

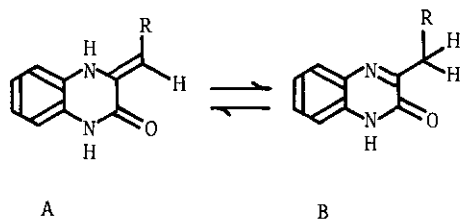
TAUTOMERIC BEHAVIORS OF 3-(1,3,4-OXADIAZOL-2-YL)METHYLENE-2-OXO-1,2,3,4-TETRAHYDROQUINOXALINES

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Abstract — 3-(1,3,4-Oxadiazol-2-yl)methylene-2-oxo-1,2,3,4-tetrahydroquinoxalines (2a,b) were found to exhibit the two tautomers in dimethylsulfoxide and three tautomers in trifluoroacetic acid, and their tautomeric species were assumed based on the NMR and UV spectral data.

Tautomeric equilibria of 3-methoxycarbonylmethylene-2-oxo-1,2,3,4-tetrahydroquinoxaline (1a) and related compounds (1b-e) have been investigated with NMR and UV spectroscopy by Mondelli and Merlini.¹ That is, the NMR spectra in dimethylsulfoxide (DMSO) demonstrated that two tautomers A and B coexisted in 1a,b,c, and the tautomer A was predominant in 1d,e, as shown in Scheme 1 and Table I. Moreover, the NMR spectra in trifluoroacetic acid (TFA) clarified that 1a,b existed as the tautomer B, and 1c,d,e as the tautomer A. Thus the above compounds 1a-e predominate in only one tautomer A or B in TFA. To the contrary, 3-(1,3,4-oxadiazol-2-yl)methylene-2-oxo-1,2,3,4-tetrahydroquinoxaline (2a) and 3-(5-methyl-1,3,4-oxadiazol-2-yl)methylene-2-oxo-1,2,3,4-tetrahydroquinoxaline (2b) (Scheme 2), previously prepared by us,² displayed



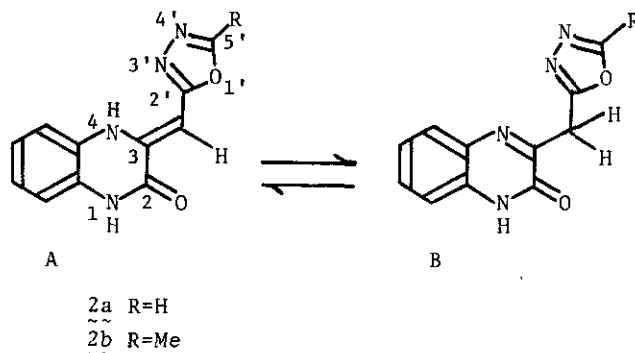
Scheme 1 Equilibria of 1 in DMSO or TFA

Table I. Tautomers of 1 assigned by NMR Spectral Data*

Compound No.	R	R'	Tautomer	
			in DMSO-d ₆	in TFA
1a	COOMe	H	A B	B
1b	COEt	H	A B	B
1c	CN	H	A B	A
1d	COMe	H	A	A
1e	COCOOEt	Me	A	A

* Reference No. 1.

the two tautomers in DMSO- d_6 and the three tautomers in TFA. We now describe the interesting tautomeric behaviors of $\underline{2a}$ and $\underline{2b}$ based on the NMR and UV spectral data. The NMR spectrum of $\underline{1a}$ in DMSO- d_6 exhibited vinyl and methylene proton signals due to the tautomers A and B at δ 5.52 and 3.83 ppm, respectively, and integral ratio of the two signals was 1:1¹ (Table II, III). The NMR spectra of $\underline{2a}$ and $\underline{2b}$ in DMSO- d_6 also represented the vinyl [δ 6.12 ($\underline{2a}$), 6.02 ($\underline{2b}$) ppm] and methylene [δ 4.47



Scheme 2 Equilibria of $\underline{2}$ in DMSO- d_6

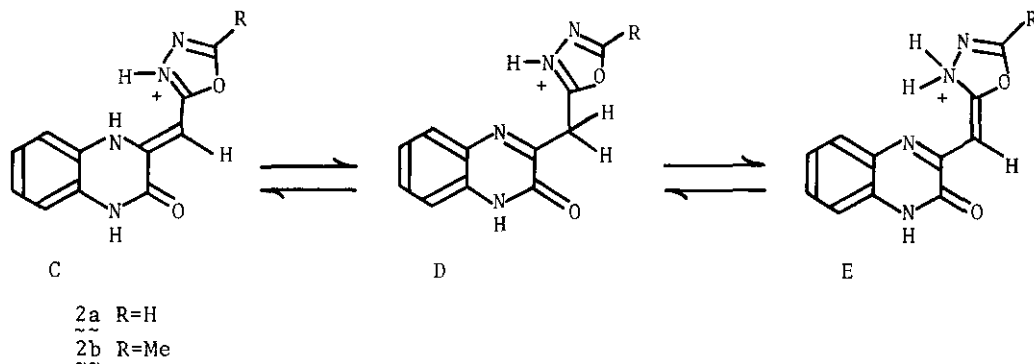
Table II. ¹H-NMR Spectral Data for $\underline{2a}$ and $\underline{2b}$ ³

Solvent	Compound	Chemical Shift (ppm)			
		Vinyl	Methylene	C ₅ , -H or C ₅ , -Me	Aromatic ^{d)}
DMSO- d_6	$\underline{1a}$	5.52	3.83		
	$\underline{2a}$	6.12	4.47	9.20, 9.13 (C ₅ , -H)	c)
	$\underline{2b}$	6.02	4.37	2.50, 2.49 (C ₅ , -Me)	c)
TFA	$\underline{1a}$ ^{a)}	—	4.55		
	$\underline{2a}$	6.63, 6.03	4.97	b), b), 8.44 (C ₅ , -H)	8.20-7.20
	$\underline{2b}$	6.52, 5.97	4.93	2.92, 2.80, 2.62 (C ₅ , -Me)	8.20-7.20
TFA- d_1	$\underline{1a}$ ^{a)}	—	—		
	$\underline{2a}$	—	—	9.05, 8.97, 8.47 (C ₅ , -H)	8.20-7.23
	$\underline{2b}$	—	—	2.95, 2.88, 2.65 (C ₅ , -Me)	8.20-7.20

a) Reference No. 1. b) hidden under signals due to TFA.

c) Reference No. 2. d) observed as multiplets (4H).

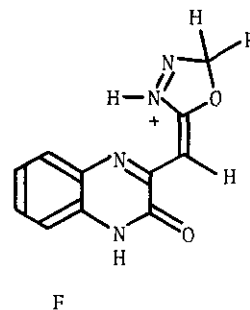
(2a), 4.37 (2b) ppm] proton signals together with the two C₅-H [δ 9.20, 9.13 ppm (2a)] or C₅-Me [δ 2.50, 2.49 ppm (2b)] proton signals. The integral ratios of the vinyl vs methylene proton signals of 2a and 2b at 30 °C were 4:1 and 3:1, respectively, suggesting more predominance of the tautomer A than the tautomer B (Scheme 2). However, these equilibria is apt to shift from the tautomer A to the tautomer B with elevation of temperature (Table III).



Scheme 3 Equilibria of 2 in TFA

Table III. Integral Ratios of Vinyl-Methylene Signals of 2a and 2b in DMSO-d₆ at Various Temperatures³

Compound	Temperature (°C)	Vinyl-Methylene
<u>1a</u> ^{a)}	34-36	1 : 1
<u>2a</u>	30	4 : 1
	50	4 : 1
	90	2 : 1
<u>2b</u>	30	3 : 1
	50	2.5 : 1
	70	2 : 1
	90	1 : 1



Scheme 4

a) Reference No. 1.

Table IV. UV Spectral Data for 2a and 2b⁴

Solvent	Compound	λ_{\max} nm (log ϵ)
CHCl ₃ EtOH	<u>1a</u> ^{a)}	262(3.92), 285(3.79), 359(4.15), 377(4.20), 396(3.99)
	<u>2a</u>	265.3(3.93), 290.0(3.84), 364.5(4.18), 384.5(4.24), 407.0(4.06)
	<u>2b</u>	265.0(3.90), 290.0(3.82), 364.5(4.19), 384.5(4.26), 407.0(4.08)
DMSO ^{b)}	<u>1a</u> ^{a)}	288(3.53), 359(4.26), 377(4.34), 396(4.09)
	<u>2a</u>	350.0(3.88), 363.0(3.93), 383.5(3.87), 406.0(3.66)
	<u>2b</u>	350.0(3.88), 363.0(3.99), 383.5(3.87), 406.0(3.66)
TFA ^{c)}	<u>1a</u> ^{a)}	331(3.74), 381(3.50)
	<u>2a</u>	398.5(3.87), 419.5(4.02), 445.0(3.83)
	<u>2b</u>	400.0(4.08), 422.0(4.14), 445.0(3.86)

a) Reference No. 1. b) 2a and 2b were measured in 70% DMSO in EtOH. c) 2a and 2b were measured in 70% TFA in EtOH.

In the spectra of 2a and 2b in TFA or TFA-d₁, the two vinyl [δ 6.63, 6.03 (2a), 6.52 5.97 (2b) ppm] and one methylene [δ 4.97 (2a), 4.93 (2b) ppm] proton signals were observed together with the three C₅-H (δ 9.05, 8.97, 8.47 ppm) or C₅-Me (δ 2.92, 2.80, 2.62 ppm in TFA, 2.95, 2.88, 2.65 ppm in TFA-d₁) proton signals. These data indicate that 2a and 2b occur in the three tautomers C, D, and E (Scheme 3) on dissolving in TFA. The literature¹ proved that the chemical shifts of the vinyl and methylene protons in DMSO-d₆ were shifted toward a lower magnetic field compared with those in TFA, presumably due to the formation of protonated species, and their

Table V. Tautomers of 2a and 2b assigned by NMR Spectral Data

Compound	Tautomer				
	in DMSO- <u>d</u> ₆		in TFA		
<u>2a</u>	A	B	C	D	E
<u>2b</u>	A	B	C	D	E

shifting values were δ 0.4-1.1 ppm in the vinyl protons and δ 0.6-0.7 ppm in the methylene protons. Therefore, it was assumed that the vinyl proton signals observed at δ 6.63 (2a) and 6.52 (2b) ppm were due to the tautomer C, the methylene proton signals observed at δ 4.97 (2a) and 4.93 (2b) ppm due to the tautomer D, and the remaining vinyl proton signals observed at δ 6.03 (2a) and 5.97 (2b) ppm due to the tautomer E (Scheme 3). The vinyl and methylene proton signals of 1a, 2a, and 2b disappeared in TFA-d₁,^{1,5} while the C₅, -H and C₅, -Me proton signals of 2a and 2b were observed as the three singlet signals in TFA-d₁. These data excluded the presence of the tautomer F (Scheme 4) in TFA. If the tautomer F was present, the C₅, -H of 2a would disappear in TFA-d₁, and the C₅, -Me of 2b would be observed as doublet in TFA.

The UV spectral data of 1a, 2a, and 2b are shown in Table IV. Interestingly, these three compounds exhibited similar spectral patterns in CHCl₃ (or EtOH), while the spectral patterns of 1a and 2a,b in DMSO varied at the shortest absorption maximum. In TFA, however, the spectral pattern of 1a is quite different from the spectral patterns of 2a and 2b. In addition, the absorption maxima of 2a and 2b appear at a much longer wavelength area than those of 1a. These results provide an additional evidence that the tautomeric behaviors of 1 are different from those of 2 in DMSO and TFA.

In conclusion, 2a and 2b were found to exist as the two tautomers A and B in DMSO and as the three tautomers C, D, and E in TFA, as shown in Table V. It is evident that the presence of the 1,3,4-oxadiazole ring in 2a and 2b leads to the above interesting tautomeric behaviors.

REFERENCES AND FOOTNOTES

1. R. Mondelli and L. Merlini, Tetrahedron, 1966, 22, 3253.
2. Y. Kurasawa, Y. Moritaki, and A. Takada, Synthesis, 1983, 238; Y. Kurasawa, Y. Moritaki, T. Ebukuro, and A. Takada, Chem. Pharm. Bull., in press.
3. NMR spectra were measured with an EM-390 spectrometer at 90 MHz.
4. UV spectra were recorded by a Hitachi model 200-20 spectrophotometer.
5. Y. Kurasawa, Y. Moritaki, and A. Takada, Heterocycles, 1982, 19, 1619.

Received, 7th June, 1983