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The electron configuration of the exocyclic nitrogen atom of allyl (5(2'-pyridyl)-[1,3,4]thiadiazol-2-yl) amine

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The electron configuration of the exocyclic nitrogen atom of allyl- (5-(2'--pyridyl)-[1,3,4] thiadiazol-2-yl)-amine has been determined on the basis of the 1H 13C 15N NMR spectra and B3LYP/6-31G(d, p) computations.

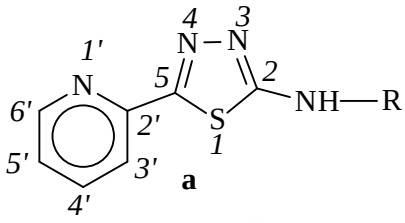
1. INTRODUCTION

The 1,3,4 - thiadiazoles possessing an amino group at C2 atom can exist in different tautomeric forms (Scheme 1). The tautomeric equilibrium is affected by the exocyclic N- atom and the C-5 of the 1,3,4-thiadiazole ring substituents [1, 2].

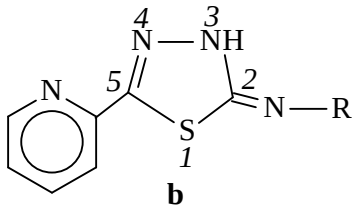
The 2-amino-[1,3,4]thiadiazole exists in the amino form either in the solution and in the solid state. This tautomer is the main species in 5-alkoxy derivatives. In the hydrazone derivatives H-atom is also attached to the exocyclic nitrogen atom, but in the sulfonamido derivatives the tautomeric equilibrium is shifted towards the imido form **b–**type. The 2-N and/or 5-substituted 2-amino[1,3,4]thiadiazole derivatives may exist in the mesoionic forms [2, 3, 4].

N-Allyl-(5-(2'-pyridyl)-[1,3,4]thiadiazol-2-yl)-amine is the subject of the present studies. The previous studies on the ^{1}H NMR spectra (100 MHz, 500 MHz) of allyl- and (3-phenyl-allyl)-(5-(2'-pyridyl)-[1,3,4]thiadiazol-2-yl)--amine point to the presence of the amino and imino tautomers **1a 1b 1c'**, **2a 2b 2c'** and various mesomeric forms of allyl- and (3-phenyl-allyl)-(5-(2'-pyridyl)--[1,3,4]thiadiazol-2-yl)-amine **1a 2a** and their tautomeric modifications 3H (allyl-(3-phenyl-allyl)-(5-(2'-pyridyl)-[1,3,4] thiadiazol-2-ylidene)-amine **1b 2b** and 3H-(allyl-(3-phenyl-allyl)-(2-(2'-pyridyl)-[1,3,4]thiadiazol-5-ylidene) amine **1c' 2c'** (Schemes 1, 2) [5, 6, 7, 8, 9].

Scheme 1



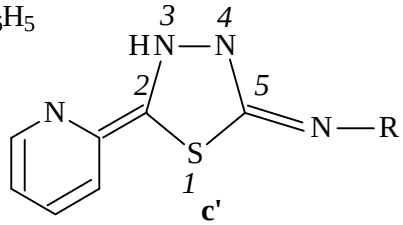
a



b

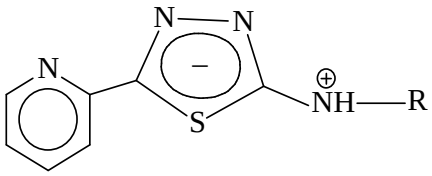
1a1b1c. R = —CH_2—CH=CH_2 (3″, 2″, 1″)

2a2b2c. R = —CH_2—CH=CH—C_6H_5

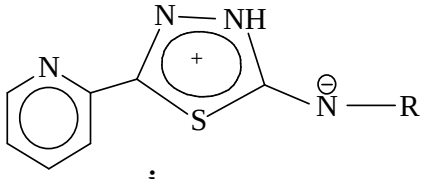


c'

Scheme 2



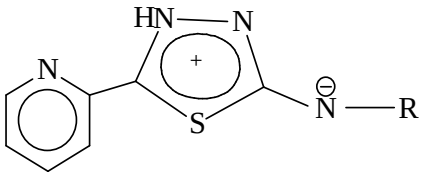
h



i

1h 1i 1j. R = —CH_2—CH=CH_2

2h 2i 2j. R = —CH_2—CH=CH—C_6H_5



j

In the molecules of the studied systems one can expect the mesoionic forms.

To describe the mesomeric forms of allyl- and (3-phenyl-allyl)-(5-(2'--pyridyl)-[1,3,4]thiadiazol-2-yl)-amine **1a 2a** and their tautomeric modifications 3H (allyl-(3-phenyl-allyl)-(5-(2'-pyridyl)-[1,3,4] thiadiazol-2-ylidene)-amine **1b 2b** and 3H-(allyl-(3-phenyl-allyl)-(2-(2'-pyridyl)-[1,3,4] thiadiazol-5-ylidene) amine **1c' 2c'** it is necessary to take into account the distribution of electrons in the molecule.

On account of the presence of allyl substituent in the molecule, the exocyclic nitrogen atom may appear as the amino–type, pyrrole–type or pyridine–type nitrogen.

In this contribution we discuss the ^{1}HNMR spectra of the product **1**. The changes of the chemical shifts from δ = 3.922 to δ = 3.954, δ = 3.978 to δ = 4.008, δ = 4.032 to δ = 4.061 may arise from different electron configurations of the exocyclic nitrogen atom C 2-N.

2. RESULTS AND DISCUSSION

According to the XRD data [9] only one tautomer **a–**type is present in the crystals of both compounds **1**, **2**. In the solid state the *egzo*-amino form **a** is stabilized by different H-bonds , and is more stable then *egzo*-imino one **b** by 35 kJ / mol according to the DFT level of theory [9].

In the ^{1}H NMR spectra of product **1** in a DMSO solution recorded at 100 MHz the signal of **NH** group appears at δ 8.270 (1.08H broaded triplet), δ 8.310 (1.05H degenerated, broaded triplet) respectively [7]. The broaded triplets suggest that this proton take part in the intermolecular hydrogen bonds. The presence of the broaded triplet at δ 8.270 indicates the slow exchange of the proton of NH group, the coupling of the protons of -NH-CH_2- and the existence of **1a** tautomer. The degenerated broaded triplet at δ 8.310 is the averaged one in consequence of the rapid transitions of hydrogen atom between the exocyclic nitrogen atom C 2-N and 3N 4N ones of 1,3,4-thiadiazole ring and support the existence of the imino tautomer. These signals disappear in D_2O. The values of the chemical shifts for the propton of NH group of **1** point to the pyrrole–type or pyridine–type nitrogen atom.

The value of the chemical shift for the proton of NH group of **1** recorded in $CDCl_3$ solution at 500.16 MHz, δ 5.81 [9] is in agreement with the resonanses of the amino protons. The signal of the nitrogen atom ^{15} N appears at δ-308.58 [9] and supports the amino–type nitrogen.

In the ^{1}H ^{1}H COSY spectrum of **1** compound the correlation signals at δ 6.750 (3 NH), δ 7.800 (4'-H) and at δ 5.950 (H-2"), δ 8.150 (H-3') support the presence of the mesomeric structure of **b**–type and the possible turned mesomeric structures of **1a 1b** tautomers, respectively.

The earlier studies [6, 7, 8] on the ^{1}H NMR spectra (100 MHz) of allyl-and (3-phenyl-allyl)-(5-(2'- pyridyl)-[1,3,4] thiadiazol-2-yl)-amine **1**, **2** point to the differences in the hybridization of the exocyclic nitrogen atom C 2-N. The differences in the chemical shifts values of the protons of -N-CH_2- group of **1** and **2** suggest the changes in $sp^3 \Leftrightarrow sp^2$ and $sp^2 \Leftrightarrow sp$ hybridization of the exocyclic nitrogen atom C 2-N of **1** and **2**, respectively [6, 7, 8].

The coupling constants of the protons of allyl substituent of **1** support the presence of these tautomers in sp^3, sp^2 hybridization of the exocyclic nitrogen atom C 2-N, the mobile **1a$_{d'}$** and rigid **1a$_{e'}$**, **1a$_d$, 1a$_e$** structures [7],.

The coupling constants J(H_bH_c) 7.6 Hz, J(H_bH_d) 7.6 Hz support the presence of the tautomers **1a$_{d'}$,** the lack of the rigid structures and sp^3 hybridization of the exocyclic nitrogen atom C 2-N [7]. The coupling constants of the protons J(H_bH_c) 8.2 Hz, J(H_bH_d) 8.2 Hz support the lack of the rigid structures and suggest the transformation of the structures **1a$_{d'}$** $\Leftrightarrow$ **1a$_{e'}$** . The coupling constants of the protons J(H_bH_c) 18.8 Hz, J(H_bH_d) 11.2 Hz confirm the existence of the rigid structure **1a$_{e'}$** and sp^2 hybridization of the exocyclic nitrogen atom C 2-N [7].

The coupling constants of the protons J(H_bH_c) 8.2 Hz, J(H_bH_d) 7.8Hz point to the transformation of the rigid structures **1a$_d$** $\Leftrightarrow$ **1a$_e$** . The coupling constants J(H_bH_c) 7.5 Hz, J(H_bH_d) 7.4 Hz confirm the presence of the structures **1a$_d$** whereas those J(H_bH_c) 18.9 Hz J(H_bH_d) 11.5 Hz support the structures **1a$_e$** in sp^3 and sp^2 hybridization of the exocyclic nitrogen atom C 2-N, respectively [7].

In the ^{1}H NMR spectra of **1** (100 MHz) the small differences appear in the chemical shifts values of the protons of -N-CH_2- group of allyl substituent (Tables 1, 2). It suggests the changes in the polarization of the bond of N-3"C resulting from the differences in the electron density distribution of N-3"C.

In the ^{1}H NMR spectra 1, 1_3, 1_4, 2-6 a signal of -N-CH_2- group appears at δ 3.999-4.088 as two doublet of a doublet (Tables 1, 2) [6, 7]. The coupling constants of the protons of allyl substituent J(H_bH_c) 7.5 Hz, J(H_bH_d) 7.4 Hz and J(H_bH_c) 18.9 Hz J(H_bH_d) 11.5 Hz indicate the presence of the rigid structures **1a$_d$** and **1a$_e$** respectively [7].

In the ^{1}H NMR spectra 1_3, 1_4 independently on the concentration of the product used the signal of the protons of -N-CH_2- group arises at δ 4.003–4.086 as two doublet of a doublet: δ 4.003–4.032, δ 4.056–4.086 and supports the presence of non-equivalent protons AB system of -N-CH_2- group of a rigid structures **1a$_d$, 1a$_e$,** the coupling constants J(H_bH_c) = J(H_cH_b) 7.5 Hz, J(H_bH_d) = J(H_dH_b) 7.4 Hz and J(H_bH_c) = J(H_cH_b) 18.9 Hz, J(H_bH_d) = J(H_dH_b) 11.5 Hz, respectively [7].

In the ^{1}H NMR spectra 1_3, 1_4 one can observe insignificant changes in time (Table 2); the small differences appear in the chemical shifts values of the protons of -N-CH_2- group of allyl substituent of the structures **1a$_d$**, **1a$_e$**.

In the ^{1}H NMR spectrum 1_3 after 10 min since preparation of the solution no changes have been observed, after 30 min the resonances lines at δ 4.0711, δ 4.0565 are shifted to the lower field δ 4.0735, δ 4.0589, respectively.

In the ^{1}H NMR spectra 1_4 and 1_4^*-recorded after 20 min since preparation of the solution the resonances lines indicate the changes in the structures of **1a$_d$**, **1a$_e$** tautomers (Table 2). This suggests the changes in the polarization of the bond of N-3"C of these tautomers [7].

In the ^{1}H NMR spectra 1_2, 1_5 a signal of -N-CH_2- group arises at δ 3.988-4.086 as a multiplet and at δ 3.988-4.069 as a doublet of a doublet respectively. The coupling constants of the protons of allyl substituent J(H_bH_c) 7.6 Hz J(H_bH_d) 7.6 Hz, J(H_bH_c) 18.8 Hz, J(H_bH_d) 11.2 Hz support the existence of the structures **1a$_{d'}$**, **1a$_{e'}$**, while J(H_bH_c) 7.5 Hz, J(H_bH_d) 7.4 Hz, J(H_bH_c) 18.9 Hz J(H_bH_d) 11.5 Hz **1a$_d$**, **1a$_e$** structures, respectively [7].

In the ^{1}H NMR spectrum 1_1 a multiplet of -N-CH_2- group undergoes splitting to three doublet of a doublet at δ 3.922-3.954, δ 3.978-4.008, δ 4.032-4.061 (Table 2). The coupling constants values of the protons of allyl substituent J(H_bH_c) 7.6 Hz J(H_bH_d) 7.6 Hz support the lack of the rigid structures the sp^3 hybridization of the exocyclic nitrogen atom C 2-N and the presence of **1a$_{d'}$** tautomer while J(H_bH_c) 18.8 Hz, J(H_bH_d) 11.2 Hz confirm the presence of **1a$_{e'}$** tautomer [7].

The doublet of a doublet at δ 3.922-3.954, δ 3.978-4.008 support the presence of the structures **1a$_{d'}$**, **1a$_{e'}$**, whereas that at δ 4.032-4.061 of **1h$_{e'}$**, (Scheme 3)

In the structure **1a$_{e'}$**, at the chemical shifts values δ 3.922-3.954 the bonding interactions occur between 2p orbitals of N-3"C with the electrons show of different spin states. At the chemical shifts values δ 3.978-4.008 in the structure **1a$_{e'}$**, the antibonding interactions between 2p orbitals of N-3"C may occur or the bonding ones. In the last case the electrons show the same spin states (Scheme 4) [10-14].

Because of the reversed electron demand of the bonding and antibonding orbitals of the structure **1a$_{e'}$**, the exocyclic nitrogen atom N-3"C may be negatively charged. The differences in the coupling constants J(H_bH_a) 17.6 Hz J(H_bH_c) 18.8Hz, J($H_bH_{a'}$) 10.6Hz J(H_bH_d) 11.2Hz (100MHz) [7] and the ^{13}C NMR signals of allyl substituent C-1" δ 117.99, C-2" δ 132.80. C-3" δ 49.28 [9] support the negatively charged pyridine–type nitrogen atom and positively charged allyl cation.

Tab. 1. The chemical shifts values of -N-CH_2- group

-N-CH_2- (δ)					
Spectrum no, Solvent					
1 ($CDCl_3$)	2 ($CDCl_3$)	3 ($CDCl_3$)	4 ($CDCl_3$)	5 ($CDCl_3$)	6 ($CDCl_3$)
δ 3.999	δ 4.003	δ 4.003	δ 4.003	δ 4.008	δ 4.003
δ 4.013	δ 4.018	δ 4.018	δ 4.022	δ 4.022	δ 4.018
δ 4.027	δ 4.032	δ 4.036	δ 4.036	δ 4.036	δ 4.032
δ 4.050	δ 4.055	δ 4.060	δ 4.060	δ 4.060	δ 4.055
δ 4.064	δ 4.069	δ 4.074	δ 4.074	δ 4.074	δ 4.074
δ 4.079	δ 4.083	δ 4.088	δ 4.088	δ 4.088	δ 4.083

Tab. 2. The chemical shifts values of -N-CH_2- group

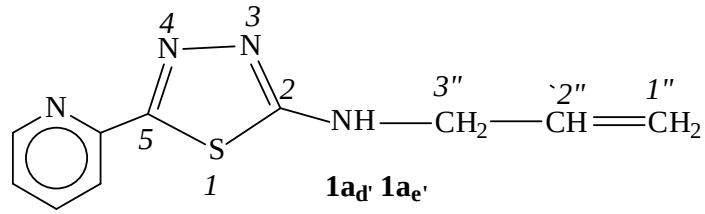
-N-CH_2- (δ)						
Spectrum no, Solvent						
1_1 (DMSO)	1_2 (DMSO)	1_5 (D_2O + DMSO)	1_3, 1_3^* ($CDCl_3$)	1_4 ($CDCl_3$)	1_4^* ($CDCl_3$)	1_3^{**} ($CDCl_3$)
δ 3.922						
δ 3.939						
δ 3.954	δ 3.988				δ 4.005	
δ 3.978	δ 4.037	δ 3.988	δ 4.003	δ 4.003	δ 4.020	δ 4.003
δ 3.993	δ 4.086	δ 4.003	δ 4.017	δ 4.017	δ 4.035	δ 4.017
δ 4.008		δ 4.017	δ 4.032	δ4.032	δ 4.059	δ 4.032
δ 4.032		δ 4.039	δ 4.056	δ 4.056	δ 4.074	δ 4.059
δ 4.047		δ 4.054	δ 4.071	δ 4.071	δ 4.088	δ 4.074
δ 4.061		δ 4.069	δ 4.086	δ 4.086		δ 4.086

1_3^*, 1_3^{**} – the ^{1}H NMR spectra have been recorded after 10 and 30 min, respectively since preparation of the solution

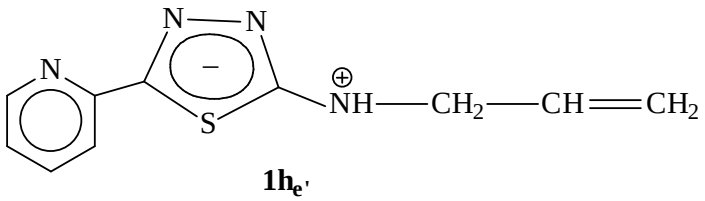
1_4^* – the ^{1}H NMR spectrum has been recorded after 20 min since preparation of the solution

The coupling constants $J(H_bH_a)$ 17.6 Hz, $J(H_bH_{a'})$ 10.6Hz $J(H_bH_a)$ 17.3 Hz $J(H_bH_{a'})$ 10.9 Hz (100 MHz) [7] point to the differences in the spin states of electrons of 2p orbitals of pyridine-type nitrogen and carbon atoms N-C 3" of **1**. The exocyclic nitrogen atom, the pyridine–type, is occupied with eight electrons. The coupling constants $J(H_bH_a)$ 17.1 Hz $J(H_aH_b)$ 17.1 Hz, $J(H_bH_{a'})$ 10.1 Hz $J(H_{a'}H_b)$ 10.1 Hz (500 MHz) [9] confirm the lack of the differences in

the spin states of electrons of 2p orbitals of pyridine-type nitrogen and carbon atoms N-C 3" of **1,** the exocyclic nitrogen atom N-C 3" is surrounded by seven electrons . The magnitude of the couplings $J(H_cH_b)$ = $J(H_bH_c)$ 5.6 Hz (500 MHz) for **1** confirms pyrrole–type nitrogen atom N-C 3" and the possible transformation of $sp^2 \Leftrightarrow sp$.



1a$_{d'}$ 1a$_{e'}$



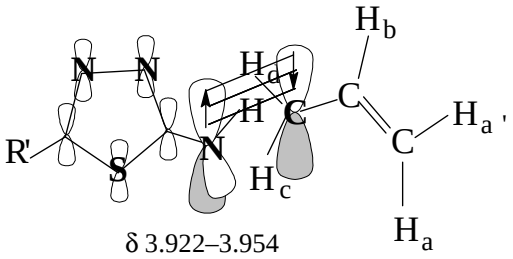
1h$_{e'}$

Scheme 3

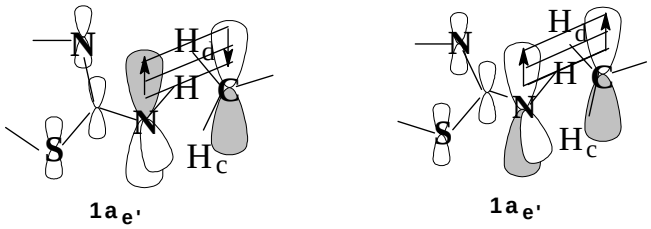
The chemical shift value of N-1' δ – 80.01 ppm of **1a** tautomer [9] supports pyrrole–type nitrogen atom of pyridyl substituent. The calculated chemical shift value of N 3 δ – 77.78 ppm [9] and ^{13}C resonances line of C 2 δ 171.42 in ^{13}C NMR spectrum [9] confirm pyridine–type nitrogen atom of **1a** tautomer and the lack of the differences in the spin states of electrons of 2p orbitals of C 2-N 3 (Scheme 5, structure **a'**). The chemical shift value of N 1' δ – 80.01 ppm and the calculated of N 3 δ – 77.78 ppm of **1a** tautomer point to the lack of the charges over pyridine and 1,3.4-thiadiazole rings.

The calculated signal at δ 8.125 (H 3') of **1a** tautomer indicates the interactions of 2p orbitals of N 1'-C 2', C 3'-C 4', C 5'-C 6'. The coupling constants $J(H_{5'}H_{3'})$ 1.0 Hz $J(H_{6'}H_{3'})$ 0.5 Hz confirm the lack of the charges on the pyridine ring.

Double signals of the protons of NH group and of pyridyl substituent that appear in the ^1H NMR spectra (100 MHz) support the presence of the **a, a'** tautomers [6].

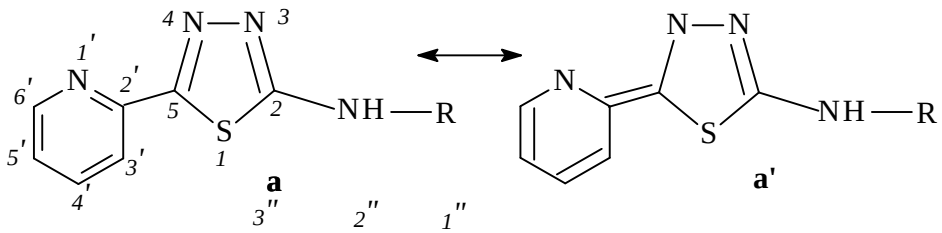


δ 3.922–3.954



δ 3.978–4.008

Scheme 4



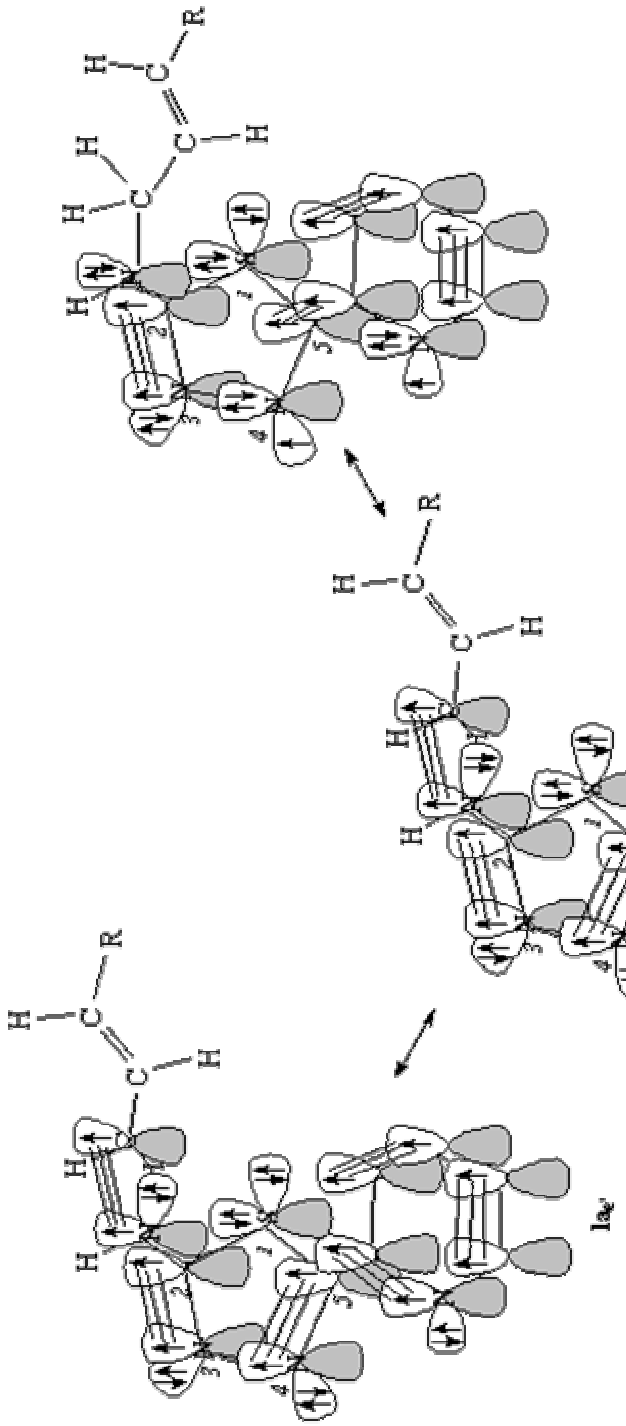
1a 1a'. R = —CH_2—CH=CH_2 (3'' 2'' 1'')

2a 2a'. R = —CH_2—CH=CH—C_6H_5

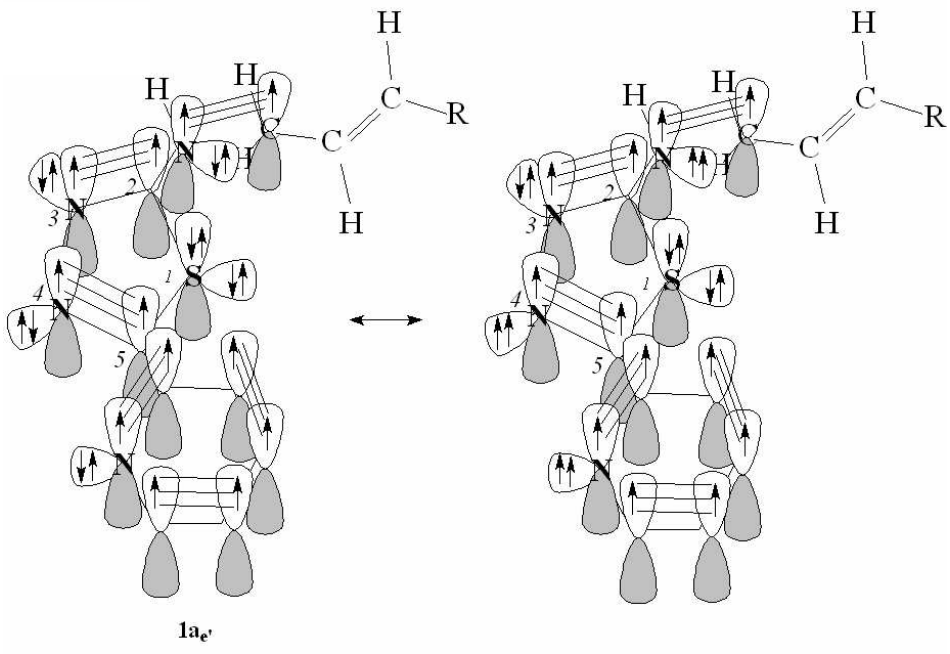
Scheme 5

The calculated chemical shift value of N 1' δ – 86.0 ppm [9] point to the amine–type nitrogen atom of **2a** tautomer. The calculated chemical shift value of NH group δ 7.5 of **2a** tautomer [9] supports sp^2 hybridization of the exocyclic nitrogen atom C 2-N , the lack of the charges over 1,3,4-thiadiazole ring and the lack of the differences in the spin states of electrons of 2p orbitals of C 5-N 4, C 2-N 3, C 2-N, N-C 3".

The data of the ^1H (100 MHz, 500 MHz) ^{13}C ^{15}N NMR spectra and the theoretical calculations point to the following changes of the electron configuration of the nitrogen atoms N 4, N 3, C 2-N , N 1' (Schemes 6, 7).



Scheme 6



$1a_{e'}$

Scheme 7

3. CONCLUSIONS

The coupling constants of the protons of allyl- substituent obtained from the ^{1}H NMR spectra (100 MHz, 500 MHz), the ^{1}H, ^{13}C and ^{15}N signals in the ^{1}H NMR, ^{13}C NMR, ^{15}N NMR spectra of **1** supported by theoretical calculations, confirm the pyridine–type, pyrrole–type and amino nitrogen atom N-C 3" of compound **1**. The ^{1}H NMR spectra (100 MHz) of compound **1** show small differences in the chemical shifts values of the protons of N-CH_2- group. It confirms the changes in the polarization of the bond of N-C 3" resulting from the differences in the electron density distribution of N-C 3". In the range of δ 3.922–3.954 the exocyclic nitrogen atom, the pyridine–type, is occupied with eight electrons. In the range of δ 3.978–4.008 the exocyclic nitrogen atom is surrounded by seven electrons, the changes in the $sp^2 \Leftrightarrow sp^3$ and $sp^2 \Leftrightarrow sp$ hybridization of the exocyclic nitrogen atom occur.

4. EXPERIMENTAL

For hydrogen the ^1H NMR spectra have been recorded at 100 MHz and 500.18 MHz. The ^1H NMR spectra at 100 MHz have been measured with 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 ^1H, ^{13}C and ^{15}N NMR measurements were taken in $CDCl_3$ and in DMSO solutions 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 ^1H ^1H 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 compound **1** was prepared according to the known method [6]. The ^1H NMR spectra 1, 1_3 1_4 2–6 have been recorded in $CDCl_3$ solution, the spectra 1_1 1_2 in DMSO solution, 1_5 in DMSO + D_2O solution at 100 MHz [6, 7]. The ^1H NMR spectra 1_1-1_4 have been taken applying various concentration of the product **1** in DMSO or $CDCl_3$ solutions [7]:

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

The ^1H NMR spectra 1–6 have been recorded in a $CDCl_3$ solution, 1_5 in a DMSO + D_2O solution without any determination of the concentration of **1** product [6, 7].

5. REFERENCES

[1] G. Kornis, in *Comprehensive Heterocyclic Compounds*, vol 6, pp. 545-577, Eds. Katritzky A. R., Ress W. C., Pergamon Press, London 1984.
[2] G. deStevens, M. Eager, C. Tarby, *Heterocycles*, 35, 763 (1993).
[3] C. G. Newton, C. A. Ramsden, *Tetrahedron*, 38 (20), 2965 (1982).
[4] C. A. Ramsden, *Comprehensive Organic Chemistry*, vol. 4, 1171-1228, (1979) ed. Barton D. H. R. and Ollis W. D., Pergamon Press, Oxford.
[5] L. Strzemecka, *Polish J. Chem.*, 64, 157 (1990).
[6] L. Strzemecka, *Annales UMCS, Sectio AA* vol. L/LI, 81-92 (1995/1996).
[7] L. Strzemecka, *Annales UMCS, Sectio AA* vol. LIV/LV, 363-377 (1999/2000).
[8] L. Strzemecka, *Annales UMCS, Sectio AA* vol. LIV/LV, 379-392 (1999/2000).
[9] L. Strzemecka, Maciejewska D., Urbańczyk-Lipkowska Z., *J. Mol. Struct*., 648, 107-113 (2003).
[10] J. March, *Chemia Organiczna. Reakcje, mechanizmy, budowa,* Wydawnictwa Naukowo-Techniczne (Scientific-Technical Publishers), Warsaw1975

[11] O, Reutov *Theoretical Principles of Organic Chemistry*, Mir Publishers, Moscow, 1970 (translated from Russian by D. Aelony, translation editor D. Sobolev).
[12] R. A. Y. Jones, *Fizyczna chemia organiczna. Mechanizmy reakcji organicznych*, Państwowe Wydawnictwo Naukowe (Polish Scientific Publishers), Warsaw 1988, (translated from English by G.Kolasińska, J. Jaszczyński).
[13] The lectures on "Ampere VII NMR School in Zakopane" 30.V.1999-4.VI.1999.
[14] R. T. Morrison, R. N. Boyd, *Chemia Organiczna*, Państwowe Wydawnictwo Naukowe (Polish Scientific Publishers), Warsaw 1985.

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