

A quantum chemical investigation of tautomerion forms of 4-phenyl-5-(4-hydroxyphenyl)-1,2,4-triazoline-3-thione

4-phenyl-5-(4-hydroxyphenyl)-1,2,4-triazoline-3-thione (TT) was obtained by the oxidative cyclization of the appropriate 4-hydroxybenzoyl phenylthiosemicarbazide. From the obtained spectral analysis it is possible to consider that the 1,2,4-triazoline-3-thiones may exist in thion-thiol tautomeric forms. The molecular conformations and electronic properties of TT containing various reaction centers were investigated by the AM1 semiempirical method. The total energies, heat of formation, dipole moments, geometric parameters, ionization potential, full atomic charges, E_{HOMO} and E_{LUMO} (energies of frontier molecular orbital) and their electron densities were calculated. Ionization constants and protonation site in TT molecule were obtained experimentally. The proton affinities for the different atoms (nitrogen, oxygen and sulfur) of the investigated triazole molecule were calculated using AM1 method, and possible protonation sites were discussed. The quantum chemical investigations of tautomerion forms of TT were in accordance with our previously experimental investigation for protonation/deprotonation process of TT: PA of TT calculated for S atom form C=S group was higher than the other atoms, meaning that the electrophilic attack of the proton on this atom is easier than the other; the most acidic hydrogen atoms were N-H/S-H (first deprotonation process) and OH (second deprotonation process).

Key words: 1,2,4-Triazolol-3-thion, AM1, Total Energies, Heats of Formation

1. INTRODUCTION

Keeping in mind the importance of triazole derivatives for living bodies, [1-4] we carry on working on triazole derivatives as one of the most biologically active classes of compounds, possessing a wide spectrum of activities. The 1,2,4-triazole nucleus is associated with diverse pharmacological activities such as antibacterial, antifungal, hypoglycemic, antihypertensive and analgesic properties. It is also known that some of aminomethyl triazole derivatives possess corrosion - inhibition activity and they can be used as additives in greasy oils or in photopolymerizing paints for improving adhesion. During the last ten years, some new 1,2,4-triazole derivatives were synthesized and investigated [5-11].

This paper reports semi empirical quantum chemical investigation of chosen triazole derivative, previously synthesized and investigated (experimentally determined acid-base constants - important from various points of view) [9,10]. Triazole compounds are five member ring containing three nitrogen atoms, which exist mainly with different structural formulas. The parent 1,2,4-triazole (1H form) is in tautomeric equilibrium with the 1,2,4-triazole (4H form). The interconversion of the two tautomeric forms occurs

rapidly and their separation is difficult. However, the 1,2,4-triazole tautomer (i) is preferred over the 1,3,4-triazole tautomer (ii) (the less symmetrical 1H form is favoured over the symmetrical 4H form) (Fig. 1).

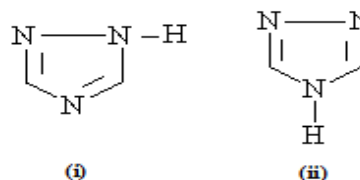


Figure 1 - Tautomeric 1,2,4-triazole:
1H-1,2,4-triazole (i) and 4H-1,2,4-triazole (ii)

Mercapto derivatives of 4,5-disubstituted-1,2,4-triazoles are especially interesting as complexing agents due to presence of four potential donor atoms: three nitrogen, one sulfur and one oxygen. Consequently many metal derivatives of ligands of this type have been prepared, and they have also been used as analytical reagents [12]. Mercapto triazoles have been proposed to exist as thion-thiol tautomers, both in solute and in solid state.

In continuation of our interest for 4,5-disubstituted-1,2,4-triazole derivatives, 4-phenyl-5-(4-hydroxyphenyl)-2,4-dihydro-3H-1,2,4-triazoline-3-thione (TT) obtained by oxidative cyclization of the appropriate 4-hydroxybenzoyl phenylthiosemicarbazide, [5] was chosen for quantum-chemical study (Fig. 2). It is important that the tautomeric interconversion must be taken into consideration to investigate the physical and chemical properties of

Author's address: University Ss. Cyril and Methodius, Faculty of Technology and Metallurgy, Rudjer Boskovic 16, Skopje, Republic of Macedonia

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the compounds which exist in a tautomeric equilibrium (thion - thiol forms).

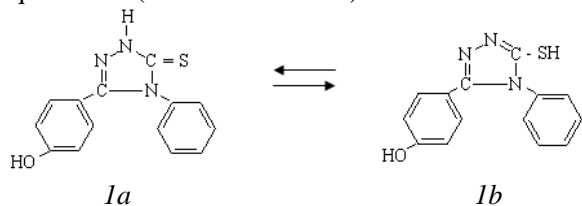


Figure 2 - Thion (1a) and thiol (1b) tautomers of 4-phenyl-5-(4-hydroxyphenyl)-2,4-dihydro-3H-1,2,4-triazoline-3-thione (TT)

The molecular conformations and electronic properties of chosen TT molecule containing various reaction centers were investigated by AM1 semi-empirical method. The total energies, heats of formation, dipole moments, rotational barriers, geometric parameters, ionization potential, full atomic charges, E_{HOMO} and E_{LUMO} (energies of frontier molecular orbitals) and their electron densities were calculated and discussed. Ionization constants and protonation site in TT molecule were obtained experimentally [9].

The proton affinities for the different atoms (nitrogen, oxygen and sulfur) of the investigated triazole molecule were calculated using AM1 and possible protonation sites were discussed. The obtained correlation between experimentally obtained acid dissociation constants and semi empirical computed data were discussed.

2. EXPERIMENTAL

2.1 Synthesis of TT

A mixture of appropriate thiosemicarbazide and NaOH solution was refluxed for 4 hours. On cooling, it was solidified (sodium salt of TT). This was dissolved in cold ice water and acidified with hydrochloric acid to pH 5-6. The solid which appeared was filtered, washed with water (neutral pH), dried and recrystallized from ethanol [5].

2.2 Identification and characterization of TT

IR [λ_{max}/cm^{-1}]: 1500 (C=N); 1330 (C=S); 1H NMR [DMSO- d_6 , ppm]: 6.68 and 7.09 (4H, ABq), 7.17-7.56 (m, 5H_{arom.}), 10.0 (bs, 1H, OH), 14.00 (bs, 1H, NH); ^{13}C NMR [DMSO- d_6 , ppm]: 115.3, 128.8, 129.3, 129.8, (CH); 116.3, 134.8, 150.7, 159.2, 168.2 (qC); UV[EtOH, λ/nm]: 255; 267; 285; Anal. calcd/found for $C_{14}H_{11}N_3OS$ (MW 269.318): C, 62.43/62.92%; H 4.08/4.44%; N 15.60/15.20%; Melting point: 250°C; Yield 95% [5].

2.3 Quantum chemical investigation

Theoretical calculations were carrying out at the restricted Hartree-Fock level (RHF) using AM1 semi empirical SCF-MO method in the HYPERCHEM program, implemented on an Intel Pentium pro 200

MHz computer. All the structures were optimized to a gradient norm of < 0.1.

3. RESULTS AND DISCUSSION

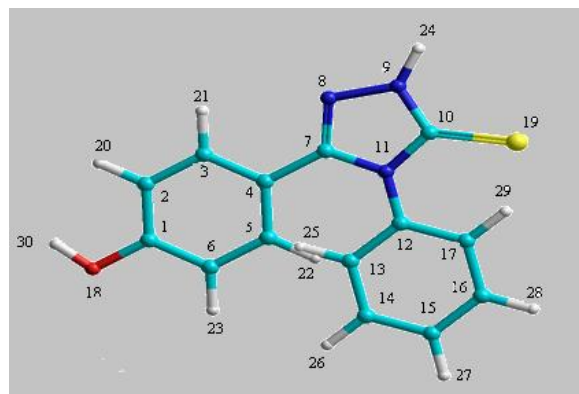


Figure 3 - Molecular structure of TT showing atomic numeration

3.1 Absorption spectra

As in the case of other heterocyclic thione, [13-16] it is possible to consider that the 1,2,4-triazoline-3-thiones may exist in thion-thiol tautomeric forms.

The UV spectra of TT in neutral media (water) was characterized by the presence of absorption maxima at about 255 nm, 267 nm and 285 nm, characteristic of electron transition in the 1,2,4-triazoline-3-thione ring [13]. Those results showed that the thione structure dominates: maximum at 255 and 285 nm, indicated that compound exist predominantly in the thion form in ethanolic solution¹⁰ and maximum at 285 nm indicated the presence of a chromophoric C=S group.

In addition to the UV data, the IR and NMR data of compound support the thion form in solid state and in nonpolar solvent; IR spectra in KBr disk showed no absorption bands at about 2600-2550 cm^{-1} which is indicative of the thiol form; the IR absorption due to C=S functions in TT appeared at about 1330 cm^{-1} . The 1H NMR spectra of TT in DMSO- d_6 exhibited the NH signals between 13.55 and 14.10 ppm (supporting the thion structure). The signals associated with other functional groups appeared in the expected regions.

Since, experimental determination of the protonation center of the triazole molecule was made, [9] the theoretical calculation of protonation parameters and the conformational analysis of TT system also appear important. The chosen molecule contains one hetero- and two aromatic rings, and interaction between them affect on the proton affinity and other properties.

On the other hand, the effect of tautomeric change on electronic properties can be evaluated by the theoretical investigation of the molecule. According

the literature data, semiempirical methods have been used widely for the quantum - chemical investigation of various heterocyclic compounds.

So, in this study, AM1 semiempirical method was used for detailed quantum-chemical investigation of 4-phenyl-5-(4-hydroxyphenyl)-2,4-dihydro-3H-1,2,4-triazoline-3-thione (TT). Molecular structure of TT showing atomic numeration is presented in Figure 3.

3.2 Geometry features of TT

The study of the geometry and preferred conformation of TT is important because of the possible usefulness of such information as an aid to the understanding of mode of action of TT as acid as and base and co-coordinative species.

Two isomeric forms, namely thion and thiol forms, of the TT are possible (Fig. 2; 1a and 1b). The

optimized geometrical parameters of 1a and 1b forms of the studied TT, such as bond length and angles are presented in Table 1.

It is reasonable for the flexible TT molecule to exist in various conformations due to rotation of the 4-hydroxy substituted phenyl and unsubstituted phenyl rings around C4 – C7 and N11 – C12 single covalent bonds (Fig. 3).

In order to investigate the effect of internal rotation on the energy of the molecule, the potential function of internal rotation around C4 – C7 (φ_1) and N11 – C12 (φ_2) single bonds were calculated. For these reasons, the φ angle was varied in the range 0 – 180° by a step of 30° and calculations were performed with AM1 geometry optimization, for both possible tautomeric forms (1a and 1b).

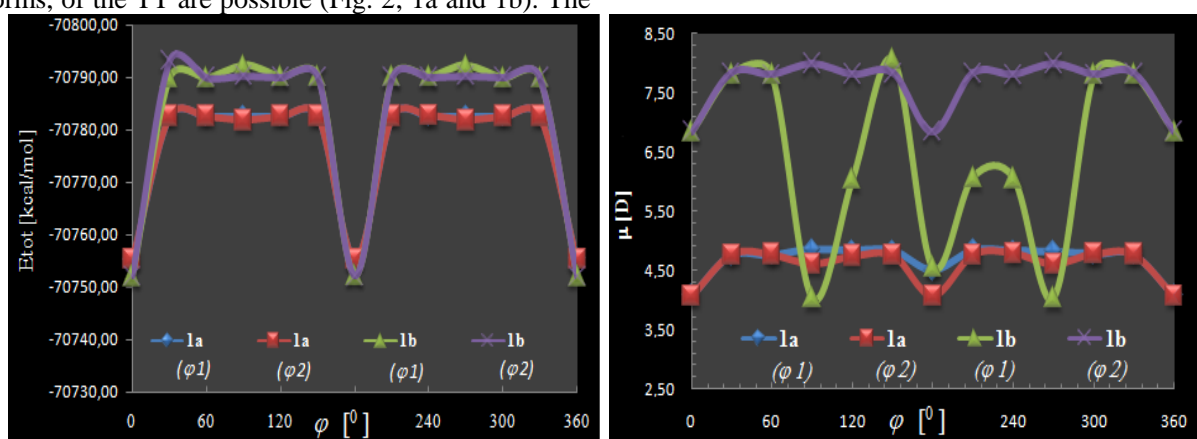


Figure 4 - Calculated E_{tot} and dipole moments varying the φ angle in the range 0 – 180° by a step of 30°

Table 1 - Selected geometrical parameters of the 1a and 1b tautomers

	Length [Å]		Angle [deg]		Torsion angle [deg]			
	1a	1b	1a	1b	1a	1b		
H30-O18	0.9689	0.9687	H30-O18-C1	108.028	108.015	H30-O18-C1-C6	1.345	1.251
O18-C1	1.3731	1.3744	O18-C1-C6	122.739	122.722	H30-O18-C1-C2	178.723	178.741
C4-C7	1.4611	1.4567	O18-C1-C2	116.522	116.524	C5-C4-C7-C8	30.727	-29.882
C7-N8	1.3546	1.3751	C3-C4-C7	121.426	121.598	C3-C4-C7-C12	32.091	-31.508
N8-N9	1.3420	1.3089	C5-C4-C7	118.860	118.714	C4-C7-N11-C12	5.221	-2.696
N9-C10	1.4124	1.3744	C4-C7-N8	124.675	125.838	C12-N11-C10-S19	4.954	2.164
C10-N11	1.4189	1.4087	C4-C7-N11	126.084	126.582	S19-C10-N9-H24	1.286	-
N11-C7	1.4267	1.4152	C7-N8-N9	106.639	109.855	C7-N8-N9-H24	178.834	-
C10-S19	1.5779	1.6882	N8-N9-C10	113.750	109.720	C7-N11-C10-S19	179.897	-179.764
N9-H24 ^a	0.9952	-	N9-C10-N11	102.609	107.89	N9-C10-S19-H24	-	-1.559
S19-H24 ^b	-	1.4154	N11-C7-N8	109.237	107.576	N11-C10-S19-H24	-	178.238
N11-C12	1.4157	1.4154	N8-N9-H24 ^a	120.866	-			
			C10-N9-H24 ^a	125.360	-			
			N9-C10-S19	127.211	127.693			
			N11-C1-S19	130.179	124.416			
			C12-N11-C10	124.048	125.511			
			C7-N11-C12	127.985	129.497			
			C10-S19-H24 ^b	-	98.429			

^aFor thion form; ^bFor thiol form

The results for E_{tot} and μ obtained by those calculations for thion and thiol form are presented in Figure 4. According to the results, in the conformation 1a when $\varphi_1=330^\circ$ and $\varphi_2=240^\circ$ and in 1b when $\varphi_1=\varphi_2=90^\circ$, the conjugation between the parent (triazole) and 4- and 5-substituted rings is minimum and the length of C4 – C7 (1a: 1.4611; 1b: 1.4567) and N11 – C12 (1a: 1.4157; 1b: 1.4154) is maximum. Bond length characteristic for 1,2,4-triazoline-3-thione/thiole moiety are: C7-N8, N8-N9, N9-C10, C10-S19 and N9-H24 (for 1a)/S19-H24 (for 1b), data presented in Table 1.

According the results obtained for those distances N-N distance in 1a is around 1.3420 Å which is little shorter form corresponding one in 1,2,4-triazole (1.350 Å), substitute 5-thione-1,2,4-triazole18 and from normal N-N bond (1.470 Å). Kipping in mind that N-N bond in 1b is between two sp^2 hybridized nitrogen atoms; more bond shortening is expected (1.3089 Å).

The C-N bonds in 1a can by divide in two sets according to the bond type observed: first set: C7-N8 and N9-C10 and second set: C7-N11 and C10-N11.

First type (C7-N8) double covalent bond in triazole ring has values of 1.3546 Å and 1.3751 Å for 1a and 1b, respectively. Those values are larger than typical C=N (1.322-1.352) and corresponding length in similar compounds (1.330 and 1.310 Å) [17].

The single N9-C10 covalent bond in **1a** is around 0.06 Å larger then C7-N8, value which is between typical single C-N bond (~1.48 Å) and double C=N bond (~1.34 Å). This probable can be explained by possibly of existence of two tautomeric forms. Values of same bond in 1b is 1.3744 Å (larger than typical C=N bond), difference that may be significant and which suggest a large double bond character in the second bond formed between two sp^2 hybridized atoms, but in same time influence of thion tautomeric form.

Second type, C7-N11 and C10-N11 bonds is in accordance with their character of single C-N bond in complex 4,5-disubstitute triazole molecule, with values of 1.4267/1.4189 Å for 1a and 1.4152/1.4087 Å for 1b, respectively, but with an evident larger values for bond distance compared with similar compounds (1.3742) [17]. Another explanation for larger C-N bond values of second type in 1a, probably is different type of hybridized N (sp^3) and C (sp^2) atoms, suggesting that the electron density is more localized among C8-N9-N10-C11-S19. Same discussion can be made for C-N bonds for thiole form, although this bond is between same type of hybridized N and C (sp^3) atoms, distance values are shorter in 1b that in 1a.

C=S bond length of 1.5779 Å in 1a are in good agreement with theoretically calculated values for C=S bond for 3,4-disubstituted-5-thione-1,2,4-triazole (1.574 Å).¹⁷ The bond length of C10-S19 (1.6882 Å) in 1b is shorter than the normal single covalent C-S bond (1.82) and same bond in some dithia-cycloalcanes (1.801~1.825 Å), bat it is still longer than the double C=S bond (1.56 Å), suggesting that it has substantial double bond character, as it is expected for compounds which may exist as tautomers (conspicuous absence of SH vibration band at 2500 cm^{-1} in the experimental (i) and theoretical (ii) IR spectrum (Fig. 5) and appearance of triazole NH signals in experimental ¹H NMR spectra) [5,9].

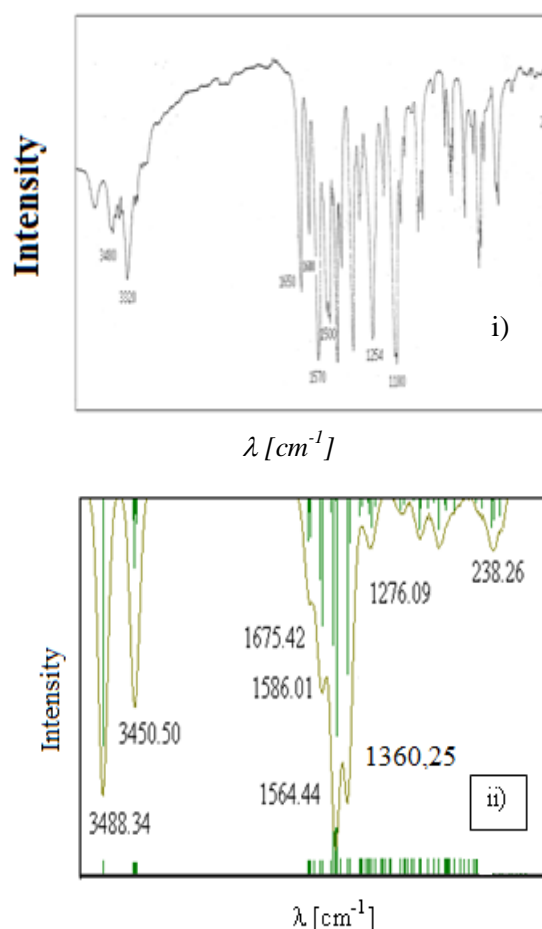


Figure 5 - Comparison between experimental (i) and theoretical (ii) IR spectra of TT

An attempt was made for comparison between experimentally obtained IR spectra and theoretically obtained (Fig. 5). As it can be seen form Figure 5, the position of characteristic bands of theoretically obtained IR spectra (ii) for TT are similar as in experimentally obtained IR spectra (i). Appearance of the bands located at 1586 cm^{-1} , 1276 cm^{-1} and 1360 cm^{-1} in theoretically obtained IR, indicated the formation of C=N N=N=C and C=S bands, res-

pectively in the preferred 1a form. Also the stretching frequency of substituted OH group and CH bands appears at 3488 and 3450 cm^{-1} .

In order to investigate the electronic properties, to find out the reaction centers and to determine the reactivity, TT has been studied using AM1 route.

Total energies (E_{tot}), the heats of formation (ΔH_f^0), E_{HOMO} and E_{LUMO} energies of frontier molecular orbitals, ionization potential ($\text{IP} = -E_{\text{HOMO}}$) and dipole moments of 1a and 1b forms of TT have been

calculated and given in Table 2. In fact, the stability of heterocyclic systems, such as TT, depends on the conjugation between the: heterocyclic ring, (in this case 1,2,4-triazole), aromatic rings and thion ($\text{C}=\text{S}$)/thiol ($\text{C}-\text{SH}$) group in position 3 in TT and the interaction between them. The calculated nucleophilicity values are collected in Tab. 2 and indicated biggest nucleophilicity of 1a form ($\mu = -8.9431$). The results support the greatest basicity of 1a compared to the 1b form.

Table 2 - Total energies, heats of formation, semi empirical calculated relative stabilities, E_{HOMO} and E_{LUMO} energies of frontier molecular orbitals, nucleophilicities and dipole moments for 1a and 1b tautomers

	E_{tot} [kcalmol ⁻¹]	ΔH_f^0 [kcalmol ⁻¹]	RS ^a	E_{HOMO}	E_{LUMO}	μ^b	$\mu \square$ [D]
1a	-70782.5	102.963	7.416	-8.4341	-0.4990	-8.9431	4.740
1b	-70792.3	95.547		-8.3751	-0.3740	-8.7491	3.998

^a RS – semi empirical calculated relative stabilities, $\text{RS} = \Delta H_f^0(\text{tautomer 1a}) - \Delta H_f^0(\text{tautomer 1b})$;

^b μ – nucleophilicities; $\mu = E_{\text{HOMO}} - E_{\text{LUMO}}$

The IP of 1a form (8.4341) was higher than that of 1b form (8.3751) (Tab. 2), but those values are relatively lower than literature reported IP for 1,2,4-triazole. According to the literature, the experimental IP of 1,2,4-triazole molecule was 10.00 eV and calculated IP using AM1 and PM3 methods, 10.27 and 10.396 eV, respectively [18].

Table 3 - Atomic charges of the 1a and 1b tautomers

Atomic charge					
Atom	1a	1b	Atom	1a	1b
C1	0.101	0.093	C16	-0.128	-0.127
C2	-0.163	-0.163	C17	-0.107	-0.103
C3	-0.067	-0.078	O18	-0.245	-0.248
C4	-0.071	-0.054	S19	-0.198	0.220
C5	-0.048	-0.048	H20	0.157	0.154
C6	-0.222	-0.221	H21	0.157	0.143
C7	0.038	-0.018	H22	0.149	0.157
N8	-0.065	-0.075	H23	0.141	0.139
N9	-0.242	-0.096	H24	0.300	0.053
C10	0.066	-0.236	H25	0.147	0.152
N11	0.195	-0.114	H26	0.141	0.142
C12	0.047	0.024	H27	0.139	0.140
C13	-0.104	0.113	H28	0.141	0.143
C14	-0.126	-0.128	H29	0.149	0.152
C15	-0.112	-0.112	H30	0.223	0.221

In order to investigate the basicity of TT, prediction of possible protonation centers in molecule with containing various proton – acceptors atoms, is very significant. The atomic charges for tautomeric forms 1a and 1b are listed in Table 3.

In accordance with the negative charge distribution on N, O and S atoms in TT, some important differences observed are that in tautomer 1a, O18, N9 and S19 were atoms with the largest electron density in the molecule (-0.245; -0.242 and -0.198). In 1b tautomer, O18 was the most negative charged atom (-0.248). In accordance with the negative charge distribution on atoms in the TT, the O18, N9 and S19 were predicted to be the main sites of the molecule for the electrophilic attack of hydrogen. In fact, the determination of the exact protonation place according to the negative atomic charge distribution was difficult because the negative atomic charges are relatively similar for previously mentioned atoms.

The most acidic hydrogen atoms were one bonded to: N9 (H24; 0.300) and to O18 (H atom from OH group; 0.223) in 1a, or H30 in tautomer 1b (0.221), but the electron deficiency was much lower in the second one. It would therefore be easier to pull the proton bonded to N9 in the first step and subsequently in the second step deprotonation process of H30 atom will take place. The molecular electrostatic potential (MESP) and total charge density of the TT molecule were calculated and presented in Figure 6.

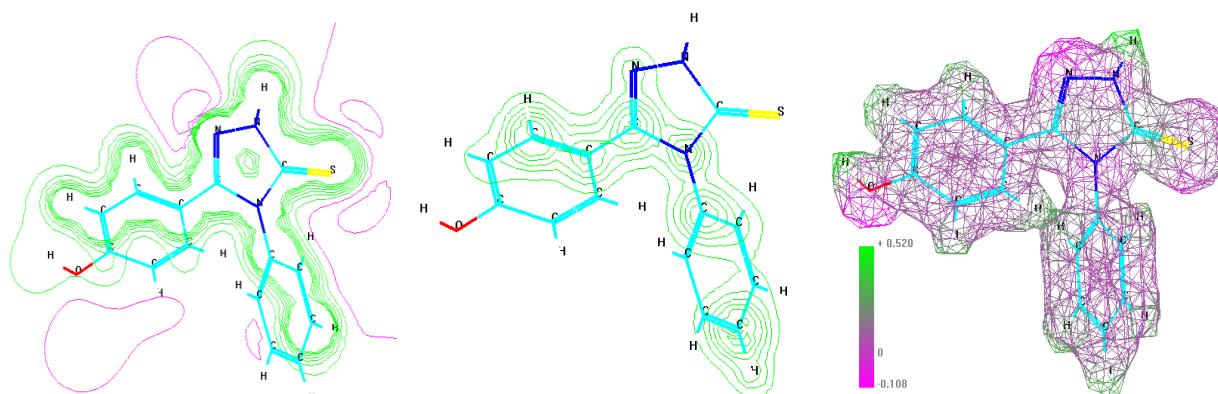


Figure 6 - Electrostatic potential and total charge density (2D contours and 3D mapped isosurface)

Next step for determination of the exact protonation center of TT system, was calculating the proton affinities for different atoms in the molecule. The possible protonation pathways (mono cations: 2, 3, 4, 5 and 6) and deprotonation pathways (mono anions: 7 and 8) for TT are described in Figure 7.

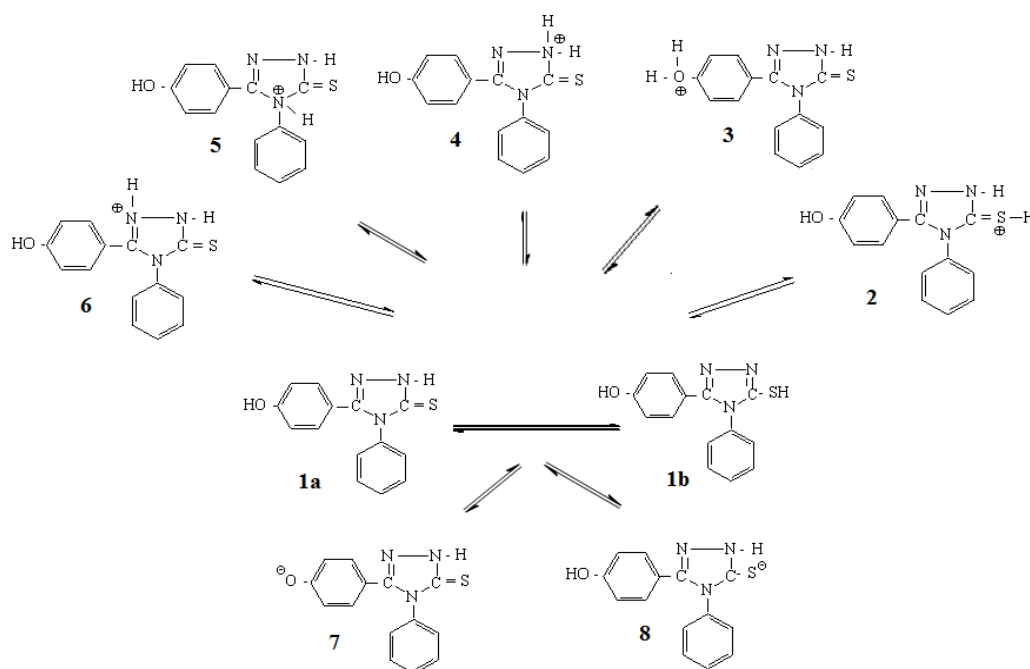


Figure 7 - Possible tautomerisation and protonation patterns for TT molecule

Hence, the stable conformations for the mono-cations formed by the protonation of different atoms in TT, such as: O18, S18, N14, N15 and N17 were determined with full geometry optimization and the heats of formation (ΔH_f^0), calculated using AM1 method (Table 4).

The proton affinity values for the different atoms were calculated using the equation (1):

$$PA = 367.2 + \Delta H_f^0(TT) + \Delta H_f^0(TTH^+) \quad (1)$$

where, PA is proton affinity, $\Delta H_f^0(TT)$ is the heat of formation for the TT molecule, $\Delta H_f^0(TTH^+)$ is the

heat of formation for the cation and 367.2 is the heat of formation for the proton.

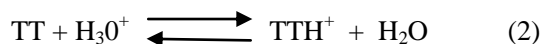
Comparing the result shown in Tab. 4 it can be concluded that the PA of TT calculated for S19 is higher than the others. In other words, the electrophilic attack of the proton on the S19 atom is easier than the other atoms. Hence, despite the fact that the stability of thiol form is higher than that thion form (E_{tot} , Tab.2), the process of proton acceptance is higher in 1a form, which together with experimentally obtained data from spectroscopic measurements are indication for dominance of thion form of TT [9].

Table 4 - Total energies, heats of formation, E_{HOMO} and E_{LUMO} energies of frontier molecular orbitals and dipol moments for protonation forms for TT

		1a	PA	1b	PA
S19	E_{tot} (kcal/mol)	-70949.5	224.041	-70935.5	199.932
	ΔH_f^0 (kcal/mol)	246.122		262.815	
	μ [D]	5.554		10.64	
O18	E_{tot} (kcal/mol)	-70892.9	199.837	-70904.2	170.717
	ΔH_f^0 (kcal/mol)	301.525		292.030	
	μ [D]	21.440		18.97	
N8	E_{tot} (kcal/mol)	-70896.2	168.862	-70906.5	170.670
	ΔH_f^0 (kcal/mol)	301.302		292.077	
	μ [D]	6.47		1.767	
N9	E_{tot} (kcal/mol)	-70922.2	168.638	-70908.1	171.999
	ΔH_f^0 (kcal/mol)	270326		290.748	
	μ [D]	5.424		5.588	
N11	E_{tot} (kcal/mol)	-70902.7	197.721	-70919.4	186.415
	ΔH_f^0 (kcal/mol)	272.442		276.332	
	μ [D]	2.086		6.537	

An attempt was made for calculation of semi empirical computed acid dissociation constants, using AM1 method.

The acidity of base as is 1,2,4-triazol-3-thione for reaction (2):



in aqueous phase can be calculated according to equation (3), where ΔG is the standard free energy:

$$\delta\Delta G_{(TTH^+)} = [\Delta G_{(TT)} + \Delta G_{(H_3O^+)}] - [\Delta G_{(TTH^+)} + \Delta G_{(H_2O)}] \quad (3)$$

The self computed thermodynamic data were used in predicting the pKa values using Eq. (4) in which the $\delta\Delta G_{(TTH^+)}$ is the standard free energy charge for reaction (2) (Table 5):

$$pKa_{(TTH^+)} = \delta\Delta G_{(TTH^+)}/2.303RT \quad (4)$$

where R is the gas constant ($R=1.987 \times 10^{-3}$ kcalmol⁻¹K⁻¹) and T is the absolute temperature in Kelvin ($T = 298^0$ K).

Table 5 - Aqueous phase calculated termodinamic parametr of neutral (1a) and S – protonated (2) TT molecule ($\epsilon = 78.4$)

	ΔH_f [kcalmol ⁻¹]	ΔS [calmol ⁻¹]	ΔG_f^a [kcalmol ⁻¹]	$\delta\Delta G$	$pKa_{(exp.)}^b$	$pKa_{(calc.)}^c$
1a (neutral)	-148.57	0.208	-210.55	-14.14	-4.4243 ^e	-10.3681
2 (S – protonated)	-18.64	0.210	-83.91		-4.7209 ^f	
H ₃ O ⁺ ^d	44.33	46.12	30.58			
H ₂ O ^d	-68.49	45.09	-81.93			

^a $\Delta G_f = \Delta H_f - T\Delta S$; ^b taken from reference [9]; ^c calculated using Eq. (4); ^d taken from reference [19]; ^e pKa using HAFM – Hammett acidity function method; ^f pKa using EAFM – “Excess acidity” function method

This quantum chemical investigations of tautomerion forms of 4-phenyl-5-(4-hydroxyphenyl)-1,2,4-triazoline-3-thion were in accordance with our previously experimental investigation for protonation place of TT [9,10]. Experimentally obtained values for

protonation pKa (-4.4243 and -4.7209) are characteristic for protonation of S atom form thiourea fragment of 1,2,4-triazoline-3-thione moiety of TT and deprotonation pK values of 7.2385 and 9.9124 correspond to first dissociation of H24 and then dissociation of H30.

As can be seen from Tab. 5, there was a difference between $pK_{a(\text{exp.})}$ and those calculated using AM1 quantum – chemical method (around 6 pKa units), which is considerable difference. This probably can be explained that a large and complex molecule such as is TT, was object of investigation. As an additional fact probably was a possibility for existence of two tautomeric forms of investigated compounds.

4. CONCLUSION

Quantum chemical investigations, in most cases can be used in structure elucidation of organic molecules and this kind of calculation should be performed as a prediction of possible synthesis and the stability of the predictive product.

When the object of investigation was a large and complex molecule, such is TT, there was overlapping of theoretical and experimental results in some areas of investigation, such as prediction of protonation place and dominance of one of tautomeric form. But there was disagreement in final calculation of pK_a value, which probably was result of structure of investigated molecule and a possibility for existence of two tautomeric forms.

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IZVOD

KVANTNO-HEMIJSKA ISPITIVANJA TAUTOMERNIH FORMI 4-FENIL-5-(4-HIDROKSIFENIL) -1,2,4-TRIAZOLIN-3-TIONA

4-Fenil-5-(4-hidroksifenil) -1,2,4-triazolin-3-tion (TT) dobijen je oksidativnom ciklizacijom odgovarajućeg 4-hidroksibenzoilfeniltiosemicarbazida. Spektralne analize ukazuju na postojanje tioniolnih tautomernih formi, 1,2,4-triazolin-3-tiona. Molekularne konformacije i elektronska svojstva TT ispitivane su AM1 semiempirijskom metodom. Ukupna energija, toplota formiranja, dipolni moment, energija jonizacije, atomske polneze E_{HOMO} i E_{LUMO} i elektronske gustine, su izračunate. Jonizacione konstante i protonaciona mesta u TT, dobijena su eksperimentalno. Protonski afiniteti (PA) za različite atome (azot, kiseonik i sumpor) izračunati su AM1 metodom. Kvantno-hemijska ispitivanja tautomernih formi TT u skladu su sa eksperimentalnim istraživanjima: PA za S atoma iz C = S grupe je veći od ostalih atoma, što ukazuje na lakši elektrofilni napad na ovaj atom.

Ključne reči: 1,2,4-triazolin-3-tion, AM1, ukupna energija, toplota formiranja

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