Quinolone Analogues 8 [1-6]. Synthesis of 3-Aminopyridazino-[3,4-*b*]quinoxalin-4(1*H*)-one

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The 3-amino-1-methylpyridazino[3,4-*b*]quinoxalin-4(1*H*)-one **6** and *N*-(l,4-dihydro-1-methyl-4-oxopyridazino[3,4-*b*]quinoxalin-3-yl)carbamates **17a,b** were synthesized from the 1,4-dihydro-1-methyl-4-oxopyridazino[3,4-*b*]quinoxaline-3-carboxylate **1b** *via* the 1,5-dihydro-4-hydroxy-1-methylpyridazino[3,4-*b*]quinoxaline-3-carbohydrazide **13b** and then 1,4-dihydro-1-methyl-4-oxopyridazino[3,4-*b*]quinoxaline-3-carboxazide **8**. Heating of compound **13b** and arylaldehydes afforded the 1,4-dihydro-1-methyl-4-oxopyridazino[3,4-*b*]quinoxaline-3-carbo(2-arylmethylene)hydrazides **14a-d**.

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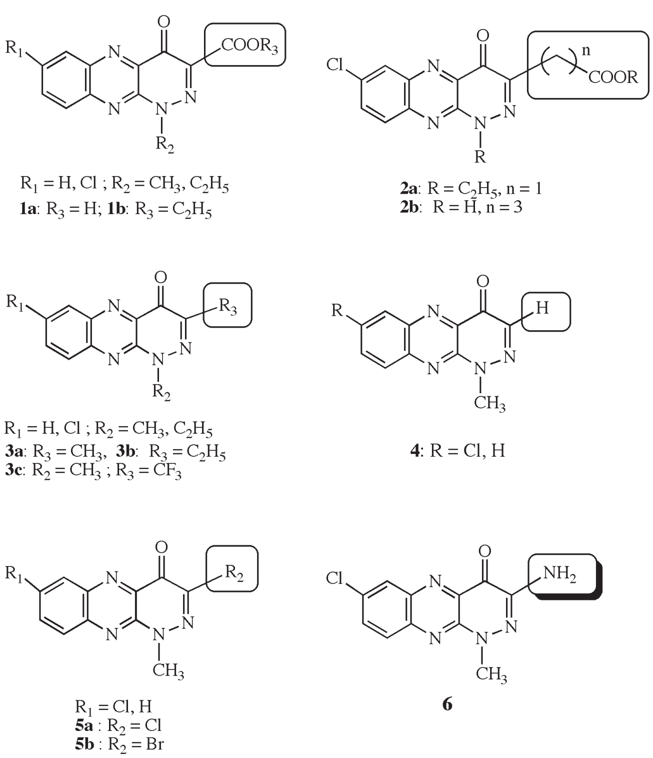
Introduction.

In previous papers [1-6], we reported the synthesis of quinolone analogues such as the 1-alkyl-1,4-dihydropyridazino[3,4-*b*]quinoxalines **1-5** (Chart 1) as candidates of antimicrobial agents. Compounds **1** and **2** having a carboxyl or carboxylate group at 3-position showed weak antibacterial activities [1,2], but the 3-alkyl **3**, 3-H **4**, and 3-halogeno **5** homologues possessing no carboxyl or carboxylate group at 3-position exhibited good antibacterial and antifungal activities [3-6]. These results suggest that 1-alkyl-1,4-dihydropyridazino[3,4-*b*]quinoxalin-4(1*H*)-ones having no carboxyl or carboxylate group at 3-position would represent some of antimicrobial activities. Accordingly, we further planned the synthesis of the 3-amino-1-methylpyridazino[3,4-*b*]quinoxalin-4(1*H*)-one **6** (Chart 1) in order to search for potent compounds.

Chart 1



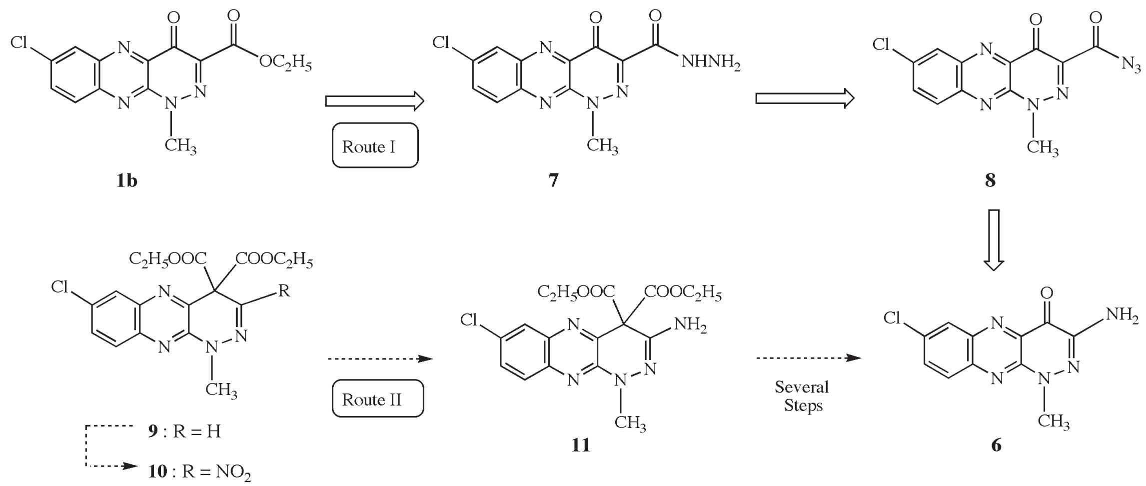
Synthetic Route.

There are at least two methods I and II for the synthesis of the 3-amino derivative **6** as shown in Scheme 1. The route I method was found to be more convenient than the route II method. Namely, if the 3-carbohydrazide **7** is successfully synthesized from the 3-carboxylate **1b**, the 3-amino derivative **6** would be easily produced *via* the Curtius rearrangement of the 3-carboxazide **8**. In fact, the reaction of the 3-carboxylate **1b** with a large amount of hydrazine hydrate (13-fold molar amount) gave the 3-carbohydrazide **13b** [7-10] instead of the 3-carbohydrazide **7** (Scheme 2), although the use of 2- or 3-fold molar amount of hydrazine hydrate recovered the starting material **1b**. Successively, the 3-carbohydrazide **13b** was converted into the 3-amino derivative **6** *via* the carboxazide **8** (Scheme 5). In the route II method, however, the yield of the 3-nitro derivative **10** from compound **9** [5,6] was very low [11]. Moreover, the direct amination of compound **9** with hydroxylamine *O*-sulfonic acid to the 3-amino derivative **11** was unsuccessful.

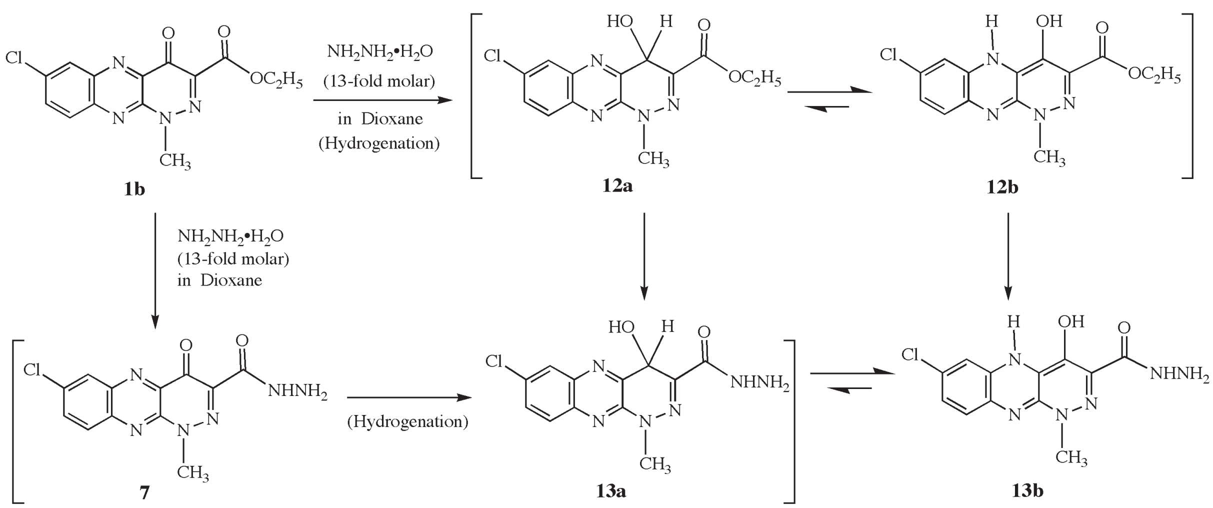
Synthesis of the 3-Amino Derivative 6.

The reaction of compound **1b** with 13-fold molar amount of hydrazine hydrate gave the 1,5-dihydro-4-hydroxy-1-methylpyridazino[3,4-*b*]quinoxaline-3-carbohydrazide **13b** presumably *via* compounds **12a/12b** or **7/13a**, wherein the 4-keto group of compound **1b** or **7** was reduced with hydrazine (Scheme 2). Oxidation of the 1,5-dihydro-4-hydroxy moiety in compound **13b** to the 1,4-dihydro-4-oxo moiety in compounds **14a-d** was found to take place easily by autoxidation. Namely, reflux of compound **13b** and arylaldehydes in *N*,*N*-dimethylformamide with stirring for 2 hours provided the 7-chloro-1-methyl-4-oxopyridazino[3,4-*b*]quinoxaline-3-carbo(2-arylmethylene)hydrazides **14a-d**, while heating of compound **13b** in dimethyl sulfoxide with stirring for 2 hours afforded the 2*H*-pyrazolo[3',4':5,6]pyridazino[3,4-*b*]quinoxalin-3(5*H*)-one **15** presumably *via* compound **7** (Scheme 3).

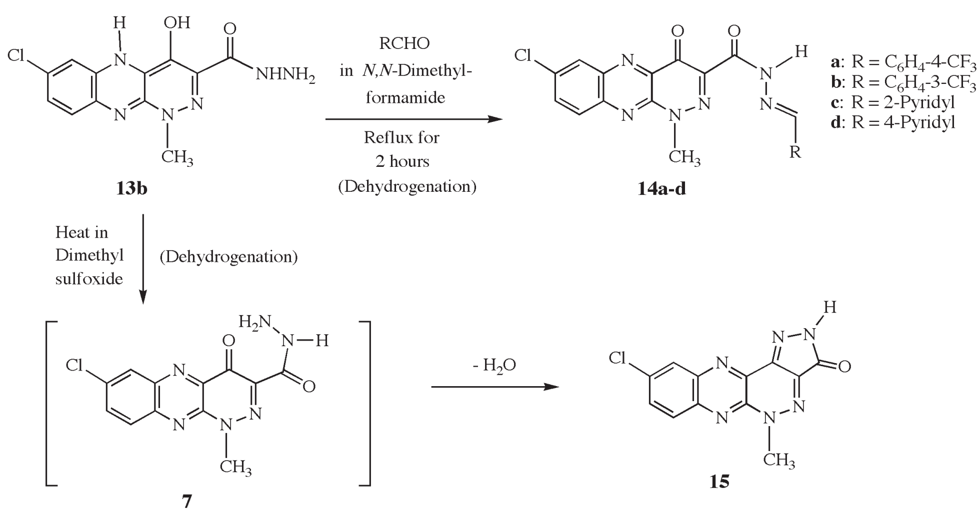
Scheme 1



Scheme 2



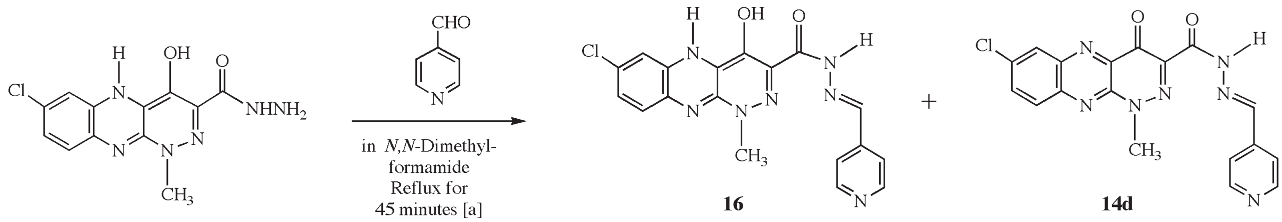
Scheme 3



However, when the mixture of compound **13b** and pyridine-4-carbaldehyde in *N*,*N*-dimethylformamide was refluxed for 45 minutes without stirring, compound **14d** and the intermediate **16** were simultaneously obtained (Scheme 4, Table 1). The nmr spectral data in Table 1 are explained later.

The reaction of compound **13b** with nitrous acid provided the 1,4-dihydro-4-oxopyridazino[3,4-*b*]quinoxaline-3-carboxazide **8** [12], whose rearrangement took place easily on heating in water/triethylamine/*N*,*N*-dimethylformamide [13] to afford the 3-amino derivative **6**. On the other hand, reflux of compound **8** in triethylamine/alcohols [13] gave the carbamate derivatives **17a,b** (Scheme 5).

Scheme 4



13b

16
1,5-Dihydroquinoxaline Form (32%)

14d
1,4-Dihydroquinoxaline Form (68%)

[a] Because of short time reflux, product was a mixture of compounds 14d and 16.

Table 1

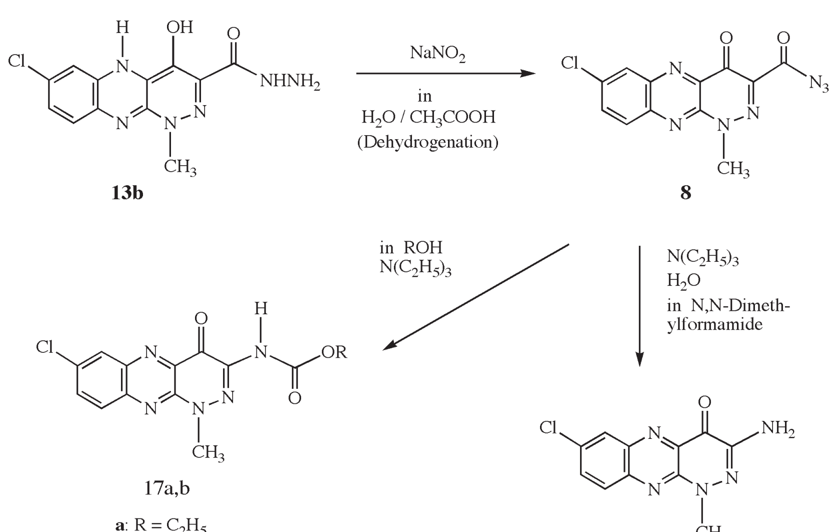
Aromatic Proton Signals of Quinoxaline Ring for Compounds **13b**, **14a-d**, and **16** [a]

Compound	Chemical Shifts (δ) 1,4-Dihydroquinoxaline Form 6-H, 8-H, 9-H	1,5-Dihydroquinoxaline Form 6-H, 8-H, 9-H
13b	———	6.52 - 6.36
14a-d	8.26 - 7.82	———
14d +16 [b]	8.08 - 7.82	6.39 - 6.25

[a] Measured in deuteriotrifluoroacetic acid. [b] Mixture of 14d and 16.

The structural assignments of new compounds were based on analytical and spectral data. Compounds **6**, **13b**, **14a-d**, and **15** were insoluble in deuteriodimethyl sulfoxide, and the nmr spectra of these compounds were measured in deuteriotrifluoroacetic acid. Accordingly, these compounds were assigned as the deuterized structure including ND and/or OD group. On the other hand, the 6-H, 8-H, and 9-H proton signals of compound **13b** (δ 6.52-6.36) with the 1,5-dihydro form were easily distinguished from those of compounds **14a-d** (δ 8.26-7.82) with the 1,4-dihydro form (Table 1), as reported by us in previous papers [2,4,6,12]. Namely, the aromatic proton signals of

Scheme 5



13b

8

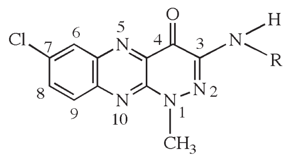
17a,b

a: R = C_2H_5
b: R = n-C_4H_9

6

Table 2

Carbon Chemical Shifts (δ) for Quinolone Analogues **6** and **17b** [a, b]



6 R = H
17b R = $COOC_4H_7$

Carbon	Compound **6**	Compound **17b**
C_3	127.2	123.8
C_4=O	163.4	162.0
C_{4a}	139.2	142.7
C_{5a}	144.3	146.1
C_6	124.3	122.7
C_7	139.5	136.5
C_8	138.3	138.8
C_9	130.2	130.6
C_{9a}	145.8	147.2
C_{10a}	144.8	144.7
NCH_3	41.2	41.3
NHCO	——	154.7

[a] Measured in deuteriotrifluoroacetic acid. [b] Assigned by HMQC and HMBC spectra.

the 1,5-dihydropyridazino[3,4-*b*]quinoxalines are observed at a higher magnetic field than those of the 1,4-dihydropyridazino[3,4-*b*]quinoxalines [2,4,6]. In a mixture of compound **16** (1,5-dihydro form) and compound **14d** (1,4-dihydro form), two pairs of the 6-H, 8-H, and 9-H proton signals were observed at δ 6.39-6.26 (due to the 1,5-dihydro compound) and at δ 8.08-7.82 (due to the 1,4-dihydro compound). Thus, the signals of compound **16** (δ 6.39-6.26) in the above mixture were easily specified by nmr spectral data. The ring carbon signals of the quinolone analogues **6** and **17b** were also assigned by HMQC and HMBC spectral data (Table 2).

The screening of novel compounds synthesized in the present investigation is in progress, and the data will be reported elsewhere.

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 XL-400 spectrometer at 400 MHz. The chemical shifts are given in the δ scale. The mass spectra were determined with a JEOL JMS-01S spectrometer. Elemental analyses were performed on a Perkin-Elmer 240B instrument.

7-Chloro-1,5-dihydro-4-hydroxy-1-methylpyridazino[3,4-*b*]quinoxaline-3-carbohydrazide (**13b**).

A suspension of compound **1b** (5 g) and hydrazine hydrate (100% purity, 10 g) in dioxane (100 ml) was refluxed for 3 hours to precipitate red needles of compound **13b**, which were collected by filtration and then washed with ethanol to give an analytically pure sample (4.59 g, 96%), mp 280-281°; ir: ν cm^{-1} 3400, 3240, 1665, 1610; ms: m/z 306 (M^+), 308 (M^+ + 2), 304 [(M^+) - 2 (H_2)]; nmr (deuteriotrifluoroacetic acid): δ 6.52 (dd, J = 8.5, 2.0 Hz, 1H, C_8-H), 6.48 (d, J = 2.0 Hz, 1H, C_6-H), 6.36 (d, J = 8.5 Hz, 1H, C_9-H), 3.59 (s, 3H, NCH_3).

Anal. Calcd. for $C_{12}H_{11}ClN_6O_2$: C, 46.99; H, 3.61; N, 27.40. Found: C, 46.95; H, 3.81; N, 27.33.

7-Chloro-1,4-dihydro-1-methyl-4-oxopyridazino[3,4-*b*]quinoxaline-3-carbo[2-(4-trifluoromethylbenzylidene)]hydrazide (**14a**).

A solution of compound **13b** (500 mg, 1.63 mmole) and 4-trifluoromethylbenzaldehyde (426 mg, 2.45 mmoles) in *N,N*-dimethylformamide (30 ml) was refluxed with stirring for 2 hours. The solution was allowed to stand overnight, precipitating yellow crystals of compound **14a**, which were collected by filtration and then washed with ethanol to give an analytically pure sample (450 mg, 60%), mp above 310°; ir: ν cm^{-1} 1690, ms: m/z 460 (M^+), 462 (M^+ + 2); nmr (deuteriotrifluoroacetic acid): δ 8.34 (s, 1H, hydrazone CH), 8.18 (d, J = 2.0 Hz, 1H, C_6-H), 8.14 (d, J = 9.5 Hz, 1H, C_9-H), 7.96 (dd, J = 2.0, 9.5 Hz, 1H, C_8-H), 7.78 (d, J = 8.0 Hz, 2H, benzene ring CH), 7.54 (d, J = 8.0 Hz, 2H, benzene ring CH), 4.52 (s, 3H, NCH_3).

Anal. Calcd. for $C_{20}H_{12}ClF_3N_6O_2$: C, 52.13; H, 2.62; N, 18.24. Found: C, 52.16; H, 2.83; N, 18.16.

7-Chloro-1,4-dihydro-1-methyl-4-oxopyridazino[3,4-*b*]-quinoxaline-3-carbo[2-(3-trifluoromethylbenzylidene)]hydrazide (**14b**).

A solution of compound **13b** (500 mg, 1.63 mmole) and 3-trifluoromethylbenzaldehyde (426 mg, 2.45 mmoles) in *N,N*-dimethylformamide (30 ml) was refluxed with stirring for 2 hours. The solution was allowed to stand overnight, precipitating yellow crystals of compound **14b**, which were collected by filtration and then washed with ethanol to give an analytically pure sample (470 mg, 63%), mp above 310°; ir: ν cm^{-1} 1690, ms: m/z 460 (M^+), 462 (M^+ + 2); nmr (deuteriotrifluoroacetic acid): δ 8.25 (s, 1H, hydrazone CH), 8.04 (d, J = 2.0 Hz, 1H, C_6-H), 8.03 (d, J = 9.5 Hz, 1H, C_9-H), 7.84 (dd, J = 2.0, 9.5 Hz, 1H, C_8-H), 7.78 (s, 1H, benzene C_2-H), 7.78 (d, J = 8.0 Hz, 1H, benzene C_6-H), 7.51 (d, J = 8.0 Hz, 1H, benzene C_4-H), 7.33 (dd, J = 8.0, 8.0 Hz, 1H, benzene C_5-H), 4.42 (s, 3H, NCH_3).

Anal. Calcd. for $C_{20}H_{12}ClF_3N_6O_2$: C, 52.13; H, 2.62; N, 18.24. Found: C, 52.17; H, 2.80; N, 18.21.

7-Chloro-1,4-dihydro-1-methyl-4-oxopyridazino[3,4-*b*]quinoxaline-3-carbo[2-(2-pyridylmethylene)]hydrazide (**14c**).

A solution of compound **13b** (1.5 g, 4.89 mmoles) and pyridine-2-carbaldehyde (0.79 g, 7.34 mmoles) in *N,N*-dimethylformamide (80 ml) was refluxed with stirring for 2 hours. Evaporation of the solvent *in vacuo* gave yellow crystals of compound **14c**, which were collected by filtration. Recrystallization from *N,N*-dimethylformamide/ethanol afforded yellow needles (1.38 g, 72%), mp 297-298°; ir: ν cm^{-1} 3230, 1695, 1640, ms: m/z 393 (M^+), 395 (M^+ + 2); nmr (deuteriotrifluoroacetic acid): δ 8.57 (dd, J = 7.0, 1.2 Hz, 1H, pyridine C_6-H), 8.48 (s, 1H, hydrazone CH), 8.47 (ddd, J = 7.0, 7.0, 1.2 Hz, 1H, pyridine C_4-H), 8.09 (d, J = 7.0 Hz, 1H, pyridine C_3-H), 8.08 (d, J = 2.0 Hz, 1H, C_6-H), 8.01 (d, J = 9.0 Hz, 1H, C_9-H), 7.88 (dd, J = 7.0, 7.0 Hz, 1H, pyridine C_5-H), 7.82 (dd, J = 2.0, 9.0 Hz, 1H, C_8-H), 4.38 (s, 3H, NCH_3).

Anal. Calcd. for $C_{18}H_{12}ClN_7O_2$: C, 54.90; H, 3.07; N, 24.90. Found: C, 54.73; H, 3.30; N, 24.60.

7-Chloro-1,4-dihydro-1-methyl-4-oxopyridazino[3,4-*b*]quinoxaline-3-carbo[2-(4-pyridylmethylene)]hydrazide (**14d**).

A solution of compound **13b** (1.5 g, 4.89 mmoles) and pyridine-4-carbaldehyde (0.79 g, 7.34 mmoles) in *N*,*N*-dimethylformamide (80 ml) was refluxed with stirring for 2 hours. Evaporation of the solvent *in vacuo* gave yellow crystals of compound **14d**, which were collected by filtration. Recrystallization from *N*,*N*-dimethylformamide/ethanol provided yellow needles (0.96 g, 50%), mp above 320°; ir: ν cm^{-1} 3240, 1690, 1620, ms: m/z 393 (M^+), 395 (M^+ + 2); nmr (deuteriotrifluoroacetic acid): δ 8.72 (d, J = 6.5 Hz, 2H, pyridine C_2-H and C_6-H), 8.59 (s, 1H, hydrazone CH), 8.48 (d, J = 6.5 Hz, 2H, pyridine C_3-H and C_5-H), 8.26 (d, J = 2.0 Hz, 1H, C_6-H), 8.08 (dd, J = 2.0, 9.0 Hz, 1H, C_8-H), 8.00 (dd, J = 9.0 Hz, 1H, C_9-H), 4.55 (s, 3H, NCH_3).

Anal. Calcd. for $C_{18}H_{12}ClN_7O_2$: C, 54.90; H, 3.07; N, 24.90. Found: C, 54.66; H, 3.34; N, 24.91.

9-Chloro-5-methyl-2*H*-pyrazolo[3',4':5,6]pyridazino[3,4-*b*]quinoxalin-3(5*H*)-one (**15**).

A solution of compound **13b** (0.5 g) in dimethyl sulfoxide (10 ml) was heated at 140-160° with stirring for 2 hours. The solution was allowed to stand overnight to precipitate purple needles of compound **15**, which were collected by filtration and then washed with ethanol to afford an analytically pure sample (0.27 g, 54%), mp above 310°; ir: ν cm^{-1} 1700, ms: m/z 286 (M^+), 288 (M^+ + 2); nmr (deuteriotrifluoroacetic acid): δ 8.10 (d, J = 2.0 Hz, 1H, C_{10}-H), 8.06 (d, J = 9.0 Hz, 1H, C_7-H), 7.84 (dd, J = 2.0, 9.0 Hz, 1H, C_8-H), 4.51 (s, 3H, NCH_3).

Anal. Calcd. for $C_{12}H_7ClN_6O$: C, 50.28; H, 2.46; N, 29.32. Found: C, 50.15; H, 2.65; N, 29.04.

7-Chloro-1,4-dihydro-1-methyl-4-oxopyridazino[3,4-*b*]quinoxalin-3-carboxazide (**8**).

(A) Preparation of compound **8** for the synthesis of the 3-amino derivative **6**: A solution of sodium nitrite (1.01 g, 14.7 mmoles) in water (20 ml) was added to a suspension of compound **13b** (3 g, 9.79 mmoles) in acetic acid (30 ml)/water (20 ml). The mixture was stirred at room temperature for 2 hours to precipitate yellow crystals of compound **8**. After addition of water (200 ml) to the stirred reaction mixture, precipitated compound **8** was collected by filtration, washed with ethanol/hexane (1:1), and then dried at room temperature; ir: ν cm^{-1} 2143 (N_3), 1700 (C=O), 1640 (C=O); ms: m/z 287 [(M^+) - N_2], 289 [(M^+ + 2) -N_2].

(B) Preparation of compound **8** for the synthesis of the 3-carbamate derivatives **17a,b**: A solution of sodium nitrite (0.34 g, 4.89 mmoles) in water (10 ml) was added to a suspension of compound **13b** (1 g, 3.26 mmoles) in acetic acid (10 ml)/water (10 ml). The mixture was stirred at room temperature for 2 hours to precipitate yellow crystals of compound **8**. After addition of water (100 ml) to the stirred reaction mixture, precipitated compound **8** was collected by filtration, washed with ethanol/hexane (1:1), and then dried at room temperature.

3-Amino-7-chloro-1-methylpyridazino[3,4-*b*]quinoxalin-4(1*H*)-one (**6**).

A solution of the above 3-caboxazide derivative **8** in water (3 ml)/triethylamine (0.3 ml)/*N,N*-dimethylformamide (60 ml) was refluxed for 2 hours to precipitate blue needles of compound **6**, which were collected by filtration and then washed with ethanol to give an analytically pure sample (1.56 g, 61%), mp above 320°; ir: ν cm^{-1} 3415, 3330, 3220, 1662, 1630; ms: m/z 261 (M^+), 263 (M^+ + 2); nmr (deuteriotrifluoroacetic acid): δ 8.13 (d, J = 2.0 Hz, 1H, C_6-H), 8.05 (d, J = 9.0 Hz, 1H, C_9-H), 7.88 (dd, J = 2.0, 9.0 Hz, 1H, C_8-H), 4.29 (s, 3H, NCH_3).

Anal. Calcd. for $C_{12}H_8ClN_5O_2$: C, 50.49; H, 3.08; N, 26.76. Found: C, 50.62; H, 3.17; N, 26.58.

Ethyl *N*-(7-Chloro-1,4-dihydro-1-methyl-4-oxopyridazino[3,4-*b*]-quinoxalin-3-yl)carbamate (**17a**).

A solution of the above 3-carboxazide derivative **8** in triethylamine (0.3 ml)/ethanol (50 ml) was refluxed for 2 hours. The solution was allowed to stand overnight to precipitate red needles of compound **17a**, which were collected by filtration and then washed with ethanol to give an analytically pure sample (0.37 g). After addition of acetic acid (0.5 ml) to the filtrate, the solvent was evaporated *in vacuo* to afford red crystals of compound **17a**, which were triturated with ethanol and then collected by filtration (0.33 g). Total yield, 0.70 g (64%).

Compound **17a** had mp 180-181°; ir: ν cm^{-1} 3385, 1740, 1725, 1635; ms: m/z 333 (M^+), 335 (M^+ + 2); nmr (deuteriodimethyl sulfoxide): δ 9.43 (s, 1H, NH), 8.38 (d, J = 2.0 Hz, 1H, C_6-H), 8.13 (d, J = 9.0 Hz, 1H, C_9-H), 8.04 (dd, J = 2.0, 9.0 Hz, 1H, C_8-H), 4.13 (q, J = 7.0 Hz, 2H, CH_2), 4.10 (s, 3H, NCH_3), 1.22 (t, J = 7.0 Hz, 3H, CH_3).

Anal. Calcd. for $C_{14}H_{12}ClN_5O_3$: C,50.39; H, 3.62; N, 20.99. Found: C, 50.35; H, 3.72; N, 20.77.

Butyl *N*-(7-Chloro-1,4-dihydro-1-methyl-4-oxopyridazino[3,4-*b*]-quinoxalin-3-yl)carbamate (**17b**).

A solution of the above 3-carboxazide derivative **8** in triethylamine (0.3 ml)/butanol (50 ml) was refluxed for 2 hours. The solution was allowed to stand overnight to precipitate red needles of compound **17b**, which were collected by filtration and then washed with ethanol to give an analytically pure sample (0.38 g). After addition of acetic acid (0.5 ml) to the filtrate, the solvent was evaporated *in vacuo* to afford red crystals of compound **17b**, which were triturated with ethanol and then collected by filtration (0.49 g). Total yield, 0.87 g (74%).

Compound **17b** had mp 164-165°; ir: ν cm^{-1} 3400, 3080, 2960, 1760, 1640; ms: m/z 361 (M^+), 363 (M^+ + 2); nmr (deuteriodimethyl sulfoxide): δ 9.43 (s, 1H, NH), 8.38 (d, J = 2.0 Hz, 1H, C_6-H), 8.13 (d, J = 9.0 Hz, 1H, C_9-H), 8.04 (dd, J = 9.0, 2.0 Hz, 1H, C_8-H), 4.10 (s, 3H, NCH_3), 4.07 (t, J = 7.0 Hz, 2H, CH_2), 1.58 (tt, J = 7.0, 7.0 Hz, 2H, CH_2), 1.37 (qt, J = 7.0, 7.0 Hz, 2H, CH_2), 0.90 (t, J = 7.0 Hz, 3H, CH_3).

Anal. Calcd. for $C_{14}H_{12}ClN_5O_3$: C, 53.12; H, 4.46; N, 19.36. Found: C, 52.90; H, 4.38; N, 19.60.

A Mixture of 7-Chloro-1,5-dihydro-4-hydroxy-1-methylpyridazino[3,4-*b*]quinoxaline-3-carbo[2-(4-pyridylmethylene)]-hydrazide (**16**) and Compound (**14d**).

A solution of compound **13b** (1.5 g, 4.89 mmoles) and pyridine-4-carbaldehyde (0.79 g, 7.34 mmoles) in *N,N*-dimethylformamide (80 ml) was refluxed for 45 minutes. The solution was allowed to stand overnight at room temperature to precipitate greenish yellow crystals of a mixture of compound **16** and compound **14d**, which were collected by filtration and washed with ethanol (1.48 g); ir: ν cm^{-1} 3240, 1690, 1620, ms: m/z 393, 395, nmr (deuteriotrifluoroacetic acid): δ [signals corresponding to compound **16** (1,5-dihydro form), 32%] 8.51 (d, J = 7.0 Hz, pyridine C_2-H and C_6-H), 8.30 (s, hydrazone CH), 8.18 (d, J = 7.0 Hz, pyridine C_3-H and C_5-H), 6.39 (dd, J = 2.0, 8.0 Hz, C_8-H), 6.26 (d, J = 2.0 Hz, C_6-H), 6.25 (d, J = 8.0 Hz, C_9-H), 3.51 (s, NCH_3); [signals corresponding to compound **14d** (1,4-dihydro form), 68%] 8.52 (d, J = 7.0 Hz, pyridine C_2-H and C_6-H), 8.40 (s, hydrazone CH), 8.28 (d, J = 7.0 Hz, pyridine C_3-H and C_5-H), 8.08 (d, J = 2.0 Hz, C_6-H), 8.00 (d, J = 8.0 Hz, C_9-H), 7.82 (dd, J = 2.0, 8.0 Hz, C_8-H), 4.37 (s, NCH_3).

REFERENCES AND NOTES

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[7] This type of compounds were clarified by us to exist as the 1,5-dihydropyridazino[3,4-*b*]quinoxaline form, but not the 1,4-dihydropyridazino[3,4-*b*]quinoxaline form, in solution and solid state [8], while dihydropyridazine [9] and dihydrocinnolines [10] were reported to predominate as the 1,4-dihydro form.

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[11] The synthesis of the 3-nitro derivative **10** will be reported elsewhere.

[12] The dehydrogenation of the 1,5-dihydro-4-hydroxy-3-carbohydrazide derivative **13b** to the 1,4-dihydro-4-oxo-3-carboxazide derivative **8** would be due to autoxidation and/or oxidation with nitrous acid. Two molar nitrous acid is known to generate two molar nitrogen monoxide and one molar nascent oxygen and water.

[13] The addition of triethylamine provided good yields.