Substituent Effects on the Tautomer Ratios between the Hydrazone Imine and Diazenyl Enamine Forms in Side-chained Quinoxalines

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The 3-(arylhydrazono)methyl-2-oxo-1,2-dihydroquinoxalines **9-11** were synthesized by the reaction of the quinoxalines **6-8** with various *p*-substituted benzenediazonium salts. Compounds **9-11** showed the tautomeric equilibria between the hydrazone imine **A** and diazenyl enamine **B** forms in dimethyl sulfoxide media. The substituent effect on the tautomer ratios of **A** to **B** was studied by the nmr spectroscopy to clarify that the presence of the ester group R^2 on the hydrazone carbon and electron-donating *p*-substituent R^1 on the side chain benzene ring exhibited a tendency to increase the ratios of the tautomer **A**.

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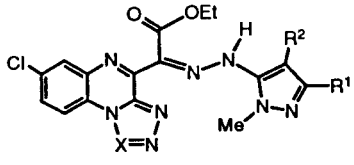
In a previous paper [1], we reported the synthesis of the side-chained quinoxaline derivatives **1a-d** (Chart 1), whose nmr spectral data showed the tautomeric equilibria between the hydrazone imine **A** and diazenyl enamine **B** forms (Scheme 1) in trifluoroacetic acid and/or dimethyl sulfoxide media. Moreover, the elevation of temperature in the nmr measurement increased the ratios of the tautomer **B** (temperature dependence), and the tautomer ratios of **A** to **B** fluctuated in a series of mixed trifluoroacetic acid/dimethyl sulfoxide media (solvent effect).

Chart 1



1a X = CH, R^1 = H, R^2 = COOEt
1b X = CH, R^1 = Me, R^2 = CN
1c X = N, R^1 = H, R^2 = COOEt
1d X = N, R^1 = Me, R^2 = CN

However, the data on the substituent effect could not be obtained from the nmr spectra of compounds **1a-d**. On the other hand, we have already reported the synthesis of the side-chained quinoxaline derivatives **2-5** together with the tautomeric equilibria between the **A** and **B** forms (Scheme 2, Table 1) [2-5], although the nmr spectral data of these compounds also provided no clue for the elucidation of the substituent effects. These results suggested that the setup of the subtituents in compounds **1-5** was not suitable for the above purposes. Accordingly, we synthesized

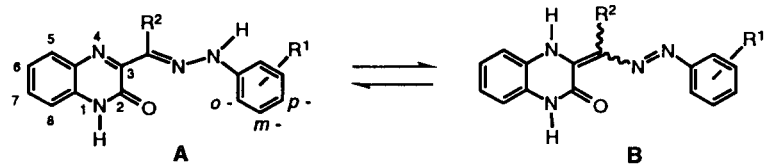
Scheme 1

A Hydrazone Imine Form

B Diazenyl Enamine Form

the side-chained quinoxalines **9-11** having various substituents R^1, R^2 and R^3 (Scheme 3) in order to study the substituent effects on the tautomer ratios of **A** to **B**. Especially, the electron-withdrawing or electron-donating groups were installed in the *p*-position of the side chain benzene ring. As the result, we found that the presence of an electron-withdrawing group in R^2 exhibited a tendency to augment the ratios of the tautomer **A**, and the existence of an electron-withdrawing group in R^1 represented a tendency to increase the ratios of the tautomer **B**. This paper describes the synthesis of novel quinoxaline derivatives **9-11** and the substituent effects on the tautomer ratios between the hydrazone imine **A** and diazenyl enamine **B** forms. The substituents in the side chain benzene ring were limited to the *p*-position in this paper.

Scheme 2

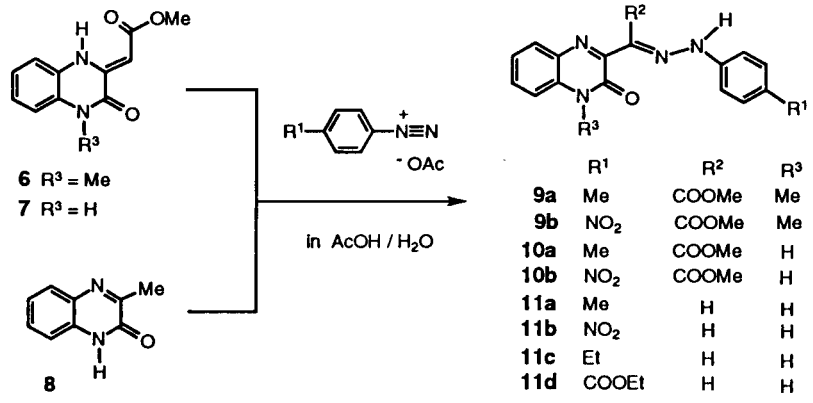


A B

2 R^2 =  3 R^2 =  4 R^2 = COOMe 5 R^2 = H

a R^1 = *o*-Cl, **b** R^1 = *p*-Cl, **c** R^1 = *m*-Cl

Scheme 3



6 R^3 = Me
7 R^3 = H

8

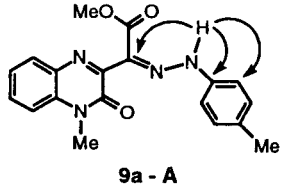
in AcOH / H_2O

	R^1	R^2	R^3
9a	Me	COOMe	Me
9b	NO_2	COOMe	Me
10a	Me	COOMe	H
10b	NO_2	COOMe	H
11a	Me	H	H
11b	NO_2	H	H
11c	Et	H	H
11d	COOEt	H	H

The reaction of 3-methoxycarbonylmethylene-1-methyl-2-oxo-1,2,3,4-tetrahydroquinoxaline **6** [6] or 3-methoxycarbonylmethylene-2-oxo-1,2,3,4-tetrahydroquinoxaline **7** [7] with *p*-methyl- or *p*-nitrobenzenediazonium acetoxide gave 1-methyl-2-oxo-3-[α-(*p*-tolylhydrazono)methoxycarbonylmethyl]-1,2-dihydroquinoxaline **9a**, 1-methyl-3-[α-(*p*-nitrophenylhydrazono)methoxycarbonylmethyl]-2-oxo-1,2-dihydroquinoxaline **9b**, 2-oxo-3-[α-(*p*-tolylhydrazono)methoxycarbonylmethyl]-1,2-dihydroquinoxaline **10a** or 3-[α-(*p*-nitrophenylhydrazono)methoxycarbonylmethyl]-2-oxo-1,2-dihydroquinoxaline **10b**, respectively (Scheme 3). The reaction of 3-methyl-2-oxo-1,2-dihydroquinoxaline **8** with *p*-methyl-, *p*-nitro-, *p*-ethyl- or *p*-ethoxycarbonylbenzenediazonium acetoxide afforded 2-oxo-3-(*p*-tolylhydrazono)methyl-1,2-dihydroquinoxaline **11a**, 3-(*p*-nitrophenylhydrazono)-methyl-2-oxo-1,2-dihydroquinoxaline **11b**, 3-(*p*-ethylphenylhydrazono)methyl-2-oxo-1,2-dihydroquinoxaline **11c** or 3-(*p*-ethoxycarbonylphenylhydrazono)methyl-2-oxo-1,2-dihydroquinoxaline **11d**, respectively.

The hydrazone NH (tautomer **A**) and N_4-H (tautomer **B**) proton signals and/or the hydrazone CH (tautomer **A**) and diazenyl CH (tautomer **B**) proton signals in compounds **2-5** (Table 1) have been empirically assigned in

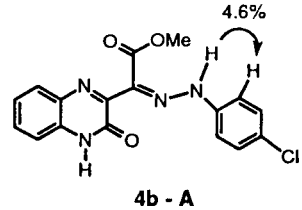
Chart 2



9a - A

Hydrazone NH (δ 11.00)
o-C (δ 114.02)
Benzene C_1 (δ 140.92)
Hydrazone C (δ 127.58)

HMBC Spectral Data for Compound **9a**



4b - A

Hydrazone NH (δ 11.17)
o-H (δ 7.24)

NOE Spectral Data (%) for Compound **4b**

Table 1

NMR Spectral Data for Compounds **2-5**

Compound	Tautomer Ratio		Chemical Shift (δ ppm)			
	A	B	Hydrazone NH A Form	N_4-H B Form	Hydrazone CH A Form	Diazenyl CH B Form
2a (*o*-Cl)	67	33	14.35	12.45	--	--
2b (*p*-Cl)	83	17	11.45	11.97	--	--
3a (*o*-Cl)	50	50	14.22	12.42	--	--
3b (*p*-Cl)	80	20	11.18	11.95	--	--
4a (*o*-Cl)	82	18	13.72	12.53	--	--
4b (*p*-Cl)	89	11	11.17	11.90	--	--
4c (*m*-Cl)	91	9	11.15	11.87	--	--
5a (*o*-Cl)	100	0	14.75	--	7.87	--
5b (*p*-Cl)	67	33	14.53	11.26	7.73	8.37
5c (*m*-Cl)	67	33	14.45	11.33	7.78	8.40

Table 2

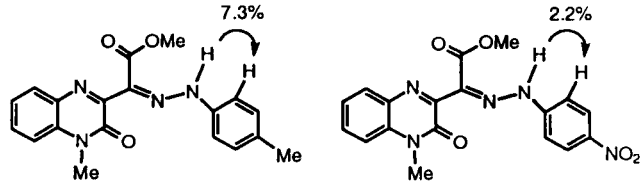
NMR Spectral Data for Compounds **9-11**

Compound	R^1	R^2	R^3	Tautomer Ratio		Chemical Shift (δ ppm)					
				A	B	Hydrazone NH A Form	N_4-H B Form	C_5-H A Form	C_5-H B Form	Hydrazone CH A Form	Diazenyl CH B Form
9a	Me	COOMe	Me	100	0	11.00	--	7.94	--	--	--
9b	NO_2	COOMe	Me	100	0	11.29	--	7.96	--	--	--
10a	Me	COOMe	H	100	0	11.13	--	7.88	--	--	--
10b	NO_2	COOMe	H	100	0	11.36	--	7.89	--	--	--
11a	Me	H	H	67	33	14.53	11.15	8.02	7.77	7.68	8.32
11c	Et	H	H	67	33	14.53	11.17	7.99	7.77	7.68	8.33
11d	COOEt	H	H	46	54	14.49	11.54	8.04	7.81	7.79	8.44
11b	NO_2	H	H	30	70	14.53	11.90	8.10	7.82	7.86	8.49

comparison with the chemical shifts of other similar compounds. These empirical assignments in compounds **2-5** were found to be in good agreement with the assignments of the hydrazone NH, N_4-H, hydrazone CH and diazenyl CH proton signals in compounds **9-11** (Table 2), which were supported by the HMBC and NOE spectral data (Charts 2-6).

Namely, the HMBC spectra of compound **9a** exhibited a correlation between the *o*-C carbon (δ 114.0 ppm) and the hydrazone NH proton (δ 11.00 ppm), between the side chain benzene C_1 carbon (δ 140.9 ppm) and the hydrazone NH proton (δ 11.00 ppm) and between the hydrazone carbon (δ 127.6 ppm) and the hydrazone NH proton (δ 11.00 ppm) (Chart 2, Table 2). In addition, the NOE was observed between the hydrazone NH and *o*-H proton signals in compounds **9a** and **9b** (Chart 3). Since compounds **9a** and **9b** are composed of a single tautomer, the above data show the predominance of the species **9a-A** and **9b-A**. Similar NOE spectral data was obtained for compound **4b** (Chart 2). Thus, the hydrazone NH proton signals of the *p*-chloro and the *m*-chloro series of compounds **2b, 3b, 4b, 4c** (δ 11.45-11.15 ppm) and the *p*-methyl and the *p*-nitro series of compounds **9a,b, 10a,b** (δ 11.36-11.00 ppm), both having the oxadiazole ring or ester group on the hydrazone carbon, were found to appear in a similar magnetic field (Table 3). Accordingly, the signals at δ 11.97-11.87 ppm were assigned to the N_4-H protons of the tautomer **B** in the *p*-chloro and the *m*-chloro series of compounds **2b, 3b, 4b, 4c** (Tables 1,3).

Chart 3



9a - A **9b - A**

Hydrazone NH (δ 11.00) Hydrazone NH (δ 11.29)

o-H (δ 7.13) *o*-H (δ 7.36)

NOE Spectral Data (%) for Compounds **9a** and **9b**

On the other hand, the HMBC spectra of compound **11a** represented the correlation between the *o*-C carbon (δ 114.1 ppm) and hydrazone NH proton (δ 14.53 ppm) and between the side chain benzene C_1 carbon (δ 141.0 ppm)

Table 3

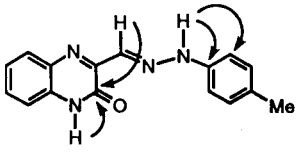
NMR Spectral Data for Compounds **2-5** and **9-11**

Compound A Form / B Form	R^1 B Form	R^2 A Form	Chemical Shift (δ ppm) Hydrazone NH B Form	N_4-H	Hydrazone CH	Diazenyl CH
2a	*o*-Cl	Oxdzl [a]				
3a	*o*-Cl	MeOxdzl [b]	14.35-13.72	12.53-12.42	--	--
4a	*o*-Cl	COOMe				
2b	*p*-Cl	Oxdzl				
3b	*p*-Cl	MeOxdzl				
4b	*p*-Cl	COOMe	11.45-11.15	11.97-11.87	--	--
4c	*m*-Cl	COOMe				
9a	*p*-Me	COOMe				
9b	*p*-NO_2	COOMe				
10a	*p*-Me	COOMe	11.36-11.00	--	--	--
10b	*p*-NO_2	COOMe				
5a	*o*-Cl	H				
5b	*p*-Cl	H	14.75-14.45	11.33-11.26	7.87-7.73	8.40-8.37
5c	*m*-Cl	H				
11a	*p*-Me	H				
11b	*p*-NO_2	H				
11c	*p*-Et	H	14.53-14.49	11.90-11.15	7.86-7.68	8.49-8.32
11d	*p*-COOEt	H				

[a] 1,3,4-Oxadiazol-2-yl. [b] 5-Methyl-1,3,4-oxadiazol-2-yl.

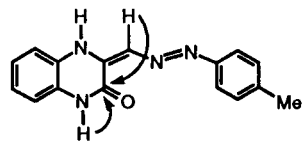
and hydrazone NH proton (δ 14.53 ppm) as well as the correlation between the C_2=O carbon and the N_1-H proton, between the C_2=O carbon and the hydrazone CH proton and between the C_2=O carbon and the diazenyl CH proton (Chart 4). These data indicated that the hydrazone

Chart 4



11a - A

Hydrazone NH (δ 14.53)
Hydrazone CH (δ 7.68)
N_1-H (δ 12.55)
Benzene C_1 (δ 141.0)
o-C (δ 114.1)
C_2=O (δ 149.5)



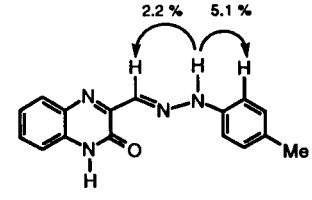
11a - B

Diazenyl CH (δ 8.32)
N_1-H (δ 12.35)
C_2 = O (δ 150.9)

HMBC Spectral Data for Compound **11a**

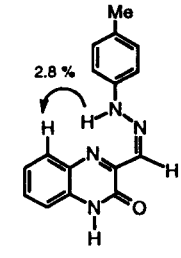
NH proton signals appeared at δ 14.75-14.45 ppm in compounds **5a-c** and **11a-d** (Tables 1-3). In general, the N_4-H proton signals did not appear at a lower magnetic field than δ 14 ppm [8-14]. Consequently, the C_5-H proton signals of the tautomer **A** were observed to appear at a lower magnetic field than those of tautomer **B** [1]. Thus, the above results supported the assignment for the signal pairs of the tautomers **A** and **B** in compounds **5a-c** and **11a-d** (Charts 5, 6, Tables 1-3), wherein the hydrazone NH, N_4-

Chart 5

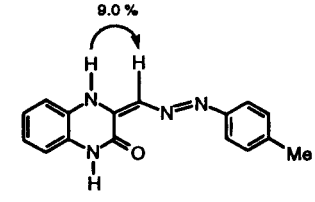


11a - A

Hydrazone NH (δ 14.53)
Hydrazone CH (δ 7.68)
o-H (δ 7.33)
C_5-H (δ 8.02)

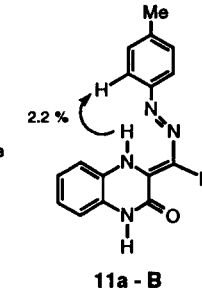


11a - A



11a - B

N_4-H (δ 11.15)
Diazenyl CH (δ 8.32)
o-H (δ 7.18)
C_5 - H (δ 7.77)



11a - B

NOE Spectral Data (%) for Compound **11a**

C_5H_4N) in boiling *n*-butanol resulted in the formation of the corresponding compounds **4a-c** in good yield. The structure of the products was established from their spectral characteristics which indicated that in addition to heterocyclization, deacetylation had taken place. Heating **4a-c** in acetic anhydride led to the formation of their acetyl derivatives **5a-c**.

For the preparation of the 1-methyl analog, **7**, compound **3** was treated with hydrazine to form **6** which on treatment with boiling acetic anhydride afforded **7**. On the other hand, treatment of **6** with acetylacetone yielded compound **8**. The structural assignment of **8** was confirmed by ^{13}C-nmr analysis.

Compound **3** was converted to tetrazolo[1,5-*a*]pyridazine **9** by the reaction of the former with sodium azide in *N,N*-dimethylformamide. The structure of **9** was supported by infrared spectroscopy.

Currently, the products isolated herein are being screened for biological activity.

EXPERIMENTAL

Melting points were determined on a Mel-Temp melting point apparatus and are reported uncorrected. Analytical tlc was performed using ascending technique with EM silica gel 60 F_{254} precoated on plastic sheets. The ir spectra were obtained on Unicam SP 1025 spectrometer, and were calibrated against the 1601 cm^{-1} band of polystyrene. The nmr spectra were recorded on Bruker AC-250 or Nicolet NT 300 MHz spectrometers. Chemical shifts are reported in parts per million downfield from internal tetramethylsilane. Apparent coupling constants (J) are given in Hertz (Hz). A Hewlett-Packard 5995 Gas Chromatograph/Mass Spectrometer was used to record eims data at 70 eV. Elemental analyses were preformed in the Chemistry Department, Faculty of Science, Alexandria, and/or Ain-Shames Universities, Egypt.

1-Aryl-4-(hydroxymethyl)-1-phenylpyrazol-3-yl][1,2,4]triazolo-[4,3-*a*]quinoxaline (**4**).

General Procedure.

A solution of **3** (2.6 mmoles) and the desired aroylhydrazine (5.9 mmoles) in butanol (20 ml) was heated under reflux for 8 hours. The reaction mixture was concentrated and the desired product that separated out was filtered off and recrystallized from ethanol or purified by flash column chromatography on silica gel using ethyl acetate as an eluent (Table).

4-[5-(Acetoxymethyl)-1-phenylpyrazol-3-yl]-1-aryl[1,2,4]triazolo[4,3-*a*]quinoxaline (**5**).

General Procedure.

A solution of **4** (0.72 mmole) in acetic anhydride (5 ml) was heated under reflux for 1 hour. The mixture was then cooled and poured onto crushed ice. The product was filtered off, washed with water, dried, and recystallized from ethanol (Table).

2-Hydrazino-3-[5-hydroxymethyl)-1-phenylpyrazol-3-yl]quinoxaline (**6**).

A suspension of **3** (0.3 g, 0.79 mmole) in hydrazine hydrate (1 ml) was heated under reflux for 1 hour. The resulting product was filtered, washed with ethanol, and dried to yield 0.25 g (95%), mp 224-226°; ir (potassium bromide): 3311, 3213, 3138 cm^{-1}; ^1H-nmr (300 MHz, DMSO-d_6): δ 4.62 (d, J = 5.52 Hz, 2 H, CH_2O), 4.77 (br s, 2H, NH_2), 5.70 (t, J = 5.52 Hz, 1H, OH), 7.35-7.90 (m, 10H, arom), 9.44 (s, 1H, NH).

Anal. Calcd. for $C_{18}H_{16}N_6O$: C, 65.04; H, 4.85; N, 25.29. Found: C, 65.24; H, 4.91; N, 25.32.

4-[5-(Acetoxymethyl)-1-phenylpyrazol-3-yl]-1-methyl[1,2,4]triazolo[4,3-*a*]quinoxaline (**7**).

A solution of **6** (0.3 g, 0.90 mmole) in acetic anhydride (5 ml) was refluxed for 1 hour. The mixture was allowed to cool to room temperature and was then poured onto crushed ice. The product was collected by filtration, washed with water and dried to yield 0.3 g (83%) mp 214-215°; ir (potassium bromide): 1745 (COO) cm^{-1}; ^1H-nmr (250 MHz, DMSO-d_6): δ 2.10 (s, 3H, CH_3CO), 3.23 (s, 3H, CH_3), 5.20 (s, 2H, CH_2O), 7.48-7.65, 8.11, 8.21, 8.30 (m, s, m, m, 10H arom).

Anal. Calcd. for $C_{22}H_{18}N_6O_2$: C, 66.32; H, 4.55; N, 21.10. Found: C, 66.11; H, 4.39; N, 20.86.

3-[5-(Hydroxymethyl)-1-phenylpyrazol-3-yl]-2-(3,5-dimethylpyrazol-1-yl)quinoxaline (**8**).

A solution of **6** (0.5 g, 1.5 mmoles) in acetylacetone (5 ml) was refluxed for 1 hour. The mixture was allowed to cool to room temperature and the precipitate was filtered and crystallized from methanol-benzene to yield 0.54 g (91%), mp 173-174°; ir (potassium bromide): 3245 (OH) cm^{-1}; ^1H-nmr (300 MHz, DMSO-d_6): δ 2.09, 2.31 (2 s, 6H, 2 CH_3), 3.19 (bs, 1H, OH), 4.53 (bs, 2H, CH_2O), 6.04, 6.18 (2s, 2H, proton at 4-positions of the pyrazolyl rings), 7.33-8.29 (5 m, 9H arom); ^{13}C-nmr (75.5 MHz, deuteriochloroform): δ 11.4, 13.5, 55.1, 106.9, 108.5, 124.1, 127.8, 127.9, 128.9, 129.1, 129.3, 130.6, 131.1, 139.3, 140.2, 141.7, 142.2, 143.7, 144.2, 144.8, 147.5, 150.0.

Anal. Calcd. for $C_{23}H_{20}N_6O$: C, 69.68; H, 5.09; N, 21.20. Found: C, 69.53; H, 4.98; N, 21.37.

4-[5-(Acetoxymethyl)-1-phenylpyrazol-3-yl]tetrazolo[1,5-*a*]-quinoxaline (**9**).

A solution of **3** (0.5 g, 1.32 mmoles) and sodium azide (0.18 g, 2.76 mmoles) in *N,N*-dimethylformamide (20 ml) was heated under reflux for 8 hours. The solution was then cooled and poured into water. The precipitate was filtered and recystallized from chloroform-ethanol to obtain **9**, (yield 0.42 g (83%) mp 185°; ir (potassium bromide): 1738 cm^{-1}; ^1H-nmr (250 MHz, DMSO-d_6): δ 2.05 (s, 3H, CH_3CO), 5.28 (s, 2H, CH_2O), 7.59-8.63 (m, 10H arom); ms: m/z 385 (M^+,2), 358 (23); 357 (49), 315 (55), 314 (100), 286 (24), 77 (24).

Anal. Calcd. for $C_{20}H_{15}N_7O_2$: C, 62.33; H, 3.92; N, 25.44. Found: C, 62.11; H, 3.74; N, 25.18.

to give a clear solution, which was added to a solution of 3-methoxycarbonylmethylene-2-oxo-1,2,3,4-tetrahydroquinoxaline (3 g, 13.4 mmoles) in acetic acid (50 ml). The mixture was heated with stirring on a boiling water bath for 1 hour to precipitate a small amount of red needles **10a**. Then, the mixture was cooled in an ice-water bath to precipitate red needles **10a**, which were collected by suction filtration and washed with ethanol to provide an analytically pure sample (1.18 g, 25%), mp 258-259°; ir: ν cm^{-1} 1715, 1650, 1585; ms: m/z 336 (M^+); pmr: 12.58 (brs, 1H, N_1-H), 11.13 (s, 1H, hydrazone NH), 7.88 (dd, J = 8.0 Hz, J = 1.5 Hz, 1H, C_5-H), 7.62 (ddd, J = 8.0 Hz, J = 8.0 Hz, J = 1.5 Hz, 1H, C_7-H), 7.38 (dd, J = 8.0 Hz, J = 1.5 Hz, 1H, C_8-H), 7.36 (ddd, J = 8.0 Hz, J = 8.0 Hz, J = 1.5 Hz, 1H, C_6-H), 7.16 (d, J = 8.5 Hz, 2H, *o*-H), 7.12 (d, J = 8.5 Hz, 2H, *m*-H), 3.73 (s, 3H, OCH_3), 2.25 (s, 3H, *p*-CH_3).

Anal. Calcd. for $C_{18}H_{16}N_4O_3$: C, 64.28; H, 4.80; N, 16.66. Found: C, 64.49; H, 4.89; N, 16.96.

3-[α-(*p*-Nitrophenylhydrazono)methoxycarbonylmethyl]-2-oxo-1,2-dihydroquinoxaline **10b**.

A solution of sodium nitrite (2.37 g, 34.4 mmoles) in water (30 ml) was added to a suspension of *p*-nitroaniline (4.75 g, 34.4 mmoles) in acetic acid (50 ml) with stirring in an ice-water bath to give yellow precipitates, which were added to a solution of 3-methoxycarbonylmethylene-2-oxo-1,2,3,4-tetrahydroquinoxaline (3 g, 13.8 mmoles) in acetic acid (50 ml). The mixture was heated with stirring on a boiling water bath for 1 hour to precipitate yellow crystals **10b**, which were collected by suction filtration (3.09 g, 61%). Recrystallization from *N,N*-dimethylformamide/ethanol afforded yellow needles, mp 295-296°; ir: ν cm^{-1} 1730, 1665, 1585; ms: m/z 367 (M^+); pmr: 12.73 (brs, 1H, N_1-H), 11.36 (brs, 1H, hydrazone NH), 8.23 (d, J = 9.0 Hz, 2H, *m*-H), 7.89 (dd, J = 8.0 Hz, J = 1.5 Hz, 1H, C_5-H), 7.66 (ddd, J = 8.0 Hz, J = 8.0 Hz, J = 1.5 Hz, 1H, C_7-H), 7.41 (dd, J = 8.0 Hz, J = 1.5 Hz, 1H, C_8-H), 7.39 (ddd, J = 8.0 Hz, J = 8.0 Hz, J = 1.5 Hz, 1H, C_6-H), 7.37 (d, J = 9.0 Hz, 2H, *o*-H), 3.77 (s, 3H, OCH_3).

Anal. Calcd. for $C_{17}H_{13}N_5O_5$: C, 55.59: H, 3.57; N, 19.07. Found: C, 55.63; H, 3.76; N, 18.80.

2-Oxo-3-(*p*-tolylhydrazono)methyl-1,2-dihydroquinoxaline **11a**.

A solution of sodium nitrite (1.47 g, 21.3 mmoles) in water (30 ml) was added to a suspension of *p*-toluidine (2.27 g, 21.3 mmoles) in acetic acid (50 ml) with stirring in an ice-water bath to give a clear solution, which was added to a solution of 3-methyl-2-oxo-1,2-dihydroquinoxaline (2 g, 12.5 mmoles) in acetic acid (50 ml). The mixture was heated with stirring on a boiling water bath for 1 hour to afford a violet clear solution. The solvent was evaporated *in vacuo* to provide an oily residue, which was crystallized from ethanol/water to give orange crystals (1.12 g, 34%). Recrystallization from *N,N*-dimethylformamide/ethanol furnished orange-red needles, mp 298-299°; ir: ν cm^{-1} 1660; ms: m/z 278 (M^+); pmr: (hydrazone imine form **A**) 14.53 (s, hydrazone NH), 12.55 (s, N_1-H), 8.02 (dd, J = 8.0 Hz, J = 1.0 Hz, C_5-H), 7.68 (s, hydrazone CH), 7.51 (ddd, J = 8.0 Hz, J = 8.0 Hz, J = 1.0 Hz, C_7-H), 7.36-7.25 (m, C_8-H and C_6-H), 7.33 (d, J = 8.0 Hz, *o*-H), 7.17 (d, J = 8.0 Hz, *m*-H), 2.28 (s, *p*-CH_3); (diazenyl enamine form **B**) 12.35 (s, N_1-H), 11.15 (s, N_4-H), 8.32 (s, diazenyl CH), 7.77 (dd, J = 8.0 Hz, J = 1.0 Hz, C_5-H), 7.45 (ddd, J = 8.0 Hz, J = 8.0 Hz, J = 1.0 Hz, C_7-H), 7.36-7.25 (m, C_8-H and C_6-H), 7.18 (d, J = 8.0 Hz, *o*-H), 7.07 (d, J = 8.0 Hz, *m*-H), 2.24 (s, *p*-CH_3).

Anal. Calcd. for $C_{16}H_{14}N_4O$: C, 69.05; H, 5.07; N, 20.13. Found: C, 68.87; H, 5.08; N, 20.03.

3-(*p*-Nitrophenylhydrazono)methyl-2-oxo-1,2-dihydroquinoxaline **11b**.

A solution of sodium nitrite (2.16 g, 31.3 mmoles) in water (30 ml) was added to a suspension of *p*-nitroaniline (4.31 g, 31.3 mmoles) in acetic acid (50 ml) with stirring in an ice-water bath to give yellow precipitates, which were added to a solution of 3-methyl-2-oxo-1,2-dihydroquinoxaline (2 g, 12.5 mmoles). The mixture was heated with stirring on a boiling water bath for 1 hour to precipitate orange crystals of **11b**, which were collected by suction filtration (2.19 g, 57%). Recrystallization from *N,N*-dimethylformamide/ethanol provided orange needles, mp above 320°; ir: ν cm^{-1} 1660, 1590; ms: m/z 309 (M^+); pmr: (hydrazone imine form **A**) 14.53 (s, hydrazone NH), 12.54 (brs, N_1-H), 8.19 (d, J = 9.0 Hz, *m*-H), 8.10 (dd, J = 8.0 Hz, J = 1.0 Hz, C_5-H), 7.86 (s, hydrazone CH), 7.56 (ddd, J = 8.0 Hz, J = 8.0 Hz, J = 1.0 Hz, C_7-H), 7.55 (d, J = 9.0 Hz, *o*-H), 7.39-7.28 (m, C_8-H and C_6-H); (diazenyl enamine form **B**) 12.54 (brs, N_1-H), 11.90 (brs, N_4-H), 8.49 (s, diazenyl CH), 8.19 (d, J = 9.0 Hz, *m*-H), 7.82 (dd, J = 8.0 Hz, J = 1.0 Hz, C_5-H), 7.51 (ddd, J = 8.0 Hz, J = 8.0 Hz, J = 1.0 Hz, C_7-H), 7.39-7.28 (m, C_8-H and C_6-H), 7.26 (d, J = 8.0 Hz, *o*-H).

Anal. Calcd. for $C_{15}H_{11}N_5O_3$: C, 58.25; H, 3.59; N, 22.65. Found: C, 58.36; H, 3.45; N, 22.39.

3-(*p*-Ethylphenylhydrazono)methyl-2-oxo-1,2-dihydroquinoxaline **11c**.

A solution of sodium nitrite (1.30 g, 18.8 mmoles) in water (50 ml) was added to a solution of *p*-ethylaniline (2.27 g, 18.8 mmoles) in acetic acid (30 ml) in an ice-water bath to give a clear solution, which was added to a suspension of 3-methyl-2-oxo-1,2-dihydroquinoxaline (2 g, 12.5 mmoles) in acetic acid (20 ml)/water (50 ml). The mixture was heated with stirring on a boiling water bath for 20 minutes to afford orange crystals **11c**, which were collected by suction filtration. Recrystallization from *N,N*-dimethylformamide/ethanol furnished orange needles (670 mg, 18%), mp 296-297°; ir: ν cm^{-1} 1650; ms: m/z 292 (M^+); pmr: (hydrazone imine form **A**) 14.53 (s, hydrazone NH), 12.50 (brs, N_1-H), 7.99 (dd, J = 8.0 Hz, J = 1.0 Hz, C_5-H), 7.68 (s, hydrazone CH), 7.50 (ddd, J = 8.0 Hz, J = 8.0 Hz, J = 1.0 Hz, C_7-H), 7.33 (d, J = 8.5 Hz, *o*-H), 7.30-7.24 (m, C_8-H and C_6-H), 7.13 (d, J = 8.5 Hz, *m*-H), 2.57 (q, J = 7.0 Hz, CH_2 of *p*-CH_2CH_3), 1.17 (t, J = 7.0 Hz, CH_3 of *p*-CH_2CH_3); (diazenyl enamine form **B**) 12.50 (brs, N_1-H), 11.17 (s, N_4-H), 8.33 (s, diazenyl CH), 7.77 (dd, J = 8.0 Hz, J = 1.0 Hz, C_5-H), 7.44 (ddd, J = 8.0 Hz, J = 8.0 Hz, J = 1.0 Hz, C_7-H), 7.30-7.24 (m, C_8-H and C_6-H), 7.19 (d, J = 8.5 Hz, *o*-H), 7.09 (d, J = 8.5 Hz, *m*-H), 2.54 (q, J = 7.0 Hz, CH_2 of *p*-CH_2CH_3), 1.16 (t, J = 7.0 Hz, CH_3 of *p*-CH_2CH_3).

Anal. Calcd. for $C_{17}H_{16}N_4O$: C, 69.84; H, 5.52; N, 19.17. Found: C, 69.89; H, 5.58; N, 19.13.

3-(*p*-Ethoxycarbonylphenylhydrazono)methyl-2-oxo-1,2-dihydroquinoxaline **11d**.

A solution of sodium nitrite (1.30 g, 18.8 mmoles) in water (50 ml) was added to a solution of ethyl *p*-aminobenzoate (3.10 g, 18.8 mmoles) in acetic acid (30 ml) in an ice-water bath to give a yellow suspension, which was added to a suspension of 3-methyl-2-oxo-1,2-dihydroquinoxaline (2 g, 12.5 mmoles) in

acetic acid (20 ml)/water (50 ml). The mixture was heated with stirring on a boiling water bath for 20 minutes to afford orange crystals of **11d**, which were collected by suction filtration. Recrystallization from *N,N*-dimethylformamide/ethanol furnished orange needles (910 mg, 22%), mp 288-289°; ir: ν cm^{-1} 1690, 1650; ms: m/z 336 (M^+); pmr: (hydrazone imine form **A**) 14.49 (s, hydrazone NH) 12.53 (brs, N_1-H), 8.04 (dd, J = 8.0 Hz, J = 1.0 Hz, C_5-H), 7.92 (d, J = 9.0 Hz, *m*-H), 7.79 (s, hydrazone CH), 7.54 (ddd, J = 8.0 Hz, J = 8.0 Hz, J = 1.0 Hz, C_7-H), 7.48 (d, J = 9.0 Hz, *o*-H), 7.33-7.27 (m, C_8-H and C_6-H), 4.27 (q, J = 7.0 Hz, CH_2 of *p*-$COOCH_2CH_3$), 1.31 (t, J = 7.0 Hz, CH_3 of *p*-$COOCH_2CH_3$); (diazenyl enamine form **B**) 12.53 (brs, N_1-H), 11.54 (s, N_4-H), 8.44 (s, diazenyl CH), 7.89 (d, J = 9.0 Hz, *m*-H), 7.81 (dd, J = 8.0 Hz, J = 1.0 Hz, C_5-H), 7.34 (ddd, J = 8.0 Hz, J = 8.0 Hz, J = 1.0 Hz, C_7-H), 7.33-7.27 (m, C_8-H and C_6-H), 7.22 (d, J = 9.0 Hz, *o*-H), 4.26 (q, J = 7.0 Hz, CH_2 of *p*-$COOCH_2CH_3$), 1.30 (t, J = 7.0 Hz, CH_3 of *p*-$COOCH_2CH_3$).

Anal. Calcd. for $C_{18}H_{16}N_4O_3$: C, 64.27; H, 4.80; N, 16.66. Found: C, 64.29; H, 4.87; N, 16.67.

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