Scientific paper

Tautomerism of (3-Phenyl-allyl-) (5-pyridin-2-yl-[1,3,4]thiadiazol-2-yl) amine

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Abstract

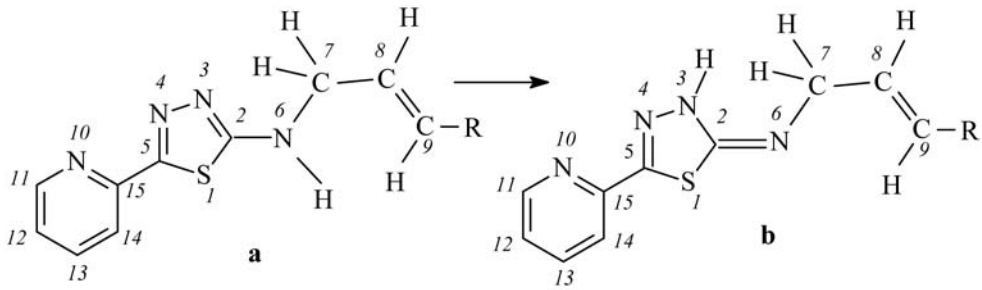
The radical and ionic structures of (3-phenyl-allyl-) (5-pyridin-2-yl-[1,3,4] thiadiazol-2-yl)-amine **2A(I)** ⟺ **2A(I)'** ⟺ **2A(I)'$_a$**, **2A(II)** ⟺ **2A(II)'** ⟺ **2A(II)'$_a$** have been determined by means of its ^{1}H (100 MHz, 500 MHz) ^{13}C and ^{15}N NMR spectra and B3LYP/6-31G** computations. The tautomeric equilibrium of **2A(I)'** ⇒ **2B'**, **2A(II)'** ⇒ **2C(II)'** has been observed in the ^{1}H NMR spectra (100 MHz)

Keywords: (3-phenyl-allyl-) (5-pyridin-2-yl-[1,3,4] thiadiazol-2-yl)-amine; electronic structure, tautomerism

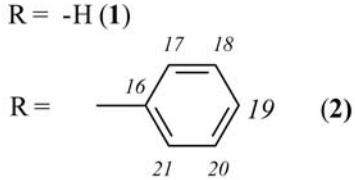
1. Introduction

(5-Pyridin-2-yl-[1,3,4] thiadiazol-2-yl)-amine bearing allyl-(**1**) and (3-phenyl-allyl-) (**2**) substituents, type **a** tautomer exist as ionic and radical forms due to the changes of the electronic structure of the endocyclic nitrogen atoms of 1,3,4-thiadiazole and pyridine rings (Figs 1–3)[1].

The XRD data confirm only one tautomer (**a-**type) in the crystals of both compounds **1** and **2**. In the solid state the *exo*-amino form **a** is stabilized by different H–bonds, and the differences in the total energy between **a** and **b** tautomers, are equal to –35.6 and –34.3 kJ/mol for **1** and **2**, respectively according to the DFT level of theory calculations[2]. The ^{1}H, ^{13}C–and ^{15}N NMR studies on the structure of allyl- (5-pyridin-2-yl-[1,3,4] thiadiazol-2-yl)-amine **1a** support the changes of the amine-type **a** nitrogen atom N-6 to pyridine-type **A** and pyrrole-type **A(I)**. Previous 100 MHz ^{1}H NMR investigations of **1** in the solution in the range from δ 8.665 to 7.233 of the chemical shift of N–H proton support the tautomeric equilibrium between allyl-(5-pyridin-2-yl-[1,3,4] thiadiazol-2-yl)-amine **1A 1A'**, 3H allyl- (5-pyridin-2 yl-[1,3,4] thiadiazol-2-ylidene)-amine **1B 1B'**



R = -H (**1**)



(**2**)

Fig 1: The tautomers **a** and **b** of allyl- (**1**) and (3-phenylallyl)-(**2**) (5-pyridin-2-yl-[1,3,4]thiadiazol-2-yl)-amine with atom numbering.

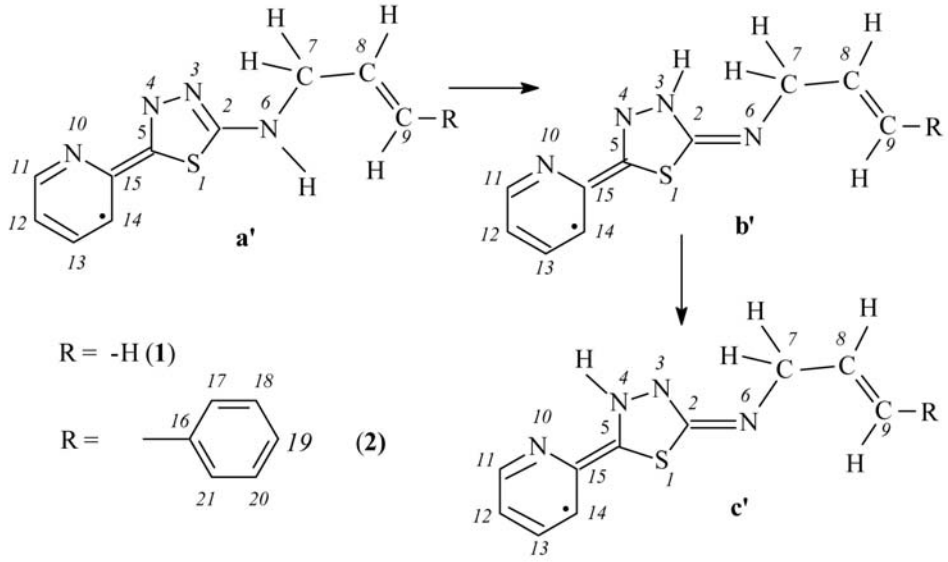


Fig 2: The tautomers **a'** and **b', c'** of allyl- (**1**) and (3-phenyl-allyl)- (**2**) (5-pyridin-2 -yl-[1,3,4]-thiadiazol-2-yl) -amine with atom numbering.

and 4H-allyl-(5-pyridin-2-yl-[1,3,4] thiadiazol-2-ylidene) amine **1C'**[1].

The intensities of the signals of N-H proton point to the interconvertions of the $\mathbf{1A'_5 \Rightarrow 1B_3 \Rightarrow 1C'_4}$ as well as to the balance of $\mathbf{1A'_7 \Rightarrow 1B'_7}$ and $\mathbf{1A'_7 \Rightarrow 1C'_7}$ tautomers and support pyridine-type nitrogen atoms N-10 N-4 N-6 and the amine-type nitrogen atoms N-4 N-3 of 1,3,4-thiadiazole ring[1], respectively.

The aim of the present paper was to describe the electronic structure of the nitrogen atoms of **2a** tautomer in the range from δ 13.64 to 7.233 of the chemical shifts of the N–H proton and its interconvertions to the imino forms in the solution in order to gain further insight into the structural features which determine biological activity. The 6-N and/or 5-substituted 2-amino[1,3,4]thiadiazole derivatives have exhibited activity against the leukemia, melanoma, lung carcinoma. They are also applied as the carbonic anhydrase inhibitors, and some of them show the antimycobacterial, anesthetic, antidepressant and anxiolytic activity[3–13]. The 2-amino-[1,3,4] thiadiazoles are used as herbicides[14], acting *via* inhibition of the imidazoleglycerol phosphate dehydrase, as well as the corrosion inhibitors[15]. The screening biological test of 3-phenyl-allyl- (5-substituted-[1,3,4] thiadiazol-2-yl)-amine has been performed under the auspices of the Developmental Therapeutics Program, Division of Cancer Treatment, National Cancer Institute, Bethesda, Maryland, USA. They have been tested against the P 388 Leukemia Tumor Test System (3PS31): Leukemia Screening Test Result (LSTR) Raport and Screening Data Summary (SDS) Raport. The presumptive activity has been confirmed by SDS Raport but they have been inactive at dose levels tested, LSTR Raport. They have been tested for in-vitro anti-HIV activity, they have been inactive.

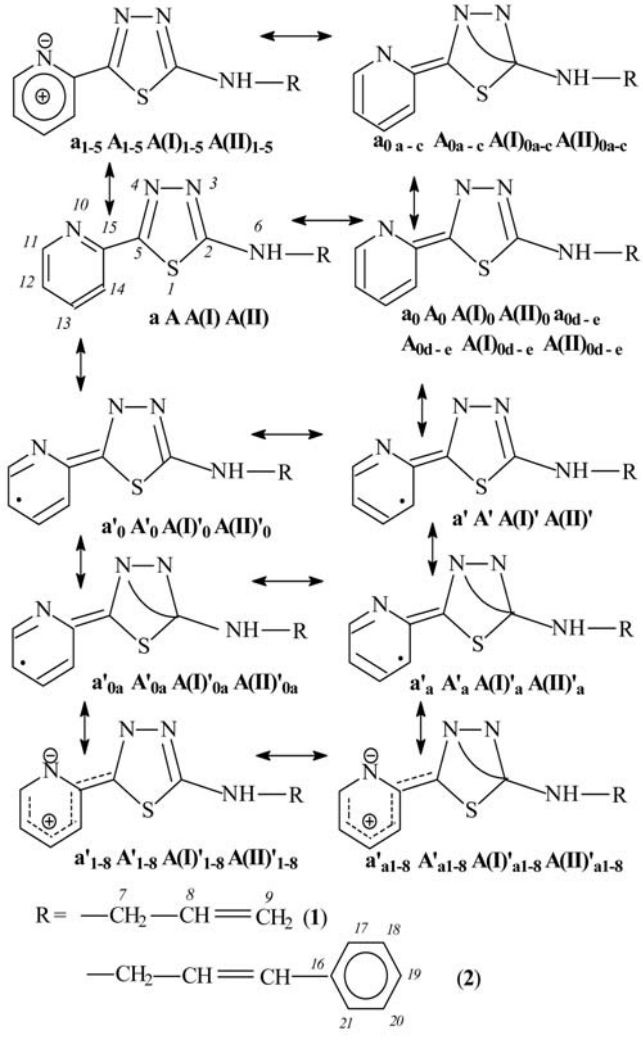


Fig 3: The resonance structures of allyl- (**1**) and (3-phenyl-allyl)- (**2**) (5-pyridin-2-yl)-[1,3,4]thiadiazol-2-yl)-amine

2. Experimental

2.1 General

The product **2** was prepared according to the published method[16] and its NMR spectra (^{1}H, ^{13}C, ^{15}N) were recorded under various conditions on Tesla BS 677 A and Bruker AM 500 spectrometers.

The ^{1}H NMR spectra 7–10 of product **2** were measured with Tesla BS 677 A spectrometer (100 MHz with T.F.) in $CDCl_3$ or DMSO solutions at room temperature with TMS as the internal standard. The ^{1}H (spectrum 8_6), ^{13}C and ^{15}N NMR measurements of **2** were taken in $CDCl_3$ and in DMSO-d_6 solutions, respectively on a Bruker AM 500 spectrometer, operating at 500.18 MHz for hydrogen, 125.76 MHz for carbon and 50.68 MHz for nitrogen, using standard conditions. The 2D spectra of ^{1}H ^{13}C HMQC, ^{1}H ^{13}C HMBC, ^{1}H ^{1}H COSY have been recorded in $CDCl_3$ solution at 500.18 MHz according to procedure given in Brucker programme library. Chemical shifts are given in δ scale.

The ^{1}H NMR spectra 8_{1-4} have been recorded, applaying various concentration of product **2** in a DMSO or $CDCl_3$ solution:

– in a DMSO solution, the concentration of product **2** amounts to (1:3) spectra 8_1 8_2, respectively
– in $CDCl_3$ solution, the concentration of product **2** amounts to: 9 mg/0.5 ccm, spectrum 8_3, 18 mg/0.5 ccm, spectrum 8_4.

The ^{1}H NMR spectra 7–10, 8_5, 8_6 have been recorded in a $CDCl_3$, 8_7 in DMSO–D_2O solutions without any determination of the concentration of **2** product.

The molecular geometries and properties corresponding to the local minima of the energy were calculated [2] at the DFT level of the theory with the B3LYP functional and the 6–31G** basis set.[17,18] The same basis set and functional were used for the ^{1}H, ^{13}C and ^{15}N NMR shielding constants calculations by applying the GIAO CPHF methods. The atomic charges were taken from the ESP fit using Breneman model (CHELPG). The Gaussian 98 package[19] was employed for these calculations.

3. Results and Discussion

The calculated chemical shifts of the nitrogen atoms ^{15}N for type **a** and type **b** tautomers of allyl- (**1**) (3-phenyl-allyl-) (**2**) (5-pyridin-2-yl-[1,3,4] thiadiazol-2-yl)-amine occur in different ranges: from about δ - 309 to about –23 for type **a** tautomer and from about δ - 225 to about –80 for **b** - one (Table 1, Fig. 4).[2]

The amino N-6 atom is strongly shielded in **1** (about δ - 308) but in **2** the shielding decreases of a few ppm (to about δ - 304). The shielding constants for the N-3 and N-10 atom in the 1,3,4-thiadiazole and pyridine rings, respectively are almost equal whereas N-4 atom is much less shielded.[2]

Table 1: Calculated ^{15}N- and ^{1}H-NMR chemical shifts δ [ppm] of type **a** and **b** tautomers

Comp.	^{15}N		^{1}H	
1a 2a	–309 – –23			
1a	N6	–131.57	H14	8.125
	N3	–77.78		
2a	N10	–86.0	H6	7.5
	N10	–72.36	H6	6.45
	N6	–133.98		
1b 2b	–225 – –80			

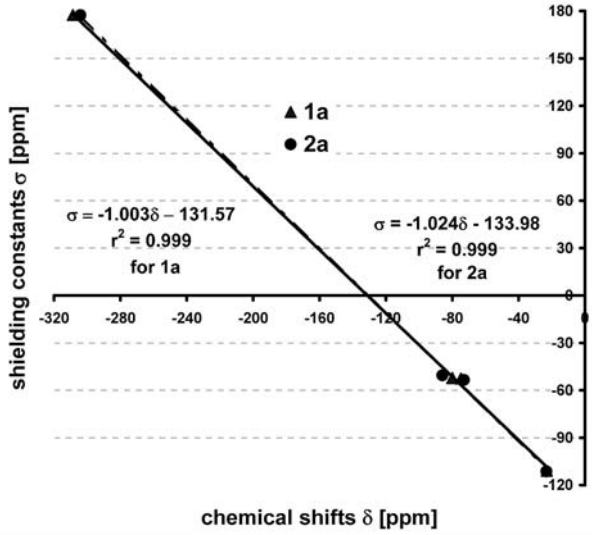


Fig 4: The linear regression of shielding constants σ [ppm] versus chemical shifts δ [ppm] for **1a** and **2a**

In the ^{1}H NMR spectra of **2** the nitrogen atom N-6 appear as amine-type **a**, pyridine-type **A**, pyrrole-type **A(I)** and in sp hybridization **A(II)** tautomers (Figs 1–3). The calculated chemical shift value for the proton of N–H group at δ 6.45 (Table 1) [2] points to the amino proton of **2a** tautomer slightly shifted by the weak intermolecular interactions of the solut-solvent type. The signal of the nitrogen atom ^{15} N appears at δ - 304.07. The calculated chemical shift of N-6 at δ - 133.98 (Table 1)[2] supports pyridine-type nitrogen, **2A** tautomer. The calculated chemical shift of N–H proton at δ 7.5 (Table 1)[2] supports sp^2 or sp hybridization of N-6, **2A, 2A(I), 2A(II)** tautomers and the lack of the charges over 1,3,4-thiadiazole ring.

The coupling constants $J(H_7H_8)$ 6.2 Hz (500 MHz),[2] $J(H_8H_{9B})$ 15.8 Hz, $J(H_{9B}H_8)$ 15.8 Hz, $J(H_8H_{9A})$ 12.6 Hz, $J(H_{9A}H_8)$ 12.6 Hz (100 MHz)[20] confirm pyrrole-type nitrogen atom N-6, **2A(I)** tautomer whereas $J(H_{7D}H_{7C})$ 1.4 Hz (500 MHz),[2] $J(H_8H_{9B})$ 15.9 Hz, $J(H_{9B}H_8)$ 15.9 Hz (500 MHz, 100 MHz),[2,20] $J(H_8H_{9A})$ 13.1 Hz, $J(H_{9A}H_8)$ 13.1 Hz (100 MHz)[20] the sp hybridization of N-6, 2**A(II)** tautomer. The coupling constants $J(H_{7C}H_8)$ 5.9 Hz, $J(H_{7D}H_8)$ 5.7 Hz and $J(H_{7C}H_8)$ 9.5 Hz, $J(H_{7D}H_8)$ 9.2 Hz (100 MHz)[20]

support the transformation of $sp^2 \Longleftrightarrow sp$ hybridization of N-6 of the rigid structures**.**

The ^{13}C NMR resonances of 3-phenyl-allyl radical C-9 at δ 133.52, C-8 at δ 123.83, C-7 at δ 49.07 and of the benzene C atoms C-16 at δ 136.20, C-19 at δ 127.97, C-18, C-20 at δ 128.60 as well as the chemical shift of the proton of phenyl group of 3-phenyl-allyl substituent H-19 at δ 7.192 (mult.)[2] confirm the positively charged cinnamyl cation. The signals of H-17, H-21 at δ 7.314 (d) and C-17, C-21 at δ 126.56 support the conjugated bonds of cinnamyl substituent. The resonances of H-18, H-20 arise at δ 7.239 (td).

The calculated signal of H-14 at δ 8.125 (Table 1) [2] as well as the ^1H ^1H coupling constants $J(H_{12}H_{14})$ 1.0 Hz, $J(H_{11}H_{14})$ 0.5 Hz of **1a** tautomer[2] confirm the absence of the charges on the pyridine ring. The calculated chemical shift of N-3 at δ - 77.78 (Table 1)[2] confirm pyridine-type nitrogen atom of **1a** tautomer and the lack of the differences in the spin states of electrons of 2p orbitals of N-3 C-2. The calculated chemical shift of N-10 at δ - 86.0 of **2a** tautomer (Table 1) [2] point to the amine-type nitrogen atom.

The ^1H ^{13}C HMQC correlation spectra of **2** show a correlation signal between H-14 at δ 8.290 and C15 at δ 149.7. The above data prove the diradical resonance structures $\mathbf{a_{0c}\ A(I)_{0c}\ A(II)_{0c}}$, $\mathbf{a_{0e}\ A(I)_{0e}\ A(II)_{0e}}$ (Fig 3) and the lack of the charges over pyridine and 1,3,4-thiadiazole rings. Pyridyl H-14 proton of the diradical resonance structures $\mathbf{a_{0c}\ A(I)_{0c}\ A(II)_{0c}}$, $\mathbf{a_{0e}\ A(I)_{0e}\ A(II)_{0e}}$ is more intensly deshielded about 0.15 ppm in relation to the structure **a A(I) A(II)**. The spectroscopic data support the conjugation of aromatic π electrons of pyridyl substituent with π electrons of double C = N bond of 1, 3, 4 thiadiazole ring in solution.

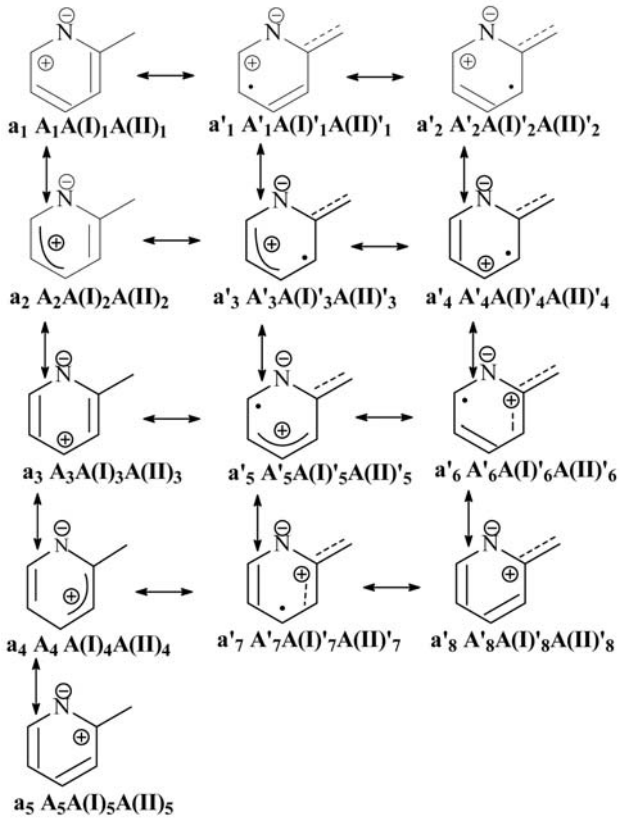


Fig. 5: The resonance structures of the pyridyl substituent

Table 2: ^1H NMR chemical shifts δ [ppm] from TMS of **2.**

Spectrum No	H 7	H 8 H 9	Benzene H atoms	Pyridin – 2- yl
8_1 (DMSO)	4.218 – 4.115 2H m	6.771 – 6.248 2H m	7.522 – 7.224 5H m	8.635 – 8.560 1H H11 8.142 – 8.037 1H H13 H14 8.003 – 7.835 1H H12 H13 7.522 – 7.224 1H H14 H12
8_2 (DMSO)	4.242 – 4.147 2H m	6.788 – 6.265 2H m	7.530 – 7.232 5H m	8.650 – 8.574 1H H11 8.169 – 8.067 1H H13 H14 8.010 – 7.842 1H H12 H13 7.530 – 7.232 1H H14 H12
8_3 ($CDCl_3$)	4.232 – 4.161 2H m	6.805 – 6.168 2H m	7.527 – 7.193 5H m	8.591 – 8.513 1H H11 8.213 – 8.110 1H H13 H14 7.830 – 7.659 1H H12 H13 7.527 – 7.193 1H H14 H12
8_4 ($CDCl_3$)	4.215 – 4.147 2H m	6.785 – 6.165 2H m	7.447 – 7.129 5H m	8.574 – 8.499 1H H11 8.179 – 8.076 1H H13 H14 7.798 – 7.627 1H H12 H13 7.447 – 7.129 1H H14 H12
8_7 (DMSO + D_2O)	4.220 – 4.169 2H m	6.785 – 6.251 2,4H m	7.527 – 7.207 5H m	8.650 – 8.577 1H H11 8.164 – 8.089 1H H13 H14 8.032 – 7.864 1H H12 H13 7.527 – 7.207 1.4H H14 H12

The signals of the N-H proton and the pyridyl substituent in the ^{1}H NMR spectra (100 MHz) support the **a A(I) A(II), a_{1-5} $A(I)_{1-5}$ $A(II)_{1-5}$** and radical resonance structures **a' A(I)' A(II)' a'_{1-8} $A(I)'_{1-8}$ $A(II)'_{1-8}$ a'_0 $A(I)'_0$ $A(II)'_0$** (Figs 1–3, 5, Tables 2–10).

In the ^{1}H NMR spectra of **2** (100 MHz) in the range from δ 8.650 to δ 7.233 of the chemical shifts of N–H proton, the nitrogen atoms N-3 N-4 N-10 appear as pyridine-type, pyrrole-type and amine-type nitrogen while N-6 as pyrrole-type, structures **$A(I)$ $A(I)'A(I)_0$** or in sp hybridization, structures **$A(II)$ $A(II)'A(II)_0$** (Fig 3).

The absence of the charges over 1,3,4 thiadiazole ring confirm the lack of the transition of electrons of p orbitals of 1S 2C 3N 4N 5C of 1,3,4-thiadiazole ring. The changes of the electronic structure of the nitrogen atoms N-3 N-4 N-10 (Fig. 3) have been described previously[1]. The ^{1}H ^{1}H long-range coupling constants in the 37.376 Hz - 43.520 Hz range (spectra 7–10)[20] (Table 8), support the coupling of the protons of the pyridyl and –N–CH_2–CH=CH–C_6H_5 groups *via* 2p orbitals of C-14 C-7 of the rigid structures **$A(II)'A(II)'_a$** and sp hybridization of the exocyclic nitrogen atom N-6 (Fig. 6).

In the 2D ^{1}H ^{13}C HMQC correlation spectra the signals of H-11 at δ 8.490 and H-14 at δ 8.080 [2] exhibit a correlation to C-12, C-8 at δ 123.8. The 2D ^{1}H ^{13}C HMQC correlation spectra show the cross-peaks of H-9A at δ 6.600, H-9B at δ 6.650 as well as the correlation signals of H-8A at δ 6.220, H-8B at δ 6.250 to C-16, C-13 at δ 136.2. Such long-range couplings can be observed if the bonds assume the planar configuration. In the 2D ^{1}H ^{13}C HMQC correlation spectra the correlation signals of H-7 at δ 4.15 to C-8, C-12 at δ 123.8, C-16, C-13 at δ 136.2, C-2 at δ 171.5 support the planar structure.

In the 2D ^{1}H ^{13}C HMBC correlation spectra the cross-peak of H-7 at δ 4.100 to C7 at δ 49.00 is observed. In the 2D ^{1}H ^{13}C HMQC correlation spectra the signals of H-6 at δ 4.200 and δ 4.000 exhibit a correlation to C-7 at δ 49.1 and support **a** tautomer. The signals at δ 0.498-4.266 (Table 8, spectra 10, 7) support the transformation of sp ↔ sp.[3]

The differences in the resonances of N–H proton in the range from δ 8.650 to 7.233 are caused by the atomic charge over the pyridine ring.

To assigne the resonance structures of **2** in the range from δ 8.650 to δ 7.233 of the chemical shifts of N–H proton, the ^{13}C, ^{15}N and ^{1}H resonances line in ^{13}C, ^{15}N and ^{1}H NMR spectra (100 MHz, 500 MHz) of **2** and the coupling constants of the pyridyl substituent have been analyzed.

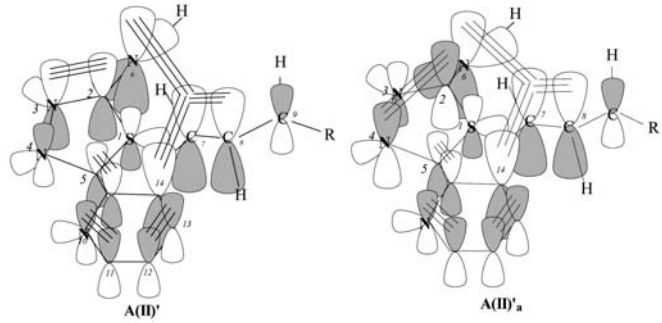


Fig 6: The resonance rigid structures **A(II)'**, **$A(II)'_a$** of (3-phenyl-allyl)- (5-pyridin-2-yl-[1,3,4] thiadiazol-2-yl)-amine

Table 3: The ^{1}H NMR chemical shifts δ [ppm] from TMS of **2**.

Spectrum No	H 7	H 8 H 9	Benzene H atoms	Pyridin – 2- yl
7($CDCl_3$)	4.266 – 4.210 2H	6.430 – 6.153 1H 6.815 – 6.660 1H	7.444 – 7.242 5H	8.580 – 8.533 1H H11 8.176 – 8.096 1H H13 H14 7.890 – 7.674 1H H12 H13 7.444 – 7.242 1H H14 H12
8($CDCl_3$)	4.224 – 4.163 2H	6.416 – 6.144 1H 6.782 - 6.622 1H	7.430 – 7.190 5H	8.547 – 8.500 1H H11 8.143 – 8.063 1H H13 H14 7.796 – 7.627 1H H12 H13 7.430 – 7.190 1H H14 H12
8_5 ($CDCl_3$)	4.2 2H	6.72 – 6.12 2H	7.280 5H	8.48 1H H11 8.08 1H H13 H14 7.64 1H H12 H13 7.28 1H H14 H12
9 ($CDCl_3$)	4.252 – 4.182 2H	6.801 – 6.641 1H 6.421 – 6.144 1H	7.448 – 7.209 5H	8.570 – 8.519 1H H11 8.162 – 8.082 1H H13 H14 7.829 – 7.655 1H H12 H13 7.448 – 7.209 1H H14 H12
10 ($CDCl_3$)	4.257 – 4.196 2H	6.646 – 6.134 2H	7.448 – 7.233 5H	8.570 – 8.523 1H H11 8.162 – 8.082 1H H13 H14 7.838 – 7.669 1H H12 H13 7.448 – 7.233 1H H14 H12

Table 4. The ^{1}H-NMR chemical shifts δ [ppm] from TMS of **2**.

Spectrum No		**Pyridin–2- yl**	
Solvent	**H 14**–of the structures	**H 14, H 13**	**H 13–**of the structures
8_3($CDCl_3$)	**$a'_4A(I)'_4A(II)'_4 \leftrightarrow a'_8A(I)'_8A(II)'_8 \leftrightarrow a'_0A(I)'_0\ A(II)'_0$**	8.213–8.110	**$a_4A(I)_4A(II)_4 \leftrightarrow a'_8A(I)'_8A(II)'_8 \leftrightarrow a'_5A(I)'_5A(II)'_5 \leftrightarrow a\ A(I)\ A(II)$**
7($CDCl_3$)	**$a'_4A(I)'_4A(II)'_4 \leftrightarrow a'_3A(I)'_3A(II)'_3 \leftrightarrow a'_0A(I)'_0\ A(II)'_0$**	8.176–8.096	**$a_4A(I)_4A(II)_4 \leftrightarrow a'_5A(I)'_5\ A(II)'_5 \leftrightarrow a'A(I)'A(II)'$**
8_7(DMSO +D_2O)	**$a'_4A(I)'_4A(II)'_4 \leftrightarrow a'_2A(I)'_2A(II)'_2 \leftrightarrow a'_0\ A(I)'_0\ A(II)'_0$**	8.164–8.089	**$a_2A(I)_2A(II)_2 \leftrightarrow a_4A(I)_4A(II)_4 \leftrightarrow a_3A(I)_3A(II)_3 \leftrightarrow a'A(I)'\ A(II)'$**
9, 10 ($CDCl_3$)	**$a'_2A(I)'_2A(II)'_2 \leftrightarrow a'_4A(I)'_4A(II)'_4$**	8.162–8.082	**$a_2A(I)_2A(II)_2 \leftrightarrow a_3A(I)_3A(II)_3 \leftrightarrow a_4A(I)_4\ A(II)_4$**
8_4($CDCl_3$)	**$a'_4A(I)'_4A(II)'_4 \leftrightarrow a'_8A(I)'_8A(II)'_8$**	8.179–8.076	**$a_4A(I)_4A(II)_4 \leftrightarrow a_2A(I)_2A(II)_2 \leftrightarrow a'_3A(I)'_3A(II)'_3 \leftrightarrow a'_5A(I)'_5\ A(II)'_5$**
8_2(DMSO)	**$a'_4A(I)'_4A(II)'_4 \leftrightarrow a'_3A(I)'_3A(II)'_3$**	8.169–8.067	**$a_2A(I)_2A(II)_2 \leftrightarrow a'_3A(I)'_3A(II)'_3$**
8($CDCl_3$)	**$a'_5A(I)'_5A(II)'_5 \leftrightarrow a'_3A(I)'_3A(II)'_3$**	8.143–8.063	**$a_3A(I)_3\ A(II)_3 \leftrightarrow a'_3\ A(I)'_3\ A(II)'_3$**
8_1(DMSO)	**$a'_5A(I)'_5A(II)'_5 \leftrightarrow a'_4A(I)'_4A(II)'_4 \leftrightarrow a'_0A(I)'_0\ A(II)'_0$**	8.142–8.037	**$a_3A(I)_3A(II)_3 \leftrightarrow a'_4A(I)'_4A(II)'_4$**

Table 5. The ^{1}H-NMR chemical shifts δ [ppm] from TMS of **2**.

Spectrum No		**Pyridin–2- yl**	
Solvent	**H 13–**of the structures	**H 13, H 12**	**H 12–**of the structures
8_7(DMSO-D_2O)	**$a_2A(I)_2A(II)_2 \leftrightarrow a_4A(I)_4A(II)_4 \leftrightarrow a'_7A(I)'_7A(II)'_7 \leftrightarrow a'_3A(I)'_3A(II)'_3$**	8.032–7.864	**$a_5A(I)_5A(II)_5 \leftrightarrow a'_8A(I)'_8A(II)'_8 \leftrightarrow a'_6A(I)'_6\ A(II)'_6 \leftrightarrow a\ A(I)\ A(II)$**
8_2(DMSO)	**$a_2A(I)_2A(II)_2 \leftrightarrow a'_3A(I)'_3A(II)'_3$**	8.010–7.842	**$a_4A(I)_4A(II)_4 \leftrightarrow a'_8A(I)'_8A(II)'_8 \leftrightarrow a'_6A(I)'_6\ A(II)'_6$**
8_1(DMSO)	**$a_4A(I)_4A(II)_4 \leftrightarrow a'_5A(I)'_5A(II)'_5$**	8.003–7.835	**$a_4A(I)_4A(II)_4 \leftrightarrow a_1A(I)_1A(II)_1 \leftrightarrow aA(I)\ A(II)$**
7($CDCl_3$)	**$a'_3A(I)'_3A(II)'_3 \leftrightarrow a'_5A(I)'_5A(II)'_5 \leftrightarrow a'_4A(I)'_4A(II)'_4 \leftrightarrow aA\ (I)\ A(II)$**	7.890–7.674	**$a'_6A(I)'_6A(II)'_6 \leftrightarrow a'_7A(I)'_7A(II)'_7 \leftrightarrow a'_4A(I)'_4A(II)'_4$**
10($CDCl_3$)	**$a'_5A(I)'_5A(II)'_5 \leftrightarrow a'_4A(I)'_4A(II)'_4 \leftrightarrow a'_0A(I)'_0\ A(II)'_0$**	7.838–7.669	**$a'_6A(I)'_6A(II)'_6 \leftrightarrow a'_1A(I)'_1A(II)'_1 \leftrightarrow a'_0A(I)'_0\ A(II)'_0$**
8_3($CDCl_3$)	**$a_3A(I)_3A(II)_3 \leftrightarrow a'_5A(I)'_5A(II)'_5 \leftrightarrow a'A(I)'A(II)'$**	7.830–7.659	**$a'_2A(I)'_2A(II)'_2 \leftrightarrow a'_1A(I)'_1A(II)'_1$**
9($CDCl_3$)	**$a_3A(I)_3A(II)_3 \leftrightarrow a'_4A(I)'_4A(II)'_4 \leftrightarrow a'A\ (I)'A(II)'$**	7.829–7.655	**$a_2A(I)_2A(II)_2 \leftrightarrow a'_5A(I)'_5\ A(II)'_5$**
8_4,8($CDCl_3$)	**$a_3A(I)_3\ A(II)_3 \leftrightarrow a'_4\ A(I)'_4\ A(II)'_4$**	7.798–7.627	**$a'_5A(I)'_5A(II)'_5 \leftrightarrow a'_3A(I)'_3A(II)'_3$**

Table 6. The ^{1}H-NMR chemical shifts δ [ppm] from TMS of **2**.

Spectrum No		**Pyridin–2- yl**	
Solvent	**H 12–**of the structures	**H 12, H 14**	**H 14–**of the structures
8_2(DMSO)	**$a_4A(I)_4A(II)_4 \leftrightarrow a_2A(I)_2A(II)_2 \leftrightarrow aA(I)\ A(II)$**	7.530– 7.232	**$a_1A(I)_1A(II)_1 \leftrightarrow a'_2A(I)'_2A(II)'_2 \leftrightarrow a'A(I)'A(II)'$**
8_7(DMSO–D_2O)	**$a_4A(I)_4A(II)_4 \leftrightarrow a'_1A(I)'_1\ A(II)'_1$**	7.527–7.207	**$a_2A(I)_2A(II)_2 \leftrightarrow a'_1A(I)'_1\ A(II)'_1 \leftrightarrow a'_5\ A(I)'_5\ A(II)'_5$**
8_1(DMSO)	**$a_4A(I)_4A(II)_4 \leftrightarrow a'_2A(I)'_2A(II)'_2 \leftrightarrow a'A(I)'\ A(II)'$**	7.522–7.224	**$a_2A(I)_2A(II)_2 \leftrightarrow a'_2A(I)'_2A(II)'_2$**
8_3($CDCl_3$)	**$a_4A(I)_4A(II)_4 \leftrightarrow a'_5A(I)'_5\ A(II)'_5$**	7.527–7.193	**$a_2A(I)_2A(II)_2 \leftrightarrow a'_1A(I)'_1A(II)'_1 \leftrightarrow a'_6A(I)'_6\ A(II)'_6$**
10($CDCl_3$)	**$a'_6A(I)'_6A(II)'_6 \leftrightarrow a'_7A(I)'_7A(II)'_7 \leftrightarrow a_4A(I)_4\ A(II)_4 \leftrightarrow aA(I)\ A(II)$**	7.448–7.233	**$a_5A(I)_5A(II)_5 \leftrightarrow a_3A(I)_3A(II)_3 \leftrightarrow a'_2A(I)'_2A(II)'_2 \leftrightarrow aA(I)A(II)$**
9($CDCl_3$)	**$a'_6A(I)'_6A(II)'_6 \leftrightarrow a'_1A(I)'_1A(II)'_1 \leftrightarrow a'_0A(I)'_0\ A(II)'_0$**	7.448–7.209	**$a_5A(I)_5A(II)_5 \leftrightarrow a_3A(I)_3A(II)_3 \leftrightarrow a'_1A(I)'_1\ A(II)'_1$**
7($CDCl_3$)	**$a'_6A(I)'_6A(II)'_6 \leftrightarrow a'_5A(I)'_5A(II)'_5 \leftrightarrow a'_8\ A(I)'_8\ A(II)'_8$**	7.444–7.242	**$a_3A(I)_3A(II)_3 \leftrightarrow a'_8A(I)'_8A(II)'_8 \leftrightarrow a'_0A(I)'_0\ A(II)'_0$**
8_4($CDCl_3$)	**$a'_6A(I)'_6A(II)'_6 \leftrightarrow a'_4A(I)'_4A(II)'_4 \leftrightarrow a'_3A(I)'_3\ A(II)'_3$**	7.447–7.129	**$a_3A(I)_3A(II)_3 \leftrightarrow a'_4A(I)'_4A(II)'_4 \leftrightarrow a'_7A(I)'_7\ A(II)'_7$**
8($CDCl_3$)	**$a'_6A(I)'_6A(II)'_6 \leftrightarrow a'_5A(I)'_5A(II)'_5$**	7.430–7.190	**$a_4A(I)_4A(II)_4 \leftrightarrow a'_4A(I)'_4A(II)'_4$**

Table 7. The ^{1}H-NMR chemical shifts δ [ppm] from TMS of **2**.

Spectrum No **Solvent**	H 11	**Pyridin–2- yl** structures
8_7(DMSO-D_2O)	8.650–8.577	**$a_5A(I)_5A(II)_5 \leftrightarrow a'_8A(I)'_8A(II)'_8 \leftrightarrow a'_4A(I)'_4A(II)'_4 \leftrightarrow a'A(I)'A(II)'$**
8_2(DMSO)	8.650–8.574	**$a_5A(I)_5A(II)_5 \leftrightarrow a'_8A(I)'_8A(II)'_8 \leftrightarrow a'_4A(I)'_4A(II)'_4 \leftrightarrow a'_0A(I)'_0 A(II)'_0$**
8_1(DMSO)	8.635 - 8.560	**$a_4A(I)_4A(II)_4 \leftrightarrow a'_4A(I)'_4 A(II)'_4 \leftrightarrow a'_6A(I)'_6 A(II)'_6$**
8_3($CDCl_3$)	8.591–8.513	**$a_2A(I)_2A(II)_2 \leftrightarrow a'_4A(I)'_4 A(II)'_4 \leftrightarrow a'_3A(I)'_3 A(II)'_3$**
7($CDCl_3$)	8.580 - 8.533	**$a'_4A(I)'_4A(II)'_4 \leftrightarrow a'_2A(I)'_2A(II)'_2 \leftrightarrow a'_8A(I)'_8A(II)'_8 \leftrightarrow aA (I) A(II)$**
8_4($CDCl_3$)	8.574–8.499	**$a'_3A(I)'_3 A(II)'_3 \leftrightarrow a'_1A(I)'_1 A(II)'_1$**
10($CDCl_3$)	8.570–8.523	**$a_2A(I)_2A(II)_2 \leftrightarrow a'_2A(I)'_2 A(II)'_2 \leftrightarrow a'A(I)' A(II)'$**
9($CDCl_3$)	8.570–8.519	**$a_2A(I)_2 A(II)_2 \leftrightarrow a'_3A(I)'_3 A(II)'_3 \leftrightarrow a'_0 A(I)'_0 A(II)'_0$**
8($CDCl_3$)	8.547–8.500	**$a'_5A(I)'_5 A(II)'_5 \leftrightarrow a'_2A(I)'_2 A(II)'_2$**

Table 8: The ^{1}H^{1}H long – range coupling constants [Hz] of 2

Spectrum No ($CDCl_3$)	**δ**	***J***	**NH**
10	0.498	$J(H_6H_{11})$ 38.400 Hz	0.279 H
7	4.210	$J(H_{7C}H_{14})$ 43.008 Hz	0.7 H
7	4.257	$J(H_{7C}H_{12})$ 43.264 Hz	
7	4.266	$J(H_{7D}H_{13})$ 41.472 Hz	
9	6.641	$J(H_{9A}H_{13})$ 37.376 Hz	0.272 H
9	8.082	$J(H_{13}H_{9A})$ 37.632 Hz	0.628 H
8	7.190	$J(H_{14}H_{9A})$ 38.784 Hz	3.08 H
8	7.369	$J(H_{14}H_{9B})$ 42.624 Hz	
10	8.523	$J(H_{11}H_{9A})$ 38.912 Hz	0,107 H
8	8.063	$J(H_{13}H_{9B})$ 42.496 Hz	0.742 H
8	7.702	$J(H_{12}H_{7C})$ 43.392 Hz	3.425 H
7	7.242	$J(H_{14}H_{9B})$ 43.520 Hz	2 H
9	7.228	$J(H_{14}H_{9B})$ 43.520 Hz	1.965 H

Table 9: The ^{1}H NMR chemical shifts δ [ppm] from TMS of NH proton of **2A(I), 2A(II)** tautomers

Spectrum No Solvent	**δ**	**NH**	**Structure**
8_5 ($CDCl_3$)	13.64	(s)	**2A(I) 2A(I)'**
8_2 (DMSO)	8.650 – 8.574	0.08 H	**2A(II) 2A (II)'**
8_1 (DMSO)	8.635 – 8.560	0.4 H	
10 ($CDCl_3$)	8.570 – 8.523	0.107 H	**$2A(I)_1$ $2A(II)_1$**
9 ($CDCl_3$)	8.570 – 8.519	0.236 H	**$2A(I)_2$ $2A(II)_2$**
8 ($CDCl_3$)	8.547 – 8.500	0.61 H	
8_5 ($CDCl_3$)	8.48	0.25 H	
8_1 (DMSO)	8.435 – 8.345	1.08 H	**$2A(I)_3$ $2A(II)_3$**
8_2 (DMSO)	8.411 – 8,306	1.5 H (t)	**$2A(I)_4$ $2A(II)_4$**

Table 10: The ^{1}H NMR chemical shifts δ [ppm] from TMS of NH proton of **2A(I)', 2A(II)'** tautomers

Spectrum No Solvent	**δ**	**NH**	**Structure**
7 ($CDCl_3$)	8.176 – 8.096	0.04 H	
9 ($CDCl_3$)	8.162 – 8.082	0.628 H	**$2A(I)_5$ $2A(II)_5$**
10 ($CDCl_3$)	8.162 – 8.082	0.358 H	**$2A(I)'_1$ $2A(II)'_1$**
8 ($CDCl_3$)	8.143 – 8.063	0.742 H	**$2A(I)'_2$ $2A(II)'_2$**
8_5 ($CDCl_3$)	8.08	0.5 H	**$2A(I)'_3$ $2A(II)'_3$**
8_1 (DMSO)	8.003 – 7.835	0.6 H	
7 ($CDCl_3$)	7.890 – 7.674	2H	
10 ($CDCl_3$)	7.838 – 7.669	2H	
8_3 ($CDCl_3$)	7.830 – 7.659	0.15 H	
9 ($CDCl_3$)	7.829 – 7.655	2H	
8 ($CDCl_3$)	7.796 – 7.627	3.425 H	
8_6 ($CDCl_3$)	7.683 – 7.680	0.089 H	
8_5 ($CDCl_3$)	7.64	2.5 H	
8_2 (DMSO)	7.530 – 7.232	0.4	**$2A(I)'_4$ $2A(II)'_4$**
8_1 (DMSO)	7.522 – 7.224	2.5 H	**$2A(I)'_5$ $2A(II)'_5$**
8_3 ($CDCl_3$)	7.527 – 7.193	0.7 H	**$2A(I)'_6$ $2A(II)'_6$**
10 ($CDCl_3$)	7.448 – 7.233	1.721H	
9 ($CDCl_3$)	7.448 – 7.209	1.965 H	**$2A(I)'_5$ $2A(II)'_5$**
7 ($CDCl_3$)	7.444 – 7.242	2H	**$2A(I)'_6$ $2A(II)'_6$**
8 ($CDCl_3$)	7.430 – 7.190	3.08 H	**$2A(I)'_7$ $2A(II)'_7$**
8_4 ($CDCl_3$)	7.447 – 7.129	0.5 H	
8_6 ($CDCl_3$)	7.323 – 7.306	0.165 H	
8_5 ($CDCl_3$)	7.280	2 H	
8_6 ($CDCl_3$)	7.252 – 7.174	0.457 H	

The resonance structures of the pyridine ring are shown on Fig. 5.

In the ^{13}C NMR spectrum of **2** the chemical shifts of C-11 at δ 149.33 and C-15 at δ 149.76 [2] confirm pyridine-type nitrogen atom N-10, the structures **a_1 $A(I)_1$ $A(II)_1$**, **$a'_1A(I)'_1$ $A(II)'_1$**, **a'_2 $A(I)'_2$ $A(II)'_2$** and **a_5 $A(I)_5$ $A(II)_5$** respectively**.**

The chemical shift of C-12 at δ 124.12 [2] of **2** support the pyridine-type nitrogen atom N-10 of the structures **a_2 $A(I)_2$ $A(II)_2$, a'_3 $A(I)'_3$ $A(II)'_3$, $a'_5A(I)'_5$ $A(II)'_5$**. The signal of C-14 at δ 119.89 [2] point to the structures **a_3 $A(I)_3$ $A(II)_3$, a'_4 $A(I)'_4$ $A(II)'_4$, a_5 $A(I)_5$ $A(II)_5$**. The signal of C-13 at δ 136.80 [2] confirms the structures **a_2 $A(I)_2$ $A(II)_2$, a_3 $A(I)_3$ $A(II)_3$, a'_3 $A(I)'_3$ $A(II)'_3$, a_4 $A(I)_4$ $A(II)_4$, a'_4 $A(I)'_4$ $A(II)'_4$, a'_5 $A(I)'_5$ $A(II)'_5$**.The chemical shift of N-10 in ^{15}N NMR spectrum of **1** at δ - 74.78 supports the structures **a_2 A_2 $A(I)_2$ $A(II)_2$, a'_3 A'_3 $A(I)'_3$ $A(II)'_3$, a_4 A_4 $A(I)_4$ $A(II)_4$, a'_{5-8} A'_{5-8} $A(I)'_{5-8}$ $A(II)'_{5-8}$**.The calculated chemical shift of N-10 of **2** at δ - 72.36 (Table 1) [2] confirms the structures **a_1 $A(I)_1$ $A(II)_1$, a'_1 $A(I)'_1$ $A(II)'_1$, a'_2 $A(I)'_2$ $A(II)'_2$, a_3 $A(I)_3$ $A(II)_3$, a'_4 $A(I)'_4$ $A(II)'_4$, a_5 $A(I)_5$ $A(II)_5$**. The ^{1}H NMR spectrum 8_6 (500 MHz) shows a signal of H-14 at δ 8.087 of the structures **a_3 $A(I)_3$ $A(II)_3$, a'_8 $A(I)'_8$ $A(II)'_8$.**

In the ^{1}H ^{13}C HMBC and HMQC correlation spectra the signal of H-14 at δ 8.080[2] exhibits a correlation to C-14 at δ 119.9 and C-12, C-8 at δ 123.8, C-15 at δ 149.7, C-5 at δ 160.0, respectively and confirms **a'$_5$ A(I)'$_5$ A(II)'$_5$**. In the 2D ^{1}H ^{13}C HMQC correlation spectra the cross-peak between H-14 at δ 7.500 and C-13 at δ 136.8 support the resonance structures **a$_3$ A(I)$_3$ A(II)$_3$ ↔ a'$_5$ A(I)'$_5$ A(II)'$_5$**. The cross-peak between H-14 at δ 7.200 and C-13, C-16 at δ 136.2 support the resonance structures **a'$_8$ A(I)'$_8$ A(II)'$_8$**.

In the ^{1}H ^{13}C HMBC and HMQC correlation spectra the signal of H-13 at δ 7.690 exhibits a correlation to C-13 at δ 136.8 and C-14 at δ 119.9, C-15 at δ 149.7, C-5 at δ 160.0, respectively and confirms **a'$_3$ A(I)'$_3$ A(II)'$_3$ ↔ a$_2$ A(I)$_2$ A(II)$_2$** and **a$_3$ A(I)$_3$ A(II)$_3$ ↔ a$_4$ A(I)$_4$ A(II)$_4$↔ a'$_4$ A(I)'$_4$ A(II)'$_4$** resonance structures.

In the 2D ^{1}H ^{13}C HMQC correlation spectra the cross-peaks between H-13 at δ 8.220, 8.200 and C-14 at δ 119.9 support the resonance structures **a'$_1$ A(I)'$_1$ A(II)'$_1$ ↔ a'$_8$ A(I)'$_8$ A(II)'$_8$**. The cross-peaks between H-13 at δ 7.920, 7.900 and C-14 at δ 119.9 support the resonance structures **a$_4$ A(I)$_4$ A(II)$_4$ ↔ a$_5$ A(I)$_5$ A(II)$_5$**. The correlation signal between H-13 at δ 7.830 and C-15 at δ 149.7 confirms **a$_4$ A(I)$_4$ A(II)$_4$ ↔ a$_3$ A(I)$_3$ A(II)$_3$↔ a$_2$ A(I)$_2$ A(II)$_2$** resonance structures.

In the 2D ^{1}H ^{13}C HMBC, HMQC correlation spectra a correlation signal between H-12 at δ 7.200 and C-12 at δ 124.1 as well as the correlation signals of H-12 at δ 7.200 to C-5 at δ 160, C-15 at δ 149.7, C-14 at δ 119.9 point to the resonance structures **a'$_5$ A(I)'$_5$ A(II)'$_5$.**

The 2D ^{1}H ^{13}C HMBC, HMQC correlation spectra show a correlation signal between H-11 at δ 8.490 and C-11 at δ 149.3 as well as the correlation signals of H-11 at δ 8.490 to C-15 at δ 149.7, C-14 at δ 119.9, C-13 at δ 136.8, C-12, C-8 at δ 123.8 and point to the resonance structures **a$_3$ A(I)$_3$ A(II)$_3$ ↔ a'$_3$ A(I)'$_3$ A(II)'$_3$, a$_2$ A(I)$_2$ A(II)$_2$ ↔ a'$_4$ A(I)'$_4$ A(II)'$_4$.**

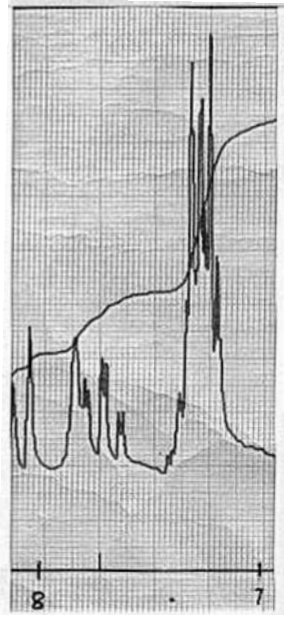
The ^{1}H ^{1}H coupling constants J($H_{13}H_{12}$) 7.8 Hz, J($H_{12}H_{13}$) 7.8 Hz [2] of **2a** tautomer support the positive charge at C-13 atom of the structures **a$_2$ A(I)$_2$ A(II)$_2$**. The coupling constants J($H_{14}H_{13}$) 7.0 Hz, J($H_{12}H_{11}$) 4.9 Hz, J($H_{11}H_{12}$) 4.9 Hz, J($H_{11}H_{14}$) 1.0 Hz, J($H_{14}H_{11}$) 1.0 Hz [2] point to the positive charge at C-15 atom and the negative one on N-10 atom of pyridine substituent of the structures **a'$_8$, A(I)'$_8$ A(II)'$_8$**. The coupling constants J($H_{12}H_{13}$) 1.7 Hz, J($H_{13}H_{12}$) 1.7 Hz [2] of **2a** confirm the lack of the charges on the pyridine ring.

In the ^{1}H NMR spectra 7–10 the signals of N–H proton in the range from δ 13.64 to 8.480 of the chemical shifts support the structures **2A(I) 2A(I)'**, **2A(II) 2A(II)'**, **2A(I)$_1$, 2A(II)$_1$ 2A(I)$_2$ 2A(II)$_2$** (Table 9) (Figs 1–3, 5).

The signals of N–H proton in the range from δ 8.435 to 8.306 (Table 9) and at δ 8.176–8.063 (Table 10) confirm the resonance structures **2A(I)$_3$, 2A(II)$_3$ 2A(I)$_4$, 2A(II)$_4$** and **2A(I)$_5$, 2A(II)$_5$ 2A(I)'$_1$ 2A(II)'$_1$** respectively. At δ 8.003–7.835 and at δ 7.830–7.627 **2A(I)'$_1$ 2A(II)'$_1$ 2A(I)'$_2$ 2A(II)'$_2$** and **2A(I)'$_3$ 2A(II)'$_3$** resonance structures arise, respectively. In the range of δ 7.530–7.193 and δ 7.448–7.129 the resonance structures **2A(I)'$_4$ 2A(II)'$_4$ 2A(I)'$_5$ 2A(II)'$_5$ 2A(I)'$_6$ 2A(II)'$_6$** and **2A(I)'$_5$ 2A(II)'$_5$ 2A(I)'$_6$ 2A(II)'$_6$ 2A(I)'$_7$ 2A(II)'$_7$** appear (Table 10).

In the ^{1}H NMR spectra 8_1 8_2 (100MHz, DMSO) the signals at δ 8.390 (1.08H, degenerated broaded triplet) and at δ 8.358 (1.5 H, broaded triplet, Table 9) correspond to the N–H proton of **2A(I)$_3$ 2A(II)$_3$** and **2A(I)$_4$ 2A(II)$_4$** tautomers, respectively.

The broaded triplets suggest that these protons take part in the intermolecular hydrogen bonds. The broaded triplet in the ^{1}H NMR spectrum 8_2 indicates the slow exchange of the N–H proton, due to this fact, the coupling of H-6 H-7 protons may be observed and support **2A$_4$ 2A(I)$_4$ 2A(II)$_4$** tautomers. These signals are the averaged ones in consequence of the rapid transitions of hydrogen atom between the exocyclic nitrogen atom N-6 and N-3 N-4 ones of 1,3,4-thiadiazole ring, then degenerated broaded triplet at δ 8.390 in the ^{1}H NMR spectrum 8_1 point to the **2A$_3$ 2B$_3$ 2C$_3$** tautomers. They disappear in D_2O (spectrum 8_7). In the ^{1}H NMR spectrum 8_5 of product **2** recorded in $CDCl_3$ solution at 100 MHz the considerable deshielding of the N–H proton at δ 13.64 indicates the possible intramolecular hydrogen bond and supports **2C' 2C(I)' 2C(II)'** tautomers. In the ^{1}H NMR spectrum 1_1 (100 MHz, DMSO) the magnitude of the couplings J(H_8H_{7D}) = J(H_8H_{7C}) 8.2 Hz support the changes of $sp^2 \Leftrightarrow sp^3$ hybridization of the nitrogen and carbon atoms N-6 C-7. The coupling constants of the protons J(H_8H_{9B}) 15.4 Hz, J(H_8H_{9A}) 8.5Hz, J(H_8H_{7C}) 7.6 Hz, J(H_8H_{7D}) 7.6 Hz support the sp^3 hybridization of C-7 carbon atom.[21]



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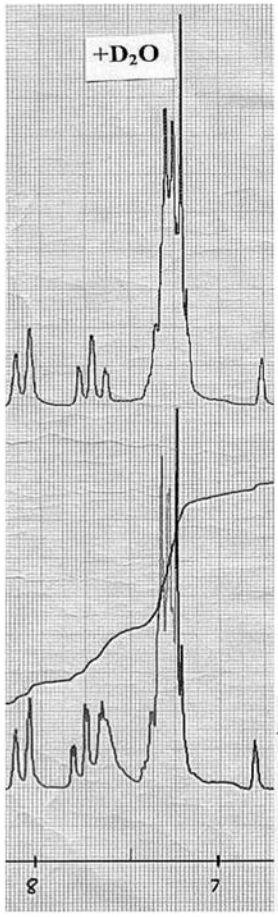
	1H 282.704
7.890	310.784
7.843	63.488
7.829	79.872
7.768	81.664
7.754	96.000
7.688	46.848
7.674	77.824

ppm	integral
	1H 282.704
7.444	16.640
7.411	107.776
7.378	135.168
7.359	347.136
7.322	271.360
7.312	167.168
7.298	176.896
7.275	364.032
7.242	635.904

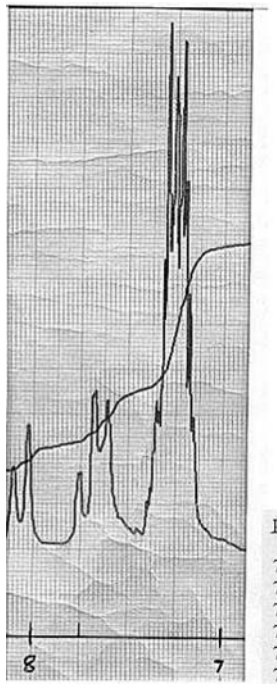
Fig. 7: The ^{1}H NMR NH group signals at δ 7.890–7.674 and δ 7.444–7.242 (spectrum 7)



ppm	integral
	1H 607.147
7.838	119.040
7.824	139.264
7.763	209.920
7.749	262.656
7.683	179.200
7.669	911.360

ppm	integral
	1H 607.147
7.448	67.840
7.430	55.040
7.397	324.352
7.364	372.736
7.345	777.216
7.308	1027.072
7.289	371.456
7.261	791.808
7.233	900.352

Fig. 8: The ^{1}H NMR NH group signals at δ 7.838–7.669 and δ 7.448–7.233 (spectrum 10)



ppm	integral
	1H 456.576
7.796	108.544
7.777	125.056
7.716	202.624
7.702	224.512
7.641	330.496
7.627	572.928

ppm	integral
	1H 456.576
7.430	93.440
7.411	61.952
7.378	251.264
7.369	82.944
7.345	333.824
7.326	658.816
7.284	994.304
7.264	299.520
7.251	309.504
7.233	461.606
7.209	202.880
7.190	400.128

Fig. 9: The ^{1}H NMR NH group signals at δ 7.796–7.627 and δ 7.430–7.190 (spectrum 8)

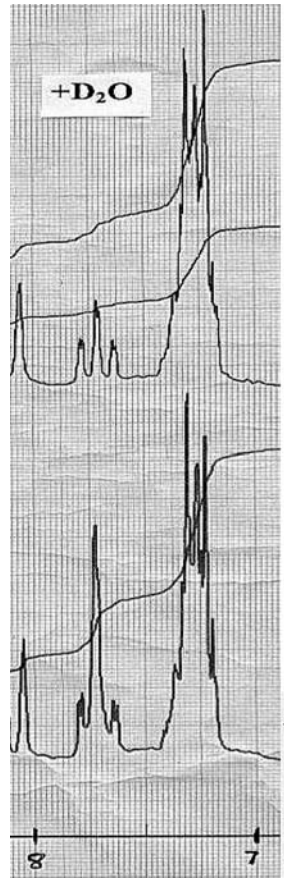
The ^{1}H NMR spectra of **2** (100 MHz) confirm the co-existence of two tautomeric forms **A(I)'** ⇒ **B'** or **A(II)'** ⇒ **C(II)'** in the solution**.**

The signals of N–H proton in the range from δ 7.890 to 7.674 (2H) and at δ 7.444 to 7.242 (2H) (Fig. 7, spectrum 7, Table 10) point to the transformation process of **2A(I)'$_1$** ⇒ **2B'$_1$**, **2A(I)'$_6$** ⇒ **2B'$_6$** or **2A(II)'$_1$** ⇒ **2C(II)'$_1$**, **2A(II)'$_6$** ⇒ **2C(II)'$_6$**, respectively.

The signals of N–H group at δ 7.838–7.669 (2 H) and at δ 7.448–7.233 (1.721 H) (Fig. 8, spectrum 10, Table 10) confirm the balance of **2A(I)'$_2$** ⇒ **2B'$_2$**, **2A(I)'$_5$** ⇒ **2B'$_5$** or **2A(II)'$_2$** ⇒ **2C(II)'$_2$**, **2A(II)'$_5$** ⇒ **2C(II)'$_5$**, respectively.

The signals of N–H proton at δ 7.796–7.627 (3.425 H) and at δ 7.430–7.190 (3.08 H) (Fig. 9, spectrum 8, Table 10) point to **2A(I)'$_3$** **2A(II)'$_3$** and **2A(I)'$_7$** **2A(II)'$_7$** resonance structures and to the interconvertion of **2A(I)'$_3$** ⇒ **2B'$_3$**, **2A(I)'$_7$** ⇒ **2B'$_7$** or **2A(II)'$_3$** ⇒ **2C(II)'$_3$**, **2A(II)'$_7$** ⇒ **2C(II)'$_7$**, respectively.

The signals of N–H proton at δ 7.64 (2.5 H) and at δ 7.28 (2 H) (spectrum 8$_5$, Table 10) confirm the **2A(I)'$_3$** **2A(II)'$_3$** and **2A(I)'$_6$** **2A(II)'$_6$** structures and the transformation process of **2A(I)'$_3$** ⇒ **2B'$_3$**, **2A(I)'$_6$** ⇒ **2B'$_6$** or **2A(II)'$_3$** ⇒ **2C(II)'$_3$**, **2A(II)'$_6$** ⇒ **2C(II)'$_6$**,respectively.



ppm	integral
	1H 311.893
7.829	67.328
7.810	98.048
7.749	394.752
7.735	230.912
7.674	60.160
7.655	84.480

ppm	integral
	1H 311.893
7.448	40.960
7.430	45.568
7.411	52.736
7.397	149.504
7.364	210.432
7.345	568.064
7.308	230.912
7.298	201.728
7.284	268.960
7.261	445.440
7.228	162.048
7.209	107.728

Fig. 10: The ^{1}H NMR NH group signals at δ 7.829–7.655 and δ 7.448–7.209 (spectrum 9)

The signal of N–H group at δ 7.829–7.655 (2 H) and at δ 7.448–7.209 (1.965 H) (Fig. 10, spectrum 9, Table 10) supports the balance of **2A(I)'$_3$ ⇒ 2B'$_3$, 2A(I)'$_5$ ⇒ 2B'$_5$** or **2A(II)'$_3$ ⇒ 2C(II)'$_3$, 2A(II)'$_5$ ⇒ 2C(II)'$_5$,** respectively. The signal of N–H group at δ 7.522–7.224 (2,5 H) (spectrum 8_1) indicates **2A(I)'$_4$ 2A(II)'$_4$** structures as well as the transformation process of **2A(I)'$_4$ ⇒ 2B'$_4$** or **2A(II)'$_4$ ⇒ 2C(II)'$_4$**. These transformation confirm the amine-type nitrogen N-4, N-3 of 1,3,4-thiadiazole ring.

Table 11: The ^{1}H–NMR chemical shifts δ [ppm] from TMS of the NH group of tautomer **1A 1A'.**

Spectrum No Solvent	δ	NH	Structure
1_1 (DMSO)	8.637 – 8.562	0.08 H	**11A 1A'**
1_3 ($CDCl_3$)	8.606 – 8.530	0.2 H	**1A$_1$ 1A$_2$**
1_4 ($CDCl_3$)	8.601 – 8.525	0.05 H	
3 ($CDCl_3$)	8.598 – 8.537	0.23 H	
6 ($CDCl_3$)	8.598 – 8.523	0.1 H	
1 ($CDCl_3$)	8.594 – 8.519	0.38 H	
5 ($CDCl_3$)	8.589 – 8.514	0.637 H	
2 ($CDCl_3$)	8.580 – 8.537	0.08 H	
5($CDCl_3$)	8.077 – 7.974	0.756 H	**1A'$_1$**
4($CDCl_3$)	7.852 – 7.683	0.13 H	**1A'$_2$**
6($CDCl_3$)	7.852 – 7.678	0.14 H	**1A'$_3$**
1($CDCl_3$)	7.847 – 7.674	0.43 H	
2($CDCl_3$)	7.847 – 7.674	0.18 H	
3($CDCl_3$)	7.847 – 7.674	0.25 H	
5($CDCl_3$)	7.838 – 7.646	1.356 H	
1_7($CDCl_3$)	7.78 – 7.73	0.505 H	

Table 12: The ^{1}H–NMR chemical shifts δ [ppm] from TMS and the ^{1}H–^{1}H long-range coupling constants [Hz] of **1**

Spectrum No ($CDCL_3$)	δ	*J*	NH
4	8.528	$J(H_{11}H_{9A})$ 37.280	
6	8.598	$J(H_{11}H_{9A})$ 38.144	0.1 H
1	7.754	$J(H_{12}H_{9A})$ 38.336	0.43 H
4	8.584	$J(H_{11}H_{9A})$ 38.400	
6	7.852	$J(H_{12}H_{9A})$ 38.912	0.14 H
5	7.974	$J(H_{13}H_{9A})$ 39.296	0.736 H
5	7.998	$J(H_{13}H_{9A})$ 40.064	
5	7.819	$J(H_{12}H_{9A})$ 40.832	1.356H
6	7.697	$J(H_{12}H_{9A})$ 41.984	0.14 H
4	8.594	$J(H_{11}H_{9B})$ 42.432	

In the ^{1}H–NMR (100 MHz) spectra of **1** the NH group signals in the δ 8.637–8.514 and δ 8.077–7.646 range confirm the **1A**, **1A', 1A$_1$**, **1A$_2$** and **1A'$_1$**, **1A'$_2$ 1A'$_3$** resonance structures, respectively (Table 11).[1] The signals at δ 8.594 $J(H_{11}H_{9B})$ 42.432 Hz, δ 8.584 $J(H_{11}H_{9A})$ 38.400 Hz, δ 8.528 $J(H_{11}H_{9A})$ 37.280 Hz and δ 7.998 $J(H_{13}H_{9A})$ 40.064 Hz (spectra 4, 5 Table 12)[1] point to the transition of **A'⇔ A** and **A'$_1$⇔ A$_1$** tautomers as well as to the rapid exchange at the NH group hydrogen of structures **A A'.**

The interconvertions of the structures **2A(I) ⇔ 2A(I)' ⇔ 2A(I)'$_a$, 2A(II) ⇔ 2A(II)' ⇔ 2A(II)'$_a$** and the rapid exchange of the NH hydrogen suggest the proton transfer of **2A(I)' ⇒ 2B',** or **2A(II)' ⇒ 2C(II)'** tautomers *via* solvent. Double signals of the protons corresponding to both tautomeric forms are present in the ^{1}H-NMR (100 MHz) spectra of **2** (Figs 7–10, Table 10). The proton transfer reactions for different systems have been described in the literature.[22,23]

4. Conclusions

The ^{1}H NMR studies (100MHz) of (3-phenyl-allyl-) (5-pyridin 2-yl-[1,3,4] thiadiazol-2-yl)-amine support the **A(I) ⇔ A(I)' ⇔ A(I)'$_a$, A(II) ⇔ A(II)' ⇔ A(II)'$_a$** structures. The intensities of the signals of N–H proton in the range from δ 7.890 to 7.190 confirm the balance of two tautomeric forms **A(I)' ⇒ B'** or **A(II)' ⇒ C(II)'** in the solution. Double signals of the NH proton in the ^{1}H–NMR (100 MHz) spectra of **2** (Figs 7–10, Table 10) confirm both tautomeric forms. Because of the rapid exchange of NH group hydrogen in this case the pathway of the proton transfer *via* solvent may take place.

5. References

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Povzetek

Določili smo strukturne oblike iona ali radikala spojine (3 – fenil **–** alil–) (5 – piridin – 2 – il – [1,3,4] tiadiazol – 2 – il)–amina **2A(I) ⟺ 2A(I)' ⟺ 2A(I)'$_a$**, 2**A(II) ⟺ 2A(II)' ⟺ 2A(II)'$_a$** s pomočjo njenih ^{1}H (100 MHz, 500 MHz), ^{13}C in ^{15}N NMR spektrov in B3LYP/6–31G** izračunov. Tavtomerno ravnotežje **2A(I)' ⇒ 2B', 2A(II)' ⇒ 2C(II)'** je določeno s pomočjo ^{1}H NMR spektra (100 MHz).