Heterocycles Structurally Influenced by a Side Chain. X. Effect of Temperature and Side Chain on the Imine-Enamine Tautomerism in the Quinoxalinone and Pyridopyrazinone Systems [1]

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3-(1-Benzoyl)ethyl-1*H*-pyrido[2,3-*b*]pyrazin-2-one (**7**), 3-(1-ethoxycarbonyl)ethyl-1*H*-pyrido[2,3-*b*]-pyrazin-2-one (**8**), and 3-(1-benzoyl)ethyl-1*H*-quinoxalin-2-one (**9**) exist only in the imine form due to the steric effect of the methyl substituent. As regards the imine-enamine tautomerism, 3-(β-carbonylmethylene) derivatives of 1,2-dihydro-4*H*-pyrido[2,3-*b*]pyrazin-3-one such as **12** and **15-18** gradually change from the enamine form to the imine form with elevated temperatures; however, 3-(carbonylmethylene) derivatives of 3,4-dihydro-1*H*-pyrido[2,3-*b*]pyrazin-2-one such as **10**, **19** and **20** show little temperature effect. 2-Phenacylidene-1,2-dihydro-4*H*-pyrido[3,4-*b*]pyrazin-3-one (**21**) and 3-phenacylidene-3,4-dihydro-1*H*-pyrido[3,4-*b*]pyrazin-2-one (**22**), which exist in the enamine form, show no temperature effect.

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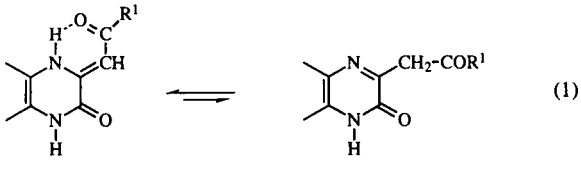
Introduction.

It has been reported that many pyrazinone derivatives having the 3-(or 2-)phenacylidene and 3-(or 2-)ethoxycarbonylmethylene groups on their side chains exist predominantly in enamine form as shown in Eq. 1; however, it was seen from the results of ^{1}H-nmr analysis that ethyl isoxanthopterin acetate and their derivatives exist in the imine form [4-11].

Furthermore, it has been disclosed that methylation with methyl iodide or diazomethane only yielded *N*-methylated compounds on the lactam NH group on the pyrazinone ring, because the NH group adjacent to the methylene group is tightly hydrogen-bonded with the carbonyl group on the side chain [12].



Enamine Form ⇌ Imine Form (1)

In this paper, we report how the imine-enamine tautomerism in the 3-(or 2-)phenacylidene and 3-(or 2-)ethoxycarbonylmethylene derivatives of pyrido[2,3-*b*]pyrazinone and pyrido[3,4-*b*]pyrazinone are influenced by various temperatures [13-15] and by changing the side chains [16-21] in equilibrium.

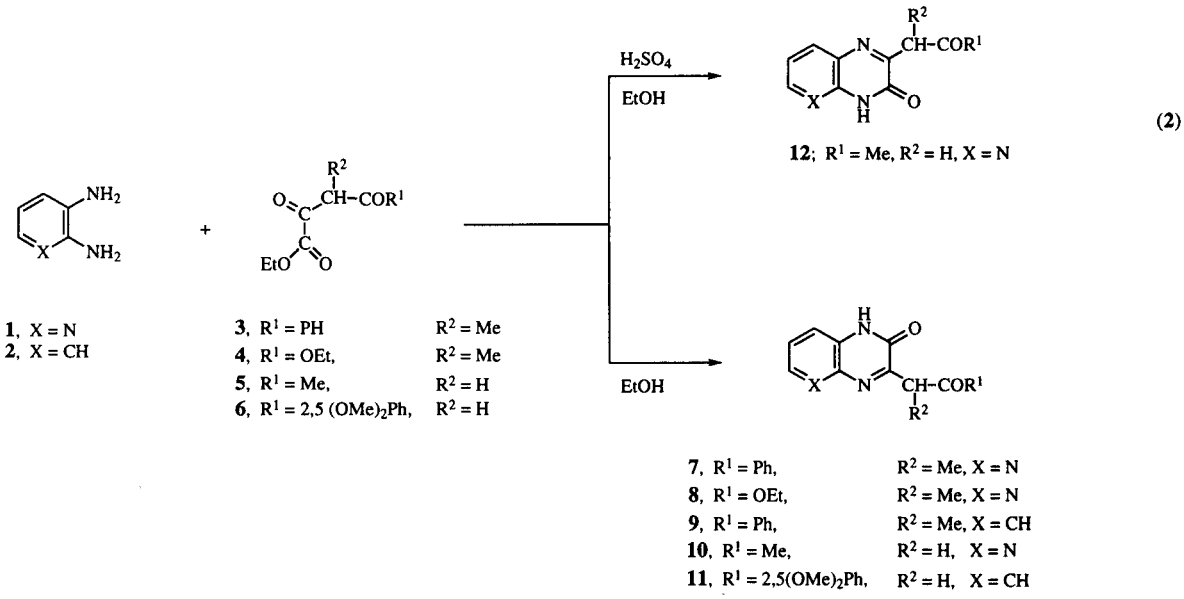
Results and Discussion.

a) Synthesis.

The syntheses of compounds **7-12** for their structural study were accomplished according to literature procedures [22-31] as shown in Eq. 2. The compounds **7**, **8**, and **10** were prepared by treatment of 2,3-diaminopyridine (**1**) with the corresponding dicarbonyl compounds **3**, **4**, and **5** in ethanol, respectively. 3-(1-Benzoyl)ethyl-1*H*-quinoxalin-2-one (**9**) and 3-(2,5-dimethoxy)phenacylidene-3,4-dihydro-1*H*-quinoxalin-2-one (**11**) were synthesized by the reaction of *o*-phenylenediamine (**2**) with **3** and **6**, respectively. In addition, 2-acetonylidene-1,2-dihydro-4*H*-pyrido[2,3-*b*]pyrazin-3-one (**12**) was synthesized from **1** and **5** in the presence of sulfuric acid in ethanol (Eq. 2).

b) Imine-Enamine Tautomerism.

In the ^{1}H-nmr spectra of **10**, **12**, and **11** in dimethyl sulfoxide (DMSO)-d_6, no methylene signals of the acetonyl or 2,5-dimethoxyphenacyl groups appear in the region between δ 6.76 and 0 ppm, except for those due to protons of the methyl groups, the solvent and water, but a singlet appears at δ 6.12-6.92 ppm. Further, the two broad signals at δ 11.7-12.1 and 12.8-13.8 ppm are assigned to amino protons. On the basis of ^{1}H-nmr and ir spectra as shown in Table 1, these compounds are concluded to exist in the enamine form similar to the related compounds [4-10]. On the other hand, in the ^{1}H-nmr spectrum of **7**, the signal due to the methine proton [-CH(CH_3)-] on the side chain was observed as a quartet at δ 5.24 ppm, and the signal of the methyl protons was revealed as a doublet at δ 1.74 ppm. The NH proton of **7** was observed as a



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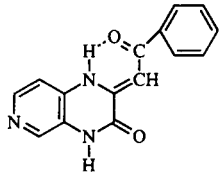

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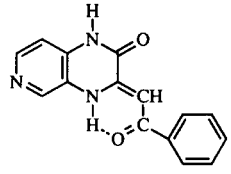

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broad singlet at δ 11.08 ppm. The relative signal intensity of the quartet and broad singlet in the spectrum of **7** represents one proton, respectively, when compared to the three protons of the doublet. Similarly, in the ^{1}H-nmr spectra of **8** and **9**, the methine and methyl signals were observed as a quartet and a doublet, respectively, as shown in Table 1. These results suggest that the compounds **7**, **8**, and **9** exist in the imine form. The imine structure of these compounds was further in evidenced by the ir spectra which were determined using potassium

Table 1

^{1}H-Nmr and Ir Spectral Data for Compounds **7-15** [a]

	^{1}H-Nmr δ (ppm)							Ir (cm^{-1})		
		(-CH(CH$_3$)-)		Ring (=CH)						
Compound	=CH (s, 1H)	CH (q, 1H)	CH$_3$ (dd, 3H)	6-H (dd, 1H)	7-H (dd, 1H)	8-H (dd, 1H)	N-H (br s, 1H)	ester	ν C=O ketone	lactam
7		5.24	1.74	8.66	7.42	8.09	11.06		1725	1690
8		4.30	1.71	8.71	7.50	7.72	11.89	1720		1690
9		5.29	1.66				11.88		1720	1690
10	6.12			8.03	7.10	7.80	11.72 12.80		1620	1690
11	6.92						11.99 13.78		1623	1690
12	6.12			8.04	7.10	7.43	11.84 12.80		1625	1695
13	6.91						12.09 13.88		1622	1689
14	6.87			8.12	7.14	7.41	12.4 13.4		1625	1710
15	5.56			7.94	7.08	7.84	11.0 12.1	1650		

[a] ^{1}H-nmr spectra of **7-9** were measured in deuteriochloroform, and those of **10-15** were measured in DMSO-d$_6$.

bromide disks. The keto carbonyl groups of **7** and **9** absorb at 1725 and 1720 cm^{-1}, respectively. The ester carbonyl of 8 absorbs at 1720 cm^{-1}. Their absorption bands appear in the ordinary carbonyl region, in contrast to the carbonyl bands (1622-1650 cm^{-1}) of 3-phenacylidene-3,4-dihydro-1*H*-quinoxalin-2-one (**13**) [5], 3-phenacylidene-3,4-dihydro-1*H*-pyrido[2,3-*b*]pyrazin-2-one (**14**) [8], and 3-ethoxycarbonylmethylene-3,4-dihydro-1*H*-pyrido-[2,3-*b*]pyrazin-2-one (**15**) [10].

Interestingly, the equilibrium of the imine-enamine tautomerism is influenced by temperature. Therefore, the temperature effect was investigated by the ^{1}H-nmr method over a temperature range from 50° to 150°: in DMSO-d_6. The ^{1}H-nmr spectra of 2-ethoxycarbonylmethylene-1,2-dihydro-4-methyl-4*H*-pyrido[2,3-*b*]pyrazin-3-one (**16**) [12] at various temperatures are shown in Figure 1. In the spectrum at 50° (the bottom spectrum), no signals appear for the methylene protons, but a singlet appears at δ 3.81 ppm, due to the methylene protons, as the temperature is elevated to 70-150°. A signal due to the methyl group in the imine form also appears at δ 3.62 ppm.

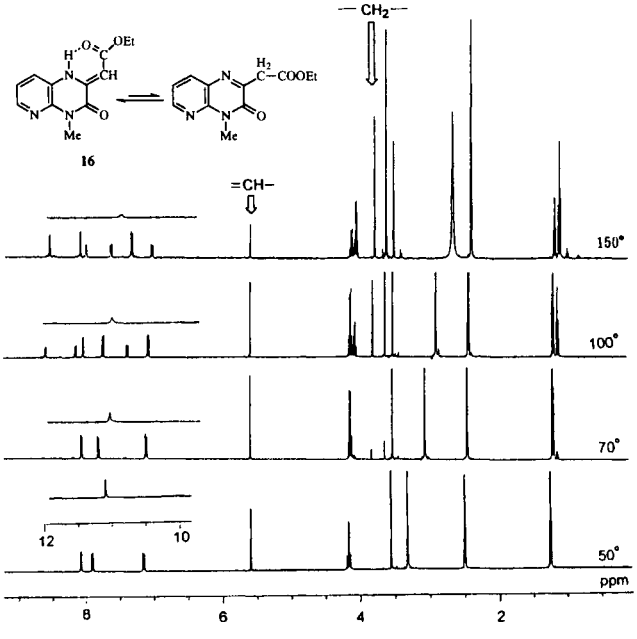


Figure 1. The ^{1}H-nmr spectra (400 MHz) of 2-ethoxycarbonylmethylene-1,2-dihydro-4-methyl-4*H*-pyrido[2,3-*b*]pyrazin-3-one (**16**) at 50, 70, 100, and 150°.

The temperature effect on the imine-enamine tautomerism in compounds **10**, **12**, and **15-20** is listed in Tables 2 and 3. The ratios of the imine and enamine forms were calculated from the ratio of the intensity of the methylene (-CH_2-) and methine (=CH-) signals.

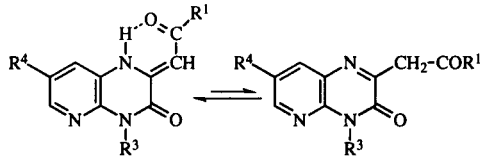
The equilibrium gradually shifts from the enamine form to the imine form for the 4*H*-pyrido[2,3-*b*]pyrazin-3-one system (Table 2) and for the 1*H*-pyrido[2,3-*b*]pyrazin-2-one system (Table 3), as the temperature rises. However, the equilibrium change from the enamine form to the imine form in the 1*H*-pyrido[2,3-*b*]pyrazin-2-one system such as **10**, **19**, and **20** is not pronounced as compared with that of 4*H*-pyrido[2,3-*b*]pyrazin-3-ones **12**, and **15-18**. It can be assumed that there is a small steric repression between the peri hydrogen atoms at the 8-position in **15** to destabilize the enamine form, whereas the hydrogen bond in **19** has no steric interaction with the neighboring nitrogen lone pair. In the 4*H*-pyrido[2,3-*b*]-pyrazin-3-one system, the order of the changes from the enamine to the imine forms at 150° is as follows: **16** (R^1 = OEt, R^3 = Me, R^4 = H, 61%) ≥ **15** (R^1 = OEt, R^3, R^4 = H, 58%) > **17** (R^1 = OMe, R^3 = H, R^4 = Br, 39%) > **12** (R^1 = Me, R^3, R^4 = H, 22%) > **18** (R^1 = Ph, R^2, R^3 = H, 7%). The replacement of an alkoxyl group in **15** by a phenyl group in **18** makes an extension of the conjugated system in the enamine form to include the benzene ring, so that the enamine form is stabilized. It is also interesting that both 2-phenacylidene-1,2-dihydro-4*H*-pyrido[3,4-*b*]-pyrazin-3-one (**21**) and 3-phenacylidene-3,4-dihydro-1*H*-pyrido[3,4-*b*]pyrazin-2-one (**22**) possess the enamine form which is entirely unchanged. On the other hand, **7** and **8** exist in the imine form which is maintained unchanged at 50-150°.

X-ray Analysis.

Because the connection between the enamine and imine forms was of interest, it was necessary to confirm the unambiguous structures of both **9** (imine form) and **11** (enamine form). The crystal structure of **9** was determined by X-ray crystallographic analysis. The single crystals of **9** were obtained by recrystallization from ethanol. The ORTEP diagram and atomic coordinates of **9** are shown in Figure 2 and Table 4. The C(7)-C(9) bond is a single bond [1.50(1) Å] and the N(2)-C(7) bond is a double bond [1.28 (1) Å]. The two C-O groups have a carbonyl character and the bond lengths are 1.22(1) Å [C(8)-O(l)] and 1.20(1) Å [C(11)-O(2)]; these are about the same. Thus, the results clearly indicate that **9** exists in the imine form. Further, the dihedral angle between C(8)-C(7) and C(9)-C(10) is 85 (1)°, almost perpendicular.

The structure of **11** was also unambiguously confirmed by X-ray crystallographic analysis. The single crystals of **11** were obtained by recrystallization from ethanol. The ORTEP diagram and atomic coordinates of **11** are shown in Figure 3 and Table 6. The quinoxalinone skeleton of **11** has a high coplanarity and the maximum atomic deviation from the least-squares plane is 0.03 Å. This compound possesses an enamine form. Thus, the C(7)-C(9) bond is a double bond [1.372(3) Å] and the N(2)-C(7) bond is a single bond [1.346(3) Å]. The N(2)-H(6) can be regarded as a single bond and the length is 1.01(3) Å. The two C-O

Table 2
Equilibrium in the 2-Derivatives of 1,2-Dihydro-4*H*-pyrido[2,3-*b*]pyrazin-3-one [a]

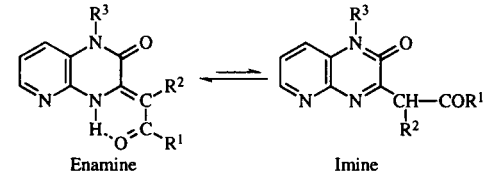


Enamine Imine

Compound	R^1	R^3	R^4	Form	Temperature (°C) 50	60	70	80	90	100	125	150
					Equilibrium (%)							
12	Me	H	H	Enamine	99.3	98.4	96.6	95.9	90.3	87.2	83.8	77.6
				Imine	0.7	1.6	3.4	4.1	9.7	12.8	16.2	22.4
18	Ph	H	H	Enamine	99.2	98.8	98.6	96.6	96.5	96.4	95.5	93.0
				Imine	0.8	1.2	1.4	3.4	3.5	3.6	4.5	7.0
15	OEt	H	H	Enamine	98.7	98.0	89.7	74.1	61.8	58.9	53.2	42.0
				Imine	1.3	2.0	10.3	25.9	38.2	41.1	46.8	58.0
16	OEt	Me	H	Enamine	98.0	97.1	92.8	85.2	74.9	64.0	49.8	39.2
				Imine	2.0	2.9	7.2	14.8	25.1	36.0	50.2	60.8
17	OMe	H	Br	Enamine	98.9	96.2	94.0	90.7	84.3	77.7	65.7	60.6
				Imine	1.1	3.8	6.0	9.3	15.7	22.3	34.3	39.4

[a] ^{1}H-nmr spectra of **12** and **15-18** were measured in DMSO-d_6.

Table 3
Equilibrium in the 3-Derivatives of 3,4-Dihydro-1*H*-pyrido[2,3-*b*]pyrazin-2-one [a]



Enamine Imine

Compound	R^1	R^2	R^3	Form	Temperature (°C) 50	60	70	80	90	100	125
					Equilibrium (%)						
10	Me	H	H	Enamine	98.1	99.9	98.0	97.4	94.8	94.5	93.8
				Imine	1.9	1.1	2.0	2.6	5.2	5.5	6.2
19	OEt	H	H	Enamine	100	100	99.6	98.6	98.1	97.4	96.9
				Imine	0	0	1.4	1.4	1.9	2.6	3.1
20	OEt	H	Me	Enamine	99.2	98.8	98.6	96.6	96.5	96.4	95.5
				Imine	0.8	1.2	1.4	3.4	3.5	3.6	4.5
7	Ph	Me	H	Enamine	0	0	0	0	0	0	0
				Imine	100	100	100	100	100	100	100
8	OEt	Me	H	Enamine	0	0	0	0	0	0	0
				Imine	100	100	100	100	100	100	100

[a] ^{1}H-nmr spectra of **10**, **19**, and **20** were measured in DMSO-d_6.

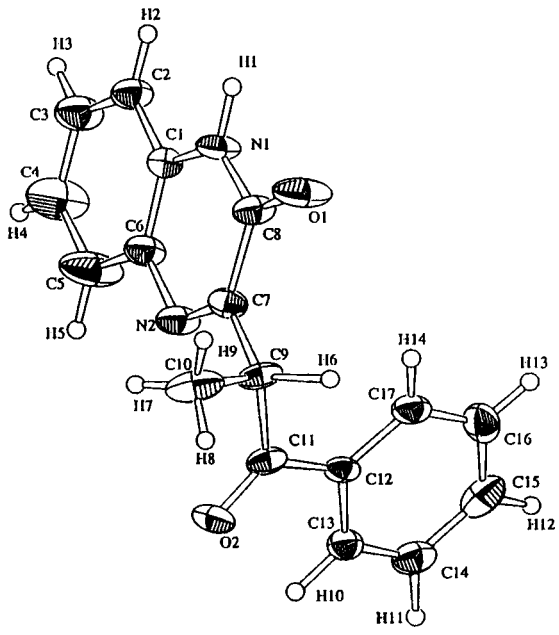


Figure 2. Molecular structure of 3-(1-benzoyl)ethyl-1*H*-quinoxalin-2-one **9**.

Table 4

Fractional Atomic Coordinates **9** with Est's in Parentheses

atom	x	y	z	B(eq)
O(1)	0.487(2)	0.483(1)	0.4278(3)	6.6(3)
O(2)	0.961(1)	0.2403(9)	0.2839(3)	4.7(2)
N(1)	0.729(2)	0.380(1)	0.4900(3)	4.4(3)
N(2)	0.965(2)	0.251(1)	0.4126(3)	4.4(3)
C(1)	0.913(2)	0.293(1)	0.5048(4)	3.5(3)
C(2)	0.979(2)	0.269(1)	0.5578(4)	4.3(3)
C(3)	1.162(2)	0.183(2)	0.5707(5)	5.7(4)
C(4)	1.282(3)	0.120(2)	0.5318(6)	8.8(6)
C(5)	1.217(3)	0.141(2)	0.4791(5)	8.4(5)
C(6)	1.032(2)	0.228(1)	0.4651(4)	4.2(3)
C(7)	0.792(2)	0.332(1)	0.3997(4)	3.6(3)
C(8)	0.653(2)	0.405(1)	0.4391(4)	4.2(3)
C(9)	0.726(2)	0.362(1)	0.3438(4)	4.0(3)
C(10)	0.851(3)	0.497(1)	0.3266(4)	6.1(4)
C(11)	0.797(2)	0.233(1)	0.3112(4)	3.5(3)
C(12)	0.652(2)	0.101(1)	0.3136(4)	3.2(3)
C(13)	0.724(2)	-0.018(1)	0.2869(4)	3.7(3)
C(14)	0.598(3)	-0.143(2)	0.287l(5)	4.7(4)
C(15)	0.395(3)	-0.151(2)	0.3135(5)	5.5(4)
C(16)	0.320(2)	-0.033(2)	0.3396(5)	5.3(4)
C(17)	0.447(2)	0.092(1)	0.3399(4)	4.1(3)
H(1)	0.6481	0.4259	0.5166	5.2286
H(2)	0.8947	0.3135	0.5842	5.113
H(3)	1.2068	0.1656	0.6062	6.8286
H(4)	1.4127	0.0604	0.5409	10.5982
H(5)	1.3017	0.0944	0.4531	10.0889
H(6)	0.53(2)	0.38(1)	0.326(5)	11(4)
H(7)	1.0091	0.4953	0.3395	7.2860
H(8)	0.8450	0.5014	0.2897	7.2860
H(9)	0.7746	0.5788	0.3398	7.2860
H(10)	0.87(2)	-0.01(1)	0.267(4)	4(2)
H(11)	0.65(2)	-0.23(1)	0.265(4)	5(3)
H(12)	0.3080	-0.2379	0.3138	6.6124
H(13)	0.1792	-0.0378	0.3576	6.3438
H(14)	0.3929	0.1732	0.3582	4.9096

groups have a carbonyl character and the bond lengths are 1.233(3) Å [C(8)-O(1)] and 1.250(3) Å [C(10)-O(2)], whereas the C(7)-C(8) and C(9)-C(10) bonds are single bonds of 1.484(4) and 1.422(4) Å, respectively. Interestingly, the bond length of the ketone-carbonyl C(10)-O(2) is elongated as compared with that of the amide-carbonyl C(8)-O(1), reflecting the hydrogen bond between O(2) and H(6).

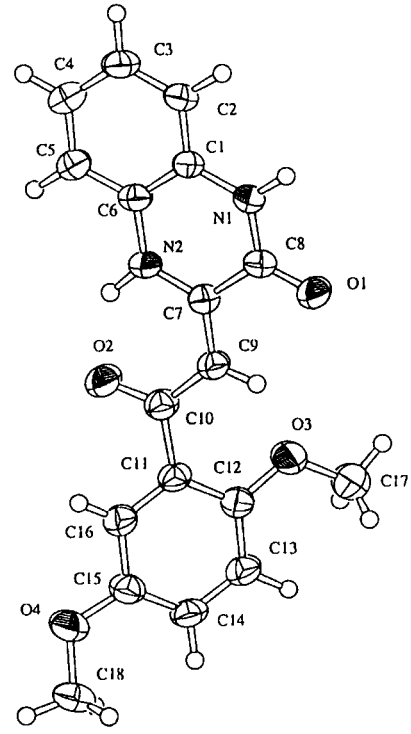


Figure 3. Molecular structure of 3-(2,5-dimethoxy)phenacylidene-3,4-dihydro-1*H*-quinoxalin-2-one **11**.

EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded on a Nippon Bunko IRA-1 spectrometer. The ^{1}H-nmr spectra were obtained on a JEOL EX-400 spectrometer in DMSO-d_6 (DMSO-d_5 δ 2.50 ppm as an internal standard) and in deuteriochloroform (TMS as an internal standard). Chemical shifts are reported in ppm (δ). X-ray analysis was measured on a Rigaku AFC7R diffractometer with graphite monochromated Mo-Kα radiation and a 12kW rotating anode generator.

Ethyl acetylpyruvate, 1-ethoxalylpropiophenone, and ethyl ethoxalylpropionate were prepared in a similar manner as described in the literature [32-33].

3-(1-Benzoyl)ethyl-1*H*-quinoxalin-2-one (**9**).

To a solution of *o*-phenylenediamine (**2**) (0.33 g, 3.0 mmoles) in ethanol (20 ml), a solution of 1-ethoxalylpropiophenone (**3**) (0.77 g, 3.3 mmoles) in ethanol (5 ml) was added dropwise with stirring at room temperature. After the mixture had been stirred for a further 4 hours, it was allowed to stand at ambient temperature for 17 hours. The precipitate was collected on a funnel. The

Table 5

Bond Lengths (Å) and Bond Angles (deg) for **9**

O(1)	C(8)	1.22(1)		O(2)	C(11)	1.20(1)	
N(1)	C(1)	1.36(1)		N(1)	C(8)	1.38(1)	
N(2)	C(6)	1.40(1)		N(2)	C(7)	1.28(1)	
C(1)	C(2)	1.42(1)		C(1)	C(6)	1.40(1)	
C(2)	C(3)	1 35(2)		C(3)	C(4)	1.38(2)	
C(4)	C(5)	1.40(2)		C(5)	C(6)	1.37(2)	
C(7)	C(8)	1.49(1)		C(7)	C(9)	1.50(1)	
C(9)	C(10)	1.53(2)		C(9)	C(11)	1.54(2)	
C(11)	C(12)	1.49(2)		C(12)	C(13)	1.38(1)	
C(12)	C(17)	1.39(1)		C(13)	C(14)	1.37(2)	
C(14)	C(15)	1.38(2)		C(15)	C(16)	1.37(2)	
C(16)	C(17)	1.38(2)					
C(l)	N(1)	C(8)	124.7(10)	C(6)	N(2)	C(7)	120(1)
N(1)	C(1)	O(2)	121(1)	N(1)	C(1)	C(6)	116(1)
C(2)	C(1)	C(6)	121(1)	C(1)	C(2)	C(3)	119(1)
C(2)	C(3)	C(4)	119(1)	C(3)	C(4)	C(5)	121(1)
C(4)	C(5)	O(6)	120(1)	N(2)	C(6)	C(1)	121(1)
N(2)	C(6)	C(5)	120(1)	C(1)	C(6)	C(5)	117(1)
N(2)	C(7)	C(8)	122(1)	N(2)	C(7)	C(9)	120(1)
C(8)	C(7)	C(9)	117(1)	O(1)	C(8)	N(1)	122(1)
O(1)	C(8)	C(7)	123(1)	N(1)	C(8)	C(7)	114(1)
C(7)	C(9)	C(10)	109(1)	C(7)	C(9)	C(11)	108.7(10)
C(10)	C(9)	C(11)	110.5(10)	O(2)	C(11)	C(9)	120(1)
O(2)	C(11)	C(12)	121(1)	C(9)	C(11)	C(12)	117(1)
C(11)	C(12)	C(13)	117(1)	C(11)	C(12)	C(17)	123(1)
C(13)	C(12)	C(17)	118(1)	C(12)	C(13)	C(14)	120(1)
C(13)	C(14)	C(15)	120(1)	C(14)	C(15)	C(16)	119(1)
C(15)	C(16)	C(17)	120(1)	C(12)	C(17)	C(16)	120(1)

Table 6
Fractional Atomic Coordinates in **11** with Est's in Parentheses

atom	x	y	z	B(eq)
O(1)	0.9199(2)	0.4567(2)	0.40105(10)	4.70(5)
O(2)	0.7122(1)	-0.0353(2)	0.29211(10)	4.81(5)
O(3)	0.6321(2)	0.3976(2)	0.19481(10)	5.00(5)
O(4)	0.6708(2)	-0.1162(2)	-0.0179(1)	5.38(5)
N(1)	0.9409(2)	0.3061(3)	0.5198(1)	3.67(5)
N(2)	0.8232(2)	0.0633(3)	0.4369(1)	3.39(5)
C(1)	0.9253(2)	0.1647(3)	0.5637(1)	3.22(6)
C(2)	0.9694(2)	0.1486(3)	0.6486(1)	3.96(6)
C(3)	0.9532(2)	0.0088(3)	0.6903(2)	4.38(7)
C(4)	0.8938(2)	-0.1160(4)	0.6481(2)	4.51(7)
C(5)	0.8508(2)	-0.1012(3)	0.5638(2)	3.98(7)
C(6)	0.8660(2)	0.0408(3)	0.5219(1)	3.19(6)
C(7)	0.8341(2)	0.2000(3)	0.3935(1)	3.16(6)
C(8)	0.9014(2)	0.3309(3)	0.4379(1)	3.54(6)
C(9)	0.7882(2)	0.2220(3)	0.3111(1)	3.37(6)
C(10)	0.7270(2)	0.1007(3)	0.2624(1)	3.55(6)
C(11)	0.6857(2)	0.1309(3)	0.1707(1)	3.19(6)
C(12)	0.6426(2)	0.2770(3)	0.1381(1)	3.56(6)
C(13)	0.6093(2)	0.2906(3)	0.0518(1)	3.89(6)
C(14)	0.6176(2)	0.1628(3)	-0.0025(2)	3.87(6)
C(15)	0.6591(2)	0.0193(3)	0.0290(1)	3.80(6)
C(16)	0.6917(2)	0.0039(3)	0.1156(2)	3.81(6)
C(17)	0.5773(4)	0.5414(4)	0.1637(2)	5.82(9)
C(18)	0.6414(3)	-0.1054(5)	-0.1081(2)	5.00(9)
H(1)	0.984(2)	0.393(3)	0.548(1)	4.8(6)
H(2)	1.014(2)	0.246(3)	0.678(1)	5.4(6)
H(3)	0.979(2)	-0.001(3)	0.754(1)	5.2(6)

Table 6 (continued)

atom	x	y	z	B(eq)
H(4)	0.885(2)	-0.216(3)	0.678(1)	4.3(6)
H(5)	0.807(2)	-0.193(3)	0.532(1)	3.9(5)
H(6)	0.786(2)	-0.019(3)	0.402(2)	7.8(8)
H(7)	0.799(2)	0.323(2)	0.287(1)	3.1(5)
H(8)	0.575(2)	0.395(3)	0.2027(1)	4.4(6)
H(9)	0.597(2)	0.176(2)	-0.062(1)	3.8(5)
H(10)	0.719(2)	-0.093(3)	0.138(1)	4.2(6)
H(111)	0.581(2)	0.615(3)	0.212(2)	7.1(8)
H(12)	0.613(2)	0.585(4)	0.115(2)	8.0(9)
H(13)	0.495(2)	0.517(4)	0.140(2)	10(1)
H(14)	0.658(2)	-0.216(3)	-0.131(2)	7.2(8)
H(15)	0.561(2)	-0.057(3)	-0.119(2)	7.3(8)
H(16)	0.689(2)	-0.024(4)	-0.133(2)	8.6(10)

crude product was recrystallized from ethanol to give **9**, mp 217-218°; ir (potassium bromide): ν 1720 (C=O), 1690 (NHC=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.66 (d, 3H, -CH(CH_3)-), 5.29 (q, 1H, -CH(CH_3)-), 6.99-8.10 (m, 9H, aromatic and phenyl protons), 11.88 (br s, 1H, N-H).

Anal. Calcd. for $C_{17}H_{14}N_2O_2$: C, 73.37; H, 5.07; N, 10.06. Found: C, 73.55; H, 4.97; N, 10.29.

3-(1-Benzoyl)ethyl-1*H*-pyrido[2,3-*b*]pyrazin-2-one (**7**).

This compound was prepared from 2,3-diaminopyridine (**1**) (0.33 g, 3.0 mmoles) and **3** (0.77 g, 3.3 mmoles) in a manner similar to that described for the synthesis of **9**, and was obtained

Table 7
Bond Lengths (Å) and Bond Angles (deg) for **11**

O(1)	C(8)	1.235(3)		C(3)	C(4)	1.386(4)	
O(2)	C(10)	1.251(3)		C(4)	C(5)	1.378(3)	
O(3)	C(12)	1.366(3)		C(5)	C(6)	1.383(3)	
O(3)	C(17)	1.427(3)		C(7)	C(8)	1.482(3)	
O(4)	C(15)	1.371(3)		C(7)	C(9)	1.367(3)	
O(4)	C(18)	1.434(3)		C(9)	C(10)	1.420(3)	
N(1)	C(1)	1.395(3)		C(10)	C(11)	1.501(3)	
N(1)	C(8)	1.343(3)		C(11)	C(12)	1.398(3)	
N(2)	C(6)	1.394(3)		C(11)	C(16)	1.381(3)	
N(2)	C(7)	1.348(3)		C(12)	C(13)	1.383(3)	
C(1)	C(2)	1.391(3)		C(13)	C(14)	1.383(3)	
C(1)	C(6)	1.377(3)		C(14)	C(15)	1.368(3)	
C(2)	C(3)	1.367(3)		C(15)	C(16)	1.388(3)	
C(12)	O(3)	C(17)	117.9(2)	O(1)	C(8)	C(7)	121.4(1)
C(15)	O(4)	C(18)	117.5(2)	N(1)	C(8)	C(7)	116.8(2)
C(1)	N(1)	C(8)	124.1(2)	C(7)	C(9)	C(10)	122.9(2)
C(6)	N(2)	C(7)	124.1(2)	O(2)	C(10)	C(9)	122.0(2)
N(1)	C(1)	C(2)	120.5(2)	O(2)	C(10)	C(11)	118.2(2)
N(1)	C(1)	C(6)	119.2(2)	C(9)	C(10)	C(11)	119.6(2)
C(2)	C(1)	C(6)	120.3(2)	C(10)	C(11)	C(12)	124.6(2)
C(1)	C(2)	C(3)	119.5((3)	C(10)	C(11)	C(16)	116.6(2)
C(2)	C(3)	C(4)	120.2(2)	C(12)	C(11)	C(16)	118.8(2)
C(3)	C(4)	C(5)	120.6(3)	O(3)	C(12)	C(11)	117.4(2)
C(1)	C(5)	C(6)	119.3(3)	O(3)	C(12)	C(13)	123.6(2)
N(2)	C(6)	C(1)	118.0(2)	C(11)	C(12)	C(13)	119.0(2)
N(2)	C(6)	C(5)	121.8(2)	C(12)	C(13)	C(14)	121.3(3)
C(1)	C(6)	C(5)	120.2(2)	C(13)	C(14)	C(15)	120.0(2)
N(2)	C(7)	C(8)	117.6(2)	O(4)	C(15)	C(14)	125.5(2)
N(2)	C(7)	C(9)	123.4(2)	O(4)	C(15)	C(16)	115.3(2)
C(8)	C(7)	C(7)	119.0(2)	C(14)	C(15)	C(16)	119.2(2)
O(1)	C(8)	N(1)	121.8(2)	C(11)	C(16)	C(15)	121.7(3)

in a yield of 0.72 g (86%). An analytical sample was recrystallized from ether, mp 264-265° dec; ir (potassium bromide): ν 1720 (C=O), 1690 (NHC=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.74 (d, 3H, -CH(CH_3)-), 5.24 (q, 1H, -CH(CH_3)-), 7.39-7.60 (m, 6H, aromatic and phenyl protons), 8.09 (dd, 1H, aromatic protons), 8.66 (dd, 1H, aromatic protons), 11.12 (br s, 1H, N-H).

Anal. Calcd. for $C_{16}H_{13}N_3O_2$: C, 68.81; H, 4.09; N, 15.04. Found: C, 68.61; H, 4.35; N, 15.01.

3-(1-Ethoxycarbonyl)ethyl-1*H*-pyrido[2,3-*b*]pyrazin-2-one (**8**).

This compound was prepared from **1** (0.33 g, 3.0 mmoles) and ethyl ethoxalylpropionate (**4**) (0.78 g, 4.1 mmoles) in a manner similar to that described for the synthesis of **9**, and was obtained in a yield of 0.52 g (70%). An analytical sample was recrystallized from ether, mp 201-202° dec; ir (potassium bromide): ν 1720 (C=O), 1690 (NHC=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.23 (t, 3H, CH_2CH_3), 1.71 (d, 3H, -CH(CH_3)-), 4.20 (q, 2H, CH_2CH_3), 4.30 (q, 1H, -CH(CH_3)-), 7.50 (dd, 1H, 7-H), 7.72 (dd, 1H, 8-H), 8.71 (dd, 1H, 6-H), 11.89 (br s, 1H, N-H).

Anal. Calcd. for $C_{12}H_{13}N_3O_3$: C, 58.29; H, 5.29; N, 16.99. Found: C, 58.20; H, 5.05; N, 16.84.

3-Acetonylidene-3,4-dihydro-1*H*-pyrido[2,3-*b*]pyrazin-2-one (**10**).

This compound was prepared from **1** (1.09 g, 10 mmoles) and ethyl acetylpyruvate (**5**) (1.58 g, 10 mmoles) in a manner similar to that described for the synthesis of **9**, and was obtained in a yield of 1.58 g (78%); mp 300° dec; ^{1}H-nmr (DMSO-d_6): δ 2.22 (s, 3H, CH_3), 6.12 (s, 1H, =CH), 7.10 (dd, 1H, aromatic proton), 7.80 (dd, 1H, aromatic proton), 8.03 (dd, 1H, aromatic proton), 11.72 (br s, 1H, N-H), 12.80 (br s, 1H, N-H).

Anal. Calcd. for $C_{10}H_9N_3O_2$: C, 59.11; H, 4.46; N, 20.68. Found: C, 59.32; H, 4.37; N, 20.96.

3-(2,5-Dimethoxy)phenacylidene-3,4-dihydro-1*H*-quinoxalin-2-one (**11**).

This compound was synthesized in a similar manner to that described for **9**, yield 76%, yellow platelets from ethanol, mp 211-212°; ^{1}H-nmr (DMSO-d_6): δ 2.22 (s, 3H, OCH_3), 2.22 (s, 3H, OCH_3), 6.92 (s, 1H, =CH), 6.99-8.10 (m, 7H, aromatic and phenyl protons), 11.99 (br s, 1H, N-H), 13.78 (br s, 1H, N-H).

2-Acetonylidene-1,2-dihydro-4*H*-pyrido[2,3-*b*]pyrazin-3-one (**12**).

To a suspension of **1** (1.09 g, 10 mmoles) in ethanol (30 ml) and 2*M* sulfuric acid (20 ml) was added dropwise a solution of **5** (1.58 g, 10 mmoles) in ethanol (10 ml) with stirring at room temperature. The mixture was refluxed for 3 hours. After cooling, the precipitate was collected by filtration and washed well with water and ethanol. The crude product was recrystallized from acetic acid-ethanol to give **12**, mp 300° dec; ^{1}H-nmr (DMSO-d_6): δ 2.22 (s, 3H, CH_3), 6.12 (s, 1H, =CH), 7.10 (dd, 1H, aromatic proton), 7.43 (dd, 1H, aromatic proton), 8.04 (dd, 1H, aromatic proton), 11.84 (br s, 1H, N-H), 12.80 (br s, 1H, N-H).

Anal. Calcd. for $C_{10}H_9N_3O_2$: C, 59.11; H, 4.46; N, 20.68. Found: C, 59.00; H, 4.39; N, 20.85.

X-Ray Analysis of **9**.

Crystal data are: $C_{17}H_{14}N_2O_2$, FW = 278.31, from ethanol, colorless prism, 0.33 x 0.18 x 0.18 mm, monoclinic, space group $P2_1/c$; a = 5.716(4) Å, b = 9.337(7) Å, c = 25.756(3) Å, β = 92.94(3)°, V = 1372(1) Å^3, Z = 4, D_{calcd} = 1.346 g cm^{-3}, F(000) = 584.00, μ (Mo-Kα) = 0.9 cm^{-1}.

Data collection was accomplished with an automatic four circle Rigaku AFC7R diffractometer operating with the teXsan program system with graphite monochromaeted Mo-Kα radiation (λ = 0.71069 Å). The intensity data were collected using the ω-2θ scan technique to a maximum 2θ value of 55.1°. A total of 3387 reflections were measured and 1257 were considered as observed [I > 4.00 ó (I) criterium]. The data were corrected for Lorentz and Polarization effects.

Structure Solution and Refinement.

The structure was solved by a direct method using SAPI91[34] and full matrix least-squares refinement (DIRDIF92 [35]). The final R and Rw values are 0.069 and 0.098, respectively.

X-Ray Analysis of **11**.

Crystal data are: $C_{18}H_{16}N_2O_4$, FW = 324.34, from ethanol, yellow plate, 0.12 x 0.50 x 0.50 mm, monoclinic, space group $P2_1/c$; a = 11.896(4) Å, b = 8.352(2) Å, c = 15.858(2) Å, β = 96.93(2)°, V = 1564.7(6) Å^3, Z = 4, D_{calcd} = 1.377 g cm^{-3}, F(000) = 680.00, μ (Mo- Kα) = 0.99 cm^{-1}.

Data collection was accomplished with an automatic four circle Rigaku AFC7R diffractometer with Mo-Kα radiation (λ = 0.71069 Å). The intensity data were collected using the ω-2θ scan technique (2θ ≤ 55.1). A total of 3874 reflections were measured and 1818 were considered as observed [I > 3.00 σ (I) criterium]. The data were corrected for Lorentz and Polarization effects.

Structure Solution and Refinement.

The structure was solved by a direct method using SAPI91 [34] and full matrix least-squares refinement (DIRDIF92 [35,36]). The final R and Rw values are 0.038 finement (DIRDIF92 [35,36]). The final R and Rw values are 0.038 and 0.033, respectively.

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