Quinolone Analogues 7 [1-6]. Synthesis of 3-Heteroaryl-1-methylpyridazino[3,4-*b*]quinoxalin-4(1*H*)-ones

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The 3-heteroaryl-1-methylpyridazino[3,4-*b*]quinoxalin-4(1*H*)-ones **6a-e** were synthesized by the oxidative-hydrolytic ring transformation of the 3-heteroaryl-1,2-diazepino[3,4-*b*]]quinoxaline-5-carbonitriles **9a-c**, which were obtained by the 1,3-dipolar cycloaddition reaction of the 2-(2-heteroarylmethylene-1-methylhydrazino)quinoxaline 4-oxides with 2-chloroacrylonitrile. The assignment of the thiophene and furan ring protons was carried out through the data of the NOE, decoupling, and coupling constants.

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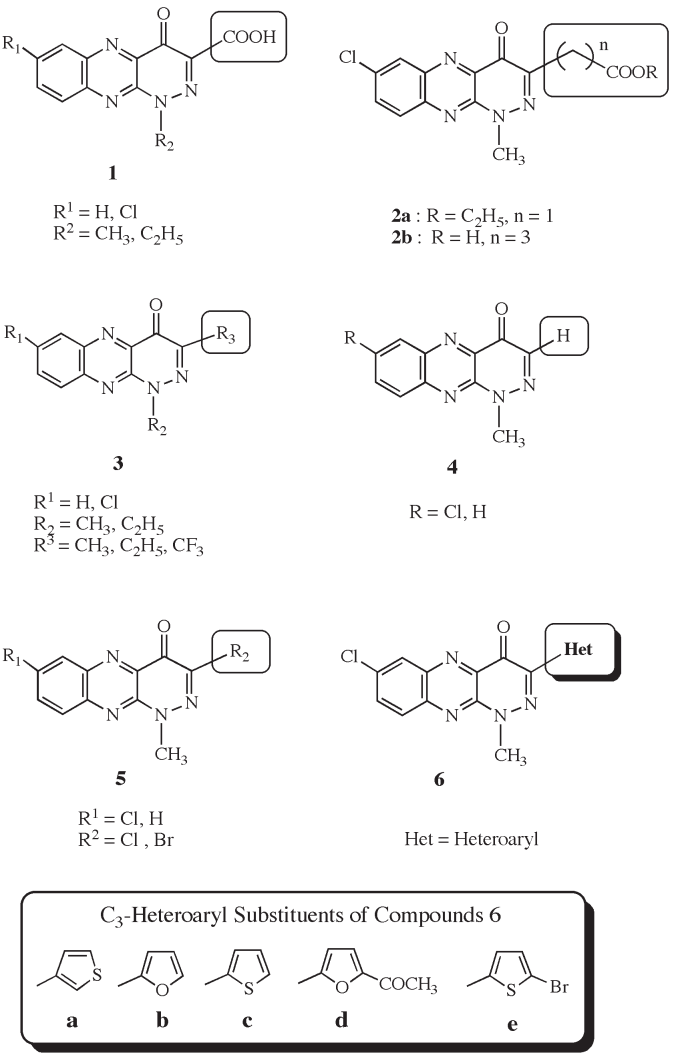
Introduction.

In previous papers [1,2], we reported the synthesis of 1-alkyl-4-oxopyridazino[3,4-*b*]quinoxaline-3-carboxylic acids **1**, 2-(7-chloro-1-methylpyridazino[3,4-*b*]quinoxalin-3-yl)acetate **2a**, and 4-(7-chloro-1-methylpyridazino[3,4-*b*]quinoxalin-3-yl)butyric acid **2b** as candidates of antibacterial quinolone analogues (Chart 1). Since compounds **1** and **2** were not so potent in the antibacterial activity, we then undertook the modification of the 3-substituent for compounds **1** and **2** in order to search for more potent compounds. Namely, we carried out the exclusion of the carboxyl or ester group from the 3-substituent of compounds **2** [2], leading to the synthesis of the 3-alkyl derivatives **3** [3,4], which were found to have good biological activities including antifungal and antibacterial activities [5]. Thereafter, we produced the 3-H **4** [6] and 3-halogeno **5** [7] derivatives, which also showed good antibacterial and antifungal activities [5]. These data suggest that the 1-alkylpyridazino[3,4-*b*]quinoxalin-4(1*H*)-ones having no carboxyl or ester group in the 3-substituent or 3-position exhibit antimicrobial activities. Thus, the above results tempted us to synthesize the 3-heteroaryl derivatives **6** (Chart 1), which would possess some antimicrobial activity. This paper describes the synthesis of several 3-heteroarylpyridazino[3,4-*b*]quinoxalin-4(1*H*)-ones **6a-e** (Schemes 2 and 3).

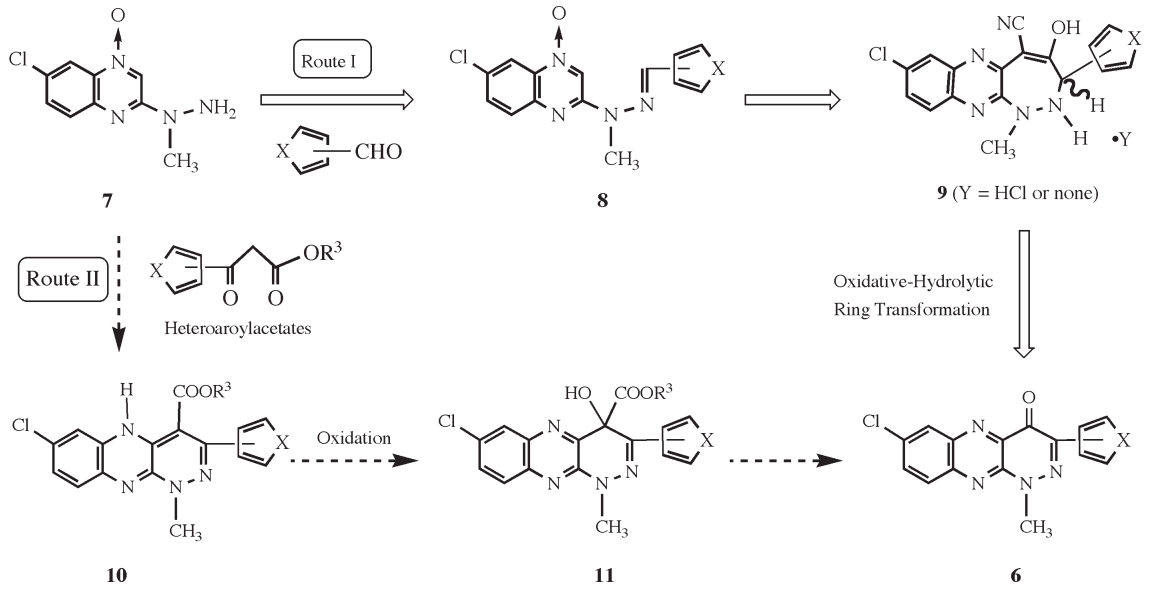
Chart 1



Synthetic Route.

We have developed several routes for the synthesis of our quinolone analogues **1-5** from the quinoxaline *N*-oxides **7** [1-6,8], some of which are applicable for the synthesis of compounds **6** as shown in Scheme 1. For example, the route I method in Scheme 1 includes the conversion of the hydrazones **8** into the 1,2-diazepino[3,4-*b*]quinoxalines **9** *via* intermediates **A**-**D** (Chart 2) [3,9,10] and then the oxidative-hydrolytic ring transformation of compounds **9** into quinolone analogues **6** *via* intermediates **E**-**H** (Chart 3) [3,8]. On the other hand, the route II method involves the synthesis of the 1,5-dihydropyridazino[3,4-*b*]quinoxalines **10** [2,4], which are converted into compounds **6** *via* the 1,4-

Scheme 1



dihydropyridazino[3,4-*b*]quinoxalines **11**. However, the route II method is not convenient, because it is not so easy to obtain various heteroaroylacetates as reagents. Thus, we have selected the route I method in the present investigation, since we can purchase some inexpensive derivatives of thiophenecarbaldehyde and furfural as commercially available compounds.

Synthesis of Quinolone Analogues **6**.

The reaction of the quinoxaline *N*-oxide **7** with thiophene-3-carbaldehyde gave the hydrazone **8a**, whose reaction with 2-chloroacrylonitrile afforded the 3-(3-thienyl)-1,2-diazepino[3,4-*b*]quinoxaline-3-carbonitrile hydrochloride **9a** (Scheme 2) presumably *via* intermediates **A**-**D** (Chart 2) [3,9,10]. The reaction of compound **9a** with selenium dioxide in water/acetic acid resulted in oxidative-hydrolytic ring transformation to provide the 3-(3-thienyl)pyridazino[3,4-*b*]quinoxalin-4(1*H*)-one **6a** presumably *via* intermediates **E**-**H** (Chart 3) [3,8]. Moreover, the reaction of the 3-(2-furyl)-1,2-diazepino[3,4-*b*]quinoxaline-5-carbonitrile **9b** [11] and 3-(2-thienyl)-1,2-diazepino[3,4-*b*]quinoxaline-5-carbonitrile **9c** [12] with selenium dioxide in water/acetic acid also produced the 3-(2-furyl)pyridazino[3,4-*b*]quinoxalin-4(1*H*)-one **6b** and 3-(2-thienyl)pyridazino[3,4-*b*]quinoxalin-4(1*H*)-one **6c**, respectively (Scheme 3). The reaction of

Chart 2

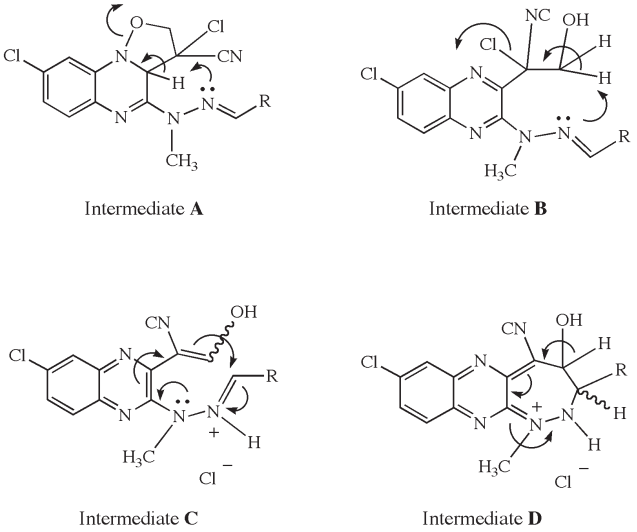
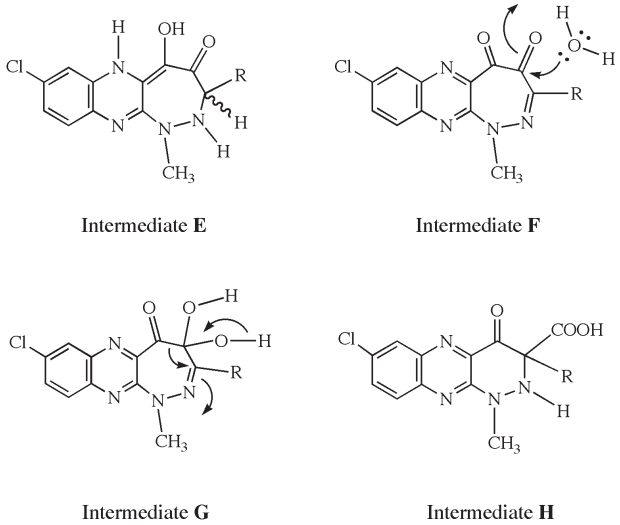
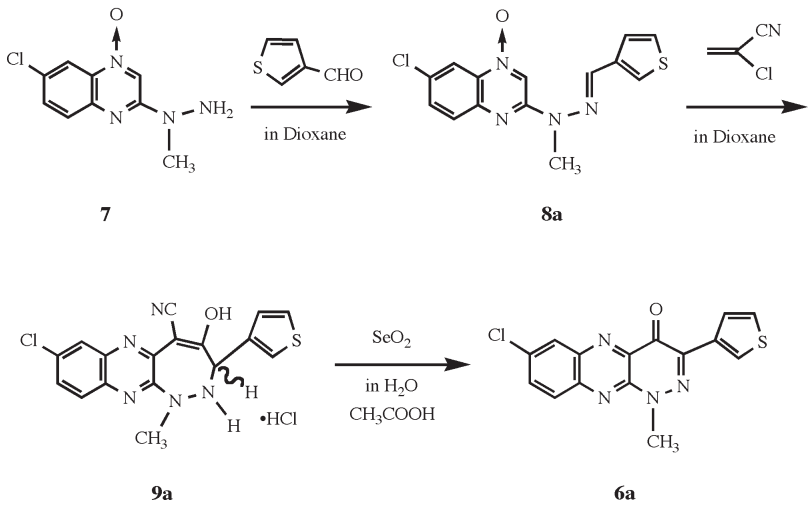


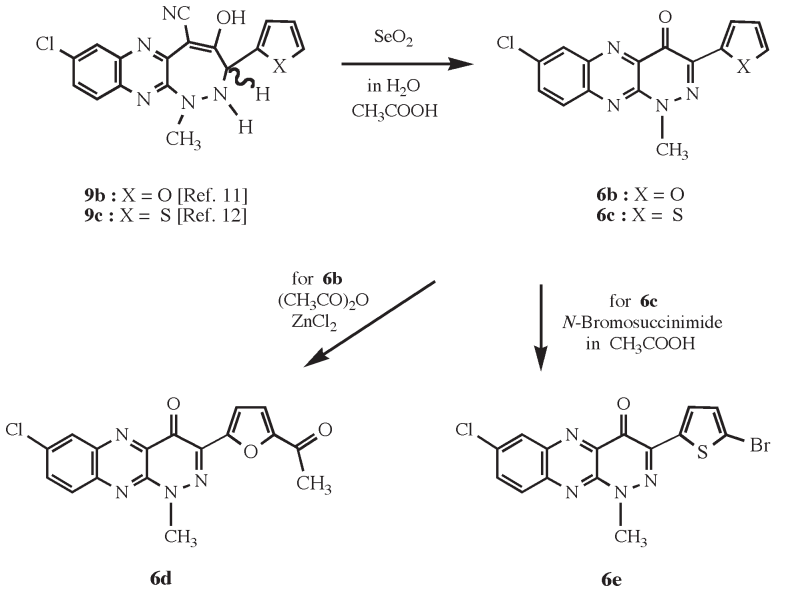
Chart 3



Scheme 2



Scheme 3



compound **6b** with acetic anhydride/zinc chloride gave the 3-(5-acetyl-2-furyl)pyridazino[3,4-*b*]quinoxalin-4(1*H*)-one **6d** in poor yield [13-15], while the reaction of compound **6c** with *N*-bromosuccinimide afforded the 3-(5-bromo-2-thienyl)pyridazino[3,4-*b*]quinoxalin-4(1*H*)-one **6e** [16-18].

Screening tests of compounds **6a-e** are now in progress, and the screening data will be reported elsewhere.

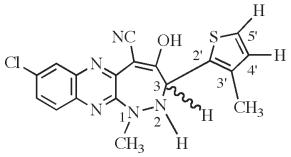
Chemical Shifts and Coupling Constants for Thiophene and Furan Ring Protons.

Thiophene and furan ring ptoton signals were assigned by the coupling constant and NOE spectral data, as described below.

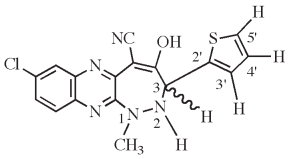
1. Thienyl Derivatives.

In previous papers, we reported the synthesis and nmr spectral data of compounds **9f** [11] and **9c** [12], whose thiophene ring proton signals were assigned by data of NOE and coupling constants, as shown in Chart 4. These data indicate that the coupling constants between 3'-H and 4'-H, between 4'-H and 5'-H, and between 3'-H and 5'-H in the thiophene ring are 3.5 Hz, 5.0 Hz, and 1.0 Hz, respectively. Similar data were obtained from compounds **12a-d** [12] (Chart 5). Based on the data of the coupling constants, thiophene ring proton signals of compounds **6c** and **6e** are assigned as shown in Chart 6, wherein the coupling

Chart 4



9f [Ref. 11] [a]



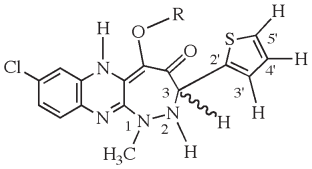
9c [Ref. 12]

Chemical Shift in δ [J in Hz (Coupling Protons)]

Proton	Compound **9f**	Compound **9c**
NH	6.12	6.30 [2.0 (NH - H_3)]
3-H	5.55	5.45 [2.0 (NH - H_3), 1.0 (H_3 - $H_{3'}$)]
3'-H	——	6.87 [1.0 (H_3 - $H_{3'}$), 1.0 ($H_{3'}$ - H_5), 3.5 ($H_{3'}$ - $H_{4'}$)]
4'-H	6.93 (5.0)	6.93 [3.5 ($H_{3'}$ - $H_{4'}$), 5.0 ($H_{4'}$ - H_5)]
5'-H	7.28 (5.0)	7.47 [5.0 ($H_{4'}$ - H_5), 1.0 ($H_{3'}$ - H_5)]

[a] Assignments for 3-, 4'-, and 5'-proton signals were based on the NOE spectral data.

Chart 5

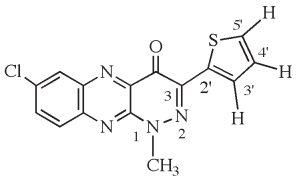


12 [Ref. 12]

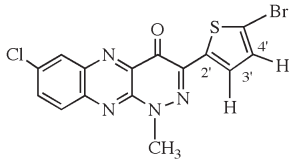
R : **a** - CH_3, **b** - C_2H_5, **c** - *n*-C_3H_7, **d** - Furfuryl

Proton	Chemical Shift in δ [J in Hz (Coupling Protons)]
NH	6.09 - 6.08 [2.5 (NH - H_3)]
3-H	5.17 - 5.12 [2.5 (NH - H_3), 1.0 (H_3 - $H_{3'}$)]
3'-H	6.81 - 6.68 [1.0 (H_3 - $H_{3'}$), 1.0 ($H_{3'}$ - H_5), 3.5 ($H_{3'}$ - $H_{4'}$)]
4'-H	6.88 - 6.83 [3.5 ($H_{3'}$ - $H_{4'}$), 5.0 ($H_{4'}$ - H_5)]
5'-H	7.34 - 7.31 [5.0 ($H_{4'}$ - H_5), 1.0 ($H_{3'}$ - H_5)]

Chart 6



6c



6e

Chemical Shift in δ [J in Hz (Coupling Protons)]

Proton	Compound **6c**	Compound **6e**
3'-H	8.16 [1.0 ($H_{3'}$ - H_5), 3.5 ($H_{3'}$ - $H_{4'}$)]	7.85 [4.0 ($H_{3'}$ - $H_{4'}$)]
4'-H	7.20 [3.5 ($H_{3'}$ - $H_{4'}$), 5.0 ($H_{4'}$ - H_5)]	7.29 [4.0 ($H_{3'}$ - $H_{4'}$)]
5'-H	7.68 [5.0 ($H_{4'}$ - H_5), 1.0 ($H_{3'}$ - H_5)]	——

constants between 3'-H and 4'-H are 3.5 and 4.0 Hz, respectively. Table 1 shows that the 3'-proton signals are

Table 1

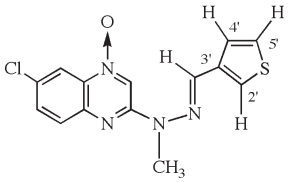
Chemical Shifts of the Thiophene Ring Protons for Compounds **6c,e**, **9c**, and **12a-d**

Compound	Chemical Shift in δ 3' - H	4' - H	5' - H
9c	6.87	6.93	7.47
12a	6.79	6.87	7.43
12b	6.81	6.88	7.32
12c	6.81	6.88	7.33
12d	6.68	6.83	7.31
6c	8.16	7.20	7.68
6e	7.85	7.29	-----

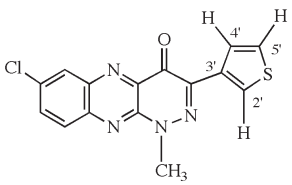
observed in higher magnetic field than the 4'- and 5'-proton signals in compounds **9c** and **12a-d**. On the contrary, the 3'-proton signals are observed in an eminently lower magnetic field than the 4'- and 5'-proton signals in compounds **6c** and **6e**. Concerning these unexpected results, we are studying further by other spectral or analytical methods.

The 2'-, 4'-, and 5'-proton signals (thiophene ring) in compound **8a** were also assigned by the data of the coupling constants and the decoupling procedure radiating on the hydrazone proton and 2'-proton (Chart 7). From the data of the coupling constants between 2'-H and 4'-H (J = 1.0 Hz) and between 2'-H and 5'-H (J = 3.0 Hz), the 2'-, 4'-, and 5'-proton signals of compounds **8a** and **6a** were assigned easily as shown in Chart 7.

Chart 7



8a



6a

Chemical Shift in δ [J in Hz (Coupling Protons)]

Proton	Compound **8a** [a]	Compound **6a** [a]
2'-H	7.92 [3.0 ($H_{2'}$ - $H_{5'}$), 1.0 ($H_{2'}$ - $H_{4'}$)]	8.60 [3.0 ($H_{2'}$ - $H_{5'}$), 1.0 ($H_{2'}$ - $H_{4'}$)]
4'-H	7.68 [1.0 ($H_{2'}$ - $H_{4'}$), 5.0 ($H_{4'}$ - $H_{5'}$)]	7.80 [1.0 ($H_{2'}$ - $H_{4'}$), 5.0 ($H_{4'}$ - $H_{5'}$)]
5'-H	7.61 [5.0 ($H_{4'}$ - $H_{5'}$), 3.0 ($H_{2'}$ - $H_{5'}$)]	7.63 [5.0 ($H_{4'}$ - $H_{5'}$), 3.0 ($H_{2'}$ - $H_{5'}$)]

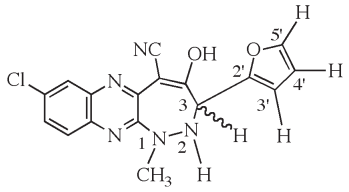
[a] Assignments for 2'-, 4'-, and 5'-proton signals were based on decoupling procedure.

2. Furyl Derivatives.

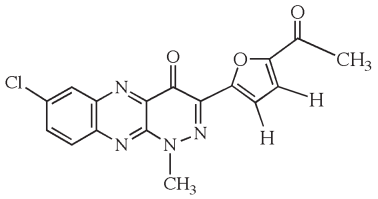
The 3'-, 4'-, and 5'-proton signals of furan ring in compound **9b** [11] were assigned by the NOE spectral data among the 2-, 3-, 3'-, 4'-, and 5'-protons (Chart 8). The 3'- and 4'-proton signals of compound **6d** and the 3'-, 4'-, and 5'-proton signals of compound **6b** were assigned by the NOE spectral data and coupling constants as shown in

Charts 8 and 9, respectively. The coupling constants between 3'-H and 4'-H, between 4'-H and 5'-H, and between 3'-H and 5'-H are 3.1-3.5 Hz, 2.0-2.5 Hz, and 0.8-1.0 Hz, respectively.

Chart 8



9b [Ref. 11] [a]



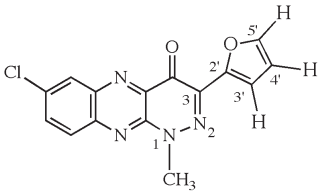
6d [b]

Chemical Shift in δ [J in Hz (Coupling Protons)]

Proton	Compound **9b**	Compound **6d**
3'-H	6.29 [0.8 ($H_{3'}$ - $H_{5'}$), 3.1 ($H_{3'}$ - $H_{4'}$)]	7.82 (3.5)
4'-H	6.39 [3.1 ($H_{3'}$ - $H_{4'}$), 2.0 ($H_{4'}$ - $H_{5'}$)]	7.33 (3.5)
5'-H	7.66 [2.0 ($H_{4'}$ - $H_{5'}$), 0.8 ($H_{3'}$ - $H_{5'}$)]	

[a] Assignments for 3'-, 4'-, and 5'-proton signals were based on NOE spectral data.
[b] Assignments for 3'-, and 4'-proton signals were based on NOE spectral data.

Chart 9



6b

Chemical Shift in δ [J in Hz (Coupling Protons)]

Proton	Compound **6b**
3'-H	7.51 [1.0 ($H_{3'}$ - $H_{5'}$), 3.5 ($H_{3'}$ - $H_{4'}$)]
4'-H	6.68 [3.5 ($H_{3'}$ - $H_{4'}$), 2.5 ($H_{4'}$ - $H_{5'}$)]
5'-H	7.88 [2.5 ($H_{4'}$ - $H_{5'}$), 1.0 ($H_{3'}$ - $H_{5'}$)]

EXPERIMENTAL

All melting points were determined on a Yazawa micro melting point BY-2 apparatus and are uncorrected. The ir spectra (potassium bromide) were recorded with a JASCO FT/IR-200 spectrophotometer. The nmr spectra were measured with a Varian UNITY 400 spectrometer at 400 MHz. The chemical shifts are given in the δ scale. The mass spectra (ms) were determined with a JEOL JMS-01S spectrometer. Elemental analyses were performed on a Perkin-Elmer 240B instrument.

6-Chloro-2-[1-methyl-2-(3-thienylmethylene)hydrazino]quinoxaline 4-Oxide (**8a**).

A solution of compound **7** (10 g, 44.5 mmoles) and thiophene-3-carbaldehyde (7.48 g, 66.8 mmoles) in dioxane (200 ml) was refluxed in an oil bath for 1 hour to precipitate yellow needles of compound **8a**. After the reaction mixture was cooled to room temperature, the yellow needles **8a** were collected by filtration and then washed with *n*-hexane to give an analytically pure sample (12.49 g, 88%), mp 255-256°; ir: ν cm^{-1} 3130, 3070, 1600, 1570, 1535, 1520; ms: m/z 318 (M^+), 320 (M^+ + 2); nmr (deuteriodimethyl sulfoxide): 8.97 (s, 1H, C_3-H), 8.26 (d, J = 2.0 Hz, 1H, C_5-H), 8.11 (s, 1H, hydrazone CH), 7.92 (dd, J = 3.0, 1.0 Hz, 1H, thiophene C_2-H), 7.80 (d, J = 9.0 Hz, 1H, C_8-H), 7.77 (dd, J = 2.0, 9.0 Hz, 1H, C_7-H), 7.68 (dd, J = 5.0, 1.0 Hz, 1H, thiophene C_4-H), 7.61 (dd, J = 5.0, 3.0 Hz, 1H, thiophene C_5-H), 3.66 (s, 3H, N-CH_3).

Anal. Calcd. for $C_{14}H_{11}ClN_4OS$: C, 52.75; H, 3.48; N, 17.58. Found: C, 52.54; H, 3.69; N, 17.48.

8-Chloro-2,3-dihydro-4-hydroxy-1-methyl-3-(3-thienyl)-1*H*-1,2-diazepino[3,4-*b*]quinoxaline-5-carbonitrile Hydrochloride (**9a**).

A solution of compound **8a** (5 g, 15.7 mmoles) and 2-chloroacrylonitrile (2.78 g, 31.4 mmoles) in dioxane (150 ml) was refluxed in an oil bath for 2 hours to precipitate yellow crystals of compound **9a**. After the reaction mixture was cooled to room temperature, the yellow crystals were collected by filtration (5.23 g, 82%), ir: ν cm^{-1} 2220 (very weak); ms: m/z 369 (M^+), 371 (M^+ + 2). This sample was used for the ring transformation into the pyridazino[3,4-*b*]quinoxaline **6a** without purification.

7-Chloro-1-methyl-3-(3-thienyl)pyridazino[3,4-*b*]quinoxalin-4(1*H*)-one (**6a**).

A solution of compound **9a** (3 g, 7.39 mmoles) and selenium dioxide (1.64 g, 14.8 mmoles) in acetic acid (150 ml)/water (5 ml) was refluxed in an oil bath for 1 hour. The reaction mixture was filtered, and the filtrate was evaporated *in vacuo* to give brick red crystals of compound **6a**, which were triturated with water and then collected by filtration. Recrystallization from *N*,*N*-dimethylformamide/ethanol/water afforded violet needles (1.56 g, 64%), mp 268-269°; ir: ν cm^{-1} 1645, 1605, 1540; ms: m/z 328 (M^+), 330 (M^+ + 2); nmr (deuteriodimethyl sulfoxide): 8.60 (dd, J = 1.0, 3.0 Hz,

1H, thiophene C_2-H), 8.41 (dd, J = 2.0, 1.0 Hz, 1H, C_6-H), 8.16 (dd, J = 9.0, 1.0 Hz, 1H, C_9-H), 8.05 (dd, J = 2.0, 9.0 Hz, 1H, C_8-H), 7.80 (dd, J = 1.0, 5.0 Hz, 1H, thiophene C_4-H), 7.63 (dd, J = 3.0, 5.0 Hz, 1H, thiophene C_5-H), 4.22 (s, 3H, N_1-CH_3).

Anal. Calcd. for $C_{15}H_9ClN_4OS$•1/2 H_2O: C, 53.34; H, 2.98; N, 16.61. Found: C, 53.55; H, 2.96; N, 16.61.

7-Chloro-3-(2-furyl)-1-methylpyridazino[3,4-*b*]quinoxalin-4(1*H*)-one (**6b**).

A solution of compound **9b** (10 g, 28.3 mmoles) and selenium dioxide (6.28 g, 56.6 mmoles) in acetic acid (250 ml)/water (10 ml) was refluxed in an oil bath for 1 hour. After cooling to room temperature, the reaction mixture was filtered. Evaporation of the filtrate *in vacuo* gave red crystals. The crystals were dissolved in hot *N*,*N*-dimethylformamide. This solution was filtered, and the filtrate was evaporated *in vacuo* to afford red crystals of compound **6b** (6.43 g, 73%). Compound **6b** was dissolved in chloroform and then submitted to column chromatography on silica gel eluting with chloroform. The fraction of red band [Rf value of compound **6b**, 0.86, silica gel, chloroform-ethanol (20:1)] was collected, and the combined eluate of this fraction was evaporated *in vacuo* to give red crystals of compound **6b**. Recrystallization from chloroform/*n*-hexane provided red cottony needles, mp 272 - 273°; ir: ν cm^{-1} 1650, 1610, 1605; ms: m/z 312 (M^+), 314 (M^+ + 2); nmr (deuteriodimethyl sulfoxide): 8.41 (d, J = 2.0 Hz, 1H, C_6-H), 8.16 (d, J = 9.0 Hz, 1H, C_9-H), 8.05 (dd, J = 2.0, 9.0 Hz, 1H, C_8-H), 7.88 (dd, J = 2.5, 1.0 Hz, 1H, furan C_5-H), 7.51 (dd, J = 1.0, 3.5 Hz, 1H, furan C_3-H), 6.68 (dd, J = 3.5, 2.5 Hz, 1H, furan C_4-H), 4.22 (s, 3H, N-CH_3).

Anal. Calcd. for $C_{15}H_9ClN_4O_2$: C, 57.61; H, 2.90; Cl, 11.34; N, 17.92. Found: C, 57.37; H, 3.18; Cl, 11.51; N, 17.88.

7-Chloro-1-methyl-3-(2-thienyl)pyridazino[3,4-*b*]quinoxalin-4(1*H*)-one (**6c**).

A solution of compound **9c** (2 g, 5.41 mmoles) and selenium dioxide (1.20 g, 10.8 mmoles) in acetic acid (90 ml)/water (10 ml) was refluxed in an oil bath for 1 hour to precipitate violet crystals, which were collected by filtration (crystals 1). Evaporation of the filtrate *in vacuo* gave violet crystals (crystals 2). The crystals 1 and 2 were combined and dissolved in hot *N*,*N*-dimethylformamide. This solution was filtered, and the filtrate was evaporated *in vacuo* to afford violet crystals. Recrystallization from *N*,*N*-dimethylformamide/ethanol twice provided analytically pure violet needles of compound **6c** (1.03 g, 58%), mp 324-325°; ir: ν cm^{-1} 1645, 1605; ms: m/z 328 (M^+), 330 (M^+ + 2); nmr (deuteriodimethyl sulfoxide): 8.44 (d, J = 2.0 Hz, 1H, C_6-H), 8.18 (d, J = 9.0 Hz, 1H, C_9-H), 8.16 (dd, J = 1.0, 3.5 Hz, 1H, thiophene C_3-H), 8.07 (dd, J = 2.0, 9.0 Hz, 1H, C_8-H), 7.68 (dd, J = 1.0, 5.0 Hz, 1H, thiophene C_5-H), 7.20 (dd, J = 3.5, 5.0 Hz, 1H, thiophene C_4-H), 4.23 (s, 3H, N-CH_3).

Anal. Calcd. for $C_{15}H_9ClN_4OS$: C, 54.80; H, 2.76; Cl, 10.78; N, 17.04. Found: C, 54.60; H, 2.98; Cl, 10.55; N, 17.05.

3-(5-Acetyl-2-furyl)-7-chloro-1-methylpyridazino[3,4-*b*]quinoxalin-4(1*H*)-one (**6d**).

A solution of compound **6b** (1 g) and zinc chloride (500 mg) in acetic anhydride (30 ml) was refluxed in an oil bath for 5 hours. Evaporation of the solvent *in vacuo* gave red crystals of compound **6d**, which were dissolved in chloroform and then submitted to column chromatography on silica gel eluting with chloroform. The fraction of red band [Rf value of compound **6d**, 0.73, silica gel, chloroform-ethanol (20:1)] was collected, and the combined eluate of this fraction was evaporated *in vacuo* to give red crystals of compound **6d**. Recrystallization from *N*,*N*-dimethylformamide/ethanol/water provided red needles (100 mg, 9%), mp 326-327°; ir: ν cm^{-1} 1680, 1645, 1600, 1570, 1535, 1520; ms: m/z 354 (M^+), 356 (M^+ + 2); nmr (deuteriochloroform): 8.41 (d, J = 2.5 Hz, 1H, C_6-H), 8.10 (d, J = 9.5 Hz, 1H, C_9-H), 7.91 (dd, J = 2.5, 9.5 Hz, 1H, C_8-H), 7.82 (d, J = 3.5 Hz, 1H, furan C_3-H), 7.33 (d, J = 3.5 Hz, 1H, furan C_4-H), 4.43 (s, 3H, N-CH_3), 2.59 (s, 3H, acetyl CH_3).

Anal. Calcd. for $C_{17}H_{11}ClN_4O_3$•1/2 H_2O: C, 56.13; H, 3.32; N, 15.40. Found: C, 56.08; H, 3.18; N, 15.13.

3-(5-Bromo-2-thienyl)-7-chloro-1-methylpyridazino[3,4-*b*]-quinoxalin-4(1*H*)-one (**6e**).

A solution of compound **6c** (1 g, 3.04 mmoles) and *N*-bromosuccinimide (0.65 g, 3.65 mmoles) in acetic acid (30 ml) was refluxed in an oil bath for 1 hour. Evaporation of the solvent *in vacuo* gave violet crystals of compound **6e**, which were triturated with hot ethanol/water and then collected by filtration (1.15 g, 93%). Recrystallization from *N*,*N*-dimethylformamide/ethanol/water provided violet needles, mp 270-271°; ir: ν cm^{-1} 1640, 1600, 1535, 1500; ms: m/z 405 (M^+), 407 (M^+ + 2), 409 (M^+ + 4); nmr (deuteriodimethyl sulfoxide): 8.41 (d, J = 2.0 Hz, 1H, C_6-H), 8.16 (d, J = 9.0 Hz, 1H, C_9-H), 8.06 (dd, J = 2.0, 9.0 Hz, 1H, C_8-H), 7.85 (d, J = 4.0 Hz, 1H, thiophene C_3-H), 7.29 (d, J = 4.0 Hz, 1H, thiophene C_4-H), 4.22 (s, 3H, N-CH_3).

Anal. Calcd. for $C_{15}H_8BrClN_4OS$•1/2 H_2O: C, 43.24; H, 2.18; N, 13.45; S, 7.69. Found: C, 43.36; H, 2.07; N, 13.52; S, 7.71.

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