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Research Article

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Equilibrium, kinetic and thermodynamic studies of silarhodanine tautomers by highly CBS-Q method

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ABSTRACT

The proton transfer processes have generated eight minimum structures of the silarhodanine molecule. These structures were studied in the gas phase by a high level theory complete basis set (CBS-Q). All the structure are heterocyclic compounds except S2 structure. The global isomeric structure was S5 at the CBS-Q levels of theory. The acyclic structure S2 is possessed the highest energy (60.17 kcal/mol) above the global minimum S5. Nine anions and nine cations of various conformers have been investigated. The protonation and deprotonation reactions in the gas phase are examined at the CBS-Q level. The S2OA showed the highest relative enthalpy (ΔH= 24.65 kcal/mol) and S3OA structure showed the highest Gibbs free energy (ΔG=23.59 kcal/mol). The S2NC cation showed the highest relative enthalpy and Gibbs free energy (ΔH= 50.25 kcal/mol, ΔG=47.07 kcal/mol) in the cations section. Energetically easiest process is the deprotonation of 2ZNA with the computed enthalpy and Gibbs free energy of 1274.52 kJ/mol and 1282.49 kJ/mol. The equilibrium constants at 298.15 K and 1 atmosphere pressure of the deprotonation reactions are very small which means the reaction at this temperature favor the reactants. The computed vibrational frequencies values for the structures are inconformity with the experimental ones.

Keywords: Global minimum, CBS-Q, enthalpies, equilibrium constant and stability.

INTRODUCTION

Heterocyclic compounds are organic compounds that contain a ring structure containing atoms in addition to carbon, such as sulfur, oxygen or nitrogen as part of the ring. A heterocyclic compound is a cyclic compound which has atoms of at least two different elements of its ring(s). Heterocyclic compounds can be spotted in hemoglobin, penicillin, vitamins (C, B6 and B12), alkaloids, flavonoids and DNA structure. The prototropic tautomerizm and rotamerization of heterocyclic compounds are including, in particular, biologically active compounds, are of great importance in many areas of chemistry and biochemistry. The term tautomerizm refers to a compound existing in an equilibrium between two or more isomeric form called tautomers [1,2]. The tautomers of Rhodanine (2-thioxothiazolidin-4-one) and its derivatives have showed many biological activities including antibacterial, antiviral, antidiabetical and anti-inflammatory action [3-7]. The molecular properties including the Gibbs free energy of salvation of doxorubicin were investigated by computational methodology [8]. The tautomerizm of substituted thiazolidine and oxazolidine heterocycles were studied theoretically at the B3LYP/6-311G(2d,p) level. The thermodynamic parameters for the molecules were calculated in the gas phase and in two different solvents, the study revealed that same tautomer is the most stable both in gas phase and in solution [9]**.** The usefulness of the quantum mechanical descriptors has been investigated by DFT, the relationship between molecular descriptors and biological activities have been produced [10]. The equilibrium geometries and harmonic frequencies of the 6-methylnicotinic acid have been investigated at density functional theory with satisfactory results [11]. Recently, we are investigated the sila- and thio- derivative of formohydroxamic acid in the same manner [12-13].

Computational Details

The calculations were investigated the relative stabilities of the various isomeric forms of Silarhodanine. The study included the analysis of the reaction enthalpies and Gibbs free energies. The geometries of Silarhodanine and its tautomers (Fig. 1.) were completely optimized at MP2(FC)/6-31G(d) level within the CBS-Q theory [14-17]. The gas-phase basicity was defined as the enthalpy of protonation (ΔH^{298}) for reaction (1).

$$X(g) + H^+(g) \rightarrow XH^+(g) \quad \text{……..(1)}$$

The enthalpy of protonation, ΔH^{298}, was computed using Eqs. (2) and (3).

$$\Delta H^{298} = \Delta E^{298} + \Delta(pV) \quad \text{…….(2)}$$

$$\Delta E^{298} = E^{298}(XH^+) - [E^{298}(X) + 3/2RT] \quad \text{……..(3)}$$

The gas-phase acidity was defined as the enthalpy of deprotonation (ΔH^{298}) for reaction (1)

$$AH\ (g) \rightarrow A^-\ (g) + H^+\ (g) \quad \text{……..(4)}$$

The enthalpy of deprotonation, ΔH^{298} was computed using the following two equations 5,6:

$$\Delta H^{298} = \Delta E^{298} + \Delta(pV) \quad \text{…….(5)}$$

$$\Delta E^{298} = [E^{298}(A^-) + 3/2RT] - E^{298}(AH) \quad \text{..……..(6)}$$

Notice that there is an inverse relationship between the magnitude of the ΔH^{298} and the strength of the acid. E^{298} stands for the total energies of the most stable conformations of acids and their anions (including the thermal energy correction at 298.15 K). In equation 2, the substitution of (ΔpV)=-RT is carried out since, one mole of gas is lost in reaction 1). Again In equation 5, the substitution of (ΔpV)=RT is carried out since, one mole of gas is obtained in reaction 4).

The equilibrium constants (K_{eq}) of the reactions were calculated from Gibbs free energies using $\Delta G = -RT\ln K_{eq}$.

The optimized structures were confirmed to be real minima by frequency calculation. The vibrational frequencies were scaled by a factor of 0.9614 [18]. The calculations were performed using Gaussian03 version 6.0 package [19].

RESULTS AND DISCUSSION

The investigation revealed that there are eight local minima structures for silarhodanine molecule. S2 is acyclic structure and the other seven forms are cyclic forms. The Selected structures are presented in Fig. 1. The description of the anions (A) and the cations (C) for the structures are as follows S7NA is an anion form of S7 molecule in which the proton is dissociated from nitrogen atom and S1NC is a cation form of S1 molecule in which the proton is added to nitrogen atom). The structural parameters from the full optimized geometry of the structures are given in Table 1.

Table 1: Selected geometrical parameters of the molecules, bond length (Å).

Sys.	Si1-S3	S3-C4	C4-S7	C4-N5	N5-C2	C2-O6	C2-Si1	Si-H	S-H	N-H	O-H
S1	2.128	1.857	1.635	1.376	1.288	1.342	1.928	1.485	-	-	0.970
S2	2.175	-	1.573	1.209	1.349	1.346	1.857	1.504	1.350	-	0.974
S3	2.256	1.735	1.758	1.326	1.333	1.338	1.923	1.512	1.350	-	0.972
S4	2.261	1.746	1.651	1.412	1.335	1.333	1.912	1.515	-	1.020	0.972
S5	2.166	1.800	1.643	1.378	1.401	1.215	1.926	1.481	-	1.018	-
S6	2.403	1.869	1.635	1.342	1.458	1.212	1.968	1.519	1.348	1.019	-
S7	2.351	1.700	1.764	1.333	1.480	1.210	1.958	1.518	1.348	1.020	-
S8	2.273	1.727	1.759	1.331	1.337	1.331	1.910	1.508	1.349	-	0.980
Exp.	-	1.735	1.645	1.367	1.374	1.220	-	-	-	0.861	-

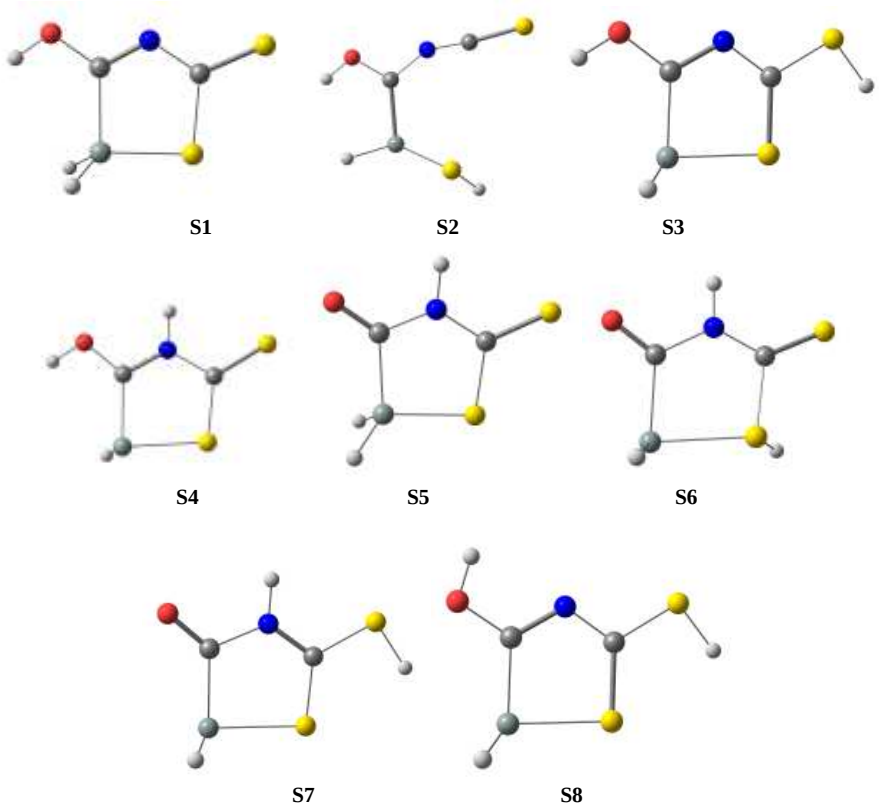

Figure1: The structures of silarhodanine conformers

The energies of the molecules are often calculated for geometries optimized at a lower level due to the large computational time required for geometry optimization; however in this paper the optimized structures at CBS-Q level of theory gave a good value for the bond distances in comparison with the available experimental related data [20]. Despite the fact that, S2 structure is acyclic it is also possessed non planner geometry similar to the other heterocyclic tautomers. The S5 is the most stable tautomer among the series and S2 structure has the highest energy (60.17 kca/mol) above the global minimum S5.

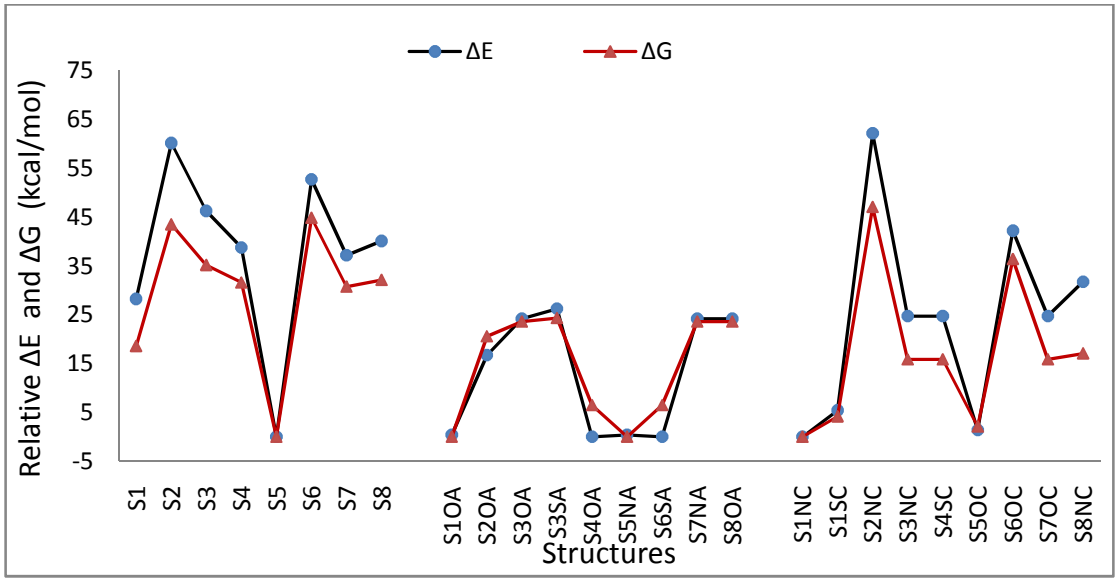

Figure 2: The relative energy and Gibbs free energy of the tautomers, anions and cations derivatives of silarhodanine molecule

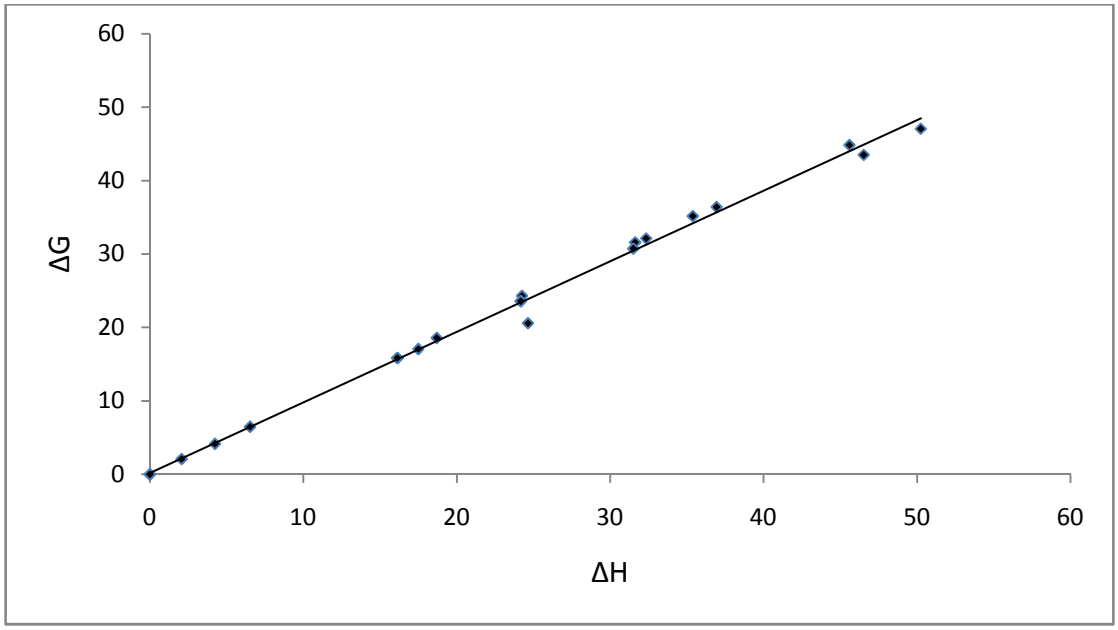

Figure 3: Relationship between enthalpies and Gibbs free energies of the structures

Table 2: The relative energies, enthalpies and free energies (kcal/mol) for the molecules at CBS-Q level of theory

Molecules	ΔE	ΔH	ΔG
S1	28.23	18.72	18.58
S2	60.17	46.53	43.51
S3	46.25	35.39	35.17
S4	38.74	31.63	31.60
S5	0.00	0.00	0.00
S6	52.73	45.60	44.85
S7	37.16	31.51	30.76
S8	40.09	32.35	32.13
S1OA	0.384	0.001	0.006
S2OA	16.72	24.65	20.58
S3OA	24.16	24.18	23.59
S3SA	26.24	24.26	24.32
S4OA	0.0	6.53	6.48
S5NA	0.384	0.00	0.00
S6SA	0.00	6.53	6.48
S7NA	24.16	24.18	23.59
S8OA	24.16	24.18	23.59
S1NC	0.0	0.0	0.0
S1SC	5.39	4.25	4.16
S2NC	62.15	50.25	47.07
S3NC	24.72	16.13	15.85
S4SC	24.72	16.13	15.85
S5OC	1.35	2.07	2.09
S6OC	42.19	36.94	36.41
S7OC	24.72	16.13	15.86
S8NC	31.71	17.50	17.07

The relationship between relative enthalpy (ΔH) and relative Gibbs free energy(ΔG) for the tautomers, anions and cations derivatives silarhodanine molecule are plotted and the correlation coefficient has the value of 0.996, this magnitude demonstrate that the ΔH and ΔG are almost identical for the various tautomers Figure 3.

In the gas-phase the relative Gibbs free energy difference (ΔG) lies between 44.85 and 18.58 kcal/mol. These data are corresponding to the $\Delta G_{S6\text{-}S5}$ and $\Delta G_{S5\text{-}S1}$ respectively; this is expected because S5 is the most stable tautomer. The equilibrium constants of tautomeric transformations were calculated using the standard equation K = exp(-ΔG /RT), where ΔG is the relative total Gibbs free energy of the reactant and product, T is the temperature, and R is the universal gas constant.

Energetically the easiest process is the deprotonation of S6SA with the computed enthalpy and Gibbs free energy of 278.91 kcal/mol and 280.58 kcal/mol. The equilibrium constants of the processes are given in Table 3. The equilibrium constants at 298.15 K and 1 atmosphere pressure of the deprotonation reactions are very small which means the reaction at this temperature favor the reactants and the protonation reactions at the same temperature showed a reverse trend.

For example, the equilibrium constant for the highest protonation reaction S3+ H+ → S3NC is 2.41×10^{152} and in contrast the deprotonation reactions S5 - H+→ S5NA is 1.10×10^{-232} in accordance with ΔG between tautomers.

The calculated frequencies of optimized structures are revealed after correction by the scaling factor of 0.9614. The vibration frequencies of the lower region (1000-4000 cm^{-1}) of the least stable structure S2 and the global minimum structure are presented in Table 4. The OH stretching frequency in S2 is at 3894 cm^{-1}, consistent with the usual OH frequency in the absence of hydrogen bonding. The SiH vibrational frequency located between 2141-2357 cm^{-1}, the highest (2357 cm^{-1}) being the symmetric stretch in S5 molecule. The experimental value for SiH stretching is 2167 cm^{-1} [21-23] which is in accord with the value of 2141 cm^{-1} calculated for the S2 isomer. Finally, the computed vibrational frequency for S2 showed the SH stretch at 2798 cm^{-1} which is higher than the reported values perhaps due to a huge electronic density on sulfur atom. The vibrational frequencies values for CN, CO and SO were in accordance with the expected range.

Table 3: The gas-phase acidity, basicities (enthalpies ΔH , Gibbs free energies ΔG in kJ/mol) and the equilibrium constants of the reactions at CBS-Q level of theory at 298.15 K

Reaction	ΔH^{298}	ΔG^{298}	K_{eq}
S1+ H+ → S1NC	-203.41	-203.67	4.04E+149
S1+ H+ → S1SC	-201.42	-201.85	1.86E+148
S2+ H+ → S2NC	-182.11	-182.96	2.48E+134
S3+ H+ → S3NC	-204.46	-207.45	2.41E+152
S4+ H+ → S4SC	-202.88	-203.87	5.66E+149
S5+ H+ → S5OC	-183.15	-183.64	7.82E+134
S6+ H+ → S6OC	-193.68	-193.77	2.16E+142
S7+ H+ → S7OC	-200.41	-199.99	8.00E+146
S8+ H+ → S8NC	-200.36	-201.29	7.21E+147
S1 - H+ → S1OA	297.16	297.73	2.0E-219
S2 - H+ → S2OA	293.90	292.11	2.69E-215
S3 - H+ → S3OA	304.73	301.93	1.65E-222
S3 - H+ → S3SA	306.78	305.26	5.00E-225
S4 - H+ → S4OA	290.86	291.11	1.46E-214
S5 - H+ → S5NA	315.49	315.78	1.10E-232
S6 - H+ → S6SA	278.91	280.58	7.93E-207
S7 - H+ → S7NA	308.78	309.37	5.64E-228
S8 - H+ → S8OA	307.79	307.32	1.81E-226

Table 4: Calculated MP2(Full)/6-31G(d) vibrational frequencies (cm^{-1}) of S2 and S5 structures

S2	Assig.	S5	Assig.
789		849	
902		1010	
910		1111	S=O
1238		1236	
1419		1321	
1486		1545	
2068	N=C	1908	C=O
2141	Si-H	2349	asy Si-H
2798	S-H	2357	sy Si-H
3894	O-H	3666	N-H

REFERENCES

[1] V Gold, *Pure Appl.Chem*. **1979** 51 1725.
[2] ED Raczynska; W Kosinska; B Osmilalowski; R Gawinecki, *Chem. Rev*. **2005** 105 3561.
[3] BCC Contello; DS Eggleston; D Haigh; RC Haltiwanger; CM Heath; RM Hindley; KR Jenning; JT Sime; SR Woroneick, *J. Chem. Soc. Perkin Trans*. **1994** 1 3319.

[4] P Villain-Guillot; M Gualtieri; L Bastide; F Roquet; J Martinez; M Amblard; M Pugniere; JP Leonetti, *J.Med*. **2007** Chem.50 (17) 4195.
[5] S Yan; G Larson; JZ Wu; T Appleby; Y Ding; R Hamatake; Z Hong; N Yao, *Bioorg. Med. Chem. Lett*. **2007** 17 (1) 63.
[6] RF Kletzien; SD Clarke; RG Ulrich, *Mol. Pharmacol*. 41 **1992** 393; Chem. Abstr. 118 **1993** 610.
[7] WA Cetenko; DT Connor; JCh Sirkar; RJ Sorenson; PCh Unangst, Eur. Pat. Appl. EP 449 216 ;chem. Abstr. **1992** 116 128921.
[8] S Bagheri; Z Bayat; SJ Mahdi Zadeh; E Taghizadeh, *J. Chem. Pharm. Res*., **2011** 3(4) 42.
[9] D Tahmassebi, *J. Mol. Struct*. **2003** 638 11.
[10] Z Bayat; M Zanoozi, *J. Chem. Pharm. Res.*, **2010** 2(6) 416.
[11] RK Srivastava; V Narayan; O Prasad; L Sinha, *J. Chem. Pharm. Res*., **2012** 4 (6) 3287.
[12] AA Ahmed, *Der Chemica Sinica* **2012** 3(4) 989.
[13] AA Ahmed, *Der Chemica Sinica* **2012** 3(4) 884.
[14] GA Petersson; MA Al-Laham, *J. Phys. Chem*. **1991,** 94, 6081.
[15] JA Montgomery; JW Ochterski; GA Peterson, *J. Phys. Chem*. **1994,** 101, 5900.
[16] GA Peterson; T Tensfeldt; JA Montgomery, *J. Phys. Chem*. **1991,** 94, 6091.
[17] WJ Ochterski; GA Peterson; JA Montgomery, *J. Phys. Chem*. **1996,** 104, 2598.
[18] AP Scott; L Radom, *J. Phys. Chem.;* **1996** 100, 16502.
[19] Gaussian 03, Revision C.02. Gaussian, Inc., Wallingford CT, 2004.
[20] SW NG, *Acta. Crystallogr. Sect*. E, **2007** 63 O1363.
[21] NW Mitzel; K Christoph; W. H. DWH Rankin, *Organometal*. **1999** 18 3437.
[22] R Kakkar A Dua; S Zaidi, *Org. Biomol. Chem*. **2007** 5 547.
[23] CWM Yuen; SKA Ku; PSR Choi; CW Kan; SY Tsang, *Res. J. Texti. &Appa*. (RJTA), **2005** 9 26.