A Convenient Synthesis of (Z)-3-(α-Alkoxycarbonyl-α-cyanomethylene)-2-oxo-1,2,3,4-tetrahydroquinoxalines and Related Compounds

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(Z)-3-(α-Alkoxycarbonyl-α-cyanomethylene)-2-oxo-1,2,3,4-tetrahydroquinoxalines **3** and (Z)-3-(α-alkoxycarbonyl-α-cyanomethylene)-3,4-dihydrobenzo[*g*]quinoxalin-2(1*H*)-ones **5** possessing various alkoxycarbonyl groups were prepared in good yields directly from the reaction of dialkyl (*E*)-2,3-dicyanobutendioates **1** with *o*-phenylenediamine (**2**) or with 2,3-diaminonaphthalene (**4**), respectively. Furthermore, 2,3-diaminopyridine (**6**) and 3,4-diaminopyridine (**7**) were reacted with the diethyl ester **1b** to give (Z)-2-(α-cyano-α-ethoxycarbonylmethylene)-1,2-dihydro-4*H*-pyrido[2,3-*b*]pyrazin-3-one (**8**) and (Z)-3-(α-cyano-α-ethoxycarbonylmethylene)-3,4-dihydro-1*H*-pyrido[3,4-*b*]pyrazin-2-one (**9**), respectively. The structural studies of **3**, **5**, **8**, and **9** were carried out by nmr experiments in some details.

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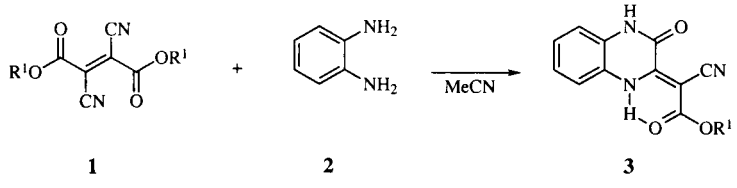
It is known that many quinoxaline derivatives, such as quinoxalinecarbonitriles [1-2], have potential biological and medicinal activities. Even though several reports on exomethylene derivatives of tetrahydroquinoxalines are known [3-10], the preparation of 2-pyrazinones, having an α-alkoxycarbonyl-α-cyanomethylene group, has not been reported. In a previous paper [11], we described a new method leading to excellent yields of dialkyl (*E*)-2,3-dicyanobutendioates **1** [12,13] as the starting material for a series of our research [14]. Thus, we have designed a simple synthesis for pyrazinone derivatives starting from *vicinal*-diamines, such as *o*-phenylenediamine (**2**) or 2,3-diaminonaphthalene (**4**), and **1** bearing alkyl groups, such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *sec*-butyl, and benzyl, respectively. We now wish to report a convenient method for a one-step synthesis of novel (Z)-3-(α-alkoxycalbonyl-α-cyanomethylene)-2-oxo-1,2,3,4-tetrahydroquinoxalines **3** and the (Z)-3-(α-alkoxycarbonyl-α-cyanomethylene)-3,4-dihydrobenzo[*g*]quinoxalin-2(1*H*)-ones **5** from **1** with **2** or **4**, respectively (Scheme 1). In general, the reaction of equimolecular amounts of 1 and the *vicinal*-diamine **2** or **4** carried out in acetonitrile at room temperature for 1 hour to yield **3** and **5**.

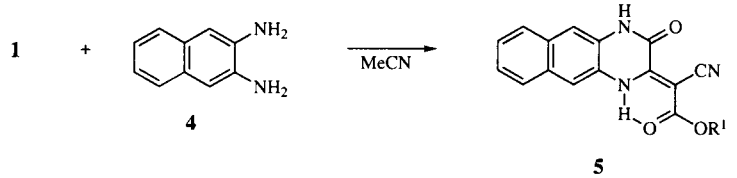
The reaction may be assumed to proceed as shown in Scheme 2 and involves the Michael addition of **2** (or **4**) to 1. The resulting adduct undergoes cyclization by intramolecular nucleophilic attack at the ester group, to give the pyrazinone ring with an elimination of hydrogen cyanide.

The ir spectra of **3** and **5** showed absorption bands due to the lactam NH stretching vibration of the 1-position in the 3200-3270 cm^{-1} region and the enamine NH stretching

Scheme 1



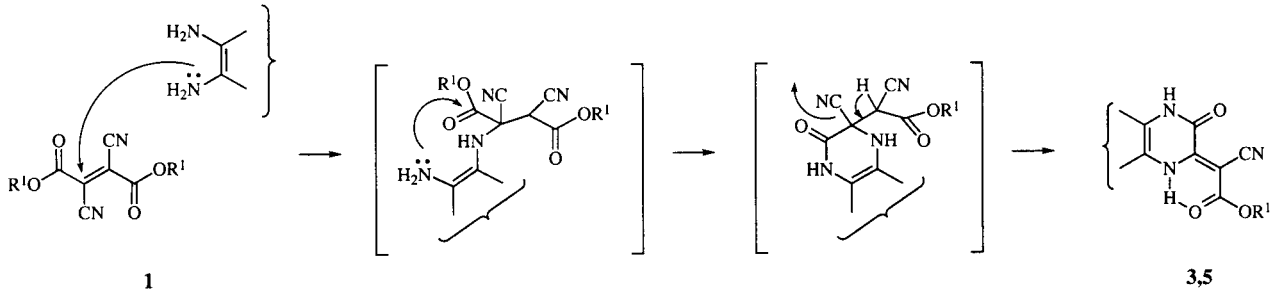
1 **2** **3**



4 **5**

1,3,5	R^1	1,3,5	R^1	1,3,5	R^1
a	Me	**d**	*i*-Pr	**g**	*s*-Bu
b	Et	**e**	Bu	**h**	benzyl
c	Pr	**f**	*i*-Bu		

Scheme 2



vibration of the 4-position in the 3105-3180 cm^{-1} region, an α,β-unsaturated nitrile at 2198-2205 cm^{-1}, and an ester carbonyl and an amide groups at 1675-1691 cm^{-1} and 1638-1658 cm^{-1}, respectively.

These observations would indicate that the presence of an intramolecular hydrogen-bond between 4-NH group and the ester group on the side chain of **3** and **5** (Scheme 1). The ester carbonyl band of lower frequency was attrib-

Scheme 3

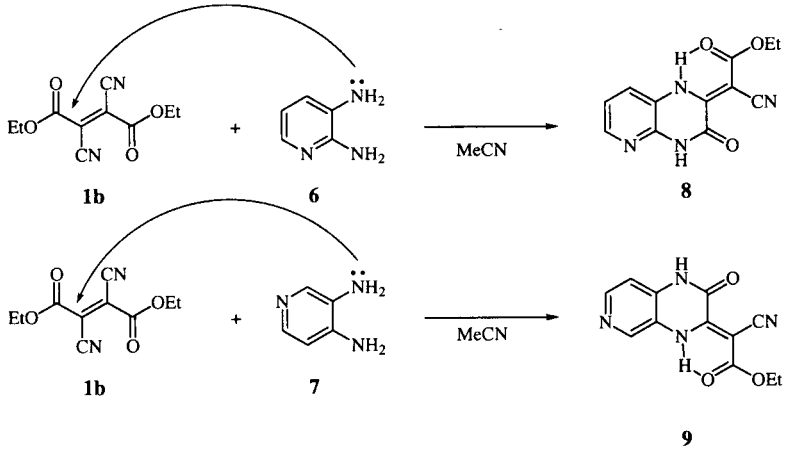


Table 1

NMR Data of Compounds **3** in Dimethyl-d_6 Sulfoxide at 30°

Product	^{1}H-NMR, δ (ppm), J (Hz)	^{13}C-NMR, δ (ppm)
3a	3.81 (s, 3H, CH_3), 7.14-7.19 (m, 1H, 6-H), 7.18 (d, 1H, J = 8.8, 8-H), 7.21-7.26 (m, 1H, 7-H), 7.60 (d, 1H, J = 8.1, 5-H), 12.32 (br s, 1H, NH), 12.68 (br s, 1H, NH)	52.2 (OCH_3), 70.4 (*C*-CN), 115.2 (CH, C8), 116.4 (CN), 117.3 (CH, C5), 123.0 (C4a), 123.7 (CH, C6), 125.4 (CH, C7), 126.9 (C8a), 150.2 (C3), 153.5 (C2), 168.9 (COO)
3b	1.29 (t, 3H, J = 7.1, CH_3), 4.28 (q, 2H, J = 7.1, OCH_2), 7.14-7.19 (m, 1H, 6-H), 7.18 (d, 1H, J = 8.8, 8-H), 7.21-7.26 (m, 1H, 7-H), 7.59 (d, 1H, J = 8.2, 5-H), 12.29 (br s, 1H, NH), 12.72 (br s, 1H, NH)	14.1 (CH_3), 60.9 (OCH_2), 70.4 (*C*-CN), 115.1 (CH, C8), 116.4 (CN), 117.3 (CH, C5), 123.0 (C4a), 123.6 (CH, C6), 125.2 (CH, C7), 126.9 (C8a), 150.2 (C3), 153.4 (C2), 168.5 (COO)
3c	0.95 (t, 3H, J = 7.4, CH_3), 1.69 (sextet, 2H, J = 7.0, CH_2CH_3), 4.19 (t, 2H, J = 6.6, OCH_2), 7.14-7.19 (m, 1H, 6-H), 7.18 (d, 1H, J = 8.8, 8-H), 7.21-7.26 (m, 1H, 7-H), 7.59 (d, 1H, J = 8.1, 5-H), 12.28 (br s, 1H, NH), 12.72 (br s, 1H, NH)	10.1 (CH_3), 21.5 (CH_2CH_3), 60.9 (OCH_2), 70.4 (*C*-CN), 115.2 (CH, C8), 116.3 (CN), 117.3 (CH, C5), 123.0 (C4a), 123.6 (CH, C6), 125.3 (CH, C7), 126.9 (C8a), 150.2 (C3), 153.5 (C2), 168.5 (COO)
3d	1.30 (d, 6H, J = 6.2, $2CH_3$), 5.09 (septet, 1H, J = 6.2, OCH), 7.13-7.18 (m, 1H, 6-H), 7.18 (d, 1H, J = 8.8, 8-H), 7.21-7.26 (m, 1H, 7-H), 7.59 (d, 1H, J = 8.1, 5-H), 12.28 (br s, 1H, NH), 12.76 (br s, 1H, NH)	21.6 ($2CH_3$), 68.6 (OCH), 70.9 (*C*-CN), 115.2 (CH, C8), 116.3 (CN), 117.2 (CH, C5), 123.0 (C4a), 123.6 (CH, C6), 125.3 (CH, C7), 126.9 (C8a), 150.2 (C3), 153.5 (C2), 168.1 (COO)
3e	0.93 (t, 3H, J = 7.4, CH_3), 1.40 (sextet, 2H, J = 7.4, CH_2CH_3), 1.66 (quintet, 2H, J = 7.0,	13.5 (CH_3), 18.5 (CH_2CH_3), 30.1 (CH_2CH_2O), 64.5 (OCH_2), 70.6 (*C*-CN), 115.2 (CH, C8),

Table 1

NMR Data of Compounds **3** in Dimethyl-d_6 Sulfoxide at 30°

Product	^{1}H-NMR, δ (ppm), J (Hz)	^{13}C-NMR, δ (ppm)
	7.19 (m, 1H, 6-H), 7.18 (d, 1H, J = 8.8, 8-H), 7.21-7.26 (m, 1H, 7-H), 7.59 (d, 1H, J = 8.1, 5-H), 12.33 (br s, 1H, NH), 12.71 (br s, 1H, NH)	(CH, C6), 125.3 (CH, C7), 126.9 (C8a), 150.2 (C3), 153.5 (C2), 168.5 (COO)
3f	0.96 (d, 6H, J = 6.6, $2CH_3$), 1.98 (nonet, 1H, J = 6.6, $CHCH_2O$), 4.03 (d, 2H, J = 6.6, OCH_2), 7.14-7.19 (m, 1H, 6-H), 7.18 (d, 1H, J = 8.8, 8-H), 7.21-7.26 (m, 1H, 7-H), 7.59 (d, 1H, J = 8.0, 5-H), 12.28 (br s, 1H, NH), 12.70 (br s, 1H, NH)	18.7 ($2CH_3$), 27.3 ($CHCH_2O$), 70.4 (OCH_2), 70.6 (*C*-CN), 115.2 (CH, C8), 116.3 (CN), 117.3 (CH, C5), 123.0 (C4a), 123.6 (CH, C6), 125.3 (CH, C7), 126.9 (C8a), 150.2 (C3), 153.5 (C2), 168.4 (COO)
3g	0.92 (t, 3H, J = 7.4, CH_3CH_2), 1.27 (d, 3H, J = 6.3, CH_3CH), 1.63 (quintet, 2H, J = 7.0, CH_2), 4.93 (sextet, 1H, J = 6.3, OCH), 7.13-7.19 (m, 1H, 6-H), 7.18 (d, 1H, J = 8.8, 8-H), 7.21-7.26 (m, 1H, 7-H), 7.59 (d, 1H, J = 8.1, 5-H), 12.26 (br s, 1H, NH), 12.75 (br s, 1H, NH)	9.3 (CH_3CH_2), 19.2 (CH_3CH), 28.2 (CH_2), 70.9 (*C*-CN), 72.9 (OCH), 115.2 (CH, C8), 116.3 (CN), 117.2 (CH, C5), 123.0 (C4a), 123.6 (CH, C6), 125.3 (CH, C7), 126.9 (C8a), 150.2 (C3), 153.5 (C2), 168.3 (COO)
3h	5.33 (s, 2H, OCH_2), 7.14-7.19 (m, 1H, 6-H), 7.18 (d, 1H, J = 8.8, 8-H), 7.22-7.27 (m, 1H, 7-H), 7.33-7.47 (m, 5H, C_6H_5), 7.61 (d, 1H, J = 8.2, 5-H), 12.31 (br s, 1H, NH), 12.69 (br s, 1H, NH)	66.0 (OCH_2), 70.4 (*C*-CN), 115.2 (CH, C8), 116.3 (CN), 117.4 (CH, C5), 123.0 (C4a), 123.6 (CH, C6), 125.4 (CH, C7), 127.0 (C8a), 127.5 (2CH, Ph), 128.0 (CH, Ph), 128.5 (2CH, Ph), 135.9 (C-CH_2O), 150.4 (C3), 153.5 (C2), 168.3 (COO)

Table 2

NMR Data of Compounds **5**, **8**, and **9** in Dimethyl-d_6 Sulfoxide at 30°

Product	^{1}H-NMR, δ (ppm), J (Hz)	^{13}C-NMR, δ (ppm)
5a	3.84 (s, 3H, CH_3), 7.41-7.48 (m, 2H, 7- and 8-H), 7.56 (s, 1H, 10-H), 7.82-7.89 (m, 2H, 6- and 9-H), 8.09 (s, 1H, 5-H), 12.39 (br s, 1H, NH), 12.70 (br s, 1H, NH)	52.3 (OCH_3), 71.8 (*C*-CN), 110.9 (CH, C10), 113.9 (CH, C5), 116.3 (CN), 123.1 (C4a), 125.3, 126.0 (each CH, C7 and C8), 126.5 (C10a), 126.8 (CH, C9), 127.1 (CH, C6), 129.5 (C5a), 130.3 (C9a), 150.0 (C3), 153.7 (C2), 168.7 (COO)
5b	1.31 (t, 3H, J = 7.1, CH_3), 4.31 (q, 2H, J = 7.1, OCH_2), 7.41-7.48 (m, 2H, 7- and 8-H), 7.56 (s, 1H, 10-H), 7.82-7.89 (m, 2H, 6- and 9-H), 8.09 (s, 1H, 5-H), 12.39 (br s, 1H, NH), 12.75 (br s, 1H, NH)	14.1 (CH_3), 61.1 (OCH_2), 71.8 (*C*-CN), 110.8 (CH, C10), 113.9 (CH, C5), 116.3 (CN), 123.3 (C4a), 125.3, 125.9 (each CH, C7 and C8), 126.5 (C10a), 126.7 (CH, C9), 127.1 (CH, C6), 129.4 (C5a), 130.2 (C9a), 150.1 (C3), 153.7 (C2), 168.3 (COO)
5c	0.97 (t, 3H, J = 7.4, CH_3), 1.71 (sextet, 2H, J = 7.1, CH_2CH_3), 4.23 (t, 2H, J = 6.3, OCH_2), 7.42-7.48 (m, 2H, 7- and 8-H), 7.57 (s, 1H, 10-H), 7.83-7.89 (m, 2H, 6- and 9-H), 8.09 (s, 1H, 5-H), 12.40 (br s, 1H, NH), 12.75 (br s, 1H, NH)	10.1 (CH_3), 21.5 (CH_2CH_3), 66.4 (OCH_2), 72.0 (*C*-CN), 110.9 (CH, C10), 113.9 (CH, C5), 116.1 (CN), 123.2 (C4a), 125.3, 125.9 (each CH, C7 and C8), 126.5 (C10a), 126.8 (CH, C9), 127.1 (CH, C6), 129.5 (C5a), 130.3 (C9a), 150.0 (C3), 153.7 (C2), 168.4 (COO)
5d	1.32 (d, 6H, J = 6.3, $2CH_3$), 5.12 (septet, 1H, J = 6.3, OCH), 7.41-7.48 (m, 2H, 7- and 8-H), 7.56 (s, 1H, 10-H), 7.82-7.89 (m, 2H, 6- and 9-H), 8.08 (s, 1H, 5-H), 12.36 (br s, 1H, NH), 12.79 (br s, 1H, NH)	21.6 ($2CH_3$), 68.9 (OCH), 72.3 (*C*-CN), 110.9 (CH, C10), 113.8 (CH, C5), 116.1 (CN), 123.2 (C4a), 125.3, 125.9 (each CH, C7 and C8), 126.5 (C10a), 126.8 (CH, C9), 127.1 (CH, C6), 129.5 (C5a), 130.3 (C9a), 150.0 (C3), 153.7 (C2), 168.0 (COO)
5e	0.94 (t, 3H, J = 6.6, CH_3), 1.41 (sextet, 2H, J = 6.0, CH_2CH_3), 1.64-1.67 (m, 2H, CH_2CH_2O), 4.26 (m, 2H, OCH_2), 7.41-7.48 (m, 2H, 7- and 8-H), 7.55 (s, 1H, 10-H), 7.82-7.89 (m, 2H, 6- and 9-H), 8.08 (s, 1H, 5-H), 12.40 (br s, 1H, NH), 12.72 (br s, 1H, NH)	13.5 (CH_3), 18.5 (CH_2CH_3), 30.1 (CH_2CH_2O), 64.7 (OCH_2), 72.0 (*C*-CN), 110.9 (CH, C10), 113.9 (CH, C5), 116.1 (CN), 123.2 (C4a), 125.3, 125.9 (each CH, C7 and C8), 126.5, (C10a), 126.8 (CH, C9), 127.1 (CH, C6), 129.5 (C5a), 130.3 (C9a), 150.0 (C3), 153.7 (C2), 168.4 (COO)
5f	0.97 (d, 6H, J = 5.9, $2CH_3$), 1.99 (nonet, 1H, J = 6.4, $CHCH_2O$), 4.05 (d, 2H, J = 5.5, OCH_2), 7.41-7.48 (m, 2H, 7- and 8-H), 7.56 (s, 1H, 10-H), 7.82-7.89 (m, 2H, 6- and 9-H), 8.08 (s, 1H, 5-H), 12.37 (br s, 1H, NH), 12.71 (br s, 1H, NH)	18.7 ($2CH_3$), 27.3 ($CHCH_2O$), 70.6 (OCH_2), 72.0 (*C*-CN), 110.9 (CH, C10), 113.9 (CH, C5), 116.1 (CN), 123.2 (C4a), 125.3, 125.9 (each CH, C7 and C8), 126.5 (C10a), 126.8 (CH, C9), 127.1 (CH, C6), 129.5 (C5a), 130.3 (C9a), 150.0 (C3), 153.7 (C2), 168.3 (COO)

Table 2 (continued)

NMR Data of Compounds **5**, **8**, and **9** in Dimethyl-d_6 Sulfoxide at 30°

Product	^{1}H-NMR, δ (ppm), J (Hz)	^{13}C-NMR, δ (ppm)
5g	0.93 (t, 3H, J = 7.3, CH_3CH_2), 1.30 (d, 3H, J = 6.1, CH_3CH), 1.65 (quintet, 2H, J = 6.9, CH_2), 4.96 (sextet, 1H, J = 6.4, OCH), 7.41-7.48 (m, 2H, 7- and 8-H), 7.56 (s, 1H, 10-H), 7.82-7.89 (m, 2H, 6- and 9-H), 8.08 (s, 1H, 5-H), 12.36 (br s, 1H, NH), 12.77 (br s, 1H, NH)	9.3 (CH_3CH_2), 19.2 (CH_3CH), 28.2 (CH_2), 72.3 (*C*-CN), 73.2 (OCH), 110.9 (CH, C10), 113.8 (CH, C5), 116.1 (CN), 123.2 (C4a), 125.3, 125.9 (each CH, C7 and C8), 126.5 (C10a), 126.8 (CH, C9), 127.1 (CH, C6), 129.5 (C5a), 130.3 (C9a), 150.0 (C3), 153.7 (C2), 168.4 (COO)
5h	5.35 (s, 2H, OCH_2), 7.34-7.51 (m, 2H, 7- and 8-H), 7.45 (s, 5H, C_6H_5), 7.56 (s, 1H, 10-H), 7.82-7.91 (m, 2H, 6- and 9-H), 8.11 (s, 1H, 5-H), 12.40 (br s, 1H, NH), 12.72 (br s, 1H, NH)	66.2 (OCH_2), 71.7 (*C*-CN), 110.9 (CH, C10), 114.0 (CH, C5), 116.2 (CN), 123.1 (C4a), 125.4, 126.0 (each CH, C7 and C8), 126.5 (C10a), 126.8 (CH, C9), 127.1 (CH, C6), 127.6 (2CH, Ph), 128.1 (CH, Ph), 128.5 (2CH, Ph), 129.5 (C5a), 130.4 (C9a), 135.8 (*C*-CH_2O), 150.2 (C3), 153.7 (C2), 168.1 (COO)
8	1.29 (t, 3H, J = 7.1, CH_3), 4.29 (q, 2H, J = 7.1, OCH_2), 7.20 (dd, 1H, J = 7.8, 4.9, 7-H), 8.07 (dd, 1H, J = 7.8, 1.5, 8-H), 8.18 (dd, 1H, J = 4.9, 1.5, 6-H), 12.62 (br s, 2H, 2NH)	14.1 (CH_3), 61.0 (OCH_2), 71.8 (*C*-CN), 116.2 (CN), 119.3 (CH, C7), 119.7 (C8a), 124.9 (CH, C8), 140.0 (C4a), 144.2 (CH, C6), 150.2 (C3), 154.9 (C2), 168.1 (COO)
9	1.30 (t, 3H, J = 7.1, CH_3), 4.29 (q, 2H, J = 7.1, OCH_2), 7.08 (d, 1H, J = 5.4, 8-H), 8.26 (d, 1H, J = 5.4, 7-H), 8.83 (s, 1H, 5-H), 12.53 (br s, 2H, 2NH)	14.1 (CH_3), 61.1 (OCH_2), 72.1 (*C*-CN), 109.2 (CH, C8), 116.1 (CN), 120.6 (C4a), 132.8 (C8a), 139.0 (CH, C5), 145.2 (CH, C7), 150.4 (C3), 154.1 (C2), 168.0 (COO)

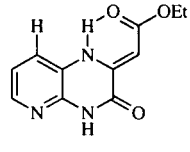
uted to an intramolecular hydrogen-bonded α,β-unsaturated ester carbonyl common to all related compounds as stated in the literature [6, 7]. The ^{1}H nmr spectra of **3** and **5** in dimethyl-d_6 sulfoxide exhibit broad signals at δ 12.6-12.8 and at δ 12.2-12.4 each corresponding to one proton. They are assigned to the 1- and 4-imino protons. However, these compounds **3** and **5** exhibit no characteristic signals for a methine proton produced by imine-enamine tautomerization [5].

2,3-Diaminopyridine (**6**) and 3,4-diaminopyridine (**7**) are of interest because they also have *vicinal*-diamino groups for the preparation of fused heterocycles. Indeed, **6** and **7** were reacted with equimolecular amounts of the ethyl ester **1b** in acetonitrile at room temperature for 3 hours to give expected (*Z*)-2-(α-cyano-α-ethoxycarbonylmethylene)-1,2-dihydro-4*H*-pyrido[2,3-*b*]pyrazin-3-one (**8**) and (*Z*)-3-(α-cyano-α-ethoxycarbonylmethylene)-3,4-dihydro-1*H*-pyrido[3,4-*b*]pyrazin-2-one (**9**), respectively (Scheme 3). The isomeric structure of **8** was assigned by the comparison of proton nmr data between **8** and related compounds, such as 2-substituted 1,2-dihydro-4*H*-pyrido[2,3-*b*]pyrazin-3-ones **10** [15] and **11** [16], and 3-substituted 3,4-dihydro-1*H*-pyrido[2,3-*b*]pyrazin-2-ones **12** [15] and **13** [16] (Table 3). The isomeric structure of **9** was also determined by the comparison between **9** and related compounds, such as 3-phenacylidene-3,4-dihydro-

Table 3

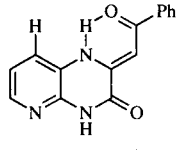
A Comparison of ^{1}H NMR Data of **8** with Known Compounds **10-13** in Dimethyl-d_6 Sulfoxide

7.84 ppm



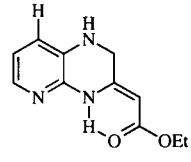
10

7.92 ppm



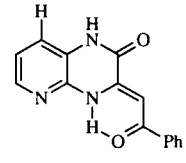
11

7.38 ppm



12

7.41 ppm

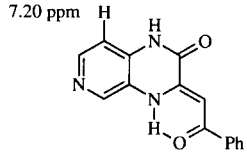


13

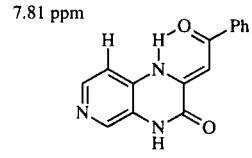
Compound	Pyrido[2,3-*b*]pyrazine Ring (=CH) at 6	7	8	N-H at 1 or 4
8	8.18 (dd)	7.20 (dd)	8.07 (dd)	12.62 (2H)
10 [15]	7.94 (dd)	7.08 (dd)	7.84 (dd)	11.0 12.1
11 [16]	8.12 (dd)	7.14 (dd)	7.92 (dd)	12.5 13.3
12 [15]	8.01 (dd)	7.07 (dd)	7.38 (dd)	11.1 11.8
13 [16]	8.12 (dd)	7.16 (dd)	7.41 (dd)	12.0 13.4

Table 4

A Comparison of ^{1}H NMR Data of **9** with Known Compounds **14-15**, in Dimethyl-d6 Sulfoxide

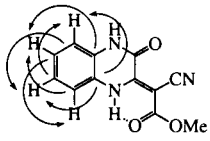


14



15

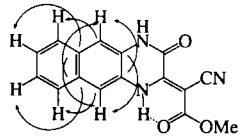
Compound	5	Pyrido[3,4-*b*]pyrazine Ring (=CH) at 7	N-H at 8	1 or 4
9	8.83 (s)	8.26 (d)	7.08 (d)	12.53 (2H)
14 [17]	8.83 (s)	8.45 (d)	7.20 (d)	12.5 13.3
15 [17]	8.96 (s)	8.31 (d)	7.81 (d)	12.3 13.3



3a

Irradiated Nucleus		$^3J_{C-H}$ Correlated Proton(s)
C4a	123.0 ppm	7.14-7.19 (6-H), 7.18 (8-H)
C5	117.3	7.21-7.26 (7-H)
C6	123.7	7.18 (8-H)
C7	125.4	7.60 (5-H)
C8	115.2	7.14-7.19 (6-H)
C8a	126.9	7.21-7.26 (7-H)

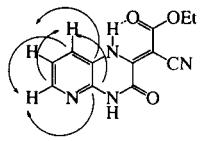
Figure 1. ^{1}H-detected long range $^3J_{C-H}$ correlation (HMBC) in **3a**.



5a

Irradiated Nucleus		$^3J_{C-H}$ Correlated Proton(s)
C4a	123.1 ppm	7.56 (10-H)
C5	113.9	7.82-7.89 (6-H)
C5a	129.5	7.41-7.48 (7-H), 7.56 (10-H)
C6	127.1	8.09 (5-H), 7.41-7.48 (8-H)
C7, C8	125.3, 126.0	7.82-7.89 (6-H, 9-H)
C9	126.8	7.41-7.48 (7-H), 7.56 (10-H)
C9a	130.3	8.09 (5-H), 7.41-7.48 (8-H),
C10	110.9	7.82-7.89 (9-H)
C10a	126.5	8.09 (5-H)

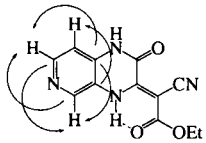
Figure 2. ^{1}H-detected long range $^3J_{C-H}$ correlation (HMBC) in **5a**.



8

Irradiated Nucleus		$^3J_{C-H}$ Correlated Proton(s)
C4a	140.0 ppm	8.18 (6-H), 8.07 (8-H)
C6	144.2	8.07 (8-H)
C7	119.3	none
C8	124.9	8.18 (6-H)
C8a	119.7	7.20 (7-H)

Figure 3. ^{1}H-detected long range $^3J_{C-H}$ correlation (HMBC) in **8**.



9

Irradiated Nucleus		$^3J_{C-H}$ Correlated Proton(s)
C4a	120.6 ppm	7.08 (8-H)
C5	144.2	8.26 (7-H)
C7	145.2	8.83 (5-H)
C8	109.2	none
C8a	132.8	8.83 (5-H), 8.26 (7-H)

Figure 4. ^{1}H-detected long range $^3J_{C-H}$ correlation (HMBC) in **9**.

1*H*-pyrido[3,4-*b*]pyrazin-2-one (**14**) [17] and 2-phenacylidene-1,2-dihydro-4*H*-pyrido[3,4-*b*]pyrazin-3-one (**15**) [17] (Table 4). In these system, the proton located on 8-position of 3-substituted pyrido[2,3-*b*]pyrazin-2-one or 3-substituted pyrido[3,4-*b*]pyrazin-2-one rings, **8**, **10**, **11**, and **15**, shows a characteristic signal in δ 7.8-8.1 ppm region. On the other hand, the proton situated on the 8-position of the 2-substituted pyrido[2,3-*b*]pyrazin-3-one or the 2-substituted pyrido[3,4-*b*]pyrazin-3-one rings, **9**, **12**, **13**, and **14**, exhibit the signal in δ 7.1-7.4 ppm region.

The reaction mechanism is similar to Scheme 2. It seems that the β-amino group in **6** and **7** predominantly attacked to ethylene double bond of **1**, followed by the intramolecular condensation between the other amino group on the pyridine ring and the ester group.

The structure of the compounds obtained, **3**, **5**, **8**, and **9**, was also confirmed by the elemental analysis and ms data. The assignment of the ^{13}C nmr spectra, summarized in Tables 1-2, was based on some 1D- and 2D-nmr techniques, such as DEPT (determination of methyl, methylene, methine, or quaternary carbon), HMQC ($^{1}J_{CH}$ correlation), and HMBC ($^{2}J_{CH}$ or $^{3}J_{CH}$ correlation). The ^{1}H-detected $^{3}J_{C\text{-}H}$ coupling correlative data (HMBC) for **3a**, **5a**, **8**, and **9** are illustrated in Figures 1-4, respectively.

The principal advantages of the method described here are that the time of reaction is short, the work up is convenient, and the reaction is easily carried out and proceeds under mild conditions to give, in general, high yields of 2-pyrazinones, such as 2-oxo-1,2,3,4-tetrahydroquinoxalines, having an α-alkoxycarbonyl-α-cyanomethylene group.

EXPERIMENTAL

Melting points were determined on a Yamato MP-21 apparatus and are uncorrected. The ir spectra were recorded on a Perkin-Elmer FT-IR 1000 PC spectrophotometer (in potassium bromide). The ^{1}H nmr spectra were recorded on either a JEOL EX-400 (400 MHz) or a Varian VXR-300 (300 MHz) instrument. The ^{13}C nmr (100 MHz) were taken on a JEOL EX-400 instrument in dimethyl-d_6 sulfoxide with tetramethylsilane as internal reference. The distortionless enhancement by polarization transfer (DEPT) spectra were run in a standard manner, using θ = 135° pulse to separate CH/CH_3 and CH_2 lines phased "up" and "down", respectively. Moreover, the signals caused by quaternary carbons were identified by the comparison between ^{13}C NMR and DEPT spectra. The ^{1}H-detected heteronuclear multiple-quantum coherence (HMQC, using C-H spin-spin coupling constant $^{1}J_{CH}$ = 140 Hz), and ^{1}H-detected multiple-bond heteronuclear multiple-quantum coherence (HMBC, using C-H long range coupling constant $^{n}J_{CH}$ = 8 Hz) experiments were also carried out with a JEOL EX-400 instrument. Mass spectra were obtained with a JEOL AX-500 spectrometer (EI: 70 eV). Elemental analyses were performed on a Perkin-Elmer 240 instrument.

General Procedure for the Preparation of (*Z*)-3-(α-Alkoxycarbonyl-α-cyanomethylene)-2-oxo-1,2,3,4-tetrahydroquinoxalines **3**.

To a magnetically stirred solution of 4.5 mmoles of dialkyl (*E*)-2,3-dicyanobutendioate (**1**) in acetonitrile (10 ml) was added a solution of 0.49 g (4.5 mmoles) of *o*-phenylenediamine (**2**) in acetonitrile (5 ml) at room temperature. When the reaction mixture was further stirred for few minutes at room temperature, a yellow precipitate began to separate from the solution. The reaction mixture was further stirred at room temperature. After 1 hour, the crystalline solid was filtered, washed with cold ethanol, and recrystallized from suitable solvent to give **3**.

(*Z*)-3-(α-Cyano-α-methoxycarbonylmethylene)-2-oxo-1,2,3,4-tetrahydroquinoxaline (**3a**).

This compound was obtained as yellow needles (dioxane:*N*,*N*-dimethylformamide), 1.0 g, 91% yield, mp 289-289.5° dec; ir: ν 3270, 3115 (NH), 2200 (CN), 1675 (COO), 1647 (N-C=O); ms: m/z 243 (M^+), 211, 185, 155, 90.

Anal. Calcd. for $C_{12}H_9N_3O_3$: C, 59.26; H, 3.73; N, 17.28. Found: C, 59.37; H, 3.70; N, 17.05.

(*Z*)-3-(α-Cyano-α-ethoxycarbonylmethylene)-2-oxo-1,2,3,4-tetrahydroquinoxaline (**3b**).

This compound was obtained as yellow needles (dioxane:ethanol), 0.94 g, 81% yield, mp 271-272° dec; ir: ν 3212, 3146 (NH), 2202 (CN), 1678 (COO), 1648 (N-C=O); ms: m/z 257 (M^+), 211, 185, 157, 155, 90.

Anal. Calcd. for $C_{13}H_{11}N_3O_3$: C, 60.70; H, 4.31; N, 16.33. Found: C, 60.53; H, 4.36; N, 16.26.

(*Z*)-3-(α-Cyano-α-propoxycarbonylmethylene)-2-oxo-1,2,3,4-tetrahydroquinoxaline (**3c**).

This compound was obtained as yellow needles (dioxane:ethanol), 0.78 g, 64% yield, mp 268-269° dec; ir: ν 3261, 3180 (NH), 2200 (CN), 1689 (COO), 1638 (N-C=O); ms: m/z 271 (M^+), 229, 211, 185, 157, 155, 90.

Anal. Calcd. for $C_{14}H_{13}N_3O_3$: C, 61.99; H, 4.83; N, 15.49. Found: C, 61.94; H, 4.96; N, 15.57.

(*Z*)-3-(α-Cyano-α-isopropyloxycarbonylmethylene)-2-oxo-1,2,3,4-tetrahydroquinoxaline (**3d**).

The reaction mixture was refluxed for 1 hour to give **3d**. This compound was obtained as yellow needles (dioxane:ethanol), 0.56 g, 46% yield, mp 260-261° dec; ir: ν 3266, 3129 (NH), 2203 (CN), 1695 (COO), 1640 (N-C=O); ms: m/z 271 (M^+), 229, 211, 185, 157, 155, 90.

Anal. Calcd. for $C_{14}H_{13}N_3O_3$: C, 61.99; H, 4.83; N, 15.49. Found: C, 62.01; H, 4.83; N, 15.20.

(*Z*)-3-(α-Butoxycarbonyl-α-cyanomethylene)-2-oxo-1,2,3,4-tetrahydroquinoxaline (**3e**).

This compound was obtained as yellow needles (dioxane:ethanol), 0.50 g, 39% yield, mp 269.5-270.5° dec; ir: ν 3261, 3110 (NH), 2200 (CN), 1691 (COO), 1640 (N-C=O); ms: m/z: 285 (M^+), 229, 211, 185, 157, 155, 90.

Anal. Calcd. for $C_{15}H_{15}N_3O_3$: C, 63.15; H, 5.30; N, 14.73. Found: C, 62.92; H, 5.58; N, 14.65.

(*Z*)-3-(α-Cyano-α-isobutyloxycarbonylmethylene)-2-oxo-1,2,3,4-tetrahydroquinoxaline (**3f**).

This compound was obtained as yellow needles (dioxane:ethanol), 0.49 g, 38% yield, mp 277-278° dec; ir: ν

3257, 3105 (NH), 2202 (CN), 1685 (COO), 1648 (N-C=O); ms: m/z 285 (M^+), 229, 211, 185, 157, 155, 90.

Anal. Calcd. for $C_{15}H_{15}N_3O_3$: C, 63.15; H, 5.30; N, 14.73. Found: C, 62.99; H, 5.41; N, 14.73.

(Z)-3-(α-Cyano-α-*sec*-butyloxycarbonylmethylene)-2-oxo-1,2,3,4-tetrahydroquinoxaline (**3g**).

The reaction mixture was refluxed for 3 hours to give **3g**. This compound was obtained as yellow needles (ethanol), 0.67 g, 52% yield, mp 228-228.5° dec; ir: ν 3267, 3135 (NH), 2202 (CN), 1685 (COO), 1645 (N-C=O); ms: m/z 285 (M^+), 229, 211, 185, 157, 155, 90.

Anal. Calcd. for $C_{15}H_{15}N_3O_3$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.03; H, 4.99; N, 14.97.

(Z)-3-(α-Benzyloxycarbonyl-α-cyanomethylene)-2-oxo-1,2,3,4-tetrahydroquinoxaline (**3h**).

This compound was obtained as yellow needles (dioxane), 1.34 g, 93% yield, mp 255.5-256° dec; ir: ν 3238, 3120 (NH), 2203 (CN), 1690 (COO), 1642 (N-C=O); ms: m/z 319 (M^+), 275, 213, 185, 91.

Anal. Calcd. for $C_{18}H_{13}N_3O_3$: C, 67.71; H, 4.10; N, 13.16. Found: C, 67.48; H, 4.04; N, 13.40.

General Procedure for the Preparation of (Z)-3-(α-Alkoxycarbonyl-α-cyanomethylene)-3,4-dihydrobenzo[*g*]quinoxalin-2(1*H*)-ones **5**.

To a magnetically stirred solution of 4.5 mmoles of dialkyl (*E*)-2,3-dicyanobutendioate (**1**) in acetonitrile (10 ml) was added a solution of 0.82 g (4.5 mmoles) of 2,3-diaminonaphthalene (**4**) in acetonitrile (5 ml) at room temperature. When the reaction mixture was further stirred for 5-8 minutes at room temperature, a yellow precipitate began to separate from the solution. The reaction mixture was further stirred at room temperature. After 1 hour, the crystalline solid was filtered, washed with cold ethanol, and recrystallized from suitable solvent to give **5**.

(Z)-3-(α-Cyano-α-methoxycarbonylmethylene)-3,4-dihydrobenzo[*g*]quinoxalin-2(1*H*)-one (**5a**).

This compound was obtained as yellow needles (ethanol:*N,N*-dimethylformamide), 0.84 g, 64% yield, mp > 320°; ir: ν 3240, 3120 (NH), 2198 (CN), 1684 (COO), 1658 (N-C=O); ms: m/z 293 (M^+), 261, 235, 205, 140.

Anal. Calcd. for $C_{16}H_{11}N_3O_3$: C, 65.53; H, 3.78; N, 14.33. Found: C, 65.38; H, 3.88; N, 14.18.

(Z)-3-(α-Cyano-α-ethoxycarbonylmethylene)-3,4-dihydrobenzo[*g*]quinoxalin-2(1*H*)-one (**5b**).

This compound was obtained as yellow needles (dioxane:*N,N*-dimethylformamide), 0.90 g, 65% yield, mp 285-286° dec; ir: ν 3200, 3110 (NH), 2204 (CN), 1690 (COO), 1655 (N-C=O); ms: m/z 307 (M^+), 261, 235, 205, 140.

Anal. Calcd. for $C_{17}H_{13}N_3O_3$: C, 66.44; H, 4.26; N, 13.67. Found: C, 66.53; H, 4.21; N, 13.86.

(Z)-3-(α-Cyano-α-propoxycarbonylmethylene)-3,4-dihydrobenzo[*g*]quinoxalin-2(1*H*)-one (**5c**).

This compound was obtained as yellow needles (dioxane:ethanol), 1.21 g, 84% yield, mp 278-279.5° dec; ir: ν 3202, 3135 (NH), 2202 (CN), 1692 (COO), 1656 (N-C=O); ms: m/z 321 (M^+), 261, 253, 207, 140.

Anal. Calcd. for $C_{18}H_{15}N_3O_3$: C, 67.28; H, 4.71; N, 13.08. Found: C, 67.13; H, 4.85; N, 13.04.

(Z)-3-(α-Cyano-α-isopropyloxycarbonylmethylene)-3,4-dihydrobenzo[*g*]quinoxalin-2(1*H*)-one (**5d**).

The reaction mixture was refluxed for 1 hour to give **5d**. This compound was obtained as yellow needles (dioxane:ethanol), 1.04 g, 72% yield, mp 284-285.5° dec; ir: ν 3244, 3110 (NH), 2202 (CN), 1693 (COO), 1656 (N-C=O); ms: m/z 321 (M^+), 279, 261, 235, 207, 140.

Anal. Calcd. for $C_{18}H_{15}N_3O_3$: C, 67.28; H, 4.71; N, 13.08. Found: C, 67.31; H, 4.94; N, 13.12.

(Z)-3-(α-Butoxycarbonyl-α-cyanomethylene)-3,4-dihydrobenzo[*g*]quinoxalin-2(1*H*)-one (**5e**).

This compound was obtained as yellow needles (dioxane:ethanol), 1.30 g, 86% yield, mp 273-274.5° dec; ir: ν 3240, 3124 (NH), 2204 (CN), 1688 (COO), 1658 (N-C=O); ms: m/z 335 (M^+), 279, 261, 235, 207, 140.

Anal. Calcd. for $C_{19}H_{17}N_3O_3$: C, 68.05; H, 5.11; N, 12.53. Found: C, 67.79; H, 5.14; N, 12.66.

(Z)-3-(α-Cyano-α-isobutyloxycarbonylmethylene)-3,4-dihydrobenzo[*g*]quinoxalin-2(1*H*)-one (**5f**).

This compound was obtained as yellow needles (dioxane:ethanol), 1.19 g, 79% yield, mp 281-283° dec; ir: ν 3216, 3108 (NH), 2200 (CN), 1689 (COO), 1658 (N-C=O); ms: m/z: 335 (M^+), 279, 261, 235, 207, 140.

Anal. Calcd. for $C_{19}H_{17}N_3O_3$: C, 68.05; H, 5.11; N, 12.53. Found: C, 67.83; H, 4.86; N, 12.65.

(Z)-3-(α-Cyano-α-*sec*-butyloxycarbonylmethylene)-3,4-dihydrobenzo[*g*]quinoxalin-2(1*H*)-one (**5g**).

The reaction mixture was refluxed for 3 hours to give **5g**. This compound was obtained as yellow needles (dioxane:ethanol), 1.19 g, 79% yield, mp 285.5-286° dec; ir: ν 3199, 3118 (NH), 2205 (CN), 1687 (COO), 1655 (N-C=O); ms: m/z 335 (M^+), 279, 261, 235, 207, 140.

Anal. Calcd. for $C_{19}H_{17}N_3O_3$: C, 68.05; H, 5.11; N, 12.53. Found: C, 67.85; H, 4.90; N, 12.69.

(Z)-3-(α-Benzyloxycarbonyl-α-cyanomethylene)-3,4-dihydrobenzo[*g*]quinoxalin-2(1*H*)-one (**5h**).

This compound was obtained as yellow needles (dioxane:ethanol), 1.62 g, 98% yield, mp 279.5-280° dec; ir: ν 3230, 3204 (NH), 2202 (CN), 1692 (COO), 1646 (N-C=O); ms: m/z: 369 (M^+), 325, 261, 235, 207, 140, 91.

Anal. Calcd. for $C_{22}H_{15}N_3O_3$: C, 71.54; H, 4.09; N, 11.38. Found: C, 71.24; H, 4.28; N, 11.39.

(Z)-2-(α-Cyano-α-ethoxycarbonylmethylene)-1,2-dihydro-4*H*-pyrido[2,3-*b*]pyrazin-3-one **8.**

To a magnetically stirred solution of 1.0 g (4.5 mmoles) of diethyl (*E*)-2,3-dicyanobutendioate (**1b**) in acetonitrile (15 ml) was added a solution of 0.49 g (4.5 mmoles) of 2,3-diaminonaphthalene (**6**) in acetonitrile (15 ml) at room temperature. When the reaction mixture was further stirred for thirty seconds, a yellow precipitate began to separate from the solution. The reaction mixture was further stirred at room temperature. After 3 hours, the crystalline solid was filtered, washed with cold ethanol, and recrystallized from pyridine to give **8** as yellow needles, 0.72 g, 62% yield, mp 286-287°; ir: ν 3428, 3204 (NH), 2204 (CN), 1687 (COO), 1659 (N-C=O); ms: m/z 258 (M^+), 212, 186, 184, 158, 120, 104.

Anal. Calcd. for $C_{12}H_{10}N_4O_3$: C, 55.81; H, 3.90; N, 21.70. Found: C, 55.72; H, 3.98; N, 21.38.

(*Z*)-3-(α-Cyano-α-ethoxycarbonylmethylene)-3,4-dihydro-1*H*-pyrido[3,4-*b*]pyrazin-2-one **9.**

To a magnetically stirred solution of 1.0 g (4.5 mmoles) of diethyl (*E*)-2,3-dicyanobutendioate (**1b**) in acetonitrile (15 ml) was added a solution of 0.49 g (4.5 mmoles) of 3,4-diaminonaphthalene (**7**) in acetonitrile (15 ml) at room temperature. When the reaction mixture was further stirred for thirty seconds, a yellow precipitate began to separate from the solution. The reaction mixture was further stirred at room temperature. After 3 hours, the crystalline solid was filtered, washed with cold ethanol, and recrystallized from pyridine to give **9** as yellow needles, 0.51 g, 44% yield, mp 237-238°; ir: ν 3430, 3228 (NH), 2215 (CN), 1680 (COO, shoulder), 1655 (N-C=O); ms: m/z 258 (M^+), 212, 186, 184, 158, 156, 104.

Anal. Calcd. for $C_{12}H_{10}N_4O_3$: C, 55.81; H, 3.90; N, 21.70. Found: C, 55.63; H, 3.88; N, 21.50.

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