



Theoretical Studies of Pyridine-2-carbaldehyde Thiosemicarbazone: A Biological Active Novel Compound

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ABSTRACT

The molecular geometry, net atomic charge and atom electron densities, HOMO-LUMO energy, Hardness-Softness and thermodynamic parameters of the Pyridine-2-carbaldehyde thiosemicarbazone a novel biological active compound, are examined theoretically at the ab-initio HF/STO-3G, HF/3-21G & HF/6-31G levels. The correlation coefficients are reported for bond lengths and bond angles at different levels of calculations. Net atomic charge and atom electron density data reveal the coordination sites in Pyridine-2-carbaldehyde thiosemicarbazone when it undergoes complexation with transition metal ions. Consequently, performance of ab-initio method at different levels of calculations has been tested to find the best auxiliary tool for the designing of a novel material.

Keywords: Pyridine-2-carbaldehyde thiosemicarbazone, HF/STO-3G, HF/3-21G & HF/6-31G *ab-initio* levels, Correlation Coefficient (CC).

INTRODUCTION

Thiosemicarbazones have been known for years to show a broad spectrum of therapeutic properties against a range of diseases, with antibacterial antimalarial, antiviral and antitumor activities. Their chelating ability with transition metal ions is found to relate to their medicinal activity. X-ray crystallography studies of this compound was first reported by L. H. Song et al[1]. Its biological activity was reported by many workers. The literature contains no theoretical study of this tridentate ligand, therefore, we report here the theoretical parameters of title compound by using ab-initio quantum chemical methods[2].

The success of quantum chemical methods in predicting a large number of important molecular properties has been an important part of their emergence as a legitimate tool for many chemical problems. The most frequently used quantum chemical methods for molecular properties are semi-empirical, *ab-initio*, density functional and molecular mechanics methods. Semi-empirical methods use a simpler Hamiltonian than the correct molecular Hamiltonian and

use parameters whose values are adjusted to fit experimental data. In contrast, an *ab-initio* calculation uses the correct Hamiltonian and does not use experimental data other than the values of the fundamental physical constants.

Ab-initio methods have been employed by different workers to study molecular structure, vibrational spectra, NMR, HOMO-LUMO energy and other different parameters [3-7]. A. Amore-Bonapasta et al reported theoretical study of the conformational behavior of the S-methyl ester of dithiocarbazic acid. They studied the interconversion pathway of four planar conformers of the S-methyl ester of dithiocarbazic acid by applying HF-LCAO-MO-SCF method with a minimal basis set[8]. 1,4- dimethoxy benzaldehyde Schiff base and p-methyl acetophenone Schiff base of S-methyl dithiocarbazate have been synthesized and characterized by Kumar et al[8]. D. Kumar et al reported the theoretical studies of the benzaldehyde thiosemicarbazone[10] and also studied the geometry and IR frequency of the S-benzyl- β -N-(2-furylmethylketone) dithiocarbazate[11]. They have also studied S-benzyl- β -N-(4-nitro benzal) methylene dithiocarbazate by BILYP, B3LYP, B3P86 and B3PW91 methods[12-16]. In the present study, we have been employed *ab-initio* method at HF/3-21G, HF/6-31G & HF/STO-3G levels of calculations[17-20]. Thus, we report here the geometrical parameters like as bond lengths, bond angles, molecular orbitals, HOMO – LUMO energy, hardness- softness, atom electron densities and net atomic charges and thermodynamic parameters by the above mentioned quantum chemical methods.

MATERIALS AND METHODS

An Intel based Pentium IV machine with HT3.2 technology having 800 FSB, 2GB RAM, 7200 RPM HDD was used to run all the calculations. Quantum chemical calculations were carried out by the HF/3-21G, HF/6-31G and HF/STO-3G levels of *ab-initio* methods by Gaussian03 series of Hyperchem 7.5 package²⁰ with root mean square (RMS) gradient 0.00001 kcal (Δmol^{-1}) using Polak-Ribiere algorithm. Chemdraw[21] was used to draw the structure of molecule, bond lengths, bond angles, electron densities and net atomic charges, HOMO-LUMO energy, Hardness-Softness and thermodynamic parameters were calculated with the help of standard parameters as implemented in the software.

RESULTS AND DISCUSSION

Optimized geometry : The optimized geometry of Pyridine-2-carbaldehyde thiosemicarbazone is presented in Figure 1. The correlation coefficient for bond length obtained by HF/STO-3G, HF/3-21G and HF/6-31G levels are 0.9112, 0.9968 and 0.9884 respectively. It is evident that HF/3-21G level gives the maximum correlation (CC=0.9968) for bond length. In the case of bond angles, correlation coefficients are 0.8378, 0.9503 and 0.9271 for HF/STO-3G, HF3-21G and HF/6-31G levels respectively. It is evident that HF/3-21G level gives most satisfactory correlation (CC=0.9503). The calculated and experimental bond lengths and bond angles are given in Table- 1 & 2 respectively and graph between experimental versus calculated bond lengths and bond angles are given in Figure 2 & 3 respectively.

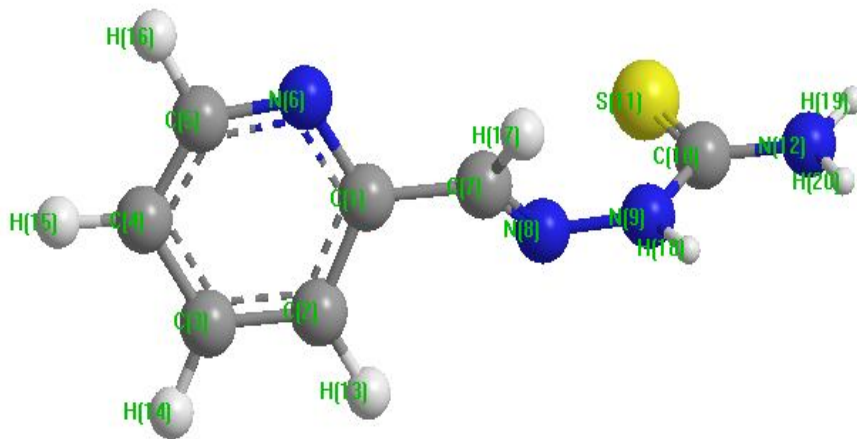


Figure 1. Pyridine-2-carbaldehyde Thiosemicarbazone

Table 1. Calculated and experimental bond lengths of Pyridine-2-carbaldehyde thiosemicarbazone by *ab-initio* HF/STO-3G, HF/3-21G and HF/6-31G levels

BOND LENGTHS		EXP.	HF/STO-3G		HF/3-21G		HF/6-31G	
C1-C2	C2-	1.388 1.367	1.394	1.383	1.384	1.380	1.390	1.380
C3	C3-C4	1.373 1.372	1.385	1.388	1.387	1.381	1.385	1.383
C4-C5	C5-N6	1.330 1.348	1.350	1.359	1.329	1.328	1.320	1.322
N6-C1	C1-C7	1.450 1.278	1.497	1.285	1.469		1.478	1.255
C7-N8	N8-N9	1.380 1.354	1.420	1.436	1.260		1.357	1.347
N9-C10	C10-	1.679 1.316	1.600	1.413	1.394	1.344	1.682	1.327
S11	C10-N12				1.743	1.319		
CC		-----	0.9112		0.9968		0.9884	

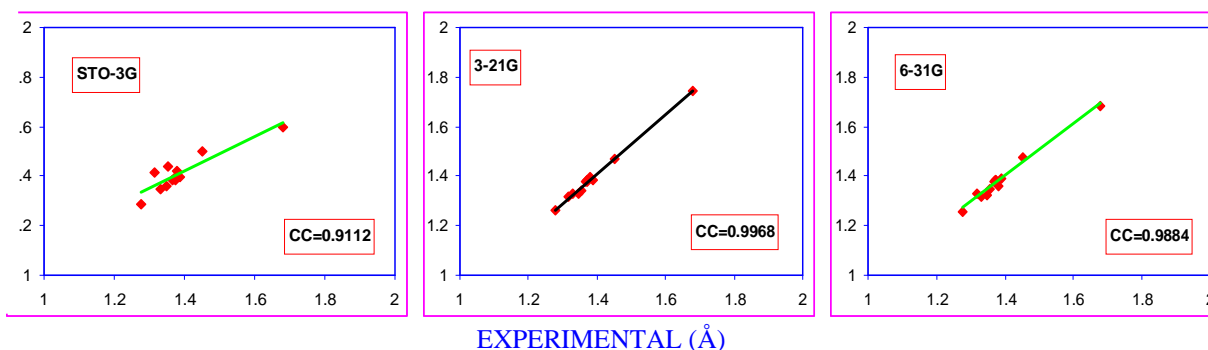


Figure 2. Graphic correlation between the experimental and calculated bond lengths obtained by *ab-initio* STO-3G, 3-21G and 6-31G levels

Table 2. Calculated and experimental bond angles of Pyridine-2-carbaldehyde thiosemicarbazone by *ab-initio* HF/STO-3G, HF/3-21G and HF/6-31G levels

BOND ANGLES		EXP.	HF/STO-3G	HF/3-21G	HF/6-31G
C1-C2-C3	C2-	119.3	119.0	118.5	118.1
	C3-C4	119.5	118.6	119.1	119.0

C3-C4-C5	118.3	118.7	118.5	118.1
C4-C5-N6	123.5	124.1	122.1	123.2
C5-N6-C1	118.0	115.8	119.3	118.4
N6- C1-C7	114.4	114.8	115.2	114.2
C1-C7-N8	121.5	120.8	122.1	122.1
C7-N8-N9	115.5	114.7	118.1	117.7
N8-N9-C10	119.9	117.7	119.9	121.9
N9-C10-S11	118.5	122.5	119.4	120.1
N9-C10-N12	116.8	111.0	116.9	116.3
S11-C10-N12	124.8	126.2	123.5	123.5
CC	-----	0.8378	0.9503	0.9271

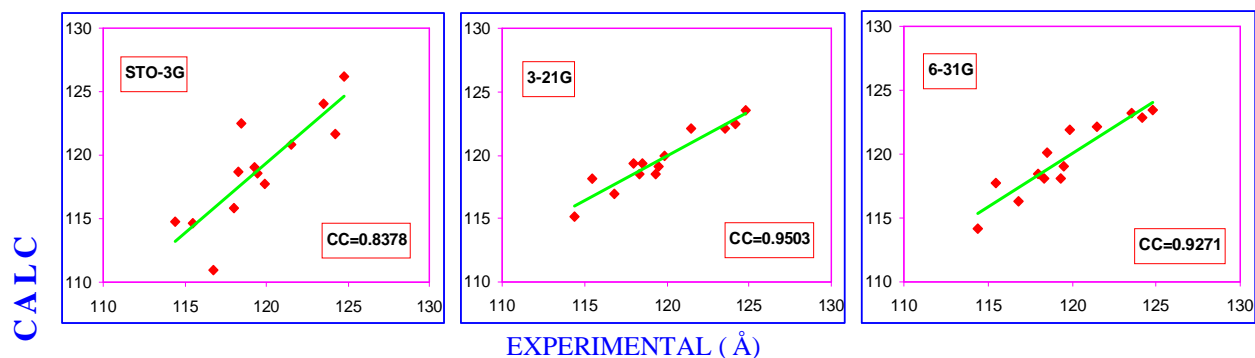


Figure 3. Graphic correlation between the experimental and calculated bond angles obtained by *ab-initio* HF/STO-3G, HF/3-21G and HF/6-31G levels

Net atomic charges and electron densities : calculated net atomic charges and electron densities are presented in Table 3. From this table, it is clear that different methods predicted different net atomic charges and electron densities on different atoms. The graphical presentation of electron densities on different atoms is also shown in Figure 4. The Table 3 shows that N(6), N(8), N(9), S(11) and N(12) have -0.242, -0.147, -0.258, -0.043 & -0.397 (HF/STO-3G) ; -0.724, -0.381, -0.688, -0.122 & -0.907 (HF/3-21G) and -0.570, -0.257, -0.571, -0.364 & -0.872 (HF/6-31G) net atomic charges and 7.242, 7.147, 7.258, 16.043 & 7.387 (HF/STO-3G) ; 7.724, 7.381, 7.688, 16.122 & 7.907 (HF/3-21G) and 7.570, 7.275, 7.571, 16.364 & 7.872 (HF/6-31G) electron densities respectively. N(6), N(8), N(9), S(11) and N(12) are the probable coordination centre in this Schiff base. However, N(9) & N(12) if coordinated to central metal ion will form a 4-membered chelating ring, which is unstable. N(8) & S(11) if coordinated to central metal ion will form a 5-membered chelating ring which is very stable.

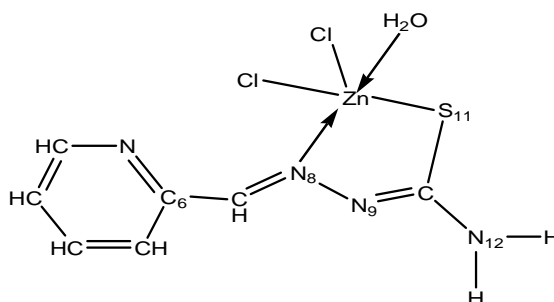


Table 3. Net atomic charges (NAC) and electron densities (ED) calculated by *ab-initio* HF/STO-3G, HF/3-21G & HF/6-31G levels for Pyridine-2-carbaldehyde thiosemicarbazone

Atom No.	HF/STO-3G		HF/3-21G		HF/6-31G	
	NAT	ED	NAT	ED	NAT	ED
N6	-0.242	7.242	-0.724	7.724	-0.570	7.570
N8	-0.147	7.147	-0.381	7.381	-0.275	7.275
N9	-0.258	7.258	-0.688	7.688	-0.571	7.571
S11	-0.043	16.043	-0.122	16.122	-0.364	16.364
N12	-0.397	7.397	-0.907	7.907	-0.872	7.872

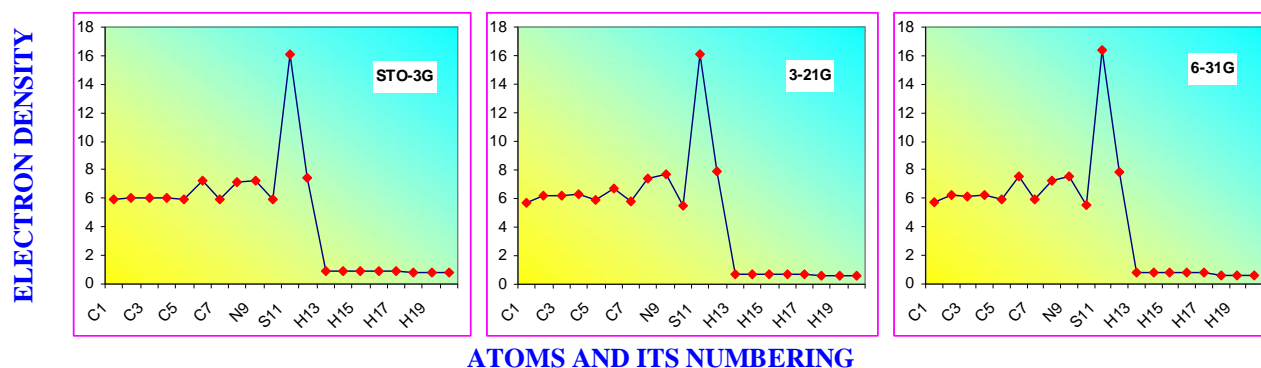


Figure 4. Graphical presentation of calculated electron densities on all atoms obtained by *ab-initio* STO-3G, 3-21G & 6-31G levels for Pyridine-2-carbaldehyde thiosemicarbazone

HOMO-LUMO energy : In the present investigation HOMO-LUMO energy gap of Pyridine-2-carbaldehyde thiosemicarbazone has been calculated by using *ab-initio* basis set at STO-3G, 3-21G and 6-31G levels and the results are presented in Table 4. It reveals that the energy gap reflects the chemical activity of the molecule. LUMO as an electron acceptor represents the ability to obtain an electron, HOMO represents the ability to donate an electron. It is clear that STO-3G and 6-31G levels give highest HOMO-LUMO gap and 3-21G lowest HOMO-LUMO gap energy.

Table 4. HOMO-LUMO energy calculated by *ab-initio* HF/STO-3G, HF/3-21G and HF/6-31G levels for Pyridine-2-carbaldehyde thiosemicarbazone

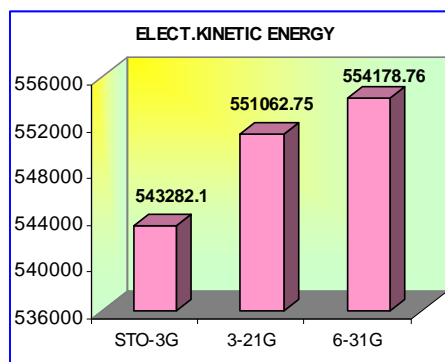
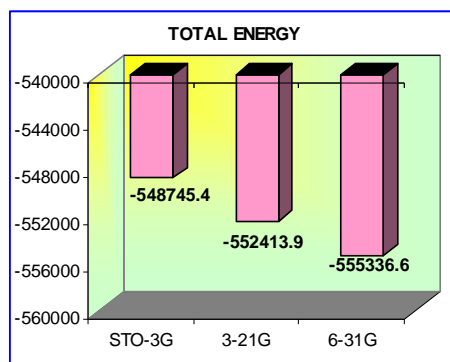
PARAMETERS	HF/STO-3G	HF/3-21G	HF/6-31G
ϵ_{HOMO}	-5.866564	-8.221558	-8.291015
ϵ_{LUMO}	5.140896	1.764823	1.863957
$\eta = \epsilon_{\text{LUMO}} - \epsilon_{\text{HOMO}}$	11.00746	9.986381	10.154972

Hardness & Softness : Hard molecule has a large HOMO-LUMO gap and a soft molecule has a small HOMO-LUMO gap. All three *ab-initio* methods predict different values for hardness. While STO-3G and 6-31G levels predict a highest value for hardness, the 3-21G level predicts a smallest value for hardness. Softness values are reciprocal of hardness value.

Thermodynamic parameters : The computed total energy, electronic Kinetic energy, Nuclear repulsion energy and RMS Gradient for Pyridine-2-carbaldehyde thiosemicarbazone by HF/STO-3G HF/3-21G and HF/6-31G *ab-initio* levels are given in Table-5 and its graphical representations are presented in Figure 6. HF/6-31G gives highest electronic kinetic energy value of 554178.7620 (ev) and HF/STO-3G gives lowest electronic kinetic energy value of 543282.0988. HF/6-31G gives higher value of Nuclear repulsion energy value of 430169.5753 (ev) and HF/STO-3G gives lowest nuclear repulsion energy value of 430169.5753 (ev). The HF/STO-3G gives higher value of RMS gradient value of 44.90445 and HF/3-21G gives lowest RMS gradient value of 24.25091.

Table 5. Computed Total energy, Electronic Kinetic energy, Nuclear repulsion energy and RMS Gradient calculated by *ab-initio* STO-3G, 3-21G and 6-31G levels

PARAMETERS	HF/STO-3G	HF/3-21G	HF/6-31G
Total energy (kcal/mol)	-548745.4082	-552413.8586	-555336.5629
Electronic Kinetic energy	543282.0988	551062.7495	554178.7620
Nuclear Repulsion Energy	433619.5552	436235.7778	438635.5083
RMS Gradient	44.90445	24.25091	30.15820



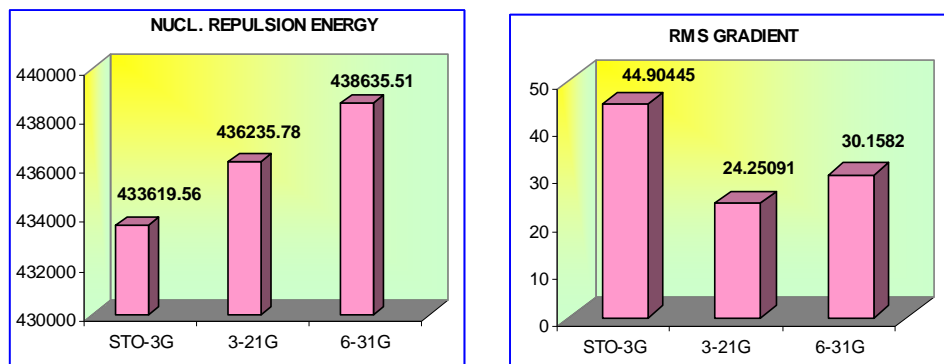


Figure 6. Graphic presentation of Total energy, Electronic kinetic energy, Nuclear repulsion energy, RMS gradient obtained by STO-3G, 3-21G and 6-31G *ab-initio* levels

APPLICATIONS

The *ab-initio* method at different levels of calculations has been applicable to find the best auxiliary tool for the designing of a novel compound.

CONCLUSIONS

Ab-initio HF/3-21G, HF/6-31G & HF/STO-3G levels proved to be important auxiliary tools for geometry optimization. The correlation coefficients for bond lengths obtained by HF/STO-3G, HF/3-21G and HF/6-31G levels are 0.9112, 0.9968 and 0.9884 respectively. It is evident that HF/3-21G level gives the maximum correlation (**CC=0.9968**) for bond length. In the case of bond angles, correlation coefficients are 0.8378, 0.9503 and 0.9271 for HF/STO-3G, HF/3-21G and HF/6-31G levels respectively. It is evident that **HF/3-21G** level yields most satisfactory correlation (**CC=0.9503**). Atom electron densities and net atomic charges indicate the coordination sites in the molecule during complex formation with transition metal ions. Almost all *ab-initio* methods for electron densities are supported by experimental data electron densities. It is clear that STO-3G method gives highest HOMO-LUMO gap and 3-21G lowest HOMO-LUMO gap energy. All three *ab-initio* methods predict different values for hardness. While STO-3G and 6-31G levels predict a highest value for hardness, the 3-21G level predicts a smallest value for hardness. Softness values are reciprocal of hardness value. Consequently, performance of *ab-initio* method at different levels of calculations has been tested to find the best auxiliary tool for the designing of a novel compound.

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