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^{13}C-NMR of Substituted Tetrazoles

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Inductive and resonance effects of phenyl substituted tetrazoles from ^{13}C NMR studies are calculated. ^{13}C NMR shifts of a series of these compounds is reported and the aminotetrazole—iminotetrazoline tautomerism of the compounds studied is discussed.

(Keywords: Inductive effects; Resonance effects; Tautomerism)

^{13}C-NMR von substituierten Tetrazolen

Aus ^{13}C-NMR-Daten werden induktive und Resonanzeffekte von phenylsubstituierten Tetrazolen berechnet. Es werden ^{13}C-NMR-Verschiebungen einer Reihe dieser Verbindungen angegeben und die Aminotetrazol—Iminotetrazolin-Tautomerie diskutiert.

Introduction

In connection with our studies[1,2] on reactivity of asymmetrically substituted carbodiimides towards some 1,3-dipoles, the 5-alkylamino-1-phenyl-1*H*-tetrazoles (**1 a–g**) have been obtained. The above products were thermally converted into 1-alkyl-5-anilino-1*H*-tetrazoles (**2 a–g**).

On the basis of ^{1}H NMR spectra[2] we have considered two possible structures **1 A** and **1 B**. It is evident that the supposed aminotetrazole—iminotetrazoline tautomerism (**I**) reflects two different structural environments of $C_{1''}$, the alkyl carbon atom directly attached to the —NH— and —N= group, respectively (*R* side chains are referred as n″). The purpose of the present work is to discuss our previous opinion and report the ^{13}C NMR data of these compounds.

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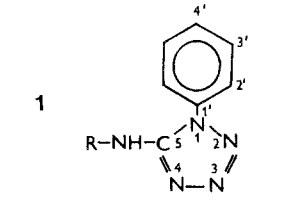
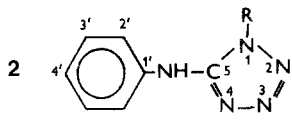


1

		R
1 and 2	a	*Me*
	b	*Et*
	c	*n-Pr*
	d	*i-Pr*
	e	*n-Bu*
	f	*i-Bu*
	g	*t-Bu*
1	h	H
2	h	*Ph*



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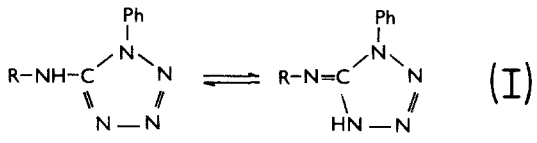

1A 1B (I)

Recently *Fong*[3] has used ^{13}C NMR shifts of *meta* and *para* atoms (C_m and C_p) of a series of phenyl substituted azoles for the evaluation of the torsional angle between phenyl and azole rings. Following equations were used:

$$\Delta(^{13}C_p) = 5.71\,\sigma_I + 20.52\,\sigma_R^0 - 0.61 \tag{1}$$

$$\Delta(^{13}C_m) = 1.80\,\sigma_I - 1.42\,\sigma_R^0 - 0.10 \tag{2}$$

and

$$(\sigma_R^0)_\Phi = (\sigma_R^0)_0 \cos^2 \Phi \tag{3}$$

$\Delta(^{13}C_p)$ and $\Delta(^{13}C_m)$ are defined

as

$$\Delta\,^{13}C_{p(m)} = \delta\,^{13}C_{p(m)} - 128.5$$

σ_I and σ_R^0 are the values representing inductive and resonance effects on the phenyl ring. Φ is the interannular angle between the planes formed by azole and the phenyl rings. The measured ^{13}C NMR shifts have been used to assess qualitatively the torsional angle between phenyl and tetrazole rings.

Results and Discussion

The ^{13}C NMR chemical shifts for the derivatives are listed in Tables 1 and 2. The shifts are given relative to *TMS* which was used as an internal standard in $CDCl_3$ solvent.

The ^{13}C NMR signals assignment was performed with the help of high resolution ^{13}C NMR spectra with NOE effect. In both series of the

Table 1. ^{13}C NMR *shifts of tetrazoles* **1a–h**

Compound	C-5	Phenyl				*R*			
		C-1′	C-2′	C-3′	C-4′	C-1″	C-2″	C-3″	C-4″
1a	155.48	133.26	123.90	130.14	129.69	30.80	—	—	—
1b	154.70	133.20	123.90	130.08	129.62	39.37	14.88	—	—
1c	154.77	133.07	123.71	129.95	129.91	46.00	22.48	11.05	—
1d	154.12	133.20	123.97	130.21	129.69	46.78	22.74	—	—
1e	154.57	132.94	123.58	129.75	129.23	43.92	31.12	19.62	13.45
1f	155.03	133.39	124.03	130.34	129.82	51.98	28.26	20.08	—
1g	154.05	133.20	123.97	130.08	129.56	53.08	28.72	—	—
1h	154.04	133.27	123.73	130.29	129.93	—	—	—	—

Table 2. ^{13}C NMR *shifts of tetrazoles* **2a–h**

Compound	C-5	Phenyl				*R*			
		C-1′	C-2′	C-3′	C-4′	C-1″	C-2″	C-3″	C-4″
2a	152.50	139.30	118.73	129.81	123.15	32.52	—	—	—
2b	152.52	139.30	118.82	129.51	123.64	40.02	14.78	—	—
2c	153.02	139.23	118.71	129.33	123.49	48.01	22.20	11.07	—
2d	152.57	139.30	118.85	129.65	123.60	48.54	22.47	—	—
2e	152.69	139.04	118.58	129.30	123.29	45.97	30.86	19.65	13.48
2f	153.92	139.60	119.02	129.51	123.77	54.00	28.00	20.10	—
2g	152.17	139.30	118.85	129.46	123.74	55.12	28.46	—	—
2h	152.01	140.01	118.45	129.56	123.64	133.39	125.01	130.73	130.65

compounds studied the two quarternary carbon atoms $C_{1'}$ and C_5 can be easily recognized. These absorptions were all of low intensity due to minimal nuclear *Overhauser* enhancement and to their relatively long relaxation times. The more deshielded C_5 of the tetrazole ring varies within the range from 151 to 156 ppm (reported value[4] for 1-phenyl-1*H*-tetrazole is 140 ppm). In the non decoupled spectra with NOE

enhancement the C_5 signal exhibits a complex structure in **1a** and **1f**. In **1a** we can observe a quartet with $^3J_{C_5H_{1''}} = 3.9$ Hz, while in **1f** the C_5 signal shows a triplet with $^3J_{C_5H_{1''}} = 3.9$ Hz. Other compounds reveal only the broadening of the C_5 signal. The two bond CH coupling caused by an adjacent hydrogen was not observed. The ipso carbon $C_{1'}$ exhibits a characteristic small triplet. The remaining benzene ring carbon atoms are assigned on the basis of the substituent effect of tetrazole and the amino group. The $C_{2'}$ and $C_{3'}$ signals can be clearly distinguished from the $C_{4'}$ signal because of different intensities in the noise decoupled spectra. Our assignment of signals in phenyl group is consistent with the results of *Könnecke* et al.[4]. The assignment of the alkyl carbon atoms was based upon the substitution effect in alkanes and the multiplicity in the non decoupled spectra.

The chemical shift difference between series **1** and **2** shows that the *ipso* $C_{1'}$ (+6 ppm) and the *ortho*-carbon $C_{2'}$ (−5 ppm) changes in opposite directions. Significant is the difference in the chemical shifts of $C_{4'}$ (about −6 ppm) due to the greater deshielding effect of directly attached tetrazole nucleus compared to the effect of an amino group. This comparison indicates that the free electron pair of the amine nitrogen participates more effectively in the benzene ring conjugation. On the other hand the transfer of electron density from tetrazole is less effective, caused by high conjugation energy of the tetrazole ring and also by the noncoplanarity between the phenyl and the tetrazole ring. Finally, it can be seen from *Dreiding* models of 5-alkylamino-1-phenyl-1*H*-tetrazoles that coplanarity of phenyl and tetrazole ring cannot be achieved due to the repulsive interaction between the *o*-phenyl hydrogen and the alkylamino group.

Table 3 gives the ^{13}C substituent chemical shifts (s.c.s.) of *ipso*-, *ortho*-, *meta*- and *para*-carbon atoms of **1a–h** and **2h** and the calculated σ_I and σ_R effects using eqs. (1) and (2). The lowest σ_R value is exhibited by **1f** which has also the highest inductive σ_I value. The evaluation of interannular angles Φ can be done according to eq. (3), taking the σ_R of **1f** as a reference. The lack of X-ray structural data of the compounds does not allow us to determine the absolute values of interannular angles. Because of the aromatic character of the substituent in **2h** Φ was not estimated. The σ_R and σ_I values differ from other compounds in series **1**. The lowest interannular conjugation is exhibited by **1c** and **1e** which has also the greatest Φ. Based on the resonance σ_R and σ_I parameters one may distinguish three groups of compounds with similar electronic structure: a) **1a**, **1b** and **1g**; b) **1c**, **1e**; c) **1d**, **1f** and **1h**. In these three groups of compounds the σ_I and σ_R values are very close.

In comparison with the series of compounds examined by *Fong*[3] on the basis of *Begtrup*'s[5,6] measurements it is necessary to realize the different character of the amino group from that of halogen substituents. The amino group is very mobile with nitrogen inversion also when hydrogen is substituted by an alkyl group. The free electron pair of the amino nitrogen is effectively included in the tetrazole ring

Table 3. *Differences in chemical shifts between the phenyl ring in tetrazoles* **1a-h** *and* **2h** *and the benzene chemical shift* (128.5 ppm)[a]

Compound	S.C.S.						
	ipso	*ortho*	*meta*	*para*	σ_R	σ_I	Φ[b] (deg)
1a	4.76	—4.60	1.64	1.19	—0.15	0.85	20.0
1b	4.70	—4.60	1.58	1.12	—0.14	0.82	25.0
1c	4.57	—4.79	1.45	1.41	—0.12	0.77	33.0
1d	4.70	—4.53	1.71	1.19	—0.16	0.88	14.0
1e	5.44	—4.92	1.25	0.73	—0.12	0.66	33.0
1f	4.89	—4.47	1.84	1.32	—0.17	0.95	0.0
1g	4.70	—4.53	1.58	1.06	—0.15	0.87	20.0
1h	4.77	—4.77	1.79	1.43	—0.16	0.93	14.0
2h	4.89	—3.49	2.23	2.15	—0.19	1.15	—

[a] See Equs. (1), (2), (3); S.C.S. *ipso* = $\delta_{C-1'} - 128.5$.
[b] **1f** was assumed as reference.

conjugation which may be seen from the C_5 chemical shift of the tetrazole nucleus (see Tables 1 and 2).

The possibility of aminotetrazole—iminotetrazoline tautomerism in some substituted 5-aminotetrazoles was the subject of intensive ^{1}H NMR studies[7–9]. In our previous work[2] the existence of both forms was supposed. In support of this idea ^{13}C NMR measurements were made. As we can see from Table 1 only single significant $C_{1''}$ and C_5 signals appear (also for series **2** single $C_{1'}$ and C_5 signals were observed). These data are conclusive and clearly show a strong preference for the amino species in solution.

The alternative explanation of the ^{1}H NMR spectra of 5-aminotetrazoles proposed by *Scott*[10] and *Katritzky*[11] consists in the role of the solvent used [*DMSO-d*$_6$ or $(CD_3)_2CO$] containing D_2O which exchanges the hydrogen of the amino group. ^{1}H NMR spectra of **1a**, **1d** and **1f** in $CDCl_3$ solution[12] promote our argumentation.

Conclusion

It is apparent that the ^{13}C NMR data presented here do not support the previously proposed tautomerism[2]. Tautomerism according to **I A**, **B** supposes the rupture of aromaticity in the tetrazole ring, which is energetically an unfavourable process. This conclusion is in agreement with published papers[10,11]. The σ_I and σ_R values calculated from equations (1) and (2) are good for characterization of electronic effects of substituents and for qualitative evaluation of interannular conjugation.

Experimental

The ^{13}C NMR spectra were measured in 10 mm o. d. tubes on a Jeol FX 100 NMR spectrometer at a frequency 25.04 MHz using 8 K data points. Spectral width was chosen 6000 Hz. The temperature of the probe was held constantly at 21 °C. Saturated solutions of each compound in $CDCl_3$ were used.

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