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The Electronic Structure of the Nitrogen Atoms of Allyl (5-pyridin-2-yl-[1,3,4]-thiadiazol-2-yl)-amine

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Abstract. The resonance structures of allyl-(5-pyridin-2-yl-[1,3,4]-thiadiazol-2-yl)-amine 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 this compound has been observed in the ^{1}H-NMR spectra (100 MHz).

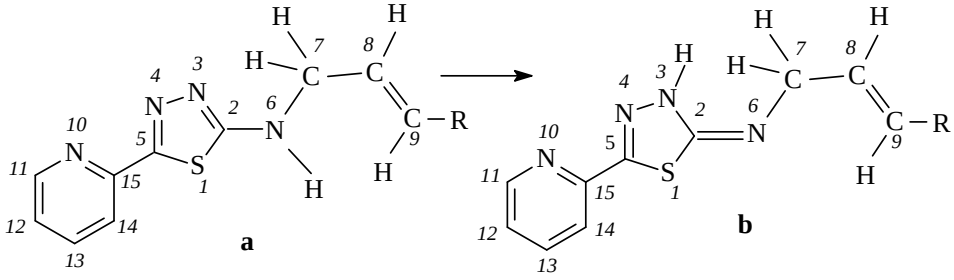
Keywords: Allyl-(5–pyridin–2-yl-[1,3,4]-thiadiazol–2–yl)-amine; electronic structure, tautomerism

Introduction

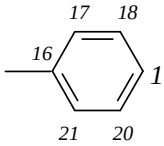
1,3,4-Thiadiazoles bearing an amino group at the C2 atom can exist in different tautomeric forms (Figure 1). The tautomeric equilibrium is influenced by the exocyclic N6 and C5 substituents on the 1,3,4-thiadiazole ring [1, 2]. 2-Amino-[1,3,4]-thiadiazole exists in the amino form in solution and in the solid state. The same tautomer is the main form in 5-alkoxy derivatives. In the case of a 2-hydrazino substituent the hydrogen atom also appears at the exocyclic N6 nitrogen atom, but in the sulfonamido group the tautomeric equilibrium shifts towards the imino form (type **b**, Figure 1). It therefore appeared of interest to examine the tautomeric equilibrium of (5-pyridin-2-yl-[1,3,4] thiadiazol-2-yl)-amine derivatives bearing allyl- and (3-phenylallyl)- substituents (compounds **1** and **2**, respectively). Earlier 100 MHz ^{1}H-NMR studies in the solution of 1-acyl-(aroyl-)-4-(3-phenylallyl)-

thiosemicarbazides [3] and N^1-[(3-phenylallyl)-thiocarbamyl]amidrazones [4] as well as of the products obtained of the result of the acid cyclization of the linear compounds [5,6] confirmed various tautomeric structures for the above mentioned compounds and the transformation products. Allyl- (**1**) and 3-phenylallyl-(5-pyridin-2-yl-[1,3,4]thiadiazol-2-yl)-amine (**2**) [6, 7], another product of the acid cyclization of the linear N^1-[allyl-(3-phenylallyl)-thiocarbamyl]-amidrazone compounds, turned out to be suitable to study the tautomeric transformations.

Figure 1. Tautomers **a** and **b** of allyl- (**1**) and 3-phenylallyl-(5-pyridin-2-yl- [1,3,4]thia-diazol-2-yl)-amine (**2**), with atom numbering.



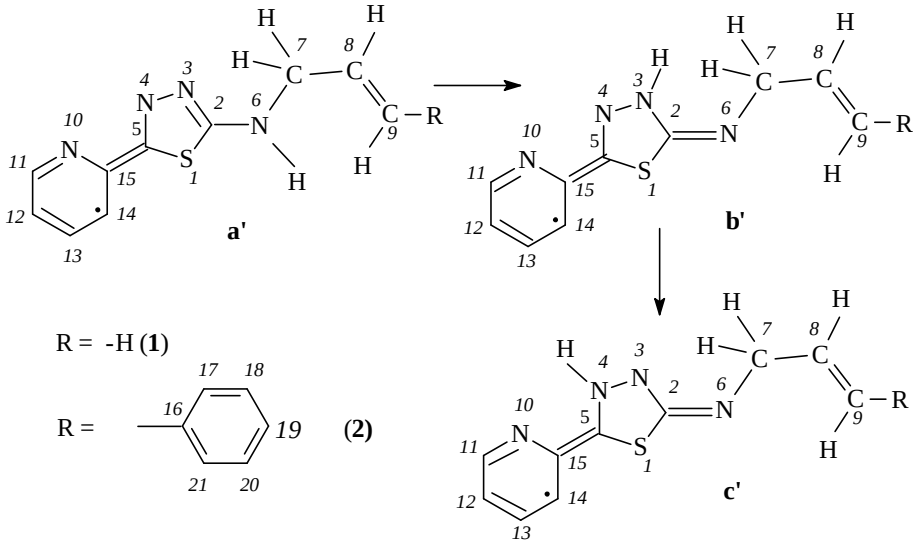
R = -H (**1**)



(**2**)

On account of the allyl- and pyridyl- substituents in the molecule, the exo- and endocyclic nitrogen atoms of 1,3,4-thiadiazole and pyridine rings may appear as amino-, pyrrole- or pyridine-type nitrogens. Consequently, allyl- (**1**) and 3-phenylallyl-(5-pyridin-2-yl-[1,3,4]thiadiazol-2-yl)-amine (**2**) can exist as **a a'**, **b b'**, **c'**, **a_0 a'_0,** tautomers (Figures 1-3).

Figure 2. Tautomers **a', b'** and **c'** of allyl- (**1**) and 3-phenylallyl-(5-pyridine-2-yl-[1,3,4]-thiadiazol-2-yl)-amine (**2**), with atom numbering.

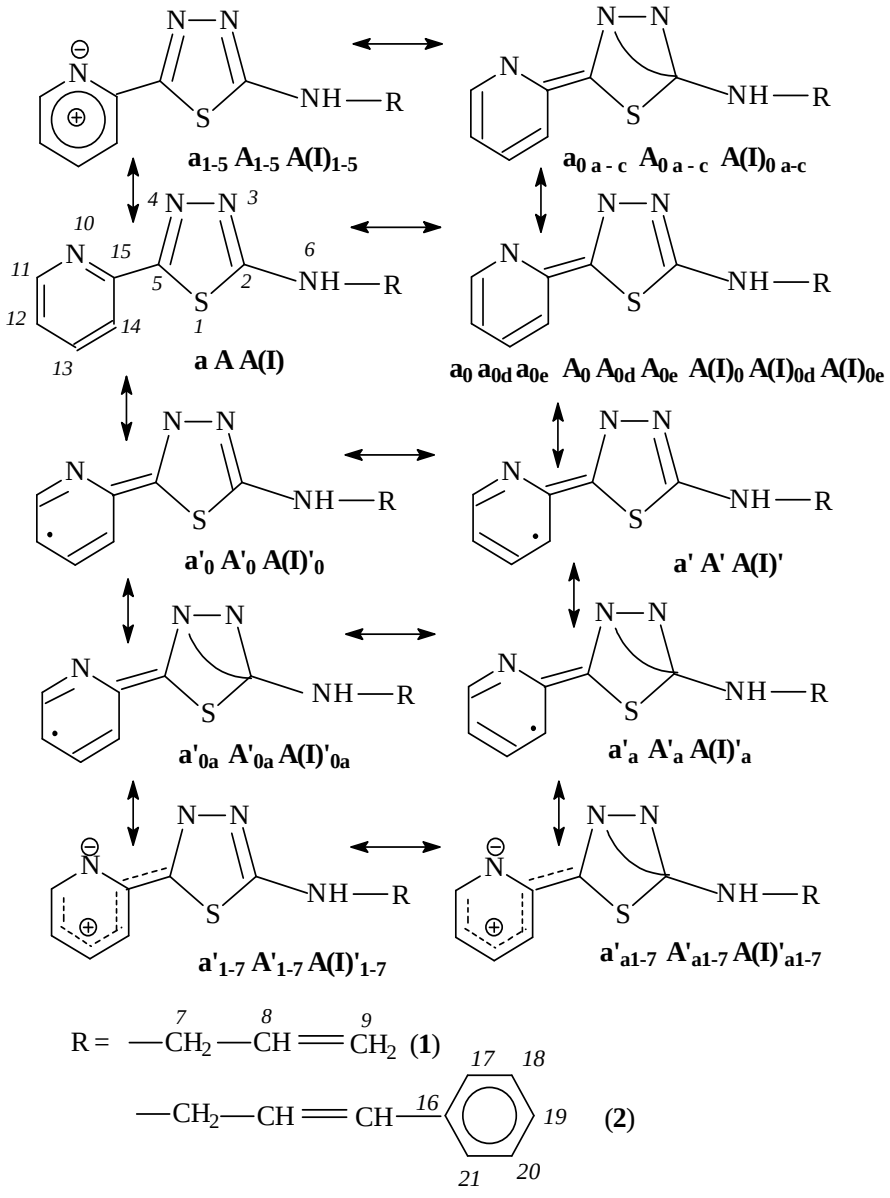


R = -H (**1**)

(**2**)

Previous 100 MHz ^{1}H-NMR investigations of 2-amino-1,3,4-thiadiazole derivatives have shown the tautomeric equilibrium in solution between allyl- and 3-phenylallyl-(5-pyridin-2-yl-[1,3,4]thiadiazol-2-yl)-amine (**1a 2a**, **1a' 2a'**), 3H-(allyl-(3-phenylallyl)-(5-pyridin-2-yl-[1,3,4]-thiadiazol-2-ylidene)-amine (**1b 2b**, **1b' 2b'**) and 4H-(allyl-(3-phenylallyl)-(5-pyridin-2-yl-[1,3,4]-thiadiazol-2-ylidene)-amine (**1c' 2c'**) (Figures 1, 2) [6-9]. The intensities of the signals prove the interconversion between these tautomeric forms. According to the XRD data only one tautomer (type **a**) is present in the crystals of both compounds **1** and **2** [10]. In the solid state the *exo*-amino form **a** is stabilized by different H bonds, and the differences in the total energy between tautomers **a** and **b** are equal to –35.6 and –34.3 kJ/mol for **1** and **2**, respectively, according to DFT level of theory calculations [10].

Figure 3. The resonance structures **a a_0, a' a'_0, A A_0, A' A'_0, A(I) $A(I)_0$, A(I)' $A(I)'_0$** of allyl-(**1**) and 3-phenylallyl-(5-pyridin–2–yl)-[1,3,4]thiadiazol–2-yl)-amine (**2**).



R = —CH_2—CH═CH_2 (**1**)

—CH_2—CH═CH— (**2**)

The calculated ^{15}N-, ^{1}H- chemical shifts and the ^{15}N-, ^{1}H-, ^{13}C- signals of the respective ^{15}N-, ^{1}H- and ^{13}C-NMR spectra suggest changes in the electron configuration of the exo - and endocyclic nitrogen atoms of the 1,3,4-thiadiazole and pyridine rings. The aim of the present paper was to describe the electronic structure of the nitrogen atoms of tautomer **1a** in the range of the chemical shifts of the NH group proton from 8.665 ppm to 7.233 ppm.

Structural studies of 2-amino-[1,3,4]-thiadiazole derivatives have been performed in order to know the properties of the compounds with the marked bioactivity. The N6 and/or 5- substituted-2-amino-[1,3,4]-thiadiazoles, depending on the nature of substituents, display varied pharmacological activities, and structural studies of new interesting [1,3,4]-thiadiazole derivatives with different medical applications may improve our understanding of their mode of action. Thus, they have shown potent activity against leukemia, melanoma and lung carcinoma. They are also known to be carbonic anhydrase inhibitors and some of them possess antimycobacterial, anesthetic, antidepressant and anxiolytic activity [11-21]. 2-Amino-[1,3,4]-thiadiazoles are also found in a new class of herbicides with a broad spectrum of activity [22], that act *via* inhibition of the enzyme imidazoleglycerol phosphate dehydrase. They are also useful as corrosion inhibitors [23].

Results and Discussion

The calculated chemical shifts of the ^{15}N nitrogen atoms for type **a** and **b** tautomers of allyl-(**1**) and 3-phenylallyl-(5-pyridin-2-yl-[1,3,4]-thiadiazol-2-yl)-amine (**2**) occur in different ranges: from about –309 ppm to about –23 ppm for the type **a** tautomer and from about -225 ppm to about -80 ppm for the **b** one (Table 1, Figure 4) [10]. The amino N6 atom is strongly shielded in **1** (about –308 ppm) but in **2** the shielding decreases by a few ppm (to about –304 ppm). The shielding constants for the N3 and N10 atom in the 1,3,4–thiadiazole and pyridine rings, respectively, are almost equal, whereas the N4 atom is much less shielded [10].

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

Compound	**^{15}N**	**^{1}H**
1a 2a	- 309 – - 23	
1a	N6 -131.57	H 14 8.125
	N3 -77.78	
2a	N10 -86.0	H 6 7.5
	N6 -133.98	
1b 2b	-225 – -80	

In the ^{1}H-NMR spectra the N6 nitrogen atom of **1a** appears as an amine – type **a**, pyridine – type **A**, pyrrole – type **A** (**I**) (Figures 1-3, 5, 6). The 5.81 ppm value of the chemical shift for the proton of NH group of **1** recorded in $CDCl_3$ solution at 500.16 MHz [10] is in agreement with the resonances of the amino protons. The signal of the N6 nitrogen atom in the ^{15}N-NMR spectrum appears at –308.58 ppm [10] and supports the amino – type nitrogen.

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

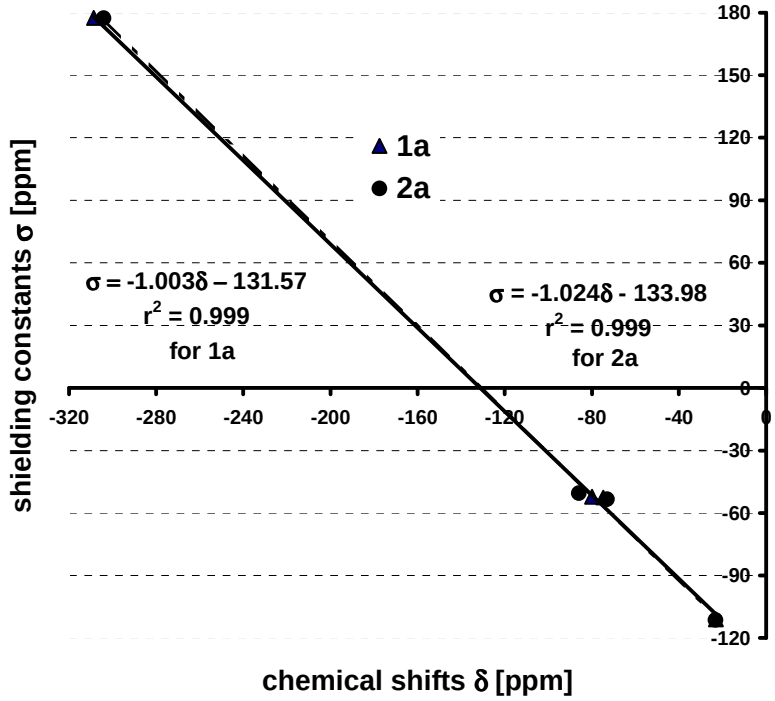


Figure 5. The resonance structures **A** **A$_0$** of allyl-(**1**) and 3-phenylallyl-(5-pyridin–2–yl)-[1,3,4]thiadiazol–2-yl)-amine (**2**)

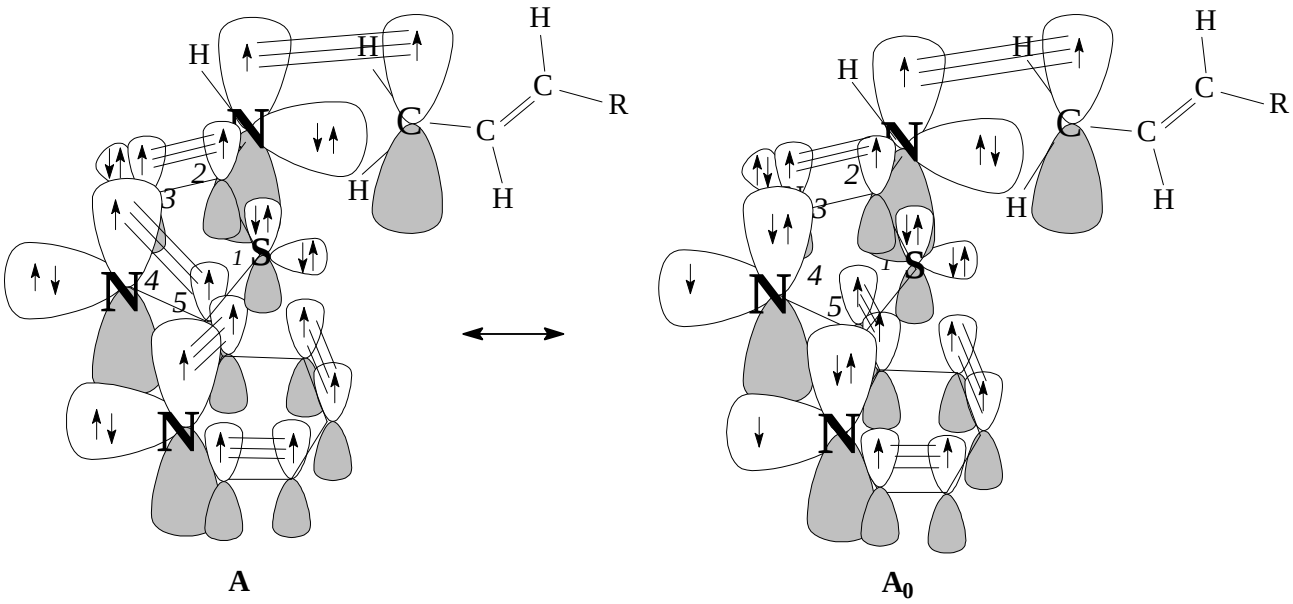
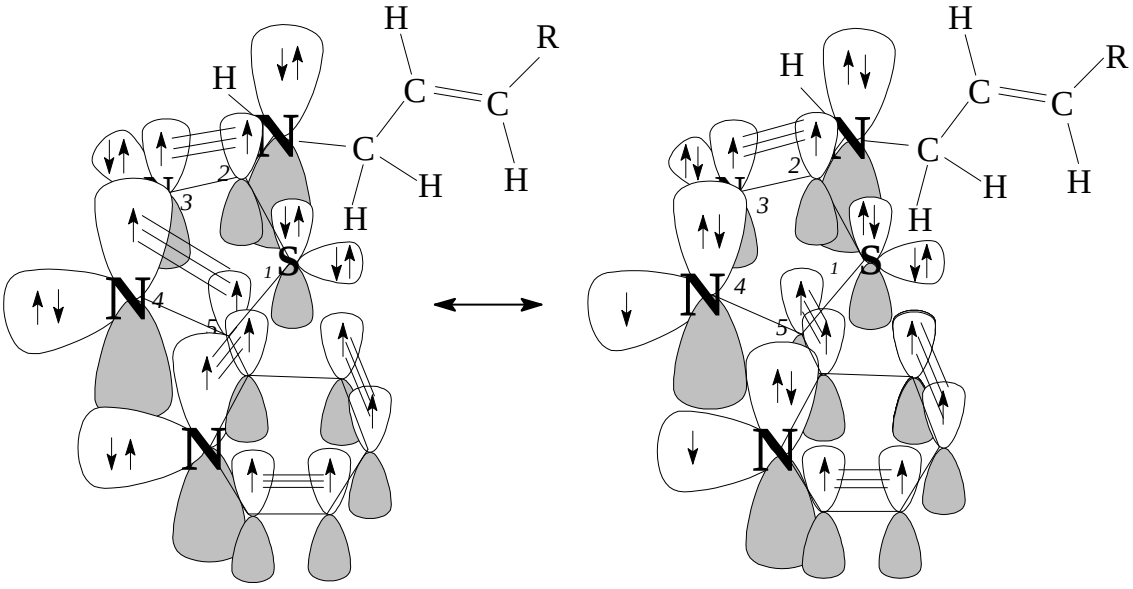


Figure 6. The resonance structures **A(I) A(I)$_0$** of allyl-(**1**) and 3-phenylallyl-(5-pyridin–2–yl)-[1,3,4]thiadiazol–2-yl)-amine (**2**)

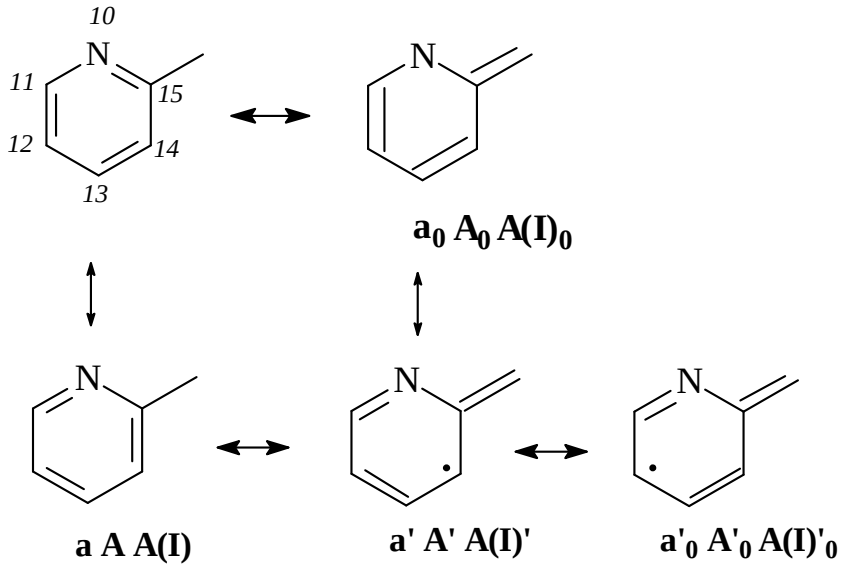


The differences in the coupling constants $J(H_8H_{9B})$ 17.6 Hz, $J(H_8H_{7C})$ 18.8Hz, $J(H_8H_{9A})$ 10.6Hz $J(H_8H_{7D})$ 11.2Hz (100MHz) [8] and the ^{13}C-NMR signals of C9 allyl substituent at 117.99 ppm, C8 at 132.80 ppm and C7 at 49.28 ppm [10] support the negatively charged pyridine – type nitrogen atom and positively charged allyl cation. The coupling constants $J(H_8H_{9B})$ 17.6 Hz, $J(H_8H_{9A})$ 10.6 Hz, $J(H_8H_{9B})$ 17.3 Hz, $J(H_8H_{9A})$ 10.9 Hz (100 MHz) [8] and $J(H_{9B}H_{9A})$ 1.2 Hz (500 MHz) confirm the reversed electron demand of the 2p orbitals of the pyridine - type nitrogen and carbon atoms N6 C7 of **1**. The exocyclic nitrogen atom, the pyridine – type, is occupied with eight electrons. The coupling constants $J(H_8H_{9B})$ 17.1 Hz, $J(H_{9B}H_8)$ 17.1 Hz, $J(H_8H_{9A})$ 10.1 Hz, $J(H_{9A}H_8)$ 10.1 Hz, $J(H_{9B}H_{9A})$ 1.0 Hz (500 MHz) [10] point to the lack of the differences in the spin states of electrons of 2p orbitals of pyridine - type nitrogen N6 and C7 atoms of **1,** the exocyclic nitrogen atom N6 is surrounded by seven electrons. The calculated chemical shift of N6 at – 131.57 ppm (Table 1) [10] supports pyridine – type nitrogen. The magnitude of the couplings $J(H_7H_8) = J(H_8H_7) = 5.6$ Hz (500 MHz) for **1** confirms a pyrrole – type nitrogen atom N6 **A(I)** and the possible transformation of $sp^2 \Leftrightarrow sp$.

The calculated signal of H14 at 8.125 ppm (Table 1) as well as the ^{1}H-^{1}H coupling constants $J(H_{12}H_{14})$ 1.0 Hz, $J(H_{11}H_{14})$ 0.5 Hz [10] of structure **a** confirm the absence of charges on the pyridine ring.

In the ^{15}N-NMR spectrum of **1a** tautomer, the chemical shift of N10 at – 80.01 ppm [10] supports the pyrrole – type nitrogen atom of the pyridyl substituent. The calculated chemical shift of N3 at – 77.78 ppm (Table 1) [10] confirm a pyridine – type nitrogen atom of tautomer **1a** and the lack of the differences in the spin states of electrons of 2p orbitals of N3 C2. The ^{1}H -^{13}C HMQC correlation spectra show a correlation signal between H14 at 8.360 ppm and C15 at 149.7 ppm. The above data prove the existence of the diradical resonance structures **a$_0$ A$_0$ A(I)$_0$ a'$_0$ A'$_0$ A(I)'$_0$** (Figures 3, 5 - 7) and the lack of the charges over the pyridine and 1,3,4 thiadiazole rings.

Figure 7. The resonance structures of the pyridyl substituent

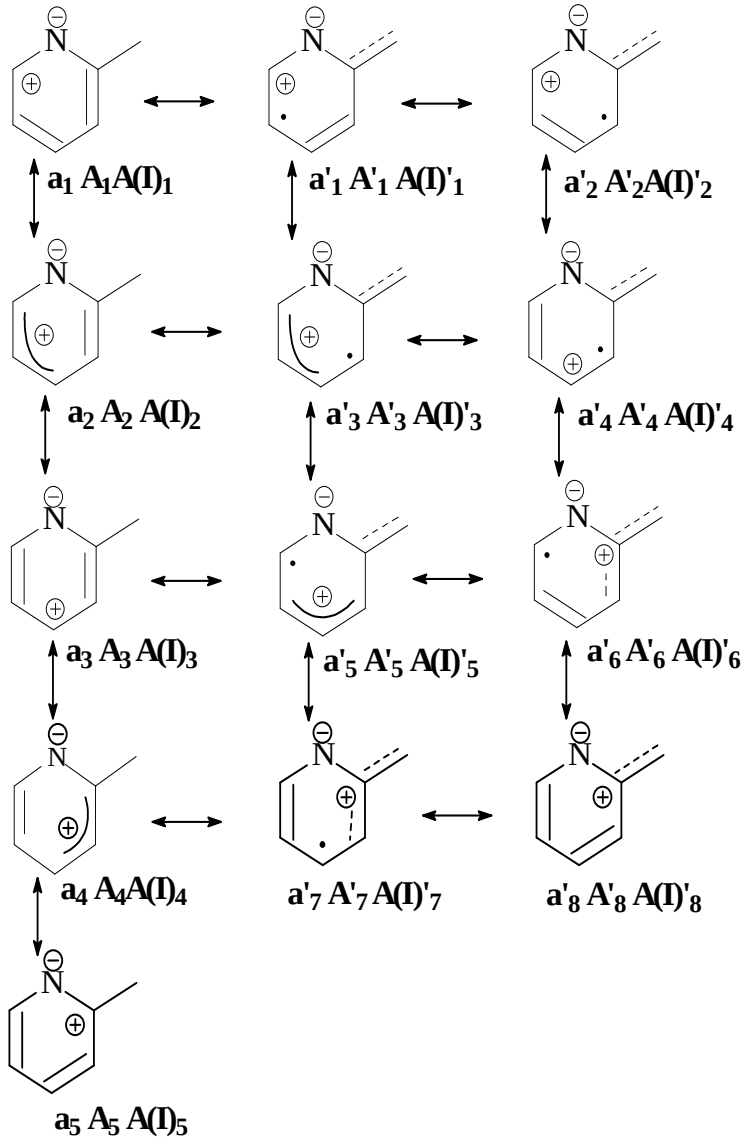


In the 2D ^{1}H-^{13}C HMBC spectra the cross – peak between H14 and C14 at 8.150 ppm and 119.7 ppm supports structures **a A A(I)** (Figures 3, 5 - 7). The pyridyl H14 proton of the diradical resonance structures **a_0 A_0 A(I)$_0$ a'$_0$ A'$_0$ A(I)'$_0$** is more intensly deshielded by about 0.2 ppm in relation to the structure **a A A(I)**. The spectroscopic data support the conjugation of the aromatic π electrons of the pyridyl substituent with the π electrons of the C = N double bond of the 1,3,4 thiadiazole ring in solution.

The signals of the NH group protons and the pyridyl substituent in the ^{1}H-NMR spectra (100 MHz) support the **a A** and diradical resonance structures **a' A', a'$_0$ A'$_0$** (Figures 1-3, 5, 7). In the ^{1}H-NMR spectra 1_3 1_4 (Tables 2, 4) the H14 signals at 8.245 ppm – 8.145 ppm and 8.237 ppm – 8.137 ppm support the resonance structures **a'$_1$ A'$_1$ ↔ a'$_2$ A'$_2$ ↔ a'$_0$ A'$_0$** and **a'$_3$ A'$_3$ ↔ a'$_1$ A'$_1$**, respectively. The H14 signals at 8.242 ppm – 8.152 ppm and 8.237 ppm – 8.148 ppm (spectra 4, 2, 3, Tables 3, 4) confirm the resonance structures **a'$_2$ A'$_2$ ↔ a'$_1$ A'$_1$ ↔ a'$_0$ A'$_0$** and **a'$_3$ A'$_3$ ↔ a'$_1$ A'$_1$ ↔ a'$_0$ A'$_0$**, respectively. The H14 signals at 8.232 ppm – 8.143 ppm and 8.223 ppm – 8.143 ppm (spectra 1, 5, Tables 3, 4) point to the resonance structures **a'$_4$ A'$_4$ ↔ a'$_1$ A'$_1$ ↔ a'$_0$ A'$_0$** and **a_4 A_4 ↔ a'$_1$ A'$_1$ ↔ a'$_0$ A'$_0$**, respectively. The H14 signals at 8.228 ppm – 8.138 ppm (spectrum 6, Tables 3, 4) indicate the resonance structures **a_2 A_2 ↔ a_4 A_4 ↔ a'$_1$ A'$_1$**.

The H14 signals at 8.174 ppm – 8.023 ppm, 8.174 ppm – 8.010 ppm and 8.135 ppm – 7.998 ppm (spectra 1_8, 1_2, 1_1, Tables 2, 4) support the resonance structures **a'$_4$ A'$_4$ ↔ a'$_5$ A'$_5$**, **a'$_4$ A'$_4$ ↔ a'$_6$ A'$_6$** and **a'$_5$ A'$_5$ ↔ a'$_6$ A'$_6$ ↔ a'$_7$ A'$_7$**, respectively. The H14 signals at 8.077 ppm – 7.974 ppm (spectrum 5, Tables 3, 4) confirm the resonance structures **a'$_8$ A'$_8$ ↔ a'$_6$ A'$_6$ ↔ a'$_7$ A'$_7$**. (Figures 7, 8).

Figure 8. The resonance structures of the pyridyl substituent



The H13 signals at 7.967 ppm – 7.869 ppm, 7.954 ppm – 7.859 ppm and 7.935 ppm – 7.837 ppm (spectra 1_8 1_2 1_1, Tables 2, 5) support the resonance structures **a$_3$ A$_3$ ↔ a'$_3$ A'$_3$ ↔ a A**, **a'$_3$ A'$_3$ ↔ a'$_5$ A'$_5$ ↔ a A** and **a'$_4$ A'$_4$ ↔ a'$_5$ A'$_5$ ↔ a A**, respectively. The H13 signals at 7.859 ppm – 7.688 ppm, 7.854 ppm – 7.681 ppm (spectra 1_3 1_4, Tables 2, 5) and 7.852 ppm – 7.683 ppm (spectrum 4, Tables 3, 5) point to the resonance structures **a'$_5$ A'$_5$ ↔ a'$_3$ A'$_3$ ↔ a'$_0$ A'$_0$**, **a'$_3$ A'$_3$ ↔ a'$_5$ A'$_5$** and **a'$_3$ A'$_3$ ↔ a'$_4$ A'$_4$ ↔ a'$_0$ A'$_0$**, respectively. The H13 signals at 7.852 ppm – 7.678 ppm, 7.847 ppm – 7.674 ppm (spectra 6, 1 – 3, Tables 3, 5) and 7.838 ppm – 7.646 ppm, (spectrum 5, Tables 3, 5) confirm the resonance structures **a'$_3$ A'$_3$ ↔ a'$_4$ A'$_4$**, **a'$_3$ A'$_3$ ↔ a'$_5$ A'$_5$ ↔ a'$_4$ A'$_4$** and **a'$_5$ A'$_5$ ↔ a'$_4$ A'$_4$**, respectively.

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

Spectrum No (Solvent)	**H 7**	**H 8**	**H 9**	**Pyridin-2-yl**
1_1 (DMSO)	3.922 – 4.061 2H m	5.772 – 6.148 1H m	5.104 – 5.399 2H m	8.637 – 8.562 1H H11 8.135 – 7.988 1H H13 H14 7.935 – 7.837 1H H12 H13 7.503 – 7.336 1H H14 H12
1_2 (DMSO)	3.988 – 4.086 2H m	5.809 – 6.187 1H m	5.133 – 5.435 2H m	8.665 – 8.589 1H H11 8.174 – 8.010 1H H13 H14 7.954 – 7.859 1H H12 H13 7.517 – 7.381 1H H14 H12
1_3 ($CDCl_3$)	4.003 – 4.086 2H m	5.782 – 6.160 1H m	5.191 – 5.482 2H m	8.606 – 8.530 1H H11 8.245 – 8.145 1H H13 H14 7.859 – 7.688 1H H12 H13 7.349 – 7.212 1H H14 H12
1_4 ($CDCl_3$)	4.003 – 4.086 2H m	5.782 – 6.160 1H m	5.191 – 5.482 2H m	8.601 – 8.525 1H H11 8.237 – 8.137 1H H13 H14 7.854 – 7.681 1H H12 H13 7.342 – 7.205 1H H14 H12
1_8 (DMSO - D_2O)	4.069 – 3.988 2.5H m	5.804 – 6.180 1.14H m	5.143 – 5.431 2.21H m	8.662 – 8.586 1.07H H11 8.174 – 8.023 1H H13 H14 7.967 – 7.869 1.42H H12 H13 7.532 – 7.395 1.21H H14 H12

The H12 signals at 7.532 ppm – 7.395 ppm, 7.517 ppm – 7.381 ppm and 7.503 ppm – 7.336 ppm (spectra 1_8 1_2 1_1, Tables 2, 6) confirm the resonance structures **a_5 A_5 ↔ a_4 A_4 ↔ a'_6 A'_6 ↔ a'_0 A'_0**, **a'_7 A'_7 ↔ a'_1 A'_1 ↔ a'_6 A'_6 ↔ a'_0 A'_0** and **a'_7 A'_7 ↔ a'_4 A'_4 ↔ a'_0 A'_0**, respectively. The H12 signals at 7.349 ppm – 7.212 ppm and 7.342 ppm – 7.205 ppm (spectra 1_3 1_4, Tables 2, 6) support the resonance structures **a'_4 A'_4 ↔ a'_2 A'_2 ↔ a_1 A_1** and **a'_4 A'_4 ↔ a'_1 A'_1 ↔ a'_0 A'_0**, respectively. The H12 signals at 7.397 ppm – 7.143 ppm (spectrum 5, Tables 3, 6) support the resonance structures **$a'_7A'_7$ ↔ a'_4 A'_4 ↔ a'_2 A'_2 ↔ a'_1 A'_1 ↔ a'_5 A'_5 ↔ a'_3 A'_3**. The H12 signals at 7.341 ppm – 7.204 ppm, 7.336 ppm – 7.200 ppm and 7.331 ppm – 7.195 ppm (spectra 4, 1, 2, 6, 3, Tables 3, 6) support the resonance structures **a'_4 A'_4 ↔ a'_2 A'_2 ↔ a'_1 A'_1., a'_2 A'_2 ↔ a'_5 A'_5 ↔ a'_0 A'_0** and **a'_1 A'_1 ↔ a'_5 A'_5**, respectively.

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

Spectrum No (Solvent)	**H 7**	**H 8**	**H 9**	**Pyridin – 2- yl**
1	4.079 – 3.999	6.101 – 5.778	5.458 – 5.196	8.594 – 8.519 1H H11
($CDCl_3$)	2H	1H	2H	8.232 – 8.143 1H H13 H14
				7.847 – 7.674 1H H12 H13
				7.336 – 7.200 1H H14 H12
2	4.083 – 4.003	6.106 – 5.782	5.463 – 5.196	8.580 – 8.537 1H H11
($CDCl_3$)	2H	1H	2H	8.237 – 8.148 1H H13 H14
				7.847 – 7.674 1H H12 H13
				7.336 – 7.200 1H H14 H12
3	4.088 – 4.003	6.111 – 5.787	5.477 – 5.182	8.598 – 8.537 1H H11
($CDCl_3$)	2H	1H	2H	8.237 – 8.148 1H H13 H14
				7.847 – 7.674 1H H12 H13
				7.331 – 7.195 1H H14 H12
4	4.088 – 4.003	6.111 – 5.787	5.482 – 5.186	8.603 – 8.528 1H H11
($CDCl_3$)	2H	1H	2H	8.242 – 8.152 1H H13 H14
				7.852 – 7.683 1H H12 H13
				7.341 – 7.204 1H H14 H12
5	4.088 – 4.008	6.101 – 5.778	5.468 – 5.177	8.589 – 8.514 1H H11
($CDCl_3$)	2H	1H	2H	8.387 – 8.345 1H H11
				8.223 – 8.143 1H H13 H14
				8.077 – 7.974 1H H13 H14
				7.838 – 7.646 2H H12 H13
				7.397 – 7.143 2H H14 H12
6	4.083 – 4.003	6.106 – 5.782	5.482 – 5.196	8.598 – 8.523 1H H11
($CDCl_3$)	2H	1H	2H	8.228 – 8.138 1H H13 H14
				7.852 – 7.678 1H H12 H13
				7.336 – 7.200 1H H14 H12

The signals of H11 at 8.665 ppm – 8.589 ppm and 8.662 ppm – 8.586 ppm (spectra 1_2, 1_8, Tables 2, 7) point to the resonance structures $\mathbf{a_4\ A_4 \leftrightarrow a'_4\ A'_4 \leftrightarrow a'_7\ A'_7 \leftrightarrow a\ A}$ and $\mathbf{a_4\ A_4 \leftrightarrow a'_6\ A'_6 \leftrightarrow a\ A}$, respectively. The signals of H11 at 8.637 ppm – 8.562 ppm (spectrum 1_1, Tables 2, 7) support the resonance structures $\mathbf{a_3\ A_3 \leftrightarrow a_5\ A_5 \leftrightarrow a'_6\ A'_6}$. The signals of H11 at 8.606 ppm – 8.530 ppm and 8.601 ppm – 8.525 ppm (spectra 1_3, 1_4, Tables 2, 7) point to the resonance structures $\mathbf{a'_7\ A'_7 \leftrightarrow a'_1\ A'_1 \leftrightarrow a'_8\ A'_8 \leftrightarrow a\ A}$ and $\mathbf{a'_6\ A'_6 \leftrightarrow a'_3\ A'_3 \leftrightarrow a\ A}$, respectively**.**

The signals of H11 at 8.603 ppm – 8.528 ppm, 8.598 ppm – 8.537 ppm and 8.598 ppm – 8.523 ppm (spectra 4, 3, 6, Tables 3, 7) confirm the resonance structures $\mathbf{a'_4\ A'_4 \leftrightarrow a'_5\ A'_5 \leftrightarrow a\ A}$, $\mathbf{a'_5\ A'_5 \leftrightarrow a'_8\ A'_8 \leftrightarrow a\ A}$ and $\mathbf{a'_5\ A'_5 \leftrightarrow a'\ A'}$, respectively. The signals of H11 at 8.594 ppm – 8.519 ppm, 8.589 ppm – 8.514 ppm and 8.580 ppm – 8.537 ppm (spectra 1, 5, 2, Tables 3, 7) indicate the $\mathbf{a'_5\ A'_5}$

↔ **a'$_3$ A'$_3$** ↔ **a'$_0$ A'$_0$**, **a'$_3$ A'$_3$** ↔ **a' A'** and **a'$_3$ A'$_3$** ↔ **a'$_5$ A'$_5$** ↔ **a'$_8$ A'$_8$** ↔ **a A**, respectively. The signals of H11 at 8.387 ppm – 8.345 ppm (spectrum 5, Tables 3, 7) point to the resonance structures **a'$_1$ A'$_1$** ↔ **a'$_2$ A'$_2$** ↔ **a$_1$ A$_1$**.

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

Spectrum No (Solvent)	**Pyridin – 2- yl**		
	H 14 – of the structures	**H 14, H 13**	**H 13** – of the structures
1_3 ($CDCl_3$)	**a'$_1$A'$_1$**↔ **a'$_2$A'$_2$**↔ **a'$_0$A'$_0$**	8.245 – 8.145	**a'$_1$A'$_1$** ↔ **a'$_2$A'$_2$**
1_4 ($CDCl_3$)	**a'$_3$A'$_3$** ↔ **a'$_1$A'$_1$**	8.237 – 8.137	**a$_2$A$_2$** ↔ **a'$_3$A'$_3$**
4 ($CDCl_3$)	**a'$_2$A'$_2$** ↔ **a'$_1$A'$_1$** ↔ **a'$_0$ A'$_0$**	8.242 – 8.152	**a$_1$A$_1$** ↔ **a'$_1$A'$_1$** ↔ **a A**
2, 3 ($CDCl_3$)	**a'$_3$A'$_3$** ↔ **a'$_1$A'$_1$** ↔ **a'$_0$A'$_0$**	8.237 – 8.148	**a$_2$A$_2$** ↔ **a'A'**
1 ($CDCl_3$)	**a'$_4$A'$_4$** ↔ **a'$_1$A'$_1$** ↔ **a'$_0$A'$_0$**	8.232 – 8.143	**a'$_3$A'$_3$** ↔ **a'A'**
5 ($CDCl_3$)	**a$_4$A$_4$** ↔ **a'$_1$A'$_1$** ↔ **a'$_0$A'$_0$**	8.223 – 8.143	**a$_4$A$_4$** ↔ **a'$_3$A'$_3$** ↔ **a'A'**
6 ($CDCl_3$)	**a$_2$A$_2$** ↔ **a$_4$A$_4$** ↔ **a'$_1$A'$_1$**	8.228 – 8.138	**a$_2$A$_2$** ↔ **a$_4$A$_4$** ↔ **a'$_3$ A'$_3$**
1_8 (DMSO-D_2O)	**a'$_4$A'$_4$** ↔ **a'$_5$A'$_5$**	8.174 – 8.023	**a$_4$A$_4$** ↔ **a'$_3$A'$_3$**
1_2 (DMSO)	**a'$_4$A'$_4$** ↔ **a'$_6$ A'$_6$**	8.174 – 8.010	**a$_4$A$_4$** ↔ **a'$_5$A'$_5$**
1_1 (DMSO)	**a'$_5$A'$_5$**↔ **a'$_6$A'$_6$** ↔ **a'$_7$A'$_7$**	8.135 – 7.998	**a'$_5$A'$_5$** ↔ **a'$_3$A'$_3$**
5 ($CDCl_3$)	**a'$_8$A'$_8$** ↔ **a'$_6$A'$_6$** ↔ **a'$_7$A'$_7$**	8.077 – 7.974	**a'$_3$A'$_3$** ↔ **a'$_5$A'$_5$** ↔ **a'$_4$A'$_4$**

The signals of H14 at 7.532 ppm – 7.395 ppm, 7.517 ppm – 7.381 ppm and 7.503 ppm – 7.336 ppm (spectra 1_8 1_2 , 1_1, Tables 2, 6) confirm the resonance structures **a$_1$ A$_1$** ↔ **a'$_1$ A'$_1$** ↔ **a A**, **a$_2$ A$_2$** ↔ **a'$_3$ A'$_3$** ↔ **a A** and **a$_2$ A$_2$** ↔ **a'$_4$ A'$_4$** ↔ **a A**, respectively. The signals of H14 at 7.349 ppm – 7.212 ppm and 7.342 ppm – 7.205 ppm (spectra 1_3 1_4, Tables 2, 6) support the resonance structures **a'$_3$ A'$_3$** ↔ **a' A'** and **a'$_4$ A'$_4$** ↔ **a' A'**, respectively. The signals of H14 at 7.397 ppm – 7.143 ppm (spectrum 5, Tables 3, 6) confirm the resonance structures **a'$_1$ A'$_1$** ↔ **a'$_3$ A'$_3$** ↔ **a'$_4$ A'$_4$** ↔ **a'$_5$ A'$_5$** ↔ **a'$_6$ A'$_6$** ↔ **a'$_7$ A'$_7$**. The signals of H14 at 7.341 ppm – 7.204 ppm, 7.336 ppm – 7.200 ppm and 7.331 ppm – 7.195 ppm (spectra 4, 1, 2, 6, 3, Tables 3, 6) confirm the resonance structures **a'$_4$ A'$_4$** ↔ **a A , a'$_4$ A'$_4$** ↔ **a' A'** ↔ **a'$_5$ A'$_5$** and **a'$_5$ A'$_5$** ↔ **a' A'** ↔ **a'$_6$ A'$_6$**, respectively.

The signals of H13 at 8.245 ppm – 8.145 ppm and 8.237 ppm – 8.137 ppm (spectra 1_3, 1_4, Tables 2, 4) point to the **a'$_1$ A'$_1$** ↔ **a'$_2$ A'$_2$** and **a$_2$ A$_2$** ↔ **a'$_3$ A'$_3$** resonance structures, respectively. The signals of H13 at 8.242 ppm – 8.152 ppm, 8.237 ppm – 8.148 ppm and 8.232 ppm – 8.143 ppm (spectra 4, 2, 3, 1, Tables 3, 4) confirm the resonance structures **a$_1$ A$_1$** ↔ **a'$_1$ A'$_1$** ↔ **a A**, **a$_2$ A$_2$** ↔ **a' A'** and **a'$_3$ A'$_3$** ↔ **a' A'**, respectively.

The signals of H13 at 8.228 ppm – 8.138 ppm and 8.223 ppm – 8.143 ppm (spectra 6, 5, Tables 3, 4) confirm the resonance structures **a$_2$ A$_2$** ↔ **a$_4$ A$_4$** ↔ **a'$_3$ A'$_3$** and **a$_4$ A$_4$** ↔ **a'$_3$ A'$_3$** ↔ **a' A'**, respectively. The signals of H13 at 8.174 ppm – 8.023 ppm, 8.174 ppm – 8.010 ppm and 8.135 ppm – 7.988 ppm (spectra 1_8, 1_2, 1_1, Tables 2, 4) support the resonance structures **a$_4$ A$_4$** ↔ **a'$_3$ A'$_3$**, **a$_4$ A$_4$** ↔ **a'$_5$ A'$_5$** and **a'$_5$ A'$_5$** ↔ **a'$_3$ A'$_3$**, respectively. The signals of H13 at 8.077 ppm – 7.974 ppm (spectrum 5, Tables 3, 4) indicate the resonance structures **a'$_3$ A'$_3$** ↔ **a'$_5$ A'$_5$** ↔ **a'$_4$ A'$_4$**.

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

Spectrum No (Solvent)	**Pyridin – 2- yl**		
	H 13 – of the structures	**H 13, H 12**	**H 12** – of the structures
1_8(DMSO-D_2O)	$\mathbf{a_3A_3 \leftrightarrow a'_3A'_3 \leftrightarrow aA}$	7.967 – 7.869	$\mathbf{a_5A_5 \leftrightarrow a_1A_1 \leftrightarrow a'_8A'_8 \leftrightarrow aA}$
1_2(DMSO)	$\mathbf{a'_3A'_3 \leftrightarrow a'_5A'_5 \leftrightarrow aA}$	7.954 – 7.859	$\mathbf{a'_8A'_8 \leftrightarrow a'_7A'_7}$
1_1(DMSO)	$\mathbf{a'_4A'_4 \leftrightarrow a'_5A'_5 \leftrightarrow aA}$	7.935 – 7.837	$\mathbf{a'_7A'_7 \leftrightarrow a'_6A'_6}$
1_3($CDCl_3$)	$\mathbf{a'_5A'_5 \leftrightarrow a'_3A'_3 \leftrightarrow a'_0A'_0}$	7.859 – 7.688	$\mathbf{a'_7A'_7 \leftrightarrow a'_1A'_1 \leftrightarrow aA}$
1_4($CDCl_3$)	$\mathbf{a'_3A'_3 \leftrightarrow a'_5A'_5}$	7.854 – 7.681	$\mathbf{a_1A_1 \leftrightarrow a'_2A'_2 \leftrightarrow a'A'}$
4($CDCl_3$)	$\mathbf{a'_3A'_3 \leftrightarrow a'_4A'_4 \leftrightarrow a'_0A'_0}$	7.852 – 7.683	$\mathbf{a_2A_2 \leftrightarrow a'_2A'_2 \leftrightarrow aA}$
6($CDCl_3$)	$\mathbf{a'_3A'_3 \leftrightarrow a'_4A'_4}$	7.852 – 7.678	$\mathbf{a_2A_2 \leftrightarrow a'_1A'_1}$
1 - 3($CDCl_3$)	$\mathbf{a'_3A'_3 \leftrightarrow a'_5A'_5 \leftrightarrow a'_4A'_4}$	7.847 - 7.674	$\mathbf{a'_1A'_1 \leftrightarrow a'_2A'_2}$
5($CDCl_3$)	$\mathbf{a'_5A'_5 \leftrightarrow a'_4A'_4}$	7.838 – 7.646	$\mathbf{a'_6A'_6 \leftrightarrow a'_1A'_1 \leftrightarrow a'_3A'_3}$

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

Spectrum No (Solvent)	**Pyridin – 2- yl**		
	H 12 – of the structures	**H 12, H 14**	**H 14** – of the structures
1_8 (DMSO-D_2O)	$\mathbf{a_5A_5 \leftrightarrow a_4A_4 \leftrightarrow a'_6\ A'_6 \leftrightarrow a'_0A'_0}$	7.532 – 7.395	$\mathbf{a_1A_1 \leftrightarrow a'_1A'_1 \leftrightarrow aA}$
1_2 (DMSO)	$\mathbf{a'_7A'_7 \leftrightarrow a'_1A'_1 \leftrightarrow a'_6A'_6 \leftrightarrow a'_0A'_0}$	7.517 – 7.381	$\mathbf{a_2A_2 \leftrightarrow a'_3A'_3 \leftrightarrow aA}$
1_1 (DMSO)	$\mathbf{a'_7A'_7 \leftrightarrow a'_4A'_4 \leftrightarrow a'_0A'_0}$	7.503 – 7.336	$\mathbf{a_2A_2 \leftrightarrow a'_4A'_4 \leftrightarrow aA}$
1_3 ($CDCl_3$)	$\mathbf{a'_4A'_4 \leftrightarrow a'_2A'_2 \leftrightarrow a_1A_1}$	7.349 – 7.212	$\mathbf{a'_3A'_3 \leftrightarrow a'A'}$
1_4 ($CDCl_3$)	$\mathbf{a'_4A'_4 \leftrightarrow a'_1A'_1 \leftrightarrow a'_0A'_0}$	7.342 – 7.205	$\mathbf{a'_4A'_4 \leftrightarrow a'A'}$
5 ($CDCl_3$)	$\mathbf{a'_7A'_7 \leftrightarrow a'_4A'_4 \leftrightarrow a'_2A'_2 \leftrightarrow a'_1A'_1 \leftrightarrow a'_5A'_5 \leftrightarrow a'_3A'_3}$	7.397 – 7.143	$\mathbf{a'_1A'_1 \leftrightarrow a'_3A'_3 \leftrightarrow a'_4A'_4 \leftrightarrow a'_5A'_5 \leftrightarrow a'_6A'_6 \leftrightarrow a'_7\ A'_7}$
4 ($CDCl_3$)	$\mathbf{a'_4A'_4 \leftrightarrow a'_2A'_2 \leftrightarrow a'_1A'_1}$	7.341 – 7.204	$\mathbf{a'_4A'_4 \leftrightarrow aA}$
1, 2, 6 ($CDCl_3$)	$\mathbf{a'_2A'_2 \leftrightarrow a'_5A'_5 \leftrightarrow a'_0A'_0}$	7.336 – 7.200	$\mathbf{a'_4A'_4 \leftrightarrow a'A' \leftrightarrow a'_5A'_5}$
3 ($CDCl_3$)	$\mathbf{a'_1A'_1 \leftrightarrow a'_5A'_5}$	7.331 – 7.195	$\mathbf{a'_5A'_5 \leftrightarrow a'A' \leftrightarrow a'_6A'_6}$

The H12 signals at 7.967 ppm – 7.869 ppm , 7.954 ppm – 7.859 ppm and 7.935 ppm – 7.837 ppm (spectra 1_8 1_2 1_1, Tables 2, 5) indicate the $\mathbf{a_5\ A_5 \leftrightarrow a_1\ A_1 \leftrightarrow a'_8\ A'_8 \leftrightarrow a\ A}$, $\mathbf{a'_8\ A'_8 \leftrightarrow a'_7\ A'_7}$ and $\mathbf{a'_7\ A'_7 \leftrightarrow a'_6\ A'_6}$ resonance structures, respectively.

The H12 signals at 7.859 ppm – 7.688 ppm and 7.854 ppm – 7.681 ppm (spectra 1_3 1_4, Tables 2, 5) support the resonance structures $\mathbf{a'_7\ A'_7 \leftrightarrow a'_1\ A'_1 \leftrightarrow a\ A}$ and $\mathbf{a_1\ A_1 \leftrightarrow a'_2\ A'_2 \leftrightarrow a'\ A'}$, respectively. The H12 signals at 7.852 ppm – 7.683 ppm and 7.852 ppm – 7.678 ppm (spectra 4, 6, Tables 3, 5) confirm the resonance structures $\mathbf{a_2\ A_2 \leftrightarrow a'_2\ A'_2 \leftrightarrow a\ A}$ and $\mathbf{a_2\ A_2 \leftrightarrow a'_1\ A'_1}$, respectively. The H12 signals at 7.847 ppm – 7.674 ppm and 7.838 ppm – 7.646 ppm (spectra 1 – 3, 5, Tables 3, 5) confirm the resonance structures $\mathbf{a'_1\ A'_1 \leftrightarrow a'_2\ A'_2}$ and $\mathbf{a'_6\ A'_6 \leftrightarrow a'_1\ A'_1 \leftrightarrow a'_3\ A'_3}$, respectively

The calculated chemical shift of N10 at – 86.0 ppm of **2a** tautomer (Table 1) [10] point to an amine – type nitrogen atom.

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

Spectrum No (Solvent)	**Pyridin – 2- yl**	
	H 11	**structures**
1_2 (DMSO)	8.665 – 8.589	**$a_4A_4 \leftrightarrow a'_4A'_4 \leftrightarrow a'_7A'_7 \leftrightarrow aA$**
1_8 (DMSO-D_2O)	8.662 – 8.586	**$a_4A_4 \leftrightarrow a'_6A'_6 \leftrightarrow aA$**
1_1 (DMSO)	8.637 - 8.562	**$a_3A_3 \leftrightarrow a_5A_5 \leftrightarrow a'_6A'_6$**
1_3 ($CDCl_3$)	8.606 – 8.530	**$a'_7A'_7 \leftrightarrow a'_1A'_1 \leftrightarrow a'_8A'_8 \leftrightarrow aA$**
4 ($CDCl_3$)	8.603- 8.528	**$a'_4A'_4 \leftrightarrow a'_5A'_5 \leftrightarrow aA$**
1_4 ($CDCl_3$)	8.601 – 8.525	**$a'_6A'_6 \leftrightarrow a'_3A'_3 \leftrightarrow aA$**
3 ($CDCl_3$)	8.598 –8.537	**$a'_5A'_5 \leftrightarrow a'_8A'_8 \leftrightarrow aA$**
6 ($CDCl_3$)	8.598 – 8.523	**$a'_5A'_5 \leftrightarrow a'A'$**
1 ($CDCl_3$)	8.594 – 8.519	**$a'_5A'_5 \leftrightarrow a'_3A'_3 \leftrightarrow a'_0A'_0$**
5 ($CDCl_3$)	8.589 – 8.514	**$a'_3A'_3 \leftrightarrow a'A'$**
2 ($CDCl_3$)	8.580 – 8.537	**$a'_3A'_3 \leftrightarrow a'_5A'_5 \leftrightarrow a'_8A'_8 \leftrightarrow aA$**
5 ($CDCl_3$)	8.387 – 8.345	**$a'_1A'_1 \leftrightarrow a'_2A'_2 \leftrightarrow a_1A_1$**

The ^{1}H- data (100 MHz, 500 MHz), ^{13}C- and ^{15}N-NMR spectra and the theoretical calculations of the studied system point to the transformation of pyridine – type nitrogen atom to pyrrole – type as well as to amine – type nitrogen of 1,3,4 – thiadiazole and pyridine rings, the structures **a A A(I) , a_0 A_0 A(I)$_0$, a'_0 A'_0 A(I)'$_0$** and **a' A' A(I) '** (Figures 1-3).

The calculated chemical shift of NH group at 7.5 ppm of tautomer **2a** (Table 1) [10] supports sp^2 hybridization of N6 as well as the absence of the charges over 1,3,4 thiadiazole ring. The calculated chemical shift of N6 at – 133.98 ppm of tautomer **2a** (Table 1) [10] supports pyridine – type nitrogen atom.

In the ^{1}H-NMR spectra of **1** (100 MHz) [7, 8] in the range of the chemical shifts of the proton of NH group from 8.637 ppm to 7.233 ppm the nitrogen atoms N3, N4, N10 appear as pyridine – type, pyrrole – type, amine – type nitrogen while N6 as pyridine – type **A** (Figures 5, 9 - 12). 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 the 1,3,4 – thiadiazole ring.

The changes concern either the phases of p orbitals of N3 N4 and N10 nitrogen atoms of 1,3,4 – thiadiazole and pyridine rings, respectively see the structures **A_{0b} A_{0d}** (Figure 11) or the spin states of electrons of sp^2 orbitals, the structures **A_0, A_{0a}**, (Figures 9, 10) and support the transformation of pyridine – type nitrogen atom to pyrrole – type nitrogen atom in the second case. The simultaneous changes of the spin states of electrons of sp^2 orbitals and of the phases of p orbitals of N3 N4 N10 nitrogen atoms of 1,3,4 – thiadiazole and pyridine rings as well as the absence of the reversed electron demand cause the transformation of pyridine nitrogen atom to amine nitrogen atom, the structures **A_{0c} A_{0e}** (Figure 12). Consequently the structures **A_0, A_{0a}**, (Figures 9, 10) show the pyrrole – type nitrogen atoms N3 N4 N10 and the lack of the differences in the phases of p orbitals of 1S 2C 3N 4N 5C 6N 10N 11C - 15C. In the structures **A_{0b} A_{0d}** (Figure 11) the nitrogen atoms N3 N4 N10 are the pyridine – type but the phases of p orbitals of N3 N10 and N4 N10 differ from p orbitals of 1S 2C 4N 5C 6N 11C – 15C and 1S 2C 3N 5C 6N 11C – 15C atoms, respectively. In the structures **A' A'_a**

and **A'$_0$ A'$_{0a}$** (Figures 13, 3) the nitrogen atom N10 is pyridine – type and p orbitals of N10 C11 – C13 and N10 C11 C13 C14, respectively show no differences in their phases.

The ^{1}H-^{1}H long-range coupling constants in the 37.280 Hz – 43.776 Hz range (spectra 1 – 6, 6$_6$) (Tables 8, 9) [8], support the coupling of the protons of the pyridyl and -N-CH$_2$- CH=CH$_2$ groups *via* 2p orbitals of C14 C7 of the rigid structures **A' A'$_a$** and sp^2 hybridization of the exocyclic nitrogen atom N6 (Figure 13). The signals at – 0.033 ppm - 5.787 ppm (Table 9, spectra 1, 3 – 5, 6$_6$) support the transformation of sp^2 ⇔ sp^3.

The differences in the resonances of NH proton in the range from 8.637 ppm to 7.233 ppm are caused by the atomic charge over the pyridine ring. To assign the resonance structures of **1** in the range from 8.637 ppm to 7.233 ppm the chemical shifts of NH group, the ^{15}N-, ^{13}C- and ^{1}H- signals in ^{15}N-, ^{13}C- and ^{1}H-NMR spectra (100 MHz, 500 MHz) of **1** as well as the ^{1}H-^{1}H coupling constants of the pyridyl substituent have been analyzed. The resonance structures of the pyridine ring are shown on Figure 8.

In the ^{13}C-NMR spectrum of **1** the chemical shifts of C11 at 149.31 ppm and C15 at 149.87 ppm confirm pyridine - type nitrogen atom N10 of the structures **a$_1$A$_1$A(I)$_1$ a'$_1$A'$_1$A(I)'$_1$ a'$_2$A'$_2$A(I)'$_2$** and **a$_5$ A$_5$ A(I)$_5$**, respectively. The chemical shift of C12 at 124.01 ppm supports the pyridine - type nitrogen atom N10 of the structures **a$_2$A$_2$A(I)$_2$ a'$_3$A'$_3$A(I)'$_3$ a'$_5$ A'$_5$A(I)'$_5$**. The signal of C14 at 119.87 ppm points to the structures **a$_3$A$_3$A(I)$_3$ a'$_4$A'$_4$A(I)'$_4$ a$_5$A$_5$A(I)$_5$**. The signal of C13 at 136.77 ppm confirms the structures **a$_2$A$_2$A(I)$_2$ a'$_3$A'$_3$A(I)'$_3$ a$_4$A$_4$ A(I)$_4$ a'$_5$A'$_5$A(I)'$_5$**.

Figure 9. The changes of the electron configuration of N4 N10 nitrogen atoms of allyl-(5-pyridin-2- yl-[1,3,4] thiadiazol-2-yl)-amine, the structure **A$_0$**

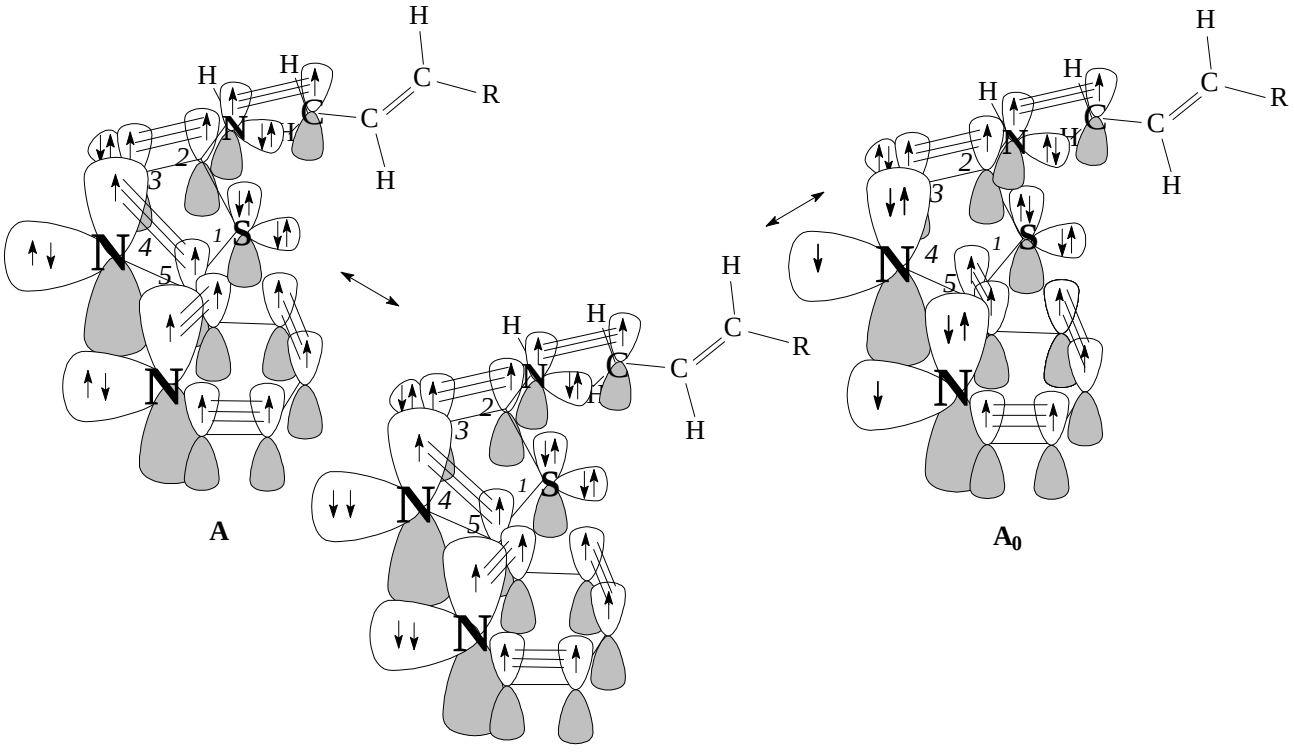


Figure 10. The changes of the electron configuration of N3 N10 nitrogen atoms of allyl- (5-pyridin – 2 – yl - [1,3,4] thiadiazol-2-yl)-amine, the structure **A_{0a}**

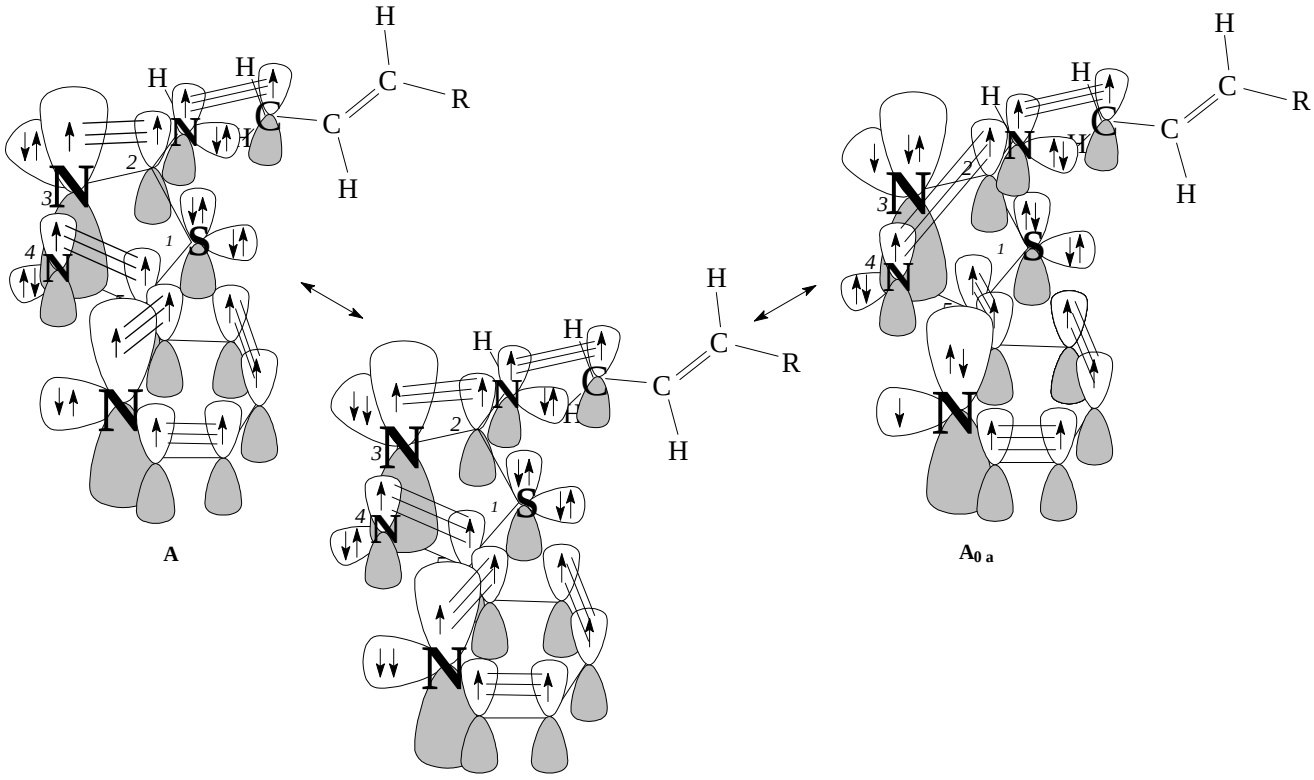


Figure 11. The changes of the electron configuration of N3 N10 and N4 N10 nitrogen atoms of allyl- (5-pyridin – 2 – yl - [1,3,4] thiadiazol – 2 - yl) - amine, the structures **A_{0b} A_{0d}**

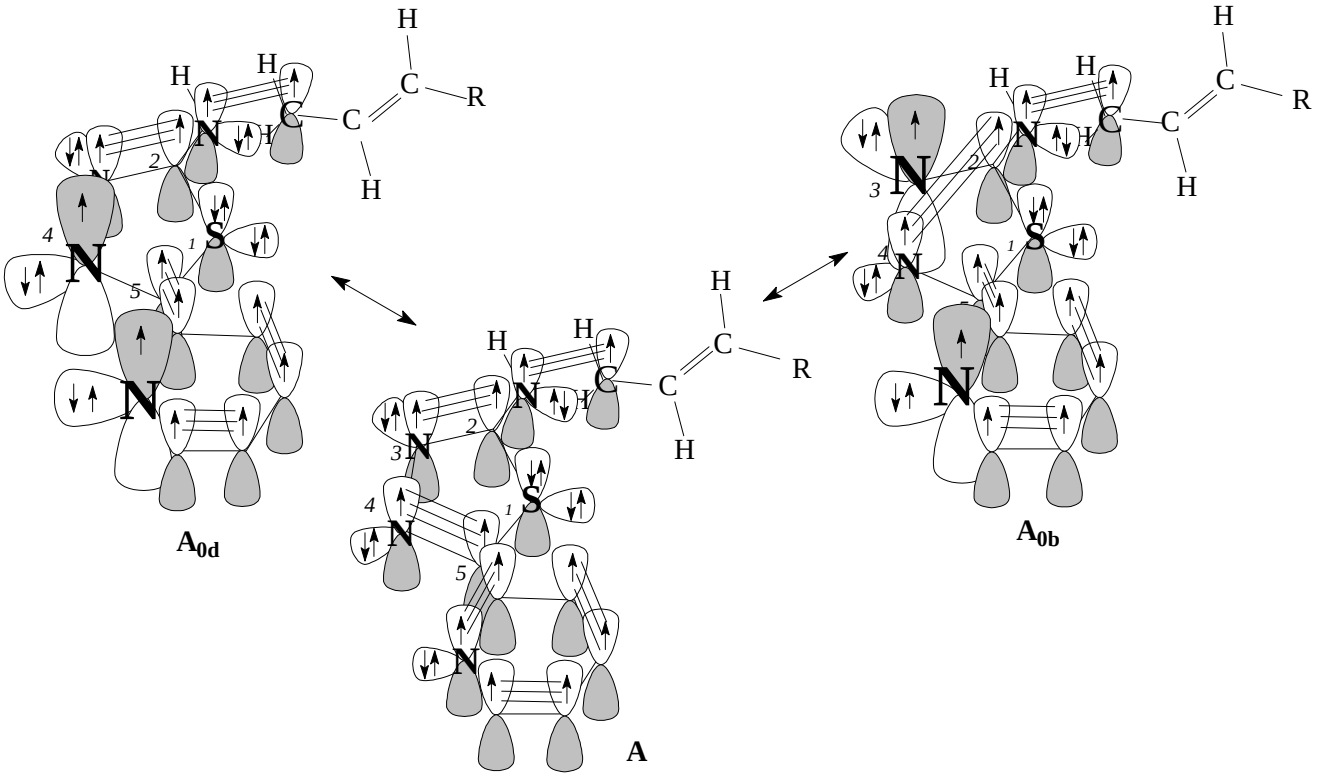


Figure 12. The changes of the electron configuration of N3 N10 and N4 N10 nitrogen atoms of allyl- (5-pyridin – 2 – yl - [1,3,4] thiadiazol-2-yl)-amine, the structures $\mathbf{A_{0c}}$ $\mathbf{A_{0e}}$

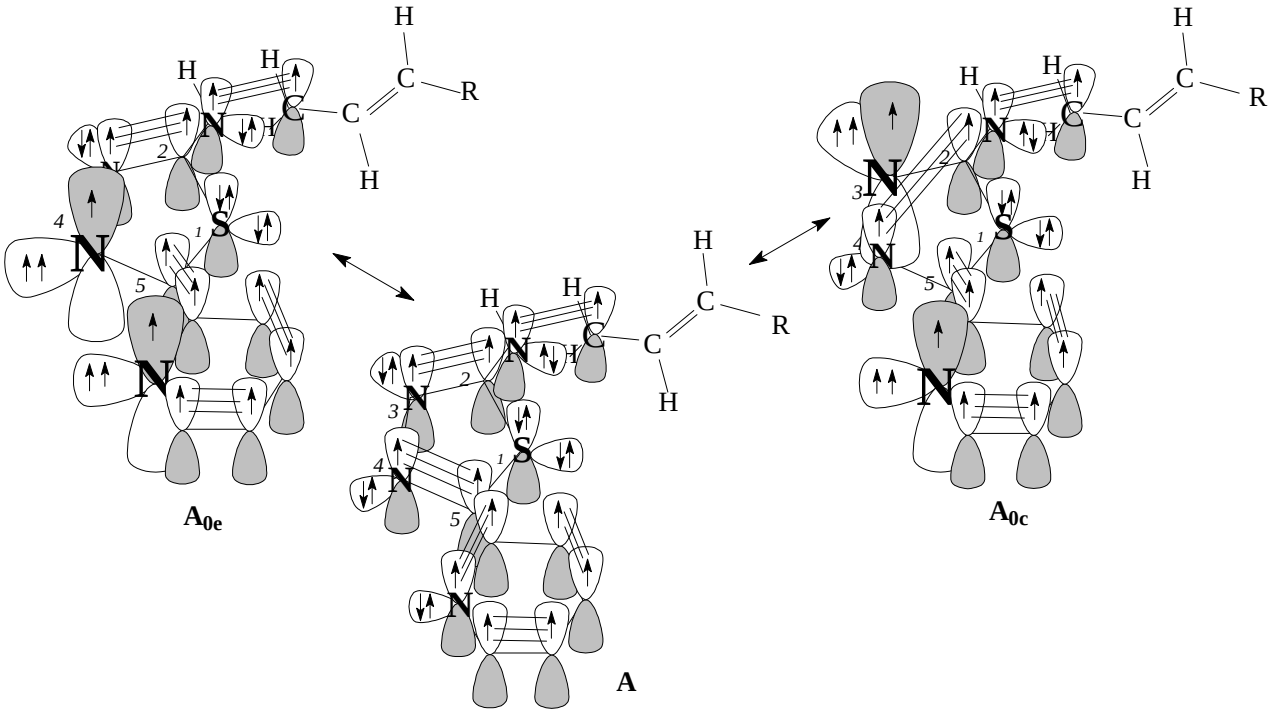
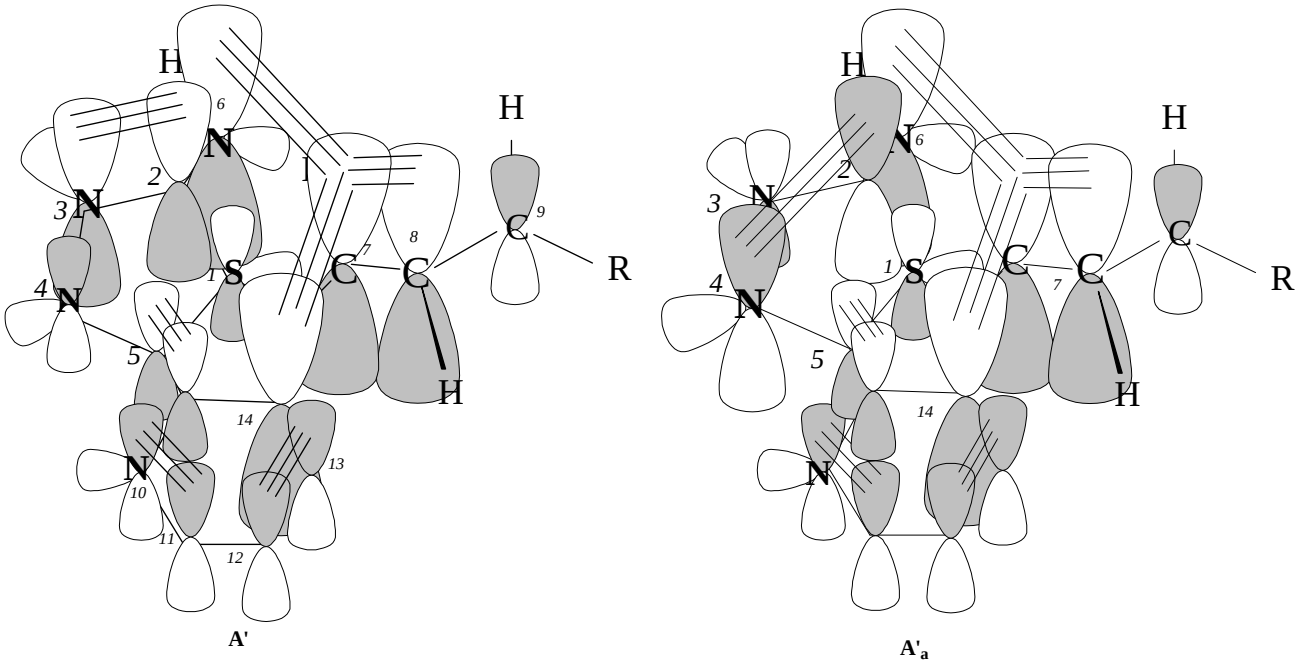


Figure 13. The resonance rigid structures **A'**, $\mathbf{A'_a}$ of allyl- (5-pyridin – 2 – yl - [1,3,4] thiadiazol-2-yl)-amine



The ^{1}H-NMR spectrum 1_7 (500 MHz) shows the signal of H14 of the structures $\mathbf{a'_1A'_1A(I)'_1}$ $\mathbf{a'_5A'_5A(I)'_5}$ $\mathbf{a'_6A'_6A(I)'_6}$ at 8.185 ppm. In the ^{1}H-^{13}C HMBC and HMQC correlatinon spectra the signal of H14 at 8.180 ppm exhibits a correlation to C14 at 119.7 ppm and C12 at 124.0 ppm, C15 at 149.7 ppm, C5 at 160.0 ppm, respectively and confirms $\mathbf{a'_5A'_5A(I)'_5}$ $\mathbf{a'_6A'_6A(I)'_6}$ structures. In the 2D ^{1}H-^{13}C HMQC spectra the cross – peak between H11 at 8.340 ppm and C14 at 119.9 ppm as well as the

correlation signals of H11 at 8.360 ppm to C14 at 119.9 ppm, C15 at 149,7 ppm support structures **a'$_2$ A'$_2$A(I)'$_2$ a$_1$A$_1$A(I)$_1$.** The chemical shift of N10 in ^{15}N-NMR spectrum of **1** at – 74.78 ppm supports the structures **a$_2$ A$_2$ A(I)$_2$ a'$_3$ A'$_3$ A(I)'$_3$ a$_4$ A$_4$ A(I)$_4$ a'$_{5-8}$A'$_{5-8}$A(I)'$_{5-8}$**.

The ^{1}H-^{1}H coupling constants J($H_{14}H_{13}$) 8.0 Hz J($H_{13}H_{14}$) 8.0 Hz J($H_{12}H_{13}$) 8.0 Hz of **1a** tautomer confirm the positive charge at C13 atom of the structures **a$_3$A$_3$A(I)$_3$ a'$_4$A'$_4$A(I)'$_4$** while the coupling constants J($H_{12}H_{13}$) 5.8 Hz J($H_{11}H_{12}$) 5.6 Hz J($H_{13}H_{11}$) 1.6 Hz indicate the positive charge at C15 and the negative one at N10 atoms of pyridine substituent of the structures **a$_4$A$_4$A(I)$_4$ a'$_7$ A(I)'$_7$**.

In the ^{1}H-NMR (100 MHz) spectra 1_1 – $_4$, 1 – 6, the NH group signals in the 8.637 ppm to 8.514 ppm and 8.387 ppm – 8.138 ppm range confirm the resonance structures **1A**, **1A', 1A$_1$**, **1A$_2$** and **1A$_3$**, **1A$_4$**, **1A$_5$** respectively (Table 10). At 8.077 ppm – 7.646 ppm and at 7.397 ppm – 7.143 ppm **1A'$_1$**, **1A'$_2$ 1A'$_3$** and **1A'$_4$ 1A'$_5$ 1A'$_6$ 1A'$_7$** resonance structures arise, respectively (spectra 1 – 6, $6_{5,6}$ 100MHz, $CDCl_3$, Table 11). The signals at 8.594 ppm *J*($H_{11}H_{9B}$) 42.432 Hz , 8.584 ppm *J*($H_{11}H_{9A}$) 38.400 Hz, 8.528 ppm *J*($H_{11}H_{9A}$) 37.280 Hz and 7.998 ppm *J*($H_{13}H_{9A}$) 40.064 Hz (spectra 4, 5 Table 8) 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 structure **A**.

Table 8. 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 (ppm)	***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
3	6.012	*J*(H_8H_{13}) 40.832	0.019 H
3	5.895	*J*(H_8H_{13}) 42.368	
3	5.886	*J*(H_8H_{14}) 39.168	
5	7.974	*J*($H_{13}H_{9A}$) 39.296	0.756 H
4	7.331	*J*($H_{14}H_{9A}$) 39.392	0.46 H
4	7.341	*J*($H_{14}H_{9A}$) 40.640	
2	6.008	*J*(H_8H_{12}) 39.872	0.071 H
2	5.890	*J*(H_8H_{13}) 41.728	
6	5.839	*J*(H_8H_{12}) 39.936	0.03 H
5	7.998	*J*($H_{13}H_{9A}$) 40.064	
1	8.152	*J*($H_{13}H_{9A}$) 40.672	0.38 H
5	7.819	*J*($H_{12}H_{9A}$) 40.832	1.356 H
1	8.223	*J*($H_{13}H_{9A}$) 41.760	0.38 H
6	7.697	*J*($H_{12}H_{9A}$) 41.984	0.14 H
6	8.218	*J*($H_{13}H_{9B}$) 42.240	0.172 H
4	8.594	*J*($H_{11}H_{9B}$) 42.432	
5	8.223	*J*($H_{13}H_{9B}$) 43.776	0.633 H

In the ^{1}H-NMR spectra 1_1 1_2 (100MHz, DMSO) [8] the signals at 8.270 ppm (1.08 H, broadened triplet) and at 8.310 ppm (1.05H, degenerated broadened triplet) (Table 10) correspond to the NH group proton of tautomers **1A$_5$** and **1A$_4$**, respectively. The broaded triplets suggest that these protons take part in the intermolecular hydrogen bonds. The broaded triplet in the ^{1}H-NMR spectrum 1_1 indicates the slow exchange of the proton of NH group, due to this fact, the coupling of the protons H6 H7 may be observed and support **1A** tautomer. These signals are the averaged ones in consequence of the rapid transitions of hydrogen atom between the exocyclic nitrogen atom N6 and N3 N4 ones of 1,3,4-thiadiazole ring, then degenerated broaded triplet at 8.310 ppm in the ^{1}H-NMR spectrum 1_2 point to the **1A$_4$ 1B$_4$ 1C$_4$** tautomers.. They disappear in D_2O (spectrum 1_8) .

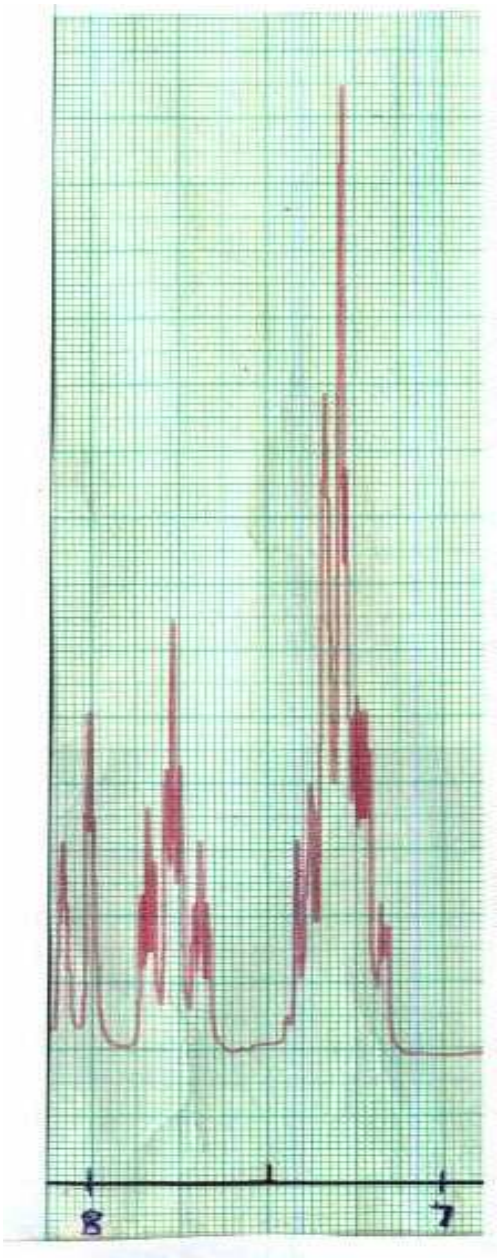
Table 9. The ^{1}H-NMR chemical shifts δ [ppm] from TMS and the ^{1}H-^{1}H long – range coupling constants [Hz] of **1**.

Spectrum No. ($CDCl_3$)	**δ**	***J***	**NH**
1	3.999	$J(H_{7D}H_{11})$ 37.696	0.822 H
3	-0.033	$J(H_6H_{11})$ 38.272	0.099 H
3	5.477	$J(H_{9A}\ H_{13})$ 40.192	0.26 H
3	5.787	$J(H_8H_{14})$ 43.136	
4	5.214	$J(H_{9B}H_{14})$ 43.712	0.24 H
4	5.280	$J(H_{9A}H_{12})$ 40.224	
5	5.266	$J(H_{9A}H_{12})$ 40.960	0.9 H
5	5.449	$J(H_{9A}H_{13})$ 39.680	
6_6	3.999	$J(H_6H_{12})$ 40.960	0.183 H
6_6	4.018	$J(H_6H_{11})$ 38.656	0.19 H

In ^{1}H-NMR spectrum 5 (100 MHz, $CDCl_3$) in the range from 7.397 ppm to 7.143 ppm a signal with an intensity of 7.5 H is seen (Figure 14, Tables 3, 11).

Two of them correspond to the proton of the pyridine ring of the resonance structures **a'$_1$ A'$_1$↔ a'$_3$ A'$_3$ ↔ a'$_4$ A'$_4$ ↔ a'$_5$ A'$_5$ ↔ a'$_6$ A'$_6$ ↔ a'$_7$ A'$_7$** (H 14) and **a'$_7$ A'$_7$ ↔ a'$_4$ A'$_4$ ↔ a'$_2$ A'$_2$ ↔ a'$_1$ A'$_1$ ↔ a'$_5$ A'$_5$↔ a'$_3$ A'$_3$** (H 12), (Tables 3, 6). The signal with the intensity of 5.5 H correspond to the proton of NH group of the resonance structures **1A'$_4$ ↔ 1A'$_5$ ↔1A'$_6$ ↔1A'$_7$** (Table 11). The NH group signal in the range from 7.397 ppm to 7.265 ppm with the intensity of 4.4H points to the transformation process of **1A'$_5$ ⇒ 1B$_3$ ⇒ 1C'$_4$** tautomers and supports pyridine – type nitrogen atoms N10, N4, N6 (Figures 1, 2, 8). The signals at 7.331 ppm $J(H_{14}H_{9A})$ 39.392 Hz and 7.341 $J(H_{14}H_{9A})$ 40.640 Hz (0.46H, Table 8. Spectrum 4) support the **1A'$_4$ 1B'$_4$ 1C'$_4$** tautomers.

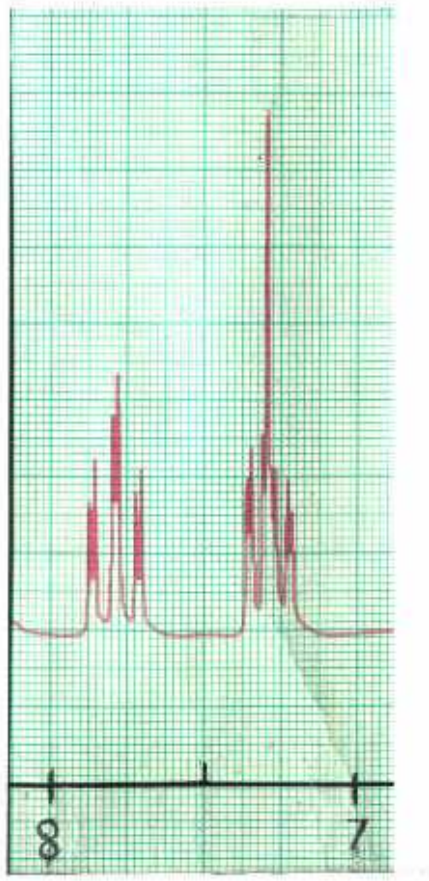
Figure 14. The ^{1}H-NMR NH group signal at 7.397 ppm – 7.143 ppm (spectrum 5)



ppm	integral
	1H 355.968
7.397	113.280
7.359	263.168
7.326	659.072
7.279	584.448
7.265	306.176
7.233	193.152
7.218	174.336
7.204	94.336
7.190	168.576
7.157	73.984
7.143	47.104

In ^{1}H-NMR spectrum 6_5 (100 MHz, $CDCl_3$) the signals at 7.317 ppm (0.74 H) and 7.256 ppm (0.34 H) (Table 11) correspond to the proton of NH group of **1A'$_5$** and **1A'$_6$** tautomers. A signal at 7.233 ppm (2H) (the spectra 6_5 and 6_6 100 MHz, $CDCl_3$, Figure 15, Table 11) confirms the transformation process of **1A'$_7$** $\Rightarrow$ **1B'$_7$**, **1A'$_7$** $\Rightarrow$ **1C'$_7$** tautomers and the amine – type nitrogen atoms N4, N3 of the 1,3,4–thiadiazole ring.

Figure 15. The ^{1}H-NMR NH group signal at 7.233 ppm (spectra 6_5, 6_6)



Spectrum No	ppm	integral
6_5	7.233	1316.352
6_6	7.233	801.792

Table 10. The ^{1}H-NMR chemical shifts δ [ppm] from TMS of the NH group of tautomer **1A**

Spectrum No (Solvent)	**NH**	**Structure**
1_1 (DMSO)	8.637 – 8.562 (0.08 H)	**1A 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 ($CDCl_3$)	8.387 – 8.345 (0.705 H)	**$1A_3$**
1_2 (DMSO)	8.310 (1.05 H)	**$1A_4$**
1_1 (DMSO)	8.270 (1.08 H)	**$1A_5$**
1 ($CDCl_3$)	8.232 – 8.143 (0.38 H)	
2 ($CDCl_3$)	8.237 – 8.148 (0.1 H)	
3 ($CDCl_3$)	8.237 – 8.148 (0.18 H)	
4 ($CDCl_3$)	8.242 – 8.152 (0.07 H)	
5 ($CDCl_3$)	8.223 – 8.143 (0.633 H)	
6 ($CDCl_3$)	8.228 – 8.138 (0.172 H)	
1_7 ($CDCl_3$)	8.20 – 8.16 (0.009 H)	

Table 11. The ^{1}H-NMR chemical shifts δ [ppm] from TMS of the NH group of tautomer **1A'** (in $CDCl_3$)

Spectrum No	NH	Structure
5	8.077 – 7.974 (0.756 H,)	**1A'$_1$**
4	7.852 – 7.683 (0.13 H)	**1A'$_2$**
6	7.852 – 7.678 (0.14 H)	**1A'$_3$**
1	7.847 – 7.674 (0.43 H)	
2	7.847 – 7.674 (0.18 H)	
3	7.847 – 7.674 (0.25 H)	
5	7.838 – 7.646 (1.356 H)	
1_7	7.78 – 7.73 (0.505 H)	
5	7.397 – 7,143 (5.5H)	**1A'$_4$**
4	7.341 – 7.204 (0.46 H)	**1A'$_5$**
1	7.336 – 7.200 (0.9 H)	**1A'$_6$**
2	7.336 – 7.200 (0.43 H)	**1A'$_7$**
6	7.336 – 7.200 (0.522 H)	
3	7.331 – 7.195 (0.41 H)	
6_5	7.317 (0.74 H)	**1A'$_5$**
1_7	7.29 – 7.25 (0.3148 H)	**1A'$_6$**
6_5	7.256 (0.34 H)	**1A'$_6$**
6_5, 6_6	7.233 (2 H)	**1A'$_7$**

Conclusions

The investigation of this specific tautomeric equilibrium support higher stability **A**, **B** and high energy diradical **A' A'$_a$**, **B'**, **C'** structures in the solution. The presently studied interconversions of the tautomeric forms **A' A'$_a$ B' C'** confirm pyridine – type nitrogen atoms for N10 N4 N6 and amine – type for N4 N3 of the pyridine and 1,3,4 – thiadiazole rings. The intensities of the signals of the NH group in the 100 MHz ^{1}H-NMR spectra in the range from 8.637 ppm to 7.143 ppm (Tables 10, 11) confirm the mesomeric resonance structures **A, B, A' B' C'** in solution.

Experimental

General

Compound **1** was prepared according to the published method [7]. The ^{1}H-, ^{13}C- and ^{15}N-NMR measurements of **1** 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 (500 MHz) have been recorded in $CDCl_3$ solution according to procedure given in the Bruker programme library. The ^{1}H-NMR spectra (1 – 6) of **1** were measured on a 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-NMR spectra 1, 1_3 1_4, 2 – 6, 6_5 6_6 (100 MHz) and 1_7 (500 MHz) have been recorded in $CDCl_3$ solution and the spectra 1_1 1_2 (100 MHz) in DMSO solution [7, 8, 10]. The ^{1}H-

NMR spectra $1_{1\text{-}4}$ (100 MHz) [8] have been taken using various concentration of **1** in DMSO or $CDCl_3$ solutions:

- in a DMSO solution, the concentration of **1** amounts to 1:3 (spectra 1_1 1_2, respectively);
- in a $CDCl_3$ solution, the concentration of **1** amounts to: 10 mg/0.5 mL and 25 mg/0.5 mL (maximal concentration, spectra 1_3 1_4, respectively).

The ^{1}H-NMR spectra 1 – 6, 6_5 6_6 [7], 1_7 [10] and 1_8 [8] have been recorded in $CDCl_3$ and DMSO – D_2O solutions, respectively, without any determination of the concentration of **1**. In the ^{1}H-NMR spectra 1 - 6 of **1** the signals of the protons of allyl, pyridyl substituents as well as of NH group of 1,3,4-thiadiazole have been recorded (Tables 2 - 7, 10, 11). In the ^{1}H-NMR spectra 6_5 6_6 of **1** [7] only the signals of the proton of NH group of the 1,3,4-thiadiazole have been recorded (Table 11).

The molecular geometries and properties corresponding to the local minima of the energy were calculated at the DFT level of the theory with the B3LYP density functional and the 6-31G* basis set [24,25]. 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 [26] was employed for these calculations.

References

1 Kornis, G. 1,3,4-Thiadiazoles. In *Comprehensive Heterocyclic Compounds*; Katritzky A.R., Ress W. C., (Eds); Pergamon Press: London. **1984**; vol. 6, pp. 545 – 577.

2 deStevens, G.; Eager, M.; Tarby, C. Steric and electronic effects controlling the synthesis of bridgehead nitrogen heterocycles. *Heterocycles* **1993**, *35*, 763 - 773.

3 Strzemecka, L. Cyclization reaction of 1,4 – disubstituted thiosemicarbasides. Part II. *Pol. J. Chem*. **1989**, *63*, 117 - 123.

4 Strzemecka, L. Cyclization of (N^1 – cinnamyl- thiocabamyl-)amidrazones. Part II. *Pol. J. Chem.* **1990**, *64*, 557 - 566.

5 Strzemecka, L. Otto T., Cyclization reaction of 1,4 – disubstituted thiosemicarbasides. Part I. *Pol. J. Chem*. **1988**, *62*, 757 - 766.

6 Strzemecka, L. Cyclization of (N^1-cinnamyl-thiocabamyl)-amidrazones. Part I. *Pol. J. Chem.* **1990**, *64*, 157 - 166.

7 Strzemecka, L. Tautomerism of 1,3,4-thiadiazole. Part I. *Annales UMCS, Sectio AA* **1995/1996**, vol. L/LI, 81 - 100.

8 Strzemecka, L. Tautomerism of 1,3,4-thiadiazole. Part II. *Annales UMCS, Sectio AA* **1999/2000**, vol. LIV/LV, 363 -377.

9 Strzemecka, L. Tautomerism of 1,3,4-thiadiazole. Part III. *Annales UMCS, Sectio AA* **1999/2000**, vol. LIV/LV, 379 - 392.

10 Strzemecka, L.; Maciejewska, D.; Urbańczyk-Lipkowska, Z. The structure of N-allyl derivatives of (5-(2'-pyridyl)-[1,3,4]thiadiazol-2-yl) amine in solution and the solid state studied by the ^{1}H, ^{13}C, ^{15}N NMR spectroscopy, X-ray crystallography and DFT computations. *J. Mol. Struct*. **2003**, *648*, 107 - 113.

11 Fremont, P.; Riverin, H.; Frenette, J.; Rogers, P. A.; Cote, C. Fatigue and recovery of rat soleus muscle are influenced by inhibition of an intracellular carbonic anhydrase isoform. *Am. J. Physiol*. **1991**, *260*, 615-21.

12 Kenny, A. D. Role of carbonic anhydraze in bone: plazma acetazolamide concentrations associated with inhibition of bone loss. *Pharmacology* **1985**, *31*, 97 - 107.

13 Potts A. C. Stable ophthalmic gel comprising methazolamide. *GB 2,223,166*, 04 Apr 1990.

14 Miyamoto, K.; Koshiura, R.; Mori, M.; Yokoi, H.; Mori, Ch.; Hasegawa, T.; Takatori, K. Antitumor activity of 5-substituted 2-acylamino-1,3,4-thiadiazoles against transplantable rodent tumors. *Chem. Pharm. Bull*. **1985**, *33*, 5126 - 9.

15 Cohen S. M, Ertruk E., Von Esch A.M., Crovetti A.. J., Bryan T. G., Carcinogenicity of 5 – nitrofurans and related compounds with amino heterocyclic substituents. *J. Natl. Cancer Inst.* **1975**, *54*, 841 - 50

16 Miyahara M., Nakadate M., Sueyohi S., Tanno M., Miyahara M., Kamiya S., Antitumor activity of 2-acylamino-1,3,4-thiadiazoles and related compounds. *Chem. Pharm. Bull.* **1982**, *30*, 4402 - 6.

17 Mamolo M. G., Falagiani V., Zampieri D., Vio L., Banfi E., Synthesis and antimycobacterial activity of [5-(pyridin-2-yl)-1,3,4-thiadiazol-2-ylthio]acetic acid arylidene-hydrazide derivatives. *Farmaco* **2001**, *56*, 587 - 92.

18 Gadad A. K., Karki S. S., Rajukar V. G., Bhongade B.A., Synthesis and biological evaluation of 5-formyl-6-arylimidazo(2,1-b)-1,3,4-thiadiazole-2-N-(dimethylaminomethino) sulfonamides as antitumor agents. *Arzneim. Forsch*. **1999**, *49*, 858 - 63.

19 Cleirci F., Pocar D., Guido M., Loche A., Perlini V, Brufani M., : Synthesis of 2-amino-5-sulfanyl-1,3,4-thiadiazole derivatives and evaluation of their antidepressant and anxiolytic activity. *J. Med. Chem*. **2001**, *44*, 931 - 6.

20 Barboiu M., Supuran C. T., Menabuoni L., Scozzafawa A., Mincione F., .Briganti F., Mincione G., Carbonic anhydrase inhibitors. Synthesis of topically effective intraocular pressure lowering agents derived from 5-(omega-aminoalkylcarboxamido)-1,3,4-thiadiazole-2-sulfonamide. *J. Enzyme Inhib. Med. Chem.* **2000**, *15*, 23 - 46.

21 Mazzone G., Pignatello R., Mazzone S., Panico A., Pennisi G., Castana R., Mazzone P., Synthesis and local anesthetic activity of alkylaminoacyl derivatives of 2-amino-1,3,4-thiadiazole. *Farmaco*. **1993**, *48*, 1207 - 24.

22 Cox J. M., Hawkes T. R., Bellini P. E., Russell M., Barrett R., The design and synthesis of inhibitors of imidazoleglycerol phosphate as potential herbicides. *Pestic. Sci*. **1997**, *50*, 297 -311.

23 Zucchi F., Trabanelli G., Gonzales N. A., Pyrimidine and thiadiazole derivatives as inhibitors of cooper corrosion in sodium chloride solution. *ACH - Mod. Chem*. **1995**, *132*, 579 -88.

24 Lee C., Yang W., Parr R.G. Development of the Colle – Salvetti corelation – energy formula into a functional of the electron density. *Phys. Rev*. **1988**, *B 37*, 785 - 9.

25 Becke A.D. Density – functional termochemistry. III. The role of exect exchange. *J. Chem. Phys.* **1993**, *98*, 5648 - 52.

26 Frisch M.J., Trucks G.W, Schlegel H. B., Scuseria G. E, Robb M. A., Cheeseman J.R., Zakrzewski V.G., Montgomery J.A.Jr, Stratmann R.E., Burant J.C., Dapprich S., Millam J. M, Daniels A. D., Kudin K. N., Strain M. C., Farkas O., Tomasi J., Barone V., Cossi M., Cammi R., Mennucci B., Pomelli C., Adamo C., Clifford S., Ochterski J., Petersson G. A., Ayala P. Y., Cui

Q., Morokuma K., Malick D. K., Rabuck A. D., .Raghavachari K, Foresman J. B., Cioslowski J., Ortiz J. V., Baboul A.G., Stefanov B. B., Liu G., Liashenko A., Piskorz P., Komaromi I., Gomperts R., Martin L. R., Fox D. J., Keith T., Al-Laham M. A., Peng C.Y., Nanayakkara A., Gonzalez C., Challacombe M., Gill P.M.W., Johnson B., Chen W., Wong M. W., Andres J.L., Gonzalez C., Head-Gordon M., Replogle E. S.; Pople J.A. *GAUSSIAN 98*, Revision A.7; Gaussian, Inc.: Pittsburgh, PA, **1998**.

Sample Availability: Available from the author.