A Convenient Synthesis of 5,14-Methano-16-oxo-1,5,6-benzoxadiazonino[3,4-*b*]quinoxalines Utilizing a 1,3-Dipolar Cycloaddition Reaction and an Intramolecular Alcoholysis [1]

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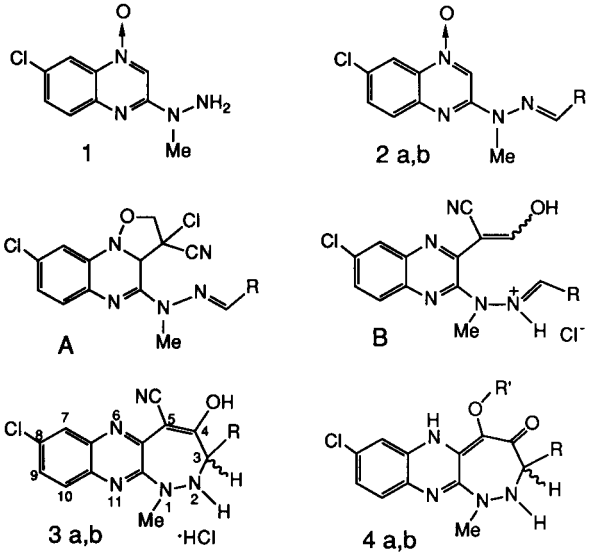
Received November 30, 1990

The reaction of the hydrazones **5a-c** with 2-chloroacrylonitrile produced the 1,2-diazepino[3,4-*b*]quinoxaline hydrochlorides **6a-c**, which were transformed into the 5,6,7,13-tetrahydro-5,14-methano-16-oxo-1,5,6-benzoxadiazonino[3,4-*b*]quinoxalines **7a-c**, respectively. The oxidation of **7a-c** with diethyl azodicarboxylate afforded the 7,13-dihydro-5,14-methano-16-oxo-1,5,6-benzoxadiazonino[3,4-*b*]quinoxalines **8a-c**, respectively. Compounds **7a-c** and **8a-c** were also obtained by a one-pot synthesis from **5a-c** and **6a-c**, respectively.

J. Heterocyclic Chem., **28**, 787 (1991).

In a previous paper [3], we reported that compound **1** was converted into the hydrazones **2a,b**, whose reaction with 2-chloroacrylonitrile gave the 5-cyano-4-hydroxy-1,2-diazepino[3,4-*b*]quinoxaline hydrochlorides **3a,b**, respectively, presumably *via* a 1,3-dipolar cycloaddition reaction to an intermediate **A**, an isoxazolidine ring opening followed by hydrogen chloride elimination to an intermediate **B** and a successive recyclization to a 1,2-diazepine ring (Chart 1). Furthermore, we found that the reaction of **3a,b** with an alcohol in the presence of a base resulted in alcoholysis to provide the 5-alkoxy-4-oxo-1,2-diazepino[3,4-*b*]-quinoxalines **4a,b**, respectively. This alcoholysis was assumed to start from an attack of the alkoxyl group to the 4-carbon atom. In order to extend the scope of the above alcoholysis, we designed an intramolecular alcoholysis in the above 1,2-diazepino[3,4-*b*]quinoxaline ring system. Namely, if the C_3-substituent of the 5-cyano-4-hydroxy-1,2-diazepino[3,4-*b*]quinoxalines **3a,b** had a hydroxyl group proximal to the 4-carbon atom, this hydroxyl group would initiate the intramolecular alcoholysis. Thus, we transformed compound **1** into the *o*-hydroxyphenylhydrazones **5a-c** (Scheme 1). The successful conversion of **5a-c** into the 3-(*o*-hydroxyphenyl)-5-cyano-4-hydroxy-1,2-diazepino[3,4-*b*]quinoxalines **6a-c** realized the expected intramolecular alcoholysis to produce the 5,6,7,13-tetrahydro-5,14-methano-16-oxo-1,5,6-benzoxadiazonino[3,4-*b*]quinoxalines **7a-c**, respectively. This paper describes a facile synthesis of **7a-c** and their related compounds **8a-c**.

Chart 1



The reaction of compound **1** with 2-hydroxybenzaldehyde, 2-hydroxy-3-methoxybenzaldehyde and 5-bromo-2-hydroxybenzaldehyde gave 6-chloro-2-[2-(2-hydroxybenzilidene)-1-methylhydrazino]quinoxaline 4-oxide **5a**, 6-chloro-2-[2-(2-hydroxy-3-methoxybenzylidene)-1-methylhydrazino]quinoxaline 4-oxide **5b** and 2-[2-(5-bromo-2-hydroxybenzilidene)-1-methylhydrazino]-6-chloroquinoxaline 4-oxide **5c**, respectively (Scheme 1). The reaction of **5a-c** with 2-chloroacrylonitrile followed by allowing to stand overnight at room temperature afforded 8-chloro-5-cyano-4-hydroxy-3-(2-hydroxyphenyl)-1-methyl-2,3-dihydro-1*H*-1,2-diazepino[3,4-*b*]quinoxaline hydrochloride **6a**, 8-chloro-5-cyano-4-hydroxy-3-(2-hydroxy-3-methoxyphenyl)-1-methyl-2,3-dihydro-1*H*-1,2-diazepino[3,4-*b*]quinoxaline hydrochloride **6b** and 3-(5-bromo-2-hydroxyphenyl)-8-chloro-5-cyano-4-hydroxy-1-methyl-2,3-dihydro-1*H*-1,2-diazepino[3,-4-*b*]quinoxaline hydrochloride **6c**, respectively [3] (Table 1). Refluxing of **6a-c** and triethylamine in 1,4-dioxane provided 11-chloro-5,6,7,13-tetrahydro-5,14-methano-7-methyl-16-oxo-1,5,6-benzoxadiazonino[3,4-*b*]quinoxaline **7a**,

Scheme 1

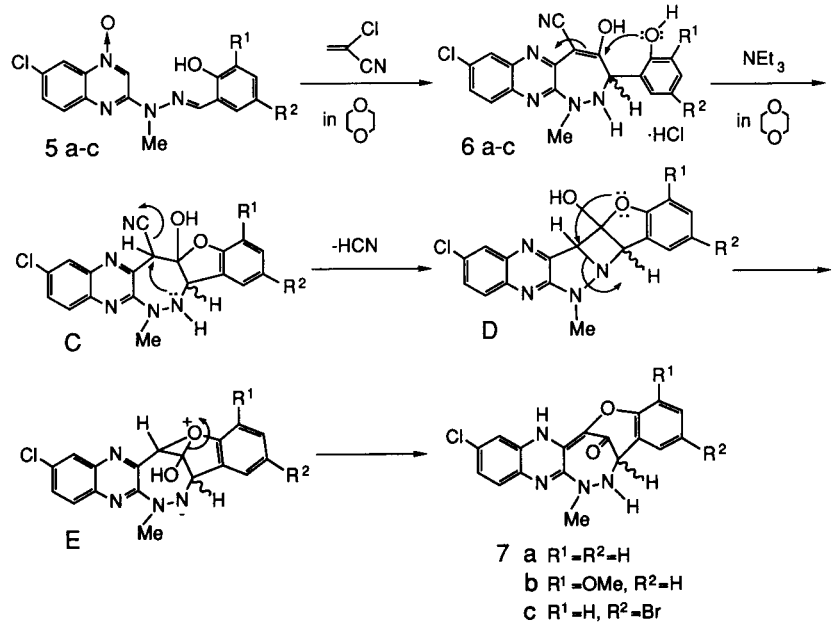


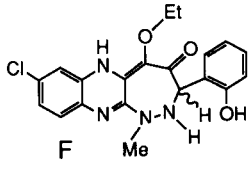
Table 1

Stepwise Yield of **7a-c** from **5a-c**

Starting Material	Product (%)
5a	**6a** (76)
5b	**6b** (92)
5c	**6c** (48)
6a	**7a** (86)
6b	**7b** (85)
6c	**7c** (73)

11-chloro-5,6,7,13-tetrahydro-5,14-methano-1-methoxy-7-methyl-16-oxo-1,5,6-benzoxadiazonino[3,4-*b*]quinoxaline **7b** and 3-bromo-11-chloro-5,6,7,13-tetrahydro-5,14-methano-7-methyl-16-oxo-1,5,6-benzoxadiazonino[3,4-*b*]quinoxaline **7c**, respectively, presumably *via* intermediates **C-E** [3]. Refluxing of **6a** and triethylamine in ethanol also effected the intramolecular alcoholysis to furnish **7a**, but not the 5-ethoxy-4-oxo-1,2-diazepino[3,4-*b*]quinoxaline **F** (Chart 2) which would be produced by the solvolysis [3].

Chart 2



The reaction of **7a-c** with diethyl azodicarboxylate resulted in the 5,6-dehydrogenation to give 11-chloro-7,13-dihydro-5,14-methano-7-methyl-16-oxo-1,5,6-benzoxadiazonino[3,4-*b*]quinoxaline **8a**, 11-chloro-7,13-dihydro-5,14-methano-1-methoxy-7-methyl-16-oxo-1,5,6-benzoxadiazonino[3,4-*b*]quinoxaline **8b** and 3-bromo-11-chloro-7,13-dihydro-5,14-methano-7-methyl-16-oxo-1,5,6-benzoxadiazonino[3,4-*b*]quinoxaline **8c**, respectively (Scheme 2, Table 2). The reaction of **6a-c** with diethyl azodicarboxylate in the presence of triethylamine directly afforded **8a-c**, respectively. The yields of **8** from **6** were higher in the stepwise synthesis than in the direct synthesis. On the other hand, **7a-c** were also obtained by one-pot synthesis from **5a-c**, respectively (Scheme 3, Table 3). The reaction of **5a-c** with 2-chloroacrylonitrile followed by an immediate evaporation of the solvent afforded intermediary free bases of **6a-c** [3], whose refluxing in triethylamine/1,4-dioxane furnished **7a-c**, respectively. In the **a** series, **8a** was obtained together with **7a**. In the **b** and **c** series, the yields of **7** from **5** were higher in the one-pot synthesis than in the stepwise synthesis.

Table 2

Yield of **8a-c** from **6a-c** or **7a-c**

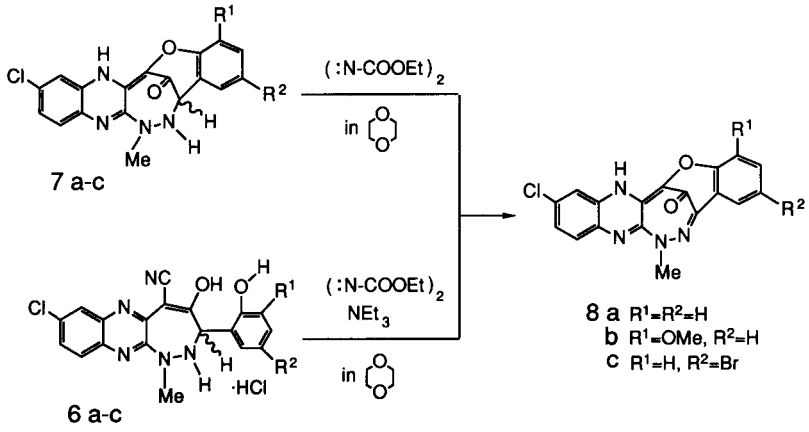
Starting Material	Product (%)
7a	**8a** (79)
7b	**8b** (87)
7c	**8c** (91)
6a	**8a** (47)
6b	**8b** (53)
6c	**8c** (44)

Table 3

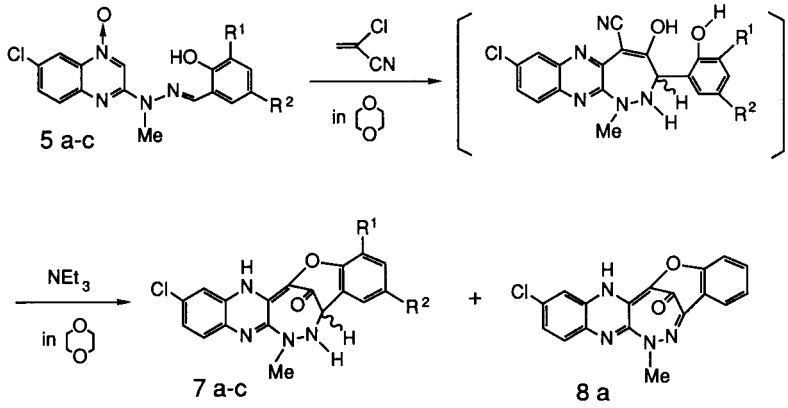
Yield for One-pot Synthesis of **7a-c** from **5a-c**

Starting Material	Product (%)	
5a	**7a** (33)	**8a** (24)
5b	**7b** (88)	—
5c	**7c** (65)	—

Scheme 2



Scheme 3



The structural assignment of **5a-c**-**8a-c** was based on the analytical and spectral data. Especially, the ^{13}C-nmr spectra of **7a-c** showed the C=O carbon signals at δ 164-162 ppm (Table 4), and the ^{1}H-nmr spectra of **7a,b** exhibited the NOE between the N_{13}-H and C_{12}-H proton signals, between the C_4-H and C_5-H proton signals and among the C_5-H, N_6-H and N_7-Me proton signals (Chart 3, Table 5) [4]. The ir spectra of **7a-c** exhibited the C=O absorption band at 1650 cm^{-1}, which was a similar value to that of **4a,b** observed at 1640 cm^{-1} [3]. These ir and nmr spectral data eliminated the structure of **H** or **I** (Chart 4), which would be produced by the hydroxyl group migration *via* intermediates **D** and **G** shown in Chart 4. The nmr spectra of **8a-c** showed the C=O carbon signals at δ 163-161 ppm, which were similar values to those of **7a-c**, and their ir spectra exhibited C=O absorption bands at 1670-1655 cm^{-1}. These data suggested that **8a-c** existed in the 7,13-dihydro-16-oxo form. The ir spectra of **6a-c** showed the nitrile absorption band at 2200 cm^{-1}. The mass spectra of **6a-c** exhibited the molecular ion peaks in the FAB method, while the spectra lacked the molecular ion peaks in the DIEI method, showing the fragment ion peaks corresponding to **7a-c** [5]. The 3-carbon atom of **3a,b**, **4a,b**

Table 4

IR and NMR Spectral Data for Carbonyl Groups of **7a-c** and **8a-c**

Compound	ν (C=O) cm^{-1} [a]	δ (C=O) ppm
7a	1650	162.73 [b]
7b	1650	162.52 [b]
7c	1650	164.97 [b]
8a	1665	163.02 [c]
8b	1670	161.87 [c]
8c	1655	162.18 [c]

[a] Measured in the solid state with potasium bromide. [b] Measured in deuteriodimethyl sulfoxide. [c] Measured in deuteriotrifluoroacetic acid.

Chart 3

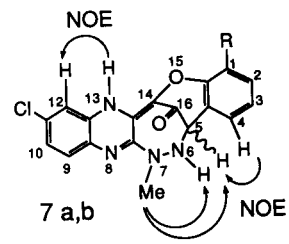


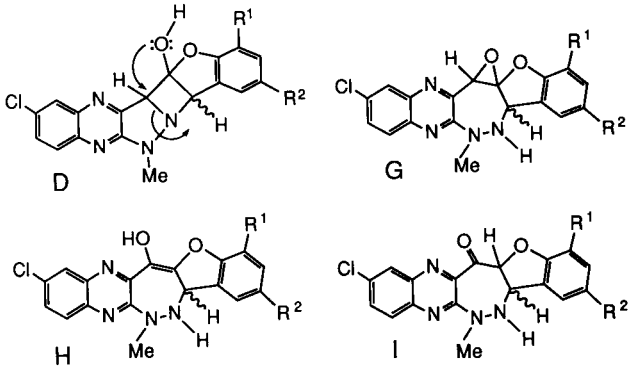
Table 5
NOE Data for Compounds **7a,b**

Radiation	NOE	Compound 7a	Compound 7b
N_{13}-H	C_{12}-H	8.7	6.3 [a]
C_4-H	C_5-H	3.1	3.1
N_7-Me	C_5-H	6.2	3.9
	N_6-H	4.5	3.6

[a] Expressed in %.

and **6a-c** and the 5-carbon of **7a-c** are the asymmetric carbon, but all these compounds are found to be optically inactive from the measurement of the optical rotation. These results would be due to the cyclization of an intermediate **B** into a C_3-racemic 1,2-diazepine ring.

Chart 4



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 in deuteriodimethyl sulfoxide, unless otherwise stated, with a VXR-300 spectrometer at 300 MHz. 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-[2-(2-hydroxybenzilidene)-1-methylhydrazino]quinoxaline 4-Oxide **5a**, 6-Chloro-2-[2-(2-hydroxy-3-methoxybenzilidene)-1-methylhydrazino]quinoxaline 4-Oxide **5b** and 2-[2-(5-Bromo-2-hydroxybenzilidene)-1-methylhydrazino]-6-chloroquinoxaline 4-Oxide **5c**.

A solution of compound **1** (10 g, 44.5 mmoles) and 2-hydroxybenzaldehyde (8.15 g, 66.8 mmoles) in *N,N*-dimethylformamide (150 ml) was refluxed in an oil bath for 2 hours to give a clear solution. The solution was cooled to room temperature to precipitate orange needles **5a**, which were collected by suction filtration. Washing with ethanol and then *n*-hexane gave an analytically pure sample (14.55 g, 100%).

Compound **5b** (orange needles, 15.80 g, 99%) was obtained in a similar manner to the above from the reaction of compound **1** (10 g, 44.5 mmoles) with 2-hydroxy-3-methoxybenzaldehyde (10.15 g, 66.75 mmoles) in *N,N*-dimethylformamide (150 ml).

Compound **5c** (yellow prisms, 17.55 g, 96%) was obtained in a similar manner to the above from the reaction of compound **1** (10 g, 44.5 mmoles) with 5-bromo-2-hydroxybenzaldehyde (13.43 g, 66.8 mmoles) in 1,4-dioxane (200 ml).

Compound **5a** had mp 275-276°; ir: ν cm^{-1} 1595, 1565, 1525; ms: m/z 328 (M^+), 330 ($M^+ + 2$); pmr: 9.60 (br, 1H, OH), 8.90 (s, 1H, C_3-H), 8.26 (d, J = 2.0 Hz, 1H, C_5-H), 8.18 (s, 1H, hydrazone CH), 7.88 (dd, J = 7.5 Hz, J = 2.0 Hz, 1H, $C_{6'}$-H), 7.81 (d, J = 8.5 Hz, 1H, C_8-H), 7.77 (dd, J = 2.0 Hz, J = 8.5 Hz, 1H, C_7-H), 7.23 (ddd, J = 7.5 Hz, J = 7.5 Hz, J = 2.0 Hz, 1H, $C_{4'}$-H), 6.92 (d, J = 7.5 Hz, 1H, $C_{3'}$-H), 6.89 (dd, J = 7.5 Hz, J = 7.5 Hz, 1H, $C_{5'}$-H), 3.69 (s, 3H, CH_3).

Anal. Calcd. for $C_{16}H_{13}ClN_4O_2$: C, 58.46; H, 3.98; Cl, 10.78; N, 17.04. Found: C, 58.33; H, 4.04; Cl, 10.93; N, 17.08.

Compound **5b** had mp 276-277°; ir: ν cm^{-1} 1595, 1565, 1520; ms: m/z 358 (M^+), 340 ($M^+ + 2$); pmr: 9.30 (br, 1H, OH), 8.89 (s, 1H, C_3-H), 8.28 (d, J = 2.5 Hz, 1H, C_5-H), 8.23 (s, 1H, hydrazone CH), 7.83 (d, J = 9.0 Hz, 1H, C_8-H), 7.78 (dd, J = 2.5 Hz, J = 9.0 Hz, 1H, C_7-H), 7.47 (dd, J = 8.0 Hz, J = 1.5 Hz, 1H, $C_{6'}$-H), 7.00 (dd, J = 8.0 Hz, J = 1.5 Hz, 1H, $C_{4'}$-H), 6.87 (dd, J = 8.0 Hz, J = 8.0 Hz, 1H, $C_{5'}$-H), 3.84 (s, 3H, OCH_3), 3.70 (s, 3H, NCH_3).

Anal. Calcd. for $C_{17}H_{15}ClN_4O_3$: C, 56.91; H, 4.21; Cl, 9.88; N, 15.62. Found: C, 56.68; H, 4.14; Cl, 9.86; N, 15.53.

Compound **5c** had mp 300-301°; ir: ν cm^{-1} 1590, 1565, 1520; ms: m/z 408 (M^+), 410 ($M^+ + 2$); pmr: 10.60 (br, 1H, OH), 8.96 (s, 1H, C_3-H), 8.28 (d, J = 2.1 Hz, 1H, C_5-H), 8.11 (s, 1H, hydrazone CH), 7.98 (d, J = 2.5 Hz, 1H, $C_{6'}$-H), 7.88 (d, J = 9.0 Hz, 1H, C_8-H), 7.78 (dd, J = 2.1 Hz, J = 9.0 Hz, 1H, C_7-H), 7.35 (dd, J = 2.5 Hz, J = 8.5 Hz, 1H, $C_{4'}$-H), 6.89 (d, J = 8.5 Hz, 1H, $C_{3'}$-H), 3.69 (s, 3H, CH_3).

Anal. Calcd. for $C_{16}H_{12}BrClN_4O_2$: C, 47.15; H, 2.95; N, 13.75. Found: C, 47.21; H, 2.89; N, 13.98.

8-Chloro-5-cyano-4-hydroxy-3-(2-hydroxyphenyl)-1-methyl-2,3-dihydro-1*H*-1,2-diazepino[3,4-*b*]quinoxaline Hydrochloride **6a**, 8-Chloro-5-cyano-4-hydroxy-3-(2-hydroxy-3-methoxyphenyl)-1-methyl-2,3-dihydro-1*H*-1,2-diazepino[3,4-*b*]quinoxaline Hydrochloride **6b** and 3-(5-Bromo-2-hydroxyphenyl)-8-chloro-5-cyano-4-hydroxy-1-methyl-2,3-dihydro-1*H*-1,2-diazepino[3,4-*b*]quinoxaline Hydrochloride **6c**.

A suspension of **5a** (10 g, 30.4 mmoles) and 2-chloroacrylonitrile (10.64 g, 121.6 mmoles) in 1,4-dioxane (500 ml) was refluxed in an oil bath for 3 hours to give a clear solution. The solution was allowed to stand overnight at room temperature to precipitate yellow needles **6a**, which were collected by suction filtration and washed with 1,4-dioxane and then *n*-hexane (9.69 g, 76%).

Compounds **6b** (yellow needles, 11.44 g, 92%) and **6c** (yellow needles, 5.75 g, 48%) were obtained in a similar manner to the above from the reaction of **5b** (10 g, 28.0 mmoles) and **5c** (10 g, 24.6 mmoles) with 2-chloroacrylonitrile [(9.80 g, 112.0 mmoles), (5.38 g, 61.5 mmoles)] in 1,4-dioxane (500 ml), respectively.

Compound **6a** had mp 228-229°; ir: ν cm^{-1} 3460, 3140, 3060, 3020, 2220, 1610, 1600, 1585, 1570; ms (FAB method): m/z 379 (M^+).

Compound **6b** had mp 185-186°; ir: ν cm^{-1} 3140, 3080, 3020, 2940, 2840, 2220, 1610, 1590, 1570; ms (FAB method): m/z 410 (M^+).

Compound **6c** had mp 168-169°; ir: ν cm^{-1} 3120, 3010, 2960,

2900, 2840, 2220, 1610, 1580, 1565; ms (FAB method): m/z 457 (M^+).

11-Chloro-5,6,7,13-tetrahydro-5,14-methano-7-methyl-16-oxo-1,5,-6-benzoxadiazonino[3,4-*b*]quinoxaline **7a**.

A solution of **6a** (5 g, 12.0 mmoles) and triethylamine (1.82 g, 18.0 mmoles) in 1,4-dioxane (200 ml) was refluxed in an oil bath for 2 hours to precipitate colorless needles of triethylamine hydrochloride. After the colorless needles were filtered off, the filtrate was evaporated *in vacuo* to give brown crystals **7a**, which were triturated with ethanol/water (1:1) and then collected by suction filtration (3.17 g). Evaporation of the filtrate *in vacuo* afforded brown crystals **7a** (0.49 g), total yield, 3.66 g (86%). Recrystallization from 1,4-dioxane/ethanol/water gave brick red needles, mp 255-256°; ir: ν cm^{-1} 1650, 1590, 1530; ms: m/z 352 (M^+), 354 ($M^+ + 2$); pmr: 11.88 (s, 1H, N_{13}-H), 7.81 (d, J = 2.0 Hz, 1H, C_{12}-H), 7.59 (d, J = 7.5 Hz, 1H, C_4-H), 7.39 (dd, J = 7.5 Hz, J = 7.5 Hz, 1H, C_2-H or C_3-H), 7.34 (d, J = 8.5 Hz, 1H, C_9-H), 7.21 (dd, J = 7.5 Hz, J = 7.5 Hz, 1H, C_3-H or C_2-H), 7.16 (dd, J = 2.0 Hz, J = 8.5 Hz, 1H, C_{10}-H), 7.12 (d, J = 7.5 Hz, 1H, C_1-H), 5.80 (d, J = 12.5 Hz, 1H, N_6-H), 5.28 (d, J = 12.5 Hz, 1H, C_5-H), 3.30 (s, 3H, CH_3).

Anal. Calcd. for $C_{18}H_{13}ClN_4O_2$: C, 61.28; H, 3.71; Cl, 10.05; N, 15.88. Found: C, 61.06; H, 3.77; Cl, 10.06; N, 15.72.

Synthesis of Compound **7a** from Compound **6a** Using Ethanol as a Solvent.

A solution of **6a** (1 g, 2.40 mmoles) and triethylamine (364 mg, 3.60 mmoles) in ethanol (50 ml) was refluxed on a boiling water bath for 30 minutes to precipitate brick red needles **7a**, which were collected by suction filtration and then washed with ethanol/water (0.58 g, 68%).

11-Chloro-5,6,7,13-tetrahydro-5,14-methano-1-methoxy-7-methyl-16-oxo-1,5,6-benzoxadiazonino[3,4-*b*]quinoxaline **7b**.

A solution of **6b** (5 g, 11.2 mmoles) and triethylamine (1.70 g, 16.8 mmoles) in 1,4-dioxane (200 ml) was refluxed in an oil bath for 2 hours to precipitate colorless needles of triethylamine hydrochloride. After the colorless needles were filtered off, the filtrate was evaporated *in vacuo* to give brown crystals **7b**, which were triturated with ethanol/water (1:1) and then collected by suction filtration (3.64 g, 85%). Recrystallization from 1,4-dioxane/ethanol/water afforded brick red needles, mp 263-264°; ir: ν cm^{-1} 1650, 1590, 1580, 1525; ms: m/z 382 (M^+), 384 ($M^+ + 2$); pmr: 11.87 (s, 1H, N_{13}-H), 7.82 (d, J = 2.5 Hz, 1H, C_{12}-H), 7.34 (d, J = 8.5 Hz, 1H, C_9-H), 7.16 (dd, J = 2.5 Hz, J = 8.5 Hz, 1H, C_{10}-H), 7.16-7.06 (m, 3H, C_2-H, C_3-H, C_4-H), 5.77 (d, J = 12.5 Hz, 1H, N_6-H), 5.27 (d, J = 12.5 Hz, 1H, C_5-H), 3.84 (s, 3H, OCH_3), 3.30 (s, 3H, NCH_3). The C_2-H and C_4-H proton signals were found to appear at δ 7.09 and 7.15 ppm, respectively, by the NOE measurement.

Anal. Calcd. for $C_{19}H_{15}ClN_4O_3$: C, 59.61; H, 3.95; Cl, 9.26; N, 14.64. Found: C, 59.57; H, 3.69; Cl, 9.21; N, 14.69.

3-Bromo-11-chloro-5,6,7,13-tetrahydro-5,14-methano-7-methyl-16-oxo-1,5,6-benzoxadiazonino[3,4-*b*]quinoxaline **7c**.

A solution of **6c** (5 g, 10.1 mmoles) and triethylamine (1.54 g, 15.2 mmoles) in 1,4-dioxane (200 ml) was refluxed in an oil bath for 2 hours to precipitate a mixture of brick red needles **7c** and colorless needles (triethylamine hydrochloride), whose collection by suction filtration and then washing with ethanol/water (1:1) gave an analytically pure sample of **7c** (2.76 g). Evaporation of filtrate *in vacuo* afforded crystals, whose trituration with 1,4-dioxane/ethanol/water provided **7c** (0.40 g), total yield, 3.16 g (73%). Compound **7c** had mp 285-286°; ir: ν cm^{-1} 1650, 1590, 1565, 1535; ms: m/z 430 (M^+), 432 ($M^+ + 2$); pmr: 11.88 (br, 1H, N_{13}-H), 7.84 (d, J = 2.5 Hz, 1H, C_{12}-H), 7.66 (dd, J = 2.5 Hz, J = 1.0 Hz, 1H, C_4-H), 7.56 (ddd, J = 8.5 Hz, J = 2.5 Hz, J = 1.0 Hz, 1H, C_2-H), 7.36 (d, J = 8.5 Hz, 1H, C_9-H), 7.18 (dd, J = 2.5 Hz, J = 8.5 Hz, 1H, C_{10}-H), 7.12 (d, J = 8.5 Hz, 1H, C_1-H), 5.87 (d, J = 12.5 Hz, 1H, N_6-H), 5.31 (d, J = 12.5 Hz, 1H, C_5-H), 3.31 (s, 3H, CH_3).

Anal. Calcd. for $C_{18}H_{12}BrClN_4O_2$: C, 50.08; H, 2.80; N, 12.98. Found: C, 50.27; H, 2.79; N, 13.24.

11-Chloro-7,13-dihydro-5,14-methano-7-methyl-16-oxo-1,5,6-benzoxadiazonino[3,4-*b*]quinoxaline **8a** and 11-Chloro-7,13-dihydro-5,14-methano-1-methoxy-7-methyl-16-oxo-1,5,6-benzoxadiazonino[3,4-*b*]quinoxaline **8b**.

From Compounds **7a,b**.

A suspension of **7a** (1 g, 2.84 mmoles) and diethyl azodicarboxylate (0.74 g, 4.26 mmoles) in 1,4-dioxane (50 ml) was heatd on a boiling water bath for 1 hour to precipitate red needles **8a**, which were collected by suction filtration. Washing with ethanol and then *n*-hexane gave analytically pure red needles (0.74 g). Addition of *n*-hexane to the filtrate precipitated additional red needles **8a**, which were collected by suction filtration (0.04 g), total yield, 0.78 g (79%).

Compound **8b** (red needles, 0.86 g, 87%) was obtained in a similar manner to the above from the reaction of **7b** (1 g, 2.61 mmoles) with diethyl azodicarboxylate (0.68 g, 3.92 mmoles) in 1,4-dioxane (50 ml).

From Compounds **6a,b**.

A solultion of **6a** (5 g, 12.0 mmoles), diethyl azodicarboxylate (3.13 g, 18.0 mmoles) and triethylamine (1.34 g, 13.2 mmoles) in 1,4-dioxane (250 ml) was refluxed in an oil bath for 1 hour to precipitate red needles **8a**, which were collected by suction filtration. Washing with ethanol/water, ethanol and then *n*-hexane gave analytically pure red needles (1.87 g). Evaporation of the filtrate *in vacuo* afforded red needles **8a**, which were treated in a similar manner to the above (0.11 g), total yield, 1.98 g (47%).

Compound **8b** (red needles, 2.24 g, 53%) was obtained in a similar manner to the above from the reaction of **6b** (5 g, 11.2 mmoles), diethyl azodicarboxylate (2.92 g, 16.8 mmoles) and triethylamine (1.24 g, 12.3 mmoles) in 1,4-dioxane (250 ml).

Compound **8a** had mp above 320°; ir: ν cm^{-1} 3230, 3070, 2940, 1665, 1610, 1590, 1580; ms: m/z 350 (M^+), 352 ($M^+ + 2$); pmr (deuteriotrifluoroacetic acid): 7.89 (d, J = 8.0 Hz, 1H, C_4-H), 7.40 (dd, J = 8.0 Hz, J = 8.0 Hz, 1H, C_3-H), 7.16 (dd, J = 8.0 Hz, J = 8.0 Hz, 1H, C_2-H), 7.04 (d, J = 8.0 Hz, 1H, C_1-H), 6.89 (d, J = 1.5 Hz, 1H, C_{12}-H), 6.85 (dd, J = 1.5 Hz, J = 8.5 Hz, 1H, C_{10}-H), 6.76 (d, J = 8.5 Hz, 1H, C_9-H), 3.67 (s, 3H, CH_3).

Anal. Calcd. for $C_{18}H_{11}ClN_4O_2$: C, 61.64; H, 3.16; Cl, 10.11; N, 15.97. Found: C, 61.45; H, 3.11; Cl, 10.21; N, 15.98.

Compound **8b** had mp 314-315°; ir: ν cm^{-1} 1670, 1610, 1580; ms: m/z: 380 (M^+), 382 ($M^+ + 2$); pmr (deuteriotrifluoroacetic acid): 7.46 (dd, J = 8.0 Hz, J = 1.0 Hz, 1H, C_4-H), 7.09 (dd, J = 8.0 Hz, J = 8.0 Hz, 1H, C_3-H), 7.01 (dd, J = 8.0 Hz, J = 1.0 Hz, 1H, C_2-H), 6.88 (d, J = 2.0 Hz, 1H, C_{12}-H), 6.83 (dd, J = 2.0 Hz, J = 8.5 Hz, 1H, C_{10}-H), 6.74 (d, J = 8.5 Hz, 1H, C_9-H), 3.73 (s, 3H, OCH_3), 3.64 (s, 3H, NCH_3).

Anal. Calcd. for $C_{19}H_{13}ClN_4O_3$: C, 59.94; H, 3.44; Cl, 9.31; N,

14.71. Found: C, 60.23; H, 3.49; Cl, 9.25; N, 14.83.

3-Bromo-11-chloro-7,13-dihydro-5,14-methano-7-methyl-16-oxo-1,5,6-benzoxadiazonino[3,4-*b*]quinoxaline **8c**.

From Compound **7c**.

A suspension of **7c** (5 g, 11.6 mmoles) and diethyl azodicarboxylate (3.03 g, 17.4 mmoles) in *N,N*-dimethylformamide (250 ml) was refluxed in an oil bath for 5 hours to precipitate red needles **8c**, which were collected by suction filtration (4.55 g, 91%). Washing with ethanol and then *n*-hexane afforded an analytically pure sample of **8c**.

From Compound **6c**.

A solution of **6c** (1 g, 2.02 mmoles) and diethyl azodicarboxylate (0.53 g, 3.03 mmoles) in triethylamine (0.22 g, 2.22 mmoles)/*N,N*-dimethylformamide (50 ml) was refluxed in an oil bath for 5 hours to precipitate red needles **8c**, which were collected by suction filtration and then washed with ethanol to give an analytically pure sample of **8c** (0.38 g, 44%).

Compound **8c** had mp above 320°; ir: ν cm^{-1} 3210, 3050, 1655, 1610, 1585; ms: m/z 428 (M^+), 430 ($M^+ + 2$); pmr (deuteriotrifluoroacetic acid): 8.16 (d, J = 2.0 Hz, 1H, C_4-H), 7.67 (dd, J = 2.0 Hz, J = 9.0 Hz, 1H, C_2-H), 7.09 (d, J = 2.0 Hz, 1H, C_{12}-H), 7.08 (d, J = 9.0 Hz, 1H, C_1-H), 7.05 (dd, J = 2.0 Hz, J = 9.0 Hz, 1H, C_{10}-H), 6.95 (d, J = 9.0 Hz, 1H, C_9-H), 3.85 (s, 3H, CH_3).

Anal. Calcd. for $C_{18}H_{10}BrClN_4O_2$: C, 50.32; H, 2.35; N, 13.04. Found: C, 50.08; H, 2.35; N, 13.12.

One-pot Synthesis of Compounds **7a** and **8a** from Compound **5a**.

A solution of **5a** (5 g, 15.2 mmoles) and 2-chloroacrylonitrile (5.32 g, 60.8 mmoles) in 1,4-dioxane (250 ml) was refluxed in an oil bath for 2 hours. While the solution was hot, the solvent was evaporated *in vacuo* to give an oily product, which was subsequently refluxed in triethylamine (1 ml)/1,4-dioxane (250 ml) in an oil bath for 30 minutes to precipitate red needles **8a**. After the reaction mixture was cooled to room temperature, the red needles were collected by suction filtration (1.30 g, 24%). Trituration with hot ethanol/water afforded an analytically pure sample of **8a**.

Evaporation of the filtrate *in vacuo* gave yellow crystals **7a**, which were triturated with hot ethanol/water and then collected by suction filtration (1.78 g, 33%).

One-Pot Synthesis of Compound **7b** from Compound **5b**.

A solution of **5b** (5 g, 14.0 mmoles) and 2-chloroacrylonitrile (4.90 g, 56.0 mmoles) in 1,4-dioxane (250 ml) was refluxed in an oil bath for 2 hours. While the solution was hot, the solvent was evaporated *in vacuo* to give an oily residue, which was subsequently refluxed in triethylamine (1 ml)/1,4-dioxane (250 ml) in an oil bath for 30 minutes. Evaporation of the solvent *in vauco* afforded yellow needles **7b**, which were triturated with hot ethanol/water and then collected by suction filtration (4.70 g, 88%).

One-pot Synthesis of Compound **7c** from Compound **5c**.

A solution of **5c** (5 g, 14.0 mmoles) and 2-chloroacrylonitrile (4.90 g, 56.0 mmoles) in 1,4-dioxane (250 ml) was refluxed in an oil bath for 2 hours. While the solution was hot, the solvent was evaporated *in vacuo* to give an oily residue, which was subsequently refluxed in triethylamine (1 ml)/1,4-dioxane (250 ml) in an oil bath for 30 minutes. Evaporation of the solvent *in vacuo* gave yellow needles **7c**, which were triturated with hot ethanol/water and then collected by suction filtration (3.63 g). Evaporation of the filtrate *in vacuo* provided yellow needles **7c**, which were triturated with hot ethanol/water and then collected by suction filtration (0.30 g), total yield, 3.93 g (65%).

REFERENCES AND NOTES

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[2] Present address: Department of Chemistry, Teacher's College, Hyosung Women's University, Gyongsan 713-900, Korea.

[3] H. S. Kim, Y. Kurasawa, C. Yoshii, M. Masuyama, A. Takada and Y. Okamoto, *J. Heterocyclic Chem.*, **27**, 819 (1990).

[4] Since compound **7c** was insoluble in an ordinary solvent other than deuteriotrifluoroacetic acid, its NOE data were not obtained. Accordingly, its ^{1}H- and ^{13}C-nmr spectra were measured in deuteriodimethyl sulfoxide and deuteriotrifluoroacetic acid, respectively.

[5] The purification of the hydrochlorides **6a-c** was very hard, since treatment of **6a-c** with a base spontaneously changed into **7a-c**, respectively. Accordingly, **6a-c** were checked by the ir and mass spectral data.