A Convenient Synthesis of 2-Amino-4*H*-1,3,4-oxadiazino[5,6-*b*]-quinoxaline Derivatives

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The reaction of 6-chloro-2-(1-methylhydrazino)quinoxaline 4-oxide **5** with a 2-fold molar amount of ethyl chloroglyoxalate gave ethyl 8-chloro-4-methyl-4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxaline-2-carboxylate **6**, whose reaction with hydrazine hydrate afforded the C_2-hydrazinocarbonyl derivative **7**. The reaction of compound **7** with nitrous acid provided the C_2-acylazide derivative **8**, which was converted into the C_2-amino **9**, C_2-carbamate **11a-c**, **12a,b**, and C_2-ureido **13a-c**, **14** derivatives. The mass spectral fragmentation patterns were examined for compounds **10-14**, wherein the molecular ion peak did not appear in the mass spectra of compounds **10c**, **11a-c**, **12a,b**, **13c**, and **14**.

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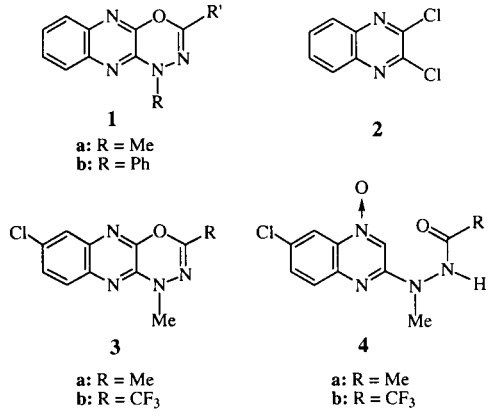
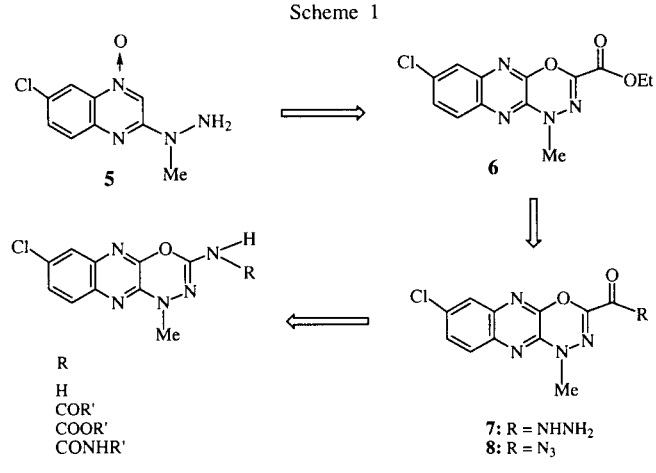
Hitherto, the 2-methyl- and 2-aryl-4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxalines **1a,b** have generally been synthesized from the reaction of 2,3-dichloroquinoxaline **2** with acyl hydrazides (Chart 1) [2]. We also reported the synthesis

Chart 1



of the 2-methyl- and 2-trifluoromethyl-4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxalines **3a,b** from the reaction of the 2-(2-acyl-1-methylhydrazino)quinoxaline 4-oxides **4a,b** with phosphoryl chloride [3]. The above 4*H*-1,3,4-oxadiazino-[5,6-*b*]quinoxalines **1a,b** and **3a,b** synthesized so far are the C_2-alkyl or C_2-phenyl analogues, which are hardly derivatized further in the C_2-side chain moiety. Accordingly, we devised the synthesis of a versatile C_2-substituted 4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxaline such as compound **6** (Scheme 1), which would be converted into multifarious C_2-(substituted)amino derivatives *via* compounds **7** and **8**, as shown in Scheme 1. In the present investigation, we succeeded in a one-step synthesis of the C_2-carboxylate **6** from

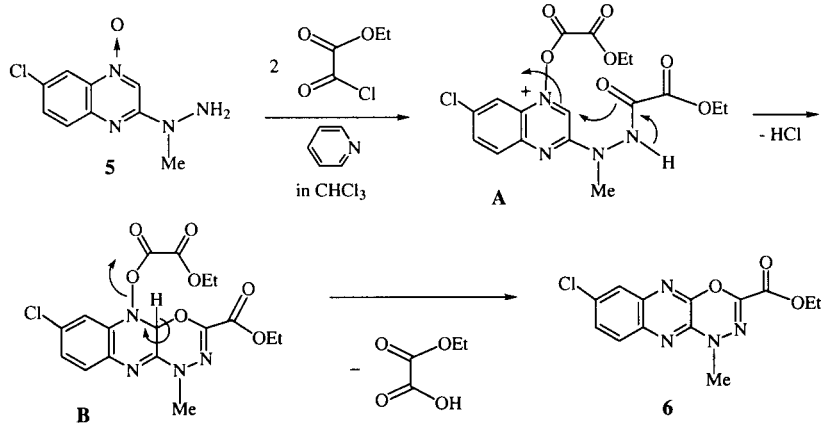
Scheme 1



the quinoxaline 4-oxide **5** together with the transformation of the C_2-carboxylate **6** into the various C_2-amino derivatives **9-14** (Scheme 2). This paper descibes the synthesis of novel 4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxalines **6-14** (Scheme 3).

The reaction of 6-chloro-2-(1-methylhydrazino)quinoxaline 4-oxide **5** with a 2-fold molar amount of ethyl chloroglyoxalate gave ethyl 8-chloro-4-methyl-4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxaline-2-carboxylate **6** presumably *via* intermediates **A** and **B** (Scheme 2). The reaction of compound **6** with hydrazine hydrate afforded 8-chloro-2-hydrazinocarbonyl-4-methyl-4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxaline **7**, whose reaction with nitrous acid provided 2-azidocarbonyl-8-chloro-4-methyl-4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxaline **8**. Heating of compound **8** in water/dioxane gave 2-amino-8-chloro-4-methyl-4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxaline **9** *via* an isocyanate intermediate **C** (Chart 2), and the reaction of

Scheme 2



Scheme 3

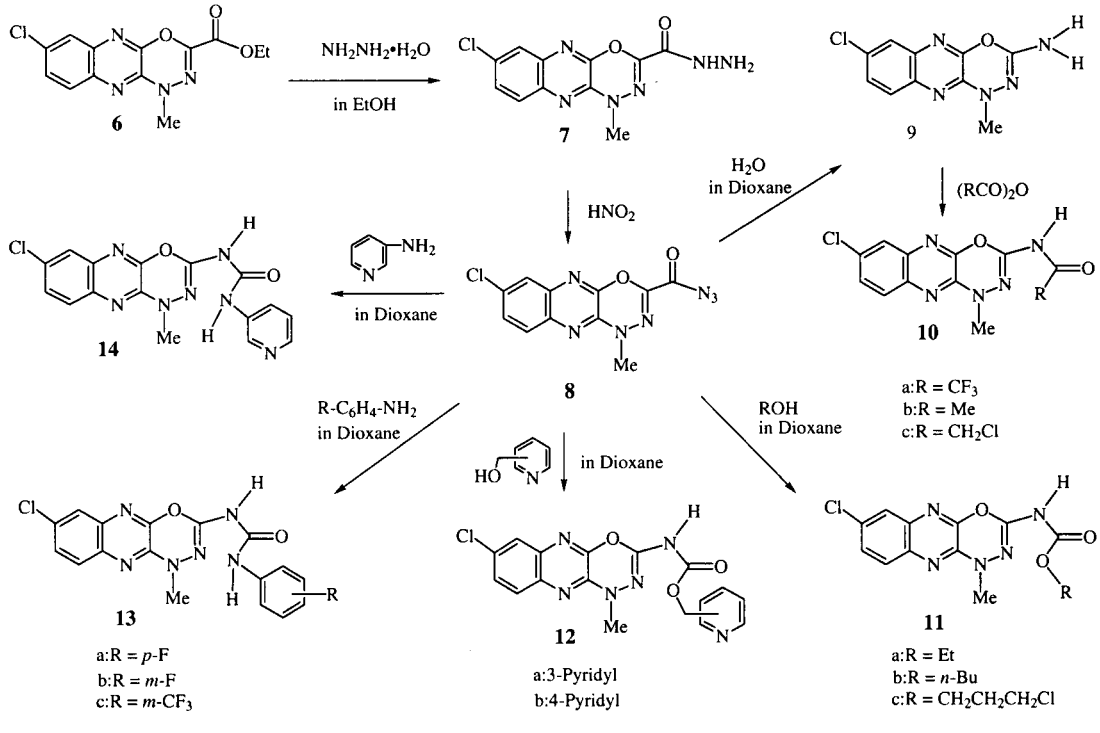
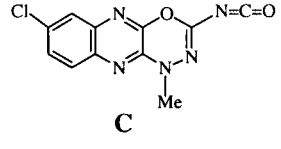


Chart 2



compound **9** with trifluoroacetic anhydride, acetic anhydride, and chloroacetic anhydride provided the 2-acylamido-8-chloro-4-methyl-4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxalines **10a-c**, respectively. The reaction of compound **9** with aromatic aldehydes under reflux in *N,N*-dimethylformamide did not afford Shiff bases presumably due to a weak nucleophilicity of the C_2-amino group of compound **9**. On the other hand, an above isocyanate intermediate **C** was trapped with alcohols or amines to afford the *N*-(8-chloro-4-methyl-4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxalin-2-yl) carbamates **11a-c**, **12a,b** or 2-(3-arylureido)-8-chloro-4-methyl-4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxalines **13a-c**, **14**, respectively.

The spectral and analytical data supported the structure of the above compounds **7-14**, except for the mass spectral data for compounds **10c**, **11a-c**, **12a,b**, **13c**, and **14**. Namely, the mass spectra of these compounds lacked the respective molecular ion peaks. Accordingly, the fragmentation patterns were inspected for compounds **10-14** (Table, Schemes 4-7). In general, the fragmentation takes

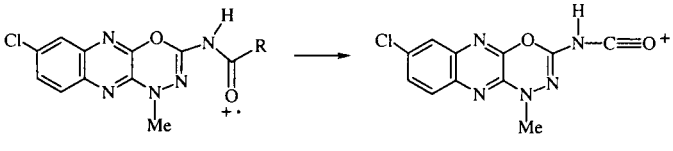
Table

Mass Spectral Data for Compounds **10-14**

Compounds	M+	M+ + 2	Selected Fragment Ion Peak			
Amide						
10a (R = CF_3)	345	347	276			
10c (R = CH_2Cl)	---	---	290 [a]	276	249	
Carbamate						
11a (R = Et)	---	---	275	247		
11b (R = *n*-Bu)	---	---	275	247		
11c [R = $(CH_2)_3Cl$]	---	---	275	249		
12a (3-Py [b])	---	---	275	247	109	108
12b (4-Py)	---	---	275	247	109	108
Ureido						
13a (R = *p*-F)	386	388	275	249	137	111
13b (R = *m*-F)	386	388	275	249	137	111
13c (R = *m*-CF_3)	---	---	275	249	187	161
14 (3-Py)	---	---	275	249	120	94

[a] M+ -Cl; [b] Py - pyridyl

Scheme 4



Amide Derivatives **10a,c** m/z 276

[RNCO, m/z 275 (**11a-c**, **12a,b**, **13a-c,** and **14**); RNHCO, m/z 276 (**10a,c**)] [4]. The fragment ion peak with a composition of RNH_2 (m/z 249) was also observed in compounds **10c**, **11c**, **13a-c**, and **14**. Thus, the absence of the molecular ion peak in compounds **10c**, **11a-c**, **12a,b**, **13c**, and **14** would be explained by the above fragmentation tendency of compounds **10-14**.

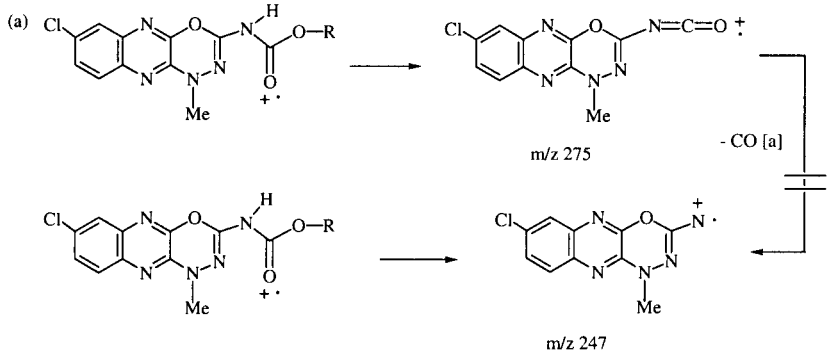
EXPERIMENTAL

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 IRA-1 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 (ms) were determined with a JEOL JMS-01S spectrometer. Elemental analyses were performed on a Perkin-Elmer 240B instrument.

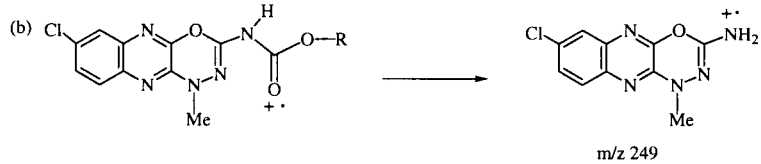
Ethyl 8-Chloro-4-methyl-4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxaline-2-carboxylate **6**.

Ethyl chloroglyoxalate (18.22 g, 133.5 mmoles) was added dropwise to a suspension of compound **5** (10 g, 44.5 mmoles) in pyridine (20 ml)/chloroform (130 ml) under cooling in an ice-water bath to give a clear solution, which was refluxed in an oil bath for 2 hours. Evaporation of the solvent *in vacuo* afforded yellow needles **6**, which were triturated with ethanol, collected by suction filtration, and then washed with ethanol to provide an analytically pure sample (10.99 g, 81%), mp 198-199°; ir: ν cm^{-1} 1735; ms: m/z 306 (M^+), 308 ($M^+ + 2$); pmr (deuteriodimethyl sulfoxide): 7.48 (dd, J =

Scheme 5



[a] The absence of this route was confirmed by the linked scan method.

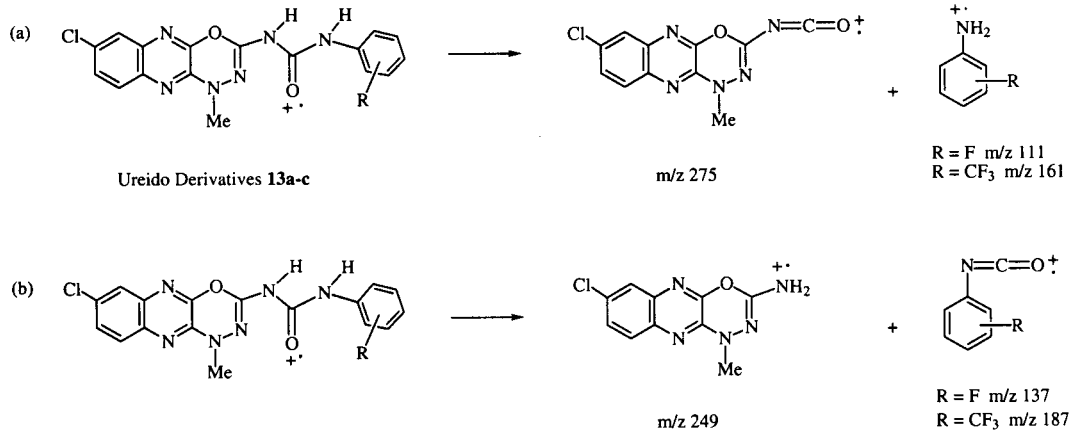


Carbamate Derivatives **11a-c**

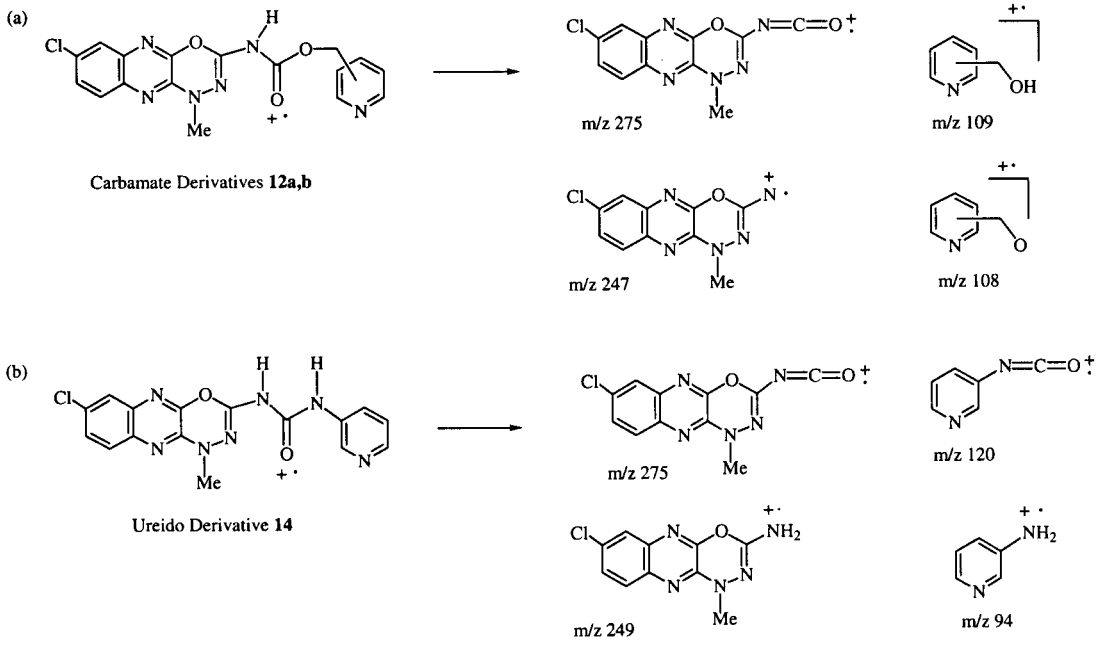
place around the carbonyl group of the C_2-side chain moiety in compounds **10-14**, and the fragment ion peak including the NCO moiety was observed in compounds **10-14**

2.0, 0.8 Hz, 1H, C_9-H), 7.46 (dd, J = 8.5, 0.8 Hz, 1H, C_6-H), 7.41 (dd, J = 2.0, 8.5 Hz, 1H, C_7-H), 4.26 (q, J = 7.0 Hz, 2H, CH_2), 3.22 (s, 3H, NCH_3), 1.26 (t, J = 7.0 Hz, 3H, CH_3).

Scheme 6



Scheme 7



Anal. Calcd. for $C_{13}H_{11}ClN_4O_3$: C, 50.91; H, 3.62; Cl, 11.56; N, 18.27. Found: C, 50.94; H, 3.73; Cl, 11.74; N, 18.30.

8-Chloro-2-hydrazinocarbonyl-4-methyl-4*H*-1,3,4-oxadiazino-[5,6-*b*]quinoxaline **7**.

A suspension of compound **6** (10 g, 32.6 mmoles) and hydrazine hydrate (4.08 g, 81.5 mmoles) in ethanol (300 ml) was refluxed on a boiling water bath for 1 hour with an intermittent stirring to precipitate pale yellow needles **7**, which were collected by suction filtration and washed with ethanol to provide an analytically pure sample (9.35 g, 98%), mp 290-291°; ir: ν cm^{-1} 3320, 3260, 1680; ms: m/z 292 (M^+), 294 (M^+ + 2); pmr (deuteriodimethyl sulfoxide): 9.77 (brs, 1H, NH), 7.47 (d, J = 2.0 Hz, 1H, C_9-H), 7.44 (d, J = 8.5 Hz, 1H, C_6-H), 7.39 (dd, J = 2.0, 8.5 Hz, 1H, C_7-H), 4.52 (brs, 2H, NH_2), 3.20 (s, 3H, NCH_3).

Anal. Calcd. for $C_{11}H_9ClN_6O_2$: C, 45.14; H, 3.10; Cl, 12.11; N, 28.71. Found: C, 45.11; H, 3.10; Cl, 12.13; N, 28.70.

2-Azidocarbonyl-8-chloro-4-methyl-4*H*-1,3,4-oxadiazino[5,6-*b*]-quinoxaline **8**.

A solution of sodium nitrite (4.25 g, 61.6 mmoles) in water (50 ml) was added dropwise to a suspension of compound **7** (10 g, 34.2 mmoles) in water (100 ml)/acetic acid (150 ml) with stirring in an ice-water bath for 1 hour to precipitate yellow needles **8**, which were collected by suction filtration and washed with ethanol and then *n*-hexane (9.76 g, 94%); ir: ν cm^{-1} 2225, 2180, 1700; ms: m/z 303 (M^+), 305 (M^+ + 2), 275 (M^+ - N_2), 277 [(M^+ - N_2) + 2]. This sample was used for later reactions.

2-Amino-8-chloro-4-methyl-4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxaline **9**.

A solution of compound **8** (10 g) in water (10 ml)/dioxane (300 ml) was heated on a boiling water bath for 1 hour. After the reaction mixture was filtrated, the filtrate was evaporated *in vacuo* to give yellow crystals **9**, which were triturated with ethanol/*n*-hexane and

then collected by suction filtration (7.13 g, 87%). Recrystallization from *N,N*-dimethylformamide/ethanol/water gave yellow needles, mp 308-309°; ir: ν cm^{-1} 3370, 3300, 3255, 3180, 1705; ms: m/z 249 (M^+), 251 ($M^+ + 2$); pmr (deuteriodimethyl sulfoxide): 7.39 (dd, J = 1.5, 1.5 Hz, 1H, C_7-H), 7.32 (d, J = 1.5 Hz, 2H, C_6-H and C_9-H), 6.39 (s, 2H, NH_2), 3.11 (s, 3H, NCH_3).

Anal. Calcd. for $C_{10}H_8ClN_5O$: C, 48.11; H, 3.23; Cl, 14.20; N, 28.05. Found: C, 48.33; H, 3.33; Cl, 14.26; N, 28.05.

8-Chloro-4-methyl-2-trifluoroacetamido-4*H*-1,3,4-oxadiazino-[5,6-*b*]quinoxaline **10a**.

Trifluoroacetic anhydride (3 ml) was added dropwise to a suspension of compound **9** (3 g) in triethylamine (2 ml)/dioxane (50 ml) to give a clear solution, and the solution was refluxed in an oil bath for 1 hour to precipitate colorless needles **10a**, which were collected by suction filtration and washed with ethanol to provide an analytically pure sample (1.85 g, 45%), mp above 320°; ir: ν cm^{-1} 1720; ms: m/z 345 (M^+), 347 ($M^+ + 2$); pmr (deuteriodimethyl sulfoxide): 12.82 (brs, 1H, NH), 9.41 (d, J = 9.0 Hz, 1H, C_6-H), 7.51 (dd, J = 2.0, 9.0 Hz, 1H, C_7-H), 7.38 (d, J = 2.0 Hz, 1H, C_9-H), 4.30 (s, 3H, NCH_3); pmr (deuteriotrifluoroacetic acid): 7.97 (d, J = 9.0 Hz, 1H, C_6-H), 7.50 (d, J = 2.0 Hz, 1H, C_9-H), 7.47 (dd, J = 2.0, 9.0 Hz, 1H, C_7-H), 4.59 (s, 3H, NCH_3).

Anal. Calcd. for $C_{12}H_7ClF_3N_5O_2$: C, 41.70; H, 2.04; N, 20.26. Found: C, 41.90; H, 2.24; N, 19.96.

2-Acetamido-8-chloro-4-methyl-4*H*-1,3,4-oxadiazino[5,6-*b*]-quinoxaline **10b**.

Acetic anhydride (10 ml) was added dropwise to a suspension of compound **9** (1.5 g) in pyridine (1 ml)/dioxane (20 ml), and the mixture was refluxed in an oil bath for 1 hour to precipitate colorless needles **10b**, which were collected by suction filtration and washed with ethanol to afford an analytically pure sample (0.93 g, 53%), mp above 320°; ir: ν cm^{-1} 1715; ms: m/z 290 ($M^+ - 1$), 292 [($M^+ - 1$) + 2]; pmr (deuteriodimethyl sulfoxide): 9.51 (d, J = 9.0 Hz, 1H, C_6-H), 7.34 (dd, J = 2.0, 9.0 Hz, 1H, C_7-H), 7.30 (d, J = 2.0 Hz, 1H, C_9-H), 4.23 (s, 3H, NCH_3), 2.03 (s, 3H, $COCH_3$), (NH proton was unobservable); pmr (deuteriotrifluoroacetic acid): 8.02 (d, J = 9.0 Hz, 1H, C_6-H), 7.47 (d, J = 2.0 Hz, 1H, C_9-H), 7.39 (dd, J = 2.0, 9.0 Hz, 1H, C_7-H), 4.50 (s, 3H, NCH_3), 2.40 (s, 3H, $COCH_3$).

Anal. Calcd. for $C_{12}H_{10}ClN_5O_2$: C, 49.41; H, 3.46; Cl, 12.15; N, 24.01. Found: C, 49.25; H, 3.53; Cl, 11.96; N, 23.77.

8-Chloro-2-chloroacetamido-4-methyl-4*H*-1,3,4-oxadiazino[5,6-*b*]-quinoxaline **10c**.

A solution of compound **9** (1 g), chloroacetic anhydride (5 g), and pyridine (1 ml) in dioxane (30 ml) was refluxed in an oil bath for 1 hour. The solvent was evaporated *in vacuo* left a mixture of crystals and oil, which was triturated with ethanol to provide analytically pure colorless needles **10c** (410 mg, 31%), mp above 330°; ir: ν cm^{-1} 1710; ms: m/z 290 (M^+ - Cl), 276 (M^+ - $ClCH_2$), 278 [(M^+ - $ClCH_2$) + 2]; pmr (deuteriodimethyl sulfoxide): 12.65 (brs, 1H, NH), 9.69 (d, J = 9.0 Hz, 1H, C_6-H), 7.39 (dd, J = 2.5, 9.0 Hz, 1H, C_7-H), 7.33 (d, J = 2.5 Hz, 1H, C_9-H), 4.24 (s, 3H, NCH_3), 4.16 (s, 2H, $COCH_2Cl$); pmr (deuteriotrifluoroacetic acid): 8.10 (d, J = 9.0 Hz, 1H, C_6-H), 7.49 (d, J = 2.0 Hz, 1H, C_9-H), 7.41 (dd, J = 2.0, 9.0 Hz, 1H, C_7-H), 4.52 (s, 3H, NCH_3), 4.35 (s, 2H, $COCH_2Cl$).

Anal. Calcd. for $C_{12}H_9Cl_2N_5O_2$: C, 44.19; H, 2.78; Cl, 21.74; N, 21.47. Found: C, 44.39; H, 2.92; Cl, 21.51; N, 21.35.

N-(8-Chloro-4-methyl-4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxalin-2-yl)-ethyl Carbamate **11a** and Related Compounds **11b,c**.

General Procedure.

A solution of compound **8** (1 g) in dioxane (30 ml)/the appropriate alcohol (5 ml) was refluxed in an oil bath for 1 hour to precipitate crystals **11**, which were collected by suction filtration and washed with ethanol and then *n*-hexane to provide an analytically pure sample.

Ethyl derivative **11a** [yield, 0.93 g (88%)] had mp 289-290°; ir: ν cm^{-1} 1720; ms: m/z 275 (M^+ - EtOH), 277 [(M^+ - EtOH) + 2]; pmr (deuteriodimethyl sulfoxide): 12.52 (brs, 1H, NH), 9.53 (d, J = 9.0 Hz, 1H, C_6-H), 7.42 (dd, J = 2.0, 9.0 Hz, 1H, C_7-H), 7.30 (d, J = 2.0 Hz, 1H, C_9-H), 4.20 (s, 3H, NCH_3), 3.95 (q, J = 7.0 Hz, 2H, CH_2), 1.17 (t, J = 7.0 Hz, 3H, CH_3); pmr (deuteriotrifluoroacetic acid): 8.42 (d, J = 9.0 Hz, 1H, C_6-H), 7.76 (d, J = 2.0 Hz, 1H, C_9-H), 7.68 (dd, J = 2.0, 9.0 Hz, 1H, C_7-H), 4.77 (s, 3H, NCH_3), 4.56 (q, J = 7.0 Hz, 2H, CH_2), 1.49 (t, J = 7.0 Hz, 3H, CH_3).

Anal. Calcd. for $C_{13}H_{12}ClN_5O_3$: C, 48.53; H, 3.76; Cl, 11.02; N, 21.77. Found: C, 48.42; H, 3.87; Cl, 11.00; N, 21.72.

n-Butyl derivative **11b** [yield, 0.93 g (81%)] had mp 286-287°; ir: ν cm^{-1} 1725; ms: m/z 275 (M^+ - BuOH), 277 [(M^+ - BuOH) + 2]; pmr (deuteriodimethyl sulfoxide): 12.54 (brs, 1H, NH), 9.52 (d, J = 9.0 Hz, 1H, C_6-H), 7.42 (dd, J = 2.0, 9.0 Hz, 1H, C_7-H), 7.30 (d, J = 2.0 Hz, 1H, C_9-H), 4.20 (s, 3H, NCH_3), 3.92 (t, J = 6.5 Hz, 2H, CH_2), 1.54 (tt, J = 6.5, 7.5 Hz, 2H, CH_2), 1.34 (qt, J = 7.5, 7.5 Hz, 2H, CH_2), 0.89 (t, J = 7.5 Hz, 3H, CH_3); pmr (deuteriotrifluoroacetic acid): 8.43 (d, J = 9.0 Hz, 1H, C_6-H), 7.77 (d, J = 2.0 Hz, 1H, C_9-H), 7.69 (dd, J = 2.0, 9.0 Hz, 1H, C_7-H), 4.77 (s, 3H, NCH_3), 4.58 (t, J = 7.0 Hz, 2H, CH_2), 1.85 (tt, J = 7.0, 7.0 Hz, 2H, CH_2), 1.53 (qt, J = 7.0, 7.0 Hz, 2H, CH_2), 1.07 (t, J = 7.0 Hz, 3H, CH_3).

Anal. Calcd. for $C_{15}H_{16}ClN_5O_3$: C, 51.51; H, 4.61; Cl, 10.13; N, 20.02. Found: C, 51.58; H, 4.56; Cl, 10.32; N, 20.07.

3-Chloropropyl derivative **11c** [yield, 0.98 g (80%)] had mp 259-260°; ir: ν cm^{-1} 1720; ms: m/z 275 (M^+ - $ClCH_2CH_2CH_2OH$), 277 [(M^+ - $ClCH_2CH_2CH_2OH$) + 2]; pmr (deuteriodimethyl sulfoxide): 12.57 (brs, 1H, NH), 9.51 (d, J = 9.0 Hz, 1H, C_6-H), 7.43 (dd, J = 2.5, 9.0 Hz, 1H, C_7-H), 7.32 (d, J = 2.5 Hz, 1H, C_9-H), 4.20 (s, 3H, NCH_3), 4.04 (t, J = 6.5 Hz, 2H, CH_2), 3.72 (t, J = 6.5 Hz, 2H, CH_2), 2.03 (tt, J = 6.5, 6.5 Hz, 2H, CH_2); pmr (deuteriotrifluoroacetic acid): 8.16 (d, J = 9.0 Hz, 1H, C_6-H), 7.48 (d, J = 2.0 Hz, 1H, C_9-H), 7.41 (dd, J = 2.0, 9.0 Hz, 1H, C_7-H), 4.49 (s, 3H, NCH_3), 4.42 (t, J = 6.0 Hz, 2H, CH_2), 3.46 (t, J = 6.0 Hz, 2H, CH_2), 2.04 (tt, J = 6.0, 6.0 Hz, 2H, CH_2).

Anal. Calcd. for $C_{14}H_{13}Cl_2N_5O_3$: C, 45.42; H, 3.54; Cl, 19.15; N, 18.92. Found: C, 45.46; H, 3.51; Cl, 19.36; N, 18.84.

N-(8-Chloro-4-methyl-4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxalin-2-yl)-(3-picolyl) Carbamate **12a**.

A solution of compound **8** (1 g) and 3-pyridyl methanol (5 ml) in dioxane (30 ml) was refluxed in an oil bath for 1 hour to precipitate colorless needles **12a**, which were collected by suction filtration and then washed with ethanol to provide an analytically pure sample (0.85 g, 67%), mp 262-263°; ir: ν cm^{-1} 3110, 1715; ms: m/z 332 (M^+ - C_3H_2N) [4,5], 318 (M^+ - C_4H_4N) [4,5], 275 (M^+ - pyridyl methanol), 109 (pyridyl methanol); pmr (deuteriotrifluoroacetic acid): 8.83 (s, 1H, pyridyl C_2-H), 8.63 (d, J = 6.0 Hz, 1H, pyridyl C_6-H), 8.58 (d, J = 9.0 Hz, 1H, pyridyl C_4-H), 8.12 (d, J = 9.0 Hz, 1H, C_6-H), 7.95 (dd, J = 6.0, 9.0 Hz, 1H, pyridyl C_5-H), 7.43 (d, J = 2.0 Hz, 1H, C_9-H), 7.33 (dd, J = 2.0, 9.0 Hz, 1H, C_7-H), 5.44 (s, 2H, CH_2), 4.43 (s, 3H, NCH_3).

Anal. Calcd. for $C_{17}H_{13}ClN_6O_3$: C, 53.07; H, 3.41; Cl, 9.21; N, 21.84. Found: C, 53.18; H, 3.59; Cl, 9.33; N, 21.73.

N-(8-Chloro-4-methyl-4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxalin-2-yl)-(4-picolyl) Carbamate **12b**.

A solution of compound **8** (1 g) and 4-pyridyl methanol (5 ml) in dioxane (30 ml) was refluxed in an oil bath for 1 hour to precipitate colorless needles **12b**, which were collected by suction filtration and then washed with ethanol to provide an analytically pure sample (0.55 g, 44%), mp 267-268°; ir: ν cm^{-1} 3110, 1715; ms: m/z 332 (M^+ - C_3H_2N) [4,5], 318 (M^+ - C_4H_4N) [4,5], 275 (M^+ - pyridyl methanol), 109 (pyridyl methanol); pmr (deuteriotrifluoroacetic acid): 8.68 (d, J = 7.0 Hz, 2H, pyridyl C_2-H and C_6-H), 8.21 (d, J = 9.0 Hz, 1H, C_6-H), 8.05 (d, J = 7.0 Hz, 2H, pyridyl C_3-H and C_5-H), 7.48 (d, J = 2.0 Hz, 1H, C_9-H), 7.39 (dd, J = 2.0, 9.0 Hz, 1H, C_7-H), 5.57 (s, 2H, CH_2), 4.49 (s, 3H, NCH_3).

Anal. Calcd. for $C_{17}H_{13}ClN_6O_3$: C, 53.07; H, 3.41; Cl, 9.21; N, 21.84. Found: C, 53.23; H, 3.68; Cl, 9.45; N, 21.93.

8-Chloro-2-(3-*p*-fluorophenylureido)-4-methyl-4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxaline **13a** and Related Compounds **13b,c**.

General Procedure.

A solution of compound **8** (1.5 g, 4.92 mmoles) and the appropriate aniline (7.38 mmoles, 1.5-fold molar amount) in dioxane (30 ml) was refluxed in an oil bath for 1 hour to precipitate yellow needles **13**, which were collected by suction filtration and washed with ethanol to afford an analytically pure sample.

p-Fluorophenyl derivative **13a** [yield, 1.63 g (88%)] had mp 276-277°; ir: ν cm^{-1} 1700, 1680; ms: m/z 386 (M^+), 388 (M^+ + 2), 275, 277; pmr (deuteriotrifluoroacetic acid): 8.27 (d, J = 9.0 Hz, 1H, C_6-H), 7.75-7.05 (m, 4H, aromatic), 7.61 (d, J = 2.0 Hz, 1H, C_9-H), 7.57 (dd, J = 2.0, 9.0 Hz, 1H, C_7-H), 4.53 (s, 3H, NCH_3).

Anal. Calcd. for $C_{17}H_{12}ClFN_6O_2$: C, 52.79; H, 3.13; N, 21.73. Found: C, 53.04; H, 3.32; N, 21.83.

m-Fluorophenyl derivative **13b** [yield, 1.63 g (88%)] had mp 255-256°; ir: ν cm^{-1} 3300, 1710, 1685; ms: m/z 386 (M^+), 388 (M^+ + 2), 275, 277; pmr (deuteriotrifluoroacetic acid): 8.29 (d, J = 9.0 Hz, 1H, C_6-H), 7.78-6.95 (m, 5H, aromatic), 7.63 (d, J = 2.0 Hz, 1H, C_9-H), 4.55 (s, 3H, NCH_3).

Anal. Calcd. for $C_{17}H_{12}ClFN_6O_2$: C, 52.79; H, 3.13; N, 21.73. Found: C, 52.78; H, 3.19; N, 21.95.

m-Trifluoromethylphenyl derivative **13c** [yield, 1.97 g (92%)] had mp 280-281°; ir: ν cm^{-1} 3220, 1715, 1620; ms: m/z 275 (M^+ - $CF_3C_6H_4NH_2$), 277 [(M^+ - $CF_3C_6H_4NH_2$) + 2]; pmr (deuteriotrifluoroacetic acid): 8.03 (d, J = 9.0 Hz, 1H, C_6-H), 7.63-7.29 (m, 4H, aromatic), 7.37 (d, J = 2.0 Hz, 1H, C_9-H), 7.33 (dd, J = 2.0, 9.0 Hz, 1H, C_7-H), 4.29 (s, 3H, NCH_3).

Anal. Calcd. for $C_{18}H_{12}ClF_3N_6O_2$: C, 49.50; H, 2.77; N, 19.24. Found: C, 49.79; H, 2.75; N, 18.98.

8-Chloro-4-methyl-2-[3-(3-pyridyl)ureido]-4*H*-1,3,4-oxadiazino[5,6-*b*]quinoxaline **14**.

A solution of compound **8** (1 g, 3.29 mmoles) and 3-aminopyridine (463 mg, 4.94 mmoles) in dioxane (30 ml) was refluxed in an oil bath for 1 hour to precipitate pale yellow needles **14**, which were collected by suction filtration and washed with ethanol to afford an analytically pure sample (0.66 g, 54%), mp 271-272°; ir: ν cm^{-1} 3300, 3220, 3110, 1705; ms: m/z 275 (M^+ - aminopyridine), 249 (M^+ - pyridyl-NCO), 120 (pyridyl-NCO), 94 (aminopyridine); pmr (deuteriotrifluoroacetic acid): 9.27 (d, J = 2.0 Hz, 1H, pyridyl C_2-H), 8.42 (dd, J = 2.0, 9.0 Hz, 1H, pyridyl C_6-H), 8.37 (d, J = 6.0 Hz, 1H, pyridyl C_4-H), 8.19 (d, J = 9.0 Hz, 1H, C_6-H), 7.88 (dd, J = 6.0, 9.0 Hz, 1H, pyridyl C_5-H), 7.45 (d, J = 2.0 Hz, 1H, C_9-H), 7.34 (dd, J = 2.0, 9.0 Hz, 1H, C_7-H), 4.48 (s, 3H, NCH_3).

Anal. Calcd. for $C_{16}H_{12}ClN_7O_2$: C, 51.97; H, 3.27; Cl, 9.59; N, 26.52. Found: C, 51.86; H, 3.32; Cl, 9.46; N, 26.73.

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