyridopyrazine monooxides is *N*-oxide and methyl substituents may thus be concluded as attached to C-2.

EXPERIMENTAL

Melting points were determined with a Yanagimoto micromelting point apparatus and are uncorrected. The ir spectra were recorded on a Jasco ir-810 spectrophotometer. The ^{1}H and ^{13}C nmr spectra were recorded on a JEOL JNM-EX 90 FT nmr and JNM-GSX 400 FT nmr System with TMS as the internal standard. The mass spectra were recorded on a Hitachi M-2000 spectrometer with an electron beam energy of 70 eV. Microanalyses were performed at microanalytical laboratory of the Center for Instrumental Analysis in College of Science & Technology, Nihon University.

Pyrido[2,3-*c*]furoxan was synthesized as described ref. 12.

General Procedure (Table 1 ,2).

To a solution of **1** (137.0 mg, 1 mmol) and benzoylacetone (243.0 mg,1.5 mmol) in dichloromethane (10 ml) was added silica gel [Silica gel A; Merck, Silica gel 40 for column chromatography (Art. 10180), Silica gel B; Merck, Silica gel 60 extra pure for column chromatography (Art. 7754), Silica gel C; Wako Pure Chemical Industries, Wakogel C-200, Silica gel D; Merck, Silica gel 100 for column chromatography (Art. 10184), 2 g] or Aluminium oxide [MERCK, Aluminium oxide 90 active basic for column chromatography (Art. 1076), Aluminium oxide 90 active neutral for column chromatography (Art. 1077), Aluminium oxide 90 active acidic for column chromatography (Art. 1078), 2 g] or molecular sieves [3A powder, 4A powder, 5A powder, 13X powder, Union Showa, 2 g]. The mixture was evaporated in an evaporator at 30°. The adsorbent containing the adsorbed reagents was allowed to stand for 2 h, at 90°.

It was then added to a silica gel column(Wako Pure Chemical Industries, Wakogel C-200) and product 3-benzoyl-2-methylpyrido[2,3-*b*]pyrazine 1,4-dioxide (**3d**) was eluted with dichloromethane/methanol (98:2) . It was purified by preparative tlc (Merck, Silica gel plate 60 F_{254} Art. 5717) with dichloromethane/methanol (96:4).Yield 181.30 mg (65%).

3-Carbomethoxy-2-methylpyrido[2,3-*b*]pyrazine 1,4-dioxide (**3a**)

This compound had mp 149 - 151°. Ir(KBr)cm^{-1}: 1737(C=O) . ^{1}H-Nmr ($CDCl_3$) δ : 2.60 (s, 3H, CH_3), 4.13 (s, 3H, OCH_3), 7.90 (dd, 1H, $J_{6,7}$=4 Hz, $J_{7,8}$=9 Hz, C7-H), 9.04 (dd, 1H, $J_{7,8}$=9 Hz, $J_{6,8}$=1.5 Hz, C8-H) , 9.10 (dd, 1H, $J_{6,7}$=4 Hz, $J_{6,8}$=1.5 Hz, C6-H). ^{13}C-Nmr ($CDCl_3$) δ : 14.36 (CH_3), 54.18 (OCH_3), 127.62 (C(7)), 130.60 (C(8)), 134.70 (C(9)), 137.81 (C(3)), 140.00 (C(2)), 145.65 (C(10)), 153.06 (C(6)), 160.01 (C=O). EI-ms m/z : 235.0627 (Calcd for $C_{10}H_9N_3O_4$: 235.0592). *Anal.* Calcd for $C_{10}H_9N_3O_4$: C, 51.06; H, 3.86; N, 17.87. Found: C, 50.94; H, 3.85; N, 17.92.

3-Carboethoxy-2-methylpyrido[2,3-*b*]pyrazine 1,4-dioxide (**3b**)

Recrystallization from *n*-hexane/ethyl acetate (50:3) afforded light yellow needles, mp 170 - 171°. Ir(KBr)cm^{-1}: 1743(C=O) . ^{1}H-Nmr ($CDCl_3$) δ : 1.48 (t, 3H, *J*=7 Hz, $C\underline{H}_3$-CH_2), 2.61 (s, 3H, CH_3), 4.60 (q, 2H, *J*=7 Hz, CH_3-$C\underline{H}_2$), 7.90 (dd, 1H, $J_{6,7}$=4 Hz, $J_{7,8}$=8 Hz, C7-H), 9.03 (dd, 1H, $J_{7,8}$=8 Hz, $J_{6,8}$=1.5 Hz, C8-H), 9.09 (dd, 1H, $J_{6,7}$=4 Hz, $J_{6,8}$=1.5 Hz, C6-H). ^{13}C-Nmr ($CDCl_3$) δ : 13.94 (CH_3), 14.27 (O-$CH_2\underline{C}H_3$), 63.85 (O-$\underline{C}H_2CH_3$), 127.55 (C(7)), 130.58 (C(8)), 134.61 (C(9)), 137.97 (C(3)), 139.93 (C(2)), 145.67 (C(10)), 153.01 (C(6)), 159.64 (C=O). EI-ms m/z : 249.0748 (Calcd for $C_{11}H_{11}N_3O_4$: 249.0744). *Anal.* Calcd for $C_{11}H_{11}N_3O_4$: C, 53.01; H, 4.45; N, 16.86. Found: C, 53.08; H, 4.43 ; N, 16.84.

3-Acetyl-2-methylpyrido[2,3-*b*]pyrazine 1,4-dioxide (**3c**)

Recrystallization from *n*-hexane/ethyl acetate (50:3) afforded light yellow needles, mp 145 - 147° . Ir(KBr)cm^{-1}: 1714(C=O) . ^{1}H-Nmr ($CDCl_3$) δ : 2.55 (s, 3H, CH_3), 2.76 (s, 3H, CH_3CO), 7.92 (dd,1H, $J_{6,7}$=4 Hz , $J_{7,8}$=9 Hz, C7-H), 9.04 (dd, 1H, $J_{7,8}$=9 Hz, $J_{6,8}$=1.5 Hz, C8-H), 9.10 (dd, 1H, $J_{6,7}$=4 Hz, $J_{6,8}$=1.5 Hz, C6-H). ^{13}C-Nmr ($CDCl_3$) δ : 13.76 (CH_3), 29.67 ($\underline{C}H_3CO$), 127.60 (C(7)), 130.62 (C(8)), 134.52 (C(9)), 140.00 (C(2)), 141.96 (C(3)), 145.42 (C(10)), 153.10 (C(6)), 193.71 (C=O). EI-ms m/z : 219.0663 (Calcd

for $C_{10}H_9N_3O_3$: 219.0643). *Anal.* Calcd for $C_{10}H_9N_3O_3$: C, 54.79; H, 4.14; N,19.17. Found: C, 54.81; H, 4.02 ; N, 19.37.

3-Benzoyl-2-methylpyrido[2,3-*b*]pyrazine 1,4-dioxide (**3d**)

Recrystallization from methanol afforded light yellow needles, mp 192 - 194°. Ir(KBr) cm^{-1} :1669(C=O) . ^{1}H-Nmr ($CDCl_3$) δ : 2.50 (s, 3H, CH_3), 7.52 (t-like, 2H, $J_{2',3'}$ or $J_{3',4'}$ or $J_{4',5'}$ or $J_{5',6'}$=7 Hz, benzoyl C3'-H and C5'-H), 7.69 (t-like, 1H, $J_{3',4'}$ or $J_{4',5'}$=7 Hz, benzoyl C4'-H) , 7.92 (d, 2H, $J_{2',3'}$ or $J_{5',6'}$=7 Hz, benzoyl C2'-H and C6'-H , 7.94 (dd, 1H, $J_{6,7}$=4 Hz, $J_{7,8}$=8 Hz, C7-H), 9.08 (d, 1H, J=8 Hz, C8-H), 9.11 (d, 1H, $J_{6,7}$=4 Hz, C6-H). ^{13}C-Nmr($CDCl_3$) δ : 14.02 (CH_3), 127.57 (C(7)), 129.29 (benzoyl C(2') and C(6')), 129.36 (benzoyl C(3') and C(5')), 130.60 (C(8)), 133.89 (benzoyl C(1')), 134.64 (C(9)), 135.38 (benzoyl C(4')), 140.51 (C(2)), 141.17 (C(3)), 145.62 (C(10)), 152.99 (C(6)), 186.12 (C=O). EI-ms m/z : 281.0805 (Calcd for $C_{15}H_{11}N_3O_3$: 281.0799). *Anal.* Calcd for $C_{15}H_{11}N_3O_3$: C, 64.05; H, 3.94; N, 14.94. Found: C, 63.98; H, 4.10 ; N, 14.84.

3-Benzoyl-2-phenylpyrido[2,3-*b*]pyrazine 1,4-dioxide (**3e**)

Recrystallization from methanol afforded light yellow needles, mp 220 - 222°. Ir(KBr)cm^{-1}:1679(C=O). ^{1}H-Nmr (DMSO-d_6) δ : 7.35 - 7.41 (m, 5H, phenyl-H), 7.50 (dd, 2H, $J_{2',3'}$ or $J_{5',6'}$=8 Hz, $J_{3',4'}$ or $J_{4',5'}$=7 Hz, benzoyl C3'-H and C5'-H), 7.68 (t-like, 1H, $J_{3',4'}$ or $J_{4',5'}$=7 Hz, benzoyl C4'-H), 8.01 (d, 2H, $J_{2',3'}$ or $J_{5',6'}$=8 Hz, benzoyl C2'-H and C6'-H), 8.12 (dd, 1H, $J_{6,7}$=4 Hz, $J_{7,8}$=9 Hz, C7-H), 9.01 (dd, 1H, $J_{7,8}$=9 Hz, $J_{6,8}$=1.5 Hz, C8-H), 9.14 (dd, 1H, $J_{6,7}$=4 Hz, $J_{6,8}$=1.5 Hz, C6-H). ^{13}C-Nmr (DMSO-d_6) δ : 127.50 (phenyl C(1")), 128.05 (C(7)), 128.31 (phenyl CH), 129.18 (benzoyl C(3') and C(5')), 129.33 (benzoyl C(2') and C(6')), 130.03 (phenyl CH), 130.21 (phenyl CH), 130.74 (C(9)), 134.40 (benzoyl C(4')), 135.02 (benzoyl C(1')), 135.77 (C(8)), 139.97 (C(2)), 140.94 (C(3)), 146.03 (C(10)), 153.23 (C(6)), 186.21 (C=O). EI-ms m/z : 343.0942 (Calcd for $C_{20}H_{13}N_3O_3$:343.0956). *Anal.* Calcd for $C_{20}H_{13}N_3O_3$: C, 69.96; H, 3.82; N, 12.24. Found: C,69.69; H, 3.88; N, 12.04.

3-Carbomethoxy-2-methylpyrido[2,3-*b*]pyrazine 1-oxide(**4a**)

Recrystallization from *n*-hexane afforded white needles, mp 145 - 147°. Ir(KBr) cm^{-1}: 1731(C=O). ^{1}H-Nmr ($CDCl_3$) δ : 2.83 (s, 3H, CH_3), 4.08 (s, 3H, OCH_3), 7.76 (dd, 1H, $J_{6,7}$=4 Hz, $J_{7,8}$=9 Hz, C7-H), 8.94 (dd, 1H, $J_{7,8}$=9 Hz, $J_{6,8}$=1.5 Hz, C8-H) , 9.21 (dd, 1H,

$J_{6,7}$=4 Hz, $J_{6,8}$=1.5 Hz, C6-H) . ^{13}C-Nmr ($CDCl_3$) δ : 13.96 (CH_3), 53.54 (OCH_3), 126.16 (C(7)), 128.43 (C(8)), 133.66 (C(9)), 141.23 (C(2)), 149.42 (C(3)), 150.76 (C(10)), 155.13 (C(6)), 164.60 (C=O). EI-ms m/z : 219.0644 (Calcd for $C_{10}H_9N_3O_3$: 219.0643). *Anal.* Calcd for $C_{10}H_9N_3O_3$: C, 54.79; H, 4.14; N, 19.17. Found: 54.85; H,4.02; N, 19.31.

3-Carboethoxy-2-methylpyrido[2,3-*b*]pyrazine 1-oxide(**4b**)

Recrystallization from *n*-hexane afforded white needles, mp 110 - 112°. Ir(KBr) cm^{-1}: 1718(C=O). ^{1}H-Nmr ($CDCl_3$) δ : 1.49 (t, 3H, J=7 Hz, $C\underline{H}_3$-CH_2), 2.80 (s, 3H, CH_3), 4.54 (q, 2H, J=7 Hz, CH_3-$C\underline{H}_2$), 7.76 (dd, 1H, $J_{6,7}$=4 Hz, $J_{7,8}$=8 Hz, C7-H), 8.94 (dd, 1H, $J_{7,8}$=8 Hz, $J_{6,8}$=2 Hz, C8-H), 9.20 (dd, 1H, $J_{6,7}$=4 Hz, $J_{6,8}$=2 Hz, C6-H). ^{13}C-Nmr ($CDCl_3$) δ : 13.94 (CH_3), 14.07 ($\underline{C}H_3$-CH_2), 62.99 (CH_3-$\underline{C}H_2$), 126.01 (C(7)), 128.39 (C(8)), 133.51 (C(9)), 140.84 (C(2)), 150.04 (C(3)), 150.83 (C(10)), 154.98 (C(6)), 164.18 (C=O). EI-ms m/z : 233.0799 (Calcd for $C_{11}H_{11}N_3O_3$: 233.0801). *Anal.* Calcd for $C_{11}H_{11}N_3O_3$: C, 56.65; H, 4.75; N, 18.02. Found: C, 56.90; H, 4.83 ; N, 17.91.

3-Acetyl-2-methylpyrido[2,3-*b*]pyrazine 1-oxide(**4c**)

Recrystallization from *n*-hexane afforded white needles, mp 108 - 110°. Ir(KBr)cm^{-1}: 1698(C=O). ^{1}H-Nmr ($CDCl_3$) δ : 2.84 (s, 3H, CH_3), 2.91 (s, 3H, CH_3CO), 7.80 (dd, 1H, $J_{6,7}$=4 Hz , $J_{7,8}$=9 Hz, C7-H), 8.95 (dd, 1H, $J_{7,8}$=9 Hz, $J_{6,8}$=2 Hz, C8-H) , 9.22 (dd, 1H, $J_{6,7}$=4 Hz, $J_{6,8}$=2 Hz, C6-H). ^{13}C-Nmr ($CDCl_3$) δ : 13.56 (CH_3), 28.15 ($\underline{C}H_3CO$), 126.18 (C(7)), 128.57 (C(8)), 133.57 (C(9)), 141.14 (C(2)), 150.19 (C(10)), 152.59 (C(3)), 154.87 (C(6)), 199.62 (C=O). EI-ms m/z : 203.0717 (Calcd for $C_{10}H_9N_3O_2$: 203.0694). *Anal.* Calcd for $C_{10}H_9N_3O_2$: C, 59.10; H ,4.46; N, 20.68. Found: C, 58.98; H, 4.50; N, 20.61.

3-Benzoyl-2-methylpyrido[2,3-*b*]pyrazine 1-oxide (**4d**)

Recrystallization from *n*-hexane/ethyl acetate (9:1) afforded white needles, mp 152 - 154°. Ir(KBr) cm^{-1}: 1667 (C=O). ^{1}H-Nmr ($CDCl_3$) δ : 2.66 (s, 3H, CH_3), 7.51 (t-like, 2H, $J_{3',4'}$ or $J_{4',5'}$=7 Hz, $J_{2',3'}$ or $J_{5',6'}$=8 Hz, benzoyl C3'-H and C5'-H), 7.67(t-like, 1H, $J_{3',4'}$ or $J_{4',5'}$=7 Hz, benzoyl C4'-H), 7.78 (dd, 1H, $J_{6,7}$=4 Hz, $J_{7,8}$=9 Hz, C7-H), 8.01 (d, 2H, $J_{2',3'}$ or $J_{5',6'}$=8 Hz, benzoyl C2'-H and C6'-H), 9.00 (dd, 1H, $J_{7,8}$=9 Hz, $J_{6,8}$=2 Hz, C8-H), 9.20 (dd, 1H, $J_{6,7}$=4 Hz, $J_{6,8}$=2 Hz, C6-H). ^{13}C-Nmr ($CDCl_3$) δ : 13.94 (CH_3), 125.74 (C(7)), 128.48 (C(8)), 128.79 (benzoyl C(3') and C(5')), 130.68 (benzoyl C(2') and C(6')), 133.24 (C(9)), 134.52 (benzoyl C(1')), 134.63 (benzoyl C(4')), 140.22 (C(2)), 150.74 (C(10)),

154.85 (C(6)), 155.82 (C(3)), 191.32 (C=O). EI-ms m/z : 265.0848 (Calcd for $C_{15}H_{11}N_3O_2$:265.0849). *Anal.* Calcd for $C_{15}H_{11}N_3O_2$: C, 67.91; H, 4.18; N, 15.84. Found: C, 67.92; H, 4.13; N, 15.58.

3-Benzoyl-2-phenylpyrido[2,3-*b*]pyrazine 1-oxide (**4e**)

Recrystallization from *n*-hexane/ethyl acetate (9:1) afforded white needles, mp 187 - 189°. Ir(KBr) cm^{-1}: 1681 (C=O). ^{1}H-Nmr ($CDCl_3$) δ : 7.40 - 7.44 (m, 5H, phenyl-H), 7.44 - 7.51 (m, 2H, benzoyl C3'-H and C'5-H), 7.59 - 7.63 (m, 1H, benzoyl C4'-H), 7.80 (dd, 1H, $J_{7,8}$=8 Hz, $J_{6,7}$=4 Hz, C7-H), 7.89 - 7.92 (m, 2H, benzoyl C2'-H and C6'-H) 9.04 (dd, 1H, $J_{7,8}$=8 Hz, $J_{6,8}$=2 Hz, C8-H), 9.25 (dd, 1H, $J_{6,7}$=4 Hz, $J_{6,8}$=2 Hz, C6-H). ^{13}C-Nmr ($CDCl_3$) δ : 125.96 (C(7)), 128.03 (C(8)), 128.73 (phenyl CH), 128.76 (phenyl CH), 129.23 (C(9)), 129.93 (benzoyl C(3') and C(5')), 130.39 (benzoyl C(2') and C(6')), 130.49 (phenyl CH), 133.89 (phenyl C(1")), 134.38 (benzoyl C(4')), 134.84 (benzoyl C(1')), 140.37 (C(2)), 151.46 (C(10)), 155.50 (C(6)), 157.07 (C(3)), 190.84 (C=O). EI-ms m/z :327.1002 (Calcd for $C_{20}H_{13}N_3O_2$:327.1006). *Anal.* Calcd for $C_{20}H_{13}N_3O_2$: C,73.38 ; H,4.00; N,12.84. Found: C,73.02; H,3.90 ; N,12.56.

3-Acetyl-2-methylpyrido[2,3-*b*]pyrazine (**5**)

A solution of **4c** (101.5 mg, 0.54 mmol) and triphenylphosphine (526.6 mg, 2 mmol) in xylene(5 ml) was heated at reflux with stirring for 20 h. The reaction mixture was then added to a silica gel column and product (**5**) was eluted with dichloromethane/methanol (98:2) . 71.1 mg (yield 66.5%) .

Recrystallization from *n*-hexane afforded white needles, mp 103 - 104°. Ir(KBr) cm^{-1}: 1690 (C=O). ^{1}H-Nmr ($CDCl_3$) δ : 2.93 (s, 3H, CH_3), 3.02 (s, 3H, CH_3CO), 7.81 (dd, 1H, $J_{7,8}$=8 Hz, $J_{6,7}$=4 Hz, C7-H), 8.43 (dd, 1H, $J_{7,8}$=8 Hz, $J_{6,8}$=2 Hz, C8-H) , 9.21 (dd, 1H, $J_{6,7}$ =4 Hz, $J_{6,8}$=2 Hz, C6-H). ^{13}C-Nmr ($CDCl_3$) δ : 24.15 (CH_3), 27.95 ($\underline{C}H_3CO$), 126.67 (C(7)), 137.41 (C(8)), 138.36 (C(9)), 148.49 (C(10)), 149.02 (C(3)), 154.10 (C(6)), 154.54 (C(2)), 200.96 (C=O). EI-ms m/z : 187.0734 (Calcd for $C_{10}H_9N_3O$:187.0744). *Anal.* Calcd for $C_{10}H_9N_3O$: C, 64.16; H ,4.85; N, 22.45. Found: C, 63.86; H, 4.86; N, 22.29.

General Procedure (Table 3).

To a solution of 3-benzoyl-2-methylpyrido[2,3-*b*]pyrazine 1,4-dioxide (**3d**)(281.2 mg, 1 mmol) in dichloromethane (10 ml) was added silica gel (Merck, Silica gel 60 Art. 7754, 2.0 g) and the mixture is evaporated in an evaporator at 30°. The silica gel containing the adsorbed reagents was allowed to stand for 2 h, at 90°. It was then added to a silica gel column (Wako Pure Chemical Industries, Wakogel C-200) and unreacted 3-benzoyl-2-methylpyrido[2,3-*b*]pyrazine 1,4-dioxide (**3d**) and 3-benzoyl-2-methylpyrido[2,3-*b*]pyrazine 1-oxide (**4d**) were eluted with dichloromethane/methanol (98:2). It was purified by preparative tlc (Merck, Silica gel plate 60 F_{254} Art. 5717) with ethyl acetate/ethanol (9:1), yield unreacted **3d** 271. 1 mg (96%) and **4d** 2.5 mg (1%). Unreacted **3d** was characterized by comparison of the melting point, and ir spectra with authentic sample (**3d**).

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