A Convenient Synthesis of 3-Formyl-2-oxo-1,2-dihydroquinoxaline Chlorophenylhydrazones: Novel Tautomeric Equilibria between Hydrazone Imine and Diazenyl Enamine Forms with Long-range Prototropy

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3-Formyl-2-oxo-1,2-dihydroquinoxaline chlorophenylhydrazones **4a-c** were synthesized from the reactions of 3-methyl-2-oxo-1,2-dihydroquinoxaline **3** with chlorophenyl diazonium salts, and **4b,c** were found to exhibit the tautomeric equilibria between the hydrazone imine and diazenyl enamine forms in the dimethylsulfoxide solutions.

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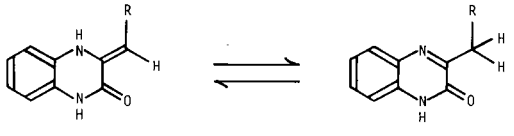
The tautomerism of 3-methoxycarbonylmethylene-2-oxo-1,2,3,4-tetrahydroquinoxaline **1a** has been studied by means of ^{1}H-nmr and uv spectroscopies by Mondelli and Merlini [1]. Namely, tautomers **A** and **B** coexist in dimethylsulfoxide (DMSO) solution of **1a** (Scheme 1).

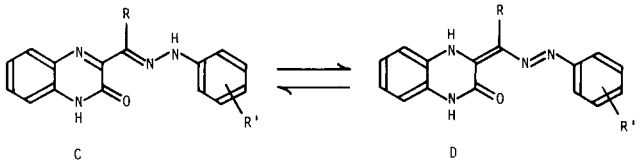


A B

1a, R=COOR'
1b, R=1,3,4-Oxadiazol-5-yl
1c, R=1,2,4-Triazol-5-yl

Scheme 1. Tautomeric Equilibria of 1 in DMSO

Recently, we have also reported the tautomeric equilibria of **1b,c** [2,3] similar to those of **1a**. Thus, the tautomeric nature of the **1** type of compounds has been well established by means of the spectral data. However, there have been few papers on the tautomeric equilibria of the quinoxaline derivatives between the hydrazone imine form **C** and diazenyl enamine form **D** (Scheme 2).

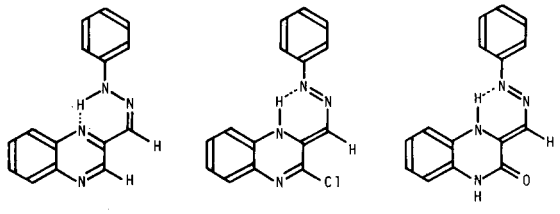


C D

hydrazone imine form diazenyl enamine form

Scheme 2. Tautomeric Equilibria in DMSO

Romanenko *et al.* [4] reported species **2a** (**C** form), **2b** (**D** form) and **2c** (**D** form), which predominated as a single tautomeric species in the ethanol solutions (Chart 1). In



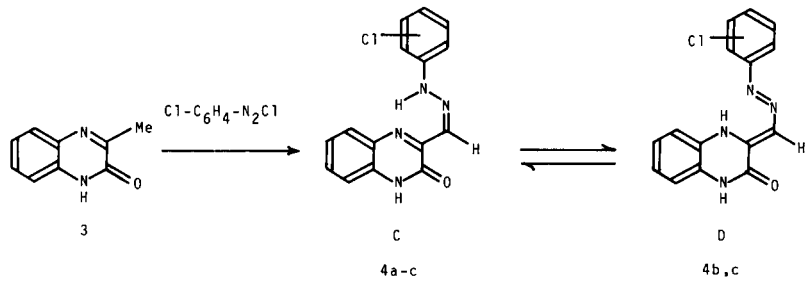
C D D

2a 2b 2c

Chart 1

the present investigation, we synthesized 3-formyl-2-oxo-1,2-dihydroquinoxaline chlorophenylhydrazones **4a-c** by direct diazotization of 3-methyl-2-oxo-1,2-dihydroquinoxaline **3**, and **4b,c** were found to exhibit the above interesting tautomeric equilibria between the **C** and **D** forms in the DMSO solutions. This paper describes the synthesis of **4a-c** and the tautomeric character of **4b,c** between the **C** and **D** forms with a long-range prototropy in the DMSO solutions.

The reactions of **3** with *o*-, *m*- and *p*-chlorophenyl diazonium salts provided orange crystals **4a-c**, whose structural assignments were based on their spectral and analytical data. The ^{1}H-nmr spectral data (Table 1) indicated that **4a** existed as the single tautomeric species **C**, and **4b,c** as the two tautomeric species **C** and **D** in the DMSO solutions. Namely, the ^{1}H-nmr spectrum of **4a** exhibited hydrazone NH (δ 14.73 ppm) and CH (δ 7.87 ppm) proton signals, while the ^{1}H-nmr spectra of **4b,c** represented the hydrazone NH [δ 14.45 (**4b**), 14.53 (**4c**) ppm] and CH [δ 7.78 (**4b**), 7.73 (**4c**) ppm] proton signals together with the N^4-H [δ 11.33 (**4b**), 11.26 (**4c**) ppm] and diazenyl CH [δ 8.40 (**4b**), 8.37 (**4c**) ppm] proton signals. The integral ratios of the hydrazone NH/N^4-H proton signals are 2 versus 1 both in **4b** and **4c**, that is, the tautomeric ratios of **C** and **D** forms are 2 versus 1 in **4b**



Scheme 3

Table 1

^{1}H-NMR Spectral Data for **4a-c**

Compound	Tautomer C	Ratio [a] D	Chemical Shift δ (ppm) N^4-H, Side Chain NH and CH		N^1-H, Aromatic H
4a	100	–	14.73 (s, 1H, =N-NH-) [b]	7.87 (s, 1H, -CH=N-N) [b]	12.60 (brs, 1H, N^1-H) 7.87-6.87 (m, 8H, aromatic)
4b	67	33	14.45 (s, ⅔ H, =N-NH-) [b] 11.33 (s, ⅓ H, N^4-H) [c]	7.78 (s, ⅔ H, -CH=N-N) [b] 8.40 (s, ⅓ H, =CH-N=N) [c]	12.53 (brs, 1H, N^1-H) 8.20-6.80 (m, 8H, aromatic)
4c	67	33	14.53 (s, ⅔ H, =N-NH-) [b] 11.26 (s, ⅓ H, N^4-H) [c]	7.73 (s, ⅔ H, -CH=N-N) [b] 8.37 (s, ⅓ H, =CH-N=N) [c]	12.52 (brs, 1H, N^1-H) 8.13-7.00 (m, 8H, aromatic)

[a] Calculated from integral curves of hydrazone NH/N^4-H and hydrazone CH/diazenyl CH proton signals. [b] Signals due to the tautomer **C**. [c] Signals due to the tautomer **D**.

and **4c**. The assignments for the above hydrazone NH and CH proton signals may be supported by the data that the hydrogen bonded hydrazone NH proton signals appear at δ 14.2 to 13.8 ppm in chloroform [5], and the hydrazone CH proton signals of benzaldehyde and pyridine-2-aldehyde phenylhydrazones in DMSO are observed at δ 7.87 and 7.93 ppm [6], respectively, whose values are similar to those of **4a-c**.

General Procedure.

All melting points are uncorrected. Infrared (ir) spectra were recorded from potassium bromide discs on a JASCO IRA-1 spectrophotometer. Mass spectra (ms) were determined with a JMS-01S spectrometer (JEOL). The ^{1}H-nmr spectra were measured in deuteriodimethylsulfoxide at 34° with an EM-390 spectrometer at 90 MHz using tetramethylsilane as an internal standard.

Preparation of **4a-c**.

A solution of sodium nitrite (5.18 g, 0.075 mole) in water (60 ml) was added dropwise to a suspension of the appropriate chloroaniline hydrochloride (12.3 g, 0.075 mole) in 5% hydrochloric acid (200 ml) with stirring in an ice-water bath to give a clear solution, which was added to a suspension of compound **3** (10 g, 0.0625 mole) in acetic acid (60 ml)/water (40 ml). The whole reaction mixture was stirred in an ice-water bath for 30 minutes, and then heated on a boiling water bath for 1 hour to precipitate orange crystals **4**. Recrystallization from *N,N*-dimethylformamide/ethanol afforded orange needles [**4a**, 18.35 g (98%); **4b**, 18.10 g (97%); **4c**, 15.10 g (81%)]; mp 318-319° (**4a**), 304-305° (**4b**), 310-311° (**4c**); ms: m/z 298 (M$^+$), 300 (M$^+$+2); ir: ν cm^{-1} 1670 (C=O) (**4a-c**).

Anal. Calcd. for $C_{15}H_{11}ClN_4O$: C, 60.31; H, 3.71; Cl, 11.87; N, 18.76. Found: C, 60.40; H, 3.66; Cl, 11.65; N, 19.04 (**4a**). C, 60.32; H, 3.65; Cl, 11.96; N, 18.83 (**4b**). C, 60.19; H, 3.66; Cl, 11.66; N, 18.76 (**4c**).

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[6] ^{1}H-nmr (deuteriodimethylsulfoxide): δ 10.27 (s, 1H, NH), 7.87 (s, 1H, hydrazone CH), 7.77-6.60 (m, 10H, aromatic) (benzaldehyde phenylhydrazone); δ 10.66 (s, 1H, NH), 8.50 (m, 1H, aromatic), 8.03-7.63 (m, 2H, aromatic), 7.93 (s, 1H, hydrazone CH), 7.40-7.03 (m, 5H, aromatic), 6.93-6.67 (m, 1H, aromatic) (pyridine-2-aldehyde phenylhydrazone).