

**Designing of a Novel Biological active compound: AB-Initio Studies of Di-2 Pyridyl Ketone Thiosemicarbazone****Hari Singh Barhadiya<sup>1\*</sup> and D. Kumar<sup>2</sup>**

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Email: [haribbb@yahoo.co.in](mailto:haribbb@yahoo.co.in)Received on 06<sup>th</sup> January and finalized on 16<sup>th</sup> January 2013**ABSTRACT**

The molecular geometry, net atomic charge and atom electron densities, HOMO-LUMO energy, vibrational frequencies and thermodynamic parameters of the Di-2 pyridyl ketone thiosemicarbazone a novel biological active compound, are examined theoretically using ab-initio method at the HF/STO-3G, HF/3-21G and HF/6-31G levels. The correlation coefficients are reported for bond lengths, bond angles and vibrational frequencies at different levels of calculations. Net atomic charge and atom electron density data reveal the coordination sites in Di-2 pyridyl ketone 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 biological active compound.

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

**INTRODUCTION**

Thiosemicarbazone belongs to a large group of thiourea derivatives, the biological activity of which are a function of the parent aldehyde or ketone. The experimental study of various physical and chemical properties and X-ray crystallographic structure of crystalline di-2- pyridyl ketone thiosemicarbazone has been reported by Chun-Ying Duan et al[1]. The literature contains no computational 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[3]. The most frequently used for quantum chemical studies of 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. *Ab-initio* methods have been employed by different workers to study molecular structure, vibrational spectra, NMR, HOMO-LUMO energy and other different parameters [4-7]. They studied the interconversion pathway of four planar conformers of the S-methyl ester of dithiocarbamic acid by applying HF-LCAO-MO-SCF method with a minimal basis set. 1,4-dimethoxy benzaldehyde Schiff

base & p-methyl acetophenone Schiff base of S-methyl dithiocarbazate have been synthesized and characterized by Kumar et al[8-9].

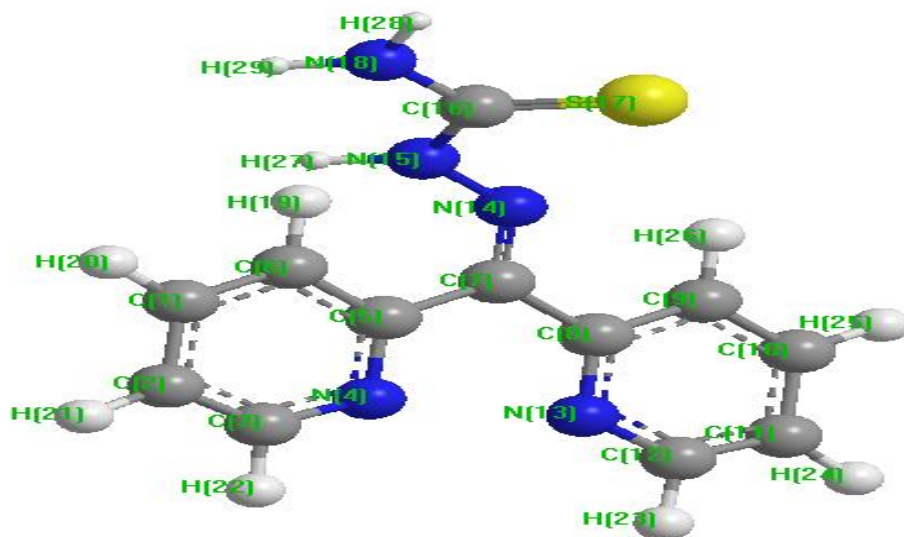
D. Kumar et al reported the theoretical studies of the benzaldehyde thiosemicarbazone and also studied the geometry and HOMO-LUMO energy of the Pyridine-2-carbaldehyde thiosemicarbazone [10-16]. In the present study, we have been employed HF/STO-3G[17], HF/3-21G[18] and HF/6-31G[19] levels of *ab-initio* methods with standard HF/STO-3G basis set. Thus, we report here the geometrical parameters like as bond length, bond angle, HOMO & LUMO energy, atom electron densities & net atomic charges, vibrational frequencies thermodynamic parameters by above mentioned quantum chemical methods.

## MATERIALS AND METHODS

Quantum chemical calculations were carried out by *ab-initio* HF/STO-3G, HF/3-21G and HF/6-31G methods by Gaussian programs of Hyperchem 7.5[20] and Chemoffice 2004 packages[21] to calculate geometry, net atomic charge, electron density, HOMO-LUMO energy, vibrational frequencies, dipole moment and thermodynamic parameters. Chemdraw was used to draw the structure of molecules. Intel based Pentium dual core T2390 @ 1.86 GHz processor machine having 2 GB RAM, 200 GB hard disc was used to run all the programmes.

## RESULTS AND DISCUSSION

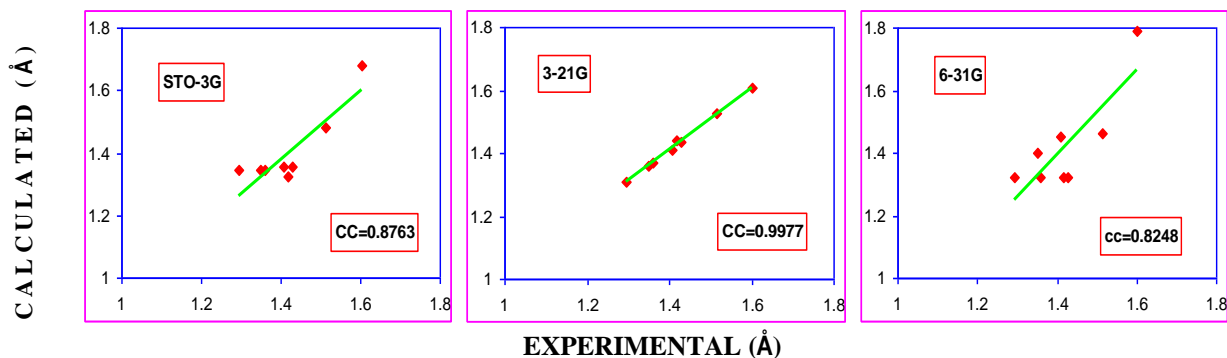
**Optimized Geometry:** The correlation coefficients (CC) for bond lengths obtained by *ab-initio* HF/STO-3G, HF/3-21G and HF/6-31G levels are 0.8763, 0.9977 and 0.8248 respectively. It is evident that HF/3-21G level gives the maximum correlation (CC=0.9977) for bond length. In the case of bond angles, correlation coefficients are 0.7810, 0.3768 and 0.3866 for HF/STO-3G, HF3-21G and HF/6-31G levels respectively. It is obvious that HF/STO-3G level gives most satisfactory correlation (CC=0.7810). The calculated and experimental bond lengths and bond angles are given in Table-1 & 2 respectively and graph between experimental versus calculated bond lengths & bond angles are given in Fig. 2 & 3 respectively.



**Figure 1.** Molecular structure of Di-2 pyridyl ketone thiosemicarbazone with numbering atoms adopted in the calculation

**Table 1.** Calculated and experimental bond lengths of Di-2 pyridyl ketone 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
C3-N4	1.354	1.344	1.361	1.402
C5-C7	1.482	1.482	1.526	1.460
N13-C8	1.343	1.345	1.372	1.321
C7-N14	1.301	1.347	1.309	1.320
N14-N15	1.354	1.354	1.408	1.450
N15-C16	1.365	1.354	1.433	1.320
C16-S17	1.682	1.682	1.610	1.790
C16-N18	1.323	1.323	1.438	1.320
CC	-----	<b>0.8763</b>	<b>0.9977</b>	<b>0.8248</b>

**Figure 2.** Graphical correlation between the experimental and calculated bond lengths obtained by *ab-initio* HF/STO-3G, HF/3-21G and HF/6-31G levels**Table 2.** Calculated and experimental bond angles of Di-2 pyridyl ketone 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
C5-C7-N14	128.1	114.9	120.0	118.2
C8-C7-N14	113.0	126.5	120.0	121.9
C5-C7-C8	118.8	120.9	119.8	123.9
C7-N14-N15	119.9	117.3	120.0	121.8
N14-N15-C16	119.6	118.0	120.6	120.0
N15-C16-S17	118.5	122.5	120.0	124.6
N15-C16-N18	116.8	117.4	115.3	111.1
S17-C16-N18	124.6	125.4	120.2	124.1
CC	-----	<b>0.7810</b>	<b>0.3768</b>	<b>0.3688</b>

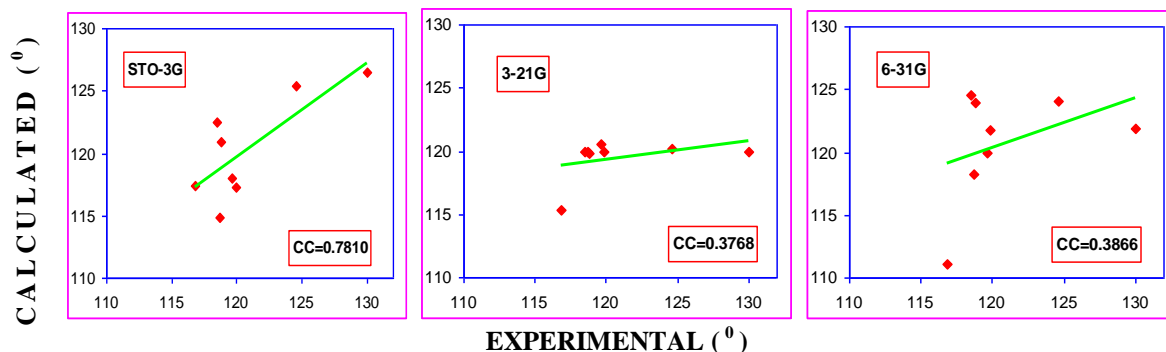
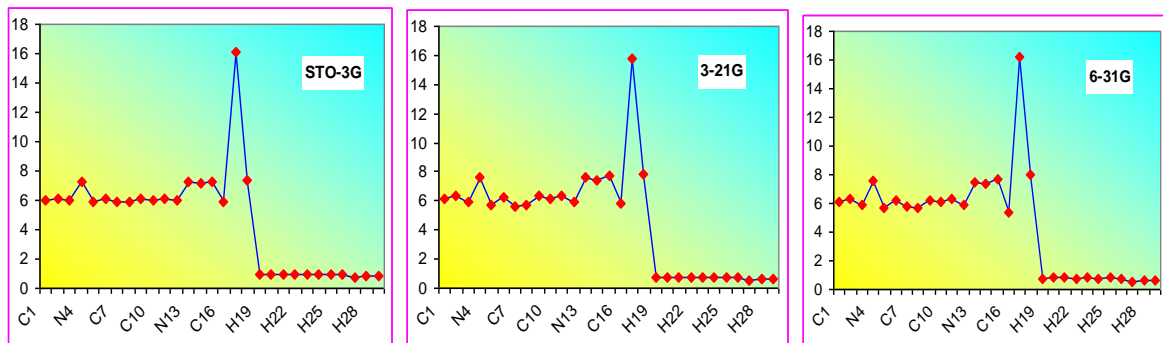


Figure 3. Graphical correlation between the experimental and calculated bond angles obtained by *ab-initio* HF/STO-3G, HF/3-21G and HF/6-31G levels

**Net Atomic Charges & Atom Electron Densities :** Calculated net atomic charges and atom 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 Nitrogen, Sulfur atoms and hence Nitrogen, Sulfur atoms can act as coordination sites while forming complexes with transition metal ions. The graphical presentation of electron density on each atom is shown in Figure 4. The graphical presentation of electron density show that N(4), N(13), N(14), N(15), S(17), and N(18) may take part in coordination in complex formation these atom show maximum net atomic charges and electron densities.

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

Atom No.	HF/STO-3G		HF/3-21G		HF/6-31G	
	NAT	ED	NAT	ED	NAT	ED
N4	-0.250	7.250	-0.653	7.653	-0.538	7.538
N13	-0.264	7.264	-0.648	7.648	-0.522	-0.522
N14	-0.144	7.144	-0.443	7.443	-0.341	-0.341
N15	-0.278	7.279	-0.726	7.726	-0.718	0.718
S17	-0.054	16.054	0.229	15.772	-0.209	-0.209
N18	-0.398	7.398	-0.883	7.883	-0.988	-0.988



Atoms and its numbering

Figure 4. Graphical presentation of calculated electron densities on all atoms obtained by *ab-initio* HF/STO-3G, HF/3-21G & HF/6-31G levels

**HOMO-LUMO Energy:** The HOMO-LUMO energy gap of the Di-2 pyridyl ketone thiosemicarbazone have been calculated by using *ab-initio* HF/STO-3G, HF/3-21G and HF/6-31G levels, reveals that the energy gap reflect the chemical activity of the molecule are presented Table 4. LUMO as an electron acceptor represents the ability to obtain an electron, HOMO represents the ability to donate an electron. It is clear that HF/STO-3G method give highest HOMO-LUMO gap and HF/6-31G lowest HOMO-LUMO gap energy. Negative value of HOMO energy is taken as ionization potential and thus HF/3-21G predicts largest value for IP while HF/STO-3G predicts smallest value for IP. Considering the chemical hardness, large HOMO-LUMO gap means a hard molecule and small HOMO-LUMO gap means a soft molecule.

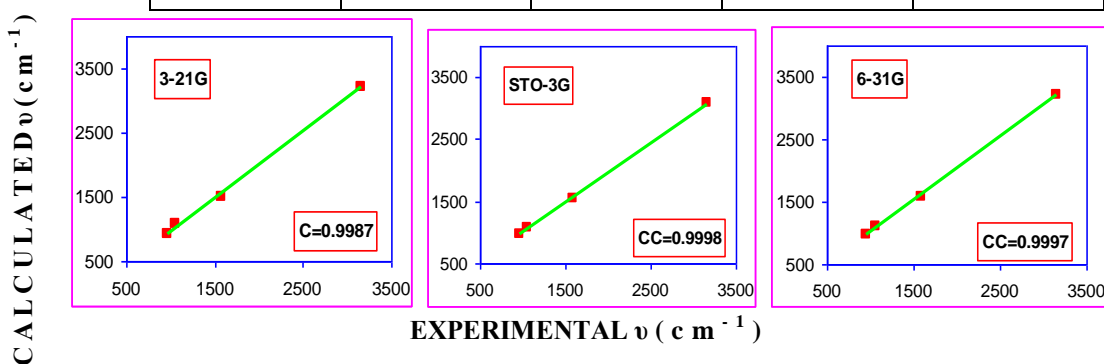
**Table 4 :** HOMO-LUMO energy (eV) calculated by *ab-initio* HF/STO-3G, HF/3-21G and HF/6-31G levels for Di-2 pyridyl ketone thiosemicarbazone

PARAMETERS	HF/STO-3G	HF/3-21G	HF/6-31G
$\epsilon_{\text{HOMO}}$	-6.063210	-8.262603	-8.094573
$\epsilon_{\text{LUMO}}$	5.247147	1.932668	1.961722
$I = -\epsilon_{\text{HOMO}}$	6.063210	8.262603	8.094573
$\eta = \epsilon_{\text{LUMO}} - \epsilon_{\text{HOMO}}$	11.310357	10.195271	10.056295

**Vibrational Frequencies :** Vibrational frequencies of Di-2 pyridyl ketone thiosemicarbazone Schiff base are presented in Table 5. The correlation coefficients obtained for HF/STO-3G, HF/3-21G and HF/6-31G are 0.9987, 0.9998 and 0.9997 respectively. For this Schiff base HF/3-21G level give more satisfactory correlation (0.9998) between experimental and calculated frequencies. Graphical correlations between experimental and calculated fundamental vibrational frequencies are presented in Figure 5.

**Table 5** Experimental and calculated fundamental vibrational frequencies of Di-2 pyridyl ketone thiosemicarbazone by *ab-initio* HF/STO-3G, HF/3-21G and HF/6-31G levels

Vibration	EXP.	HF/STO-3G	HF/3-21G	HF/6-31G
$\nu(\text{CSS})$	960	981	910	979
$\nu(\text{N-N})$	1057	1080	1089	1102
$\nu(\text{C=N})$	1584	1541	1506	1576
$\nu(\text{N-H})$	3162	3078	3216	3208
CC	-----	<b>0.9987</b>	<b>0.9998</b>	<b>0.9997</b>

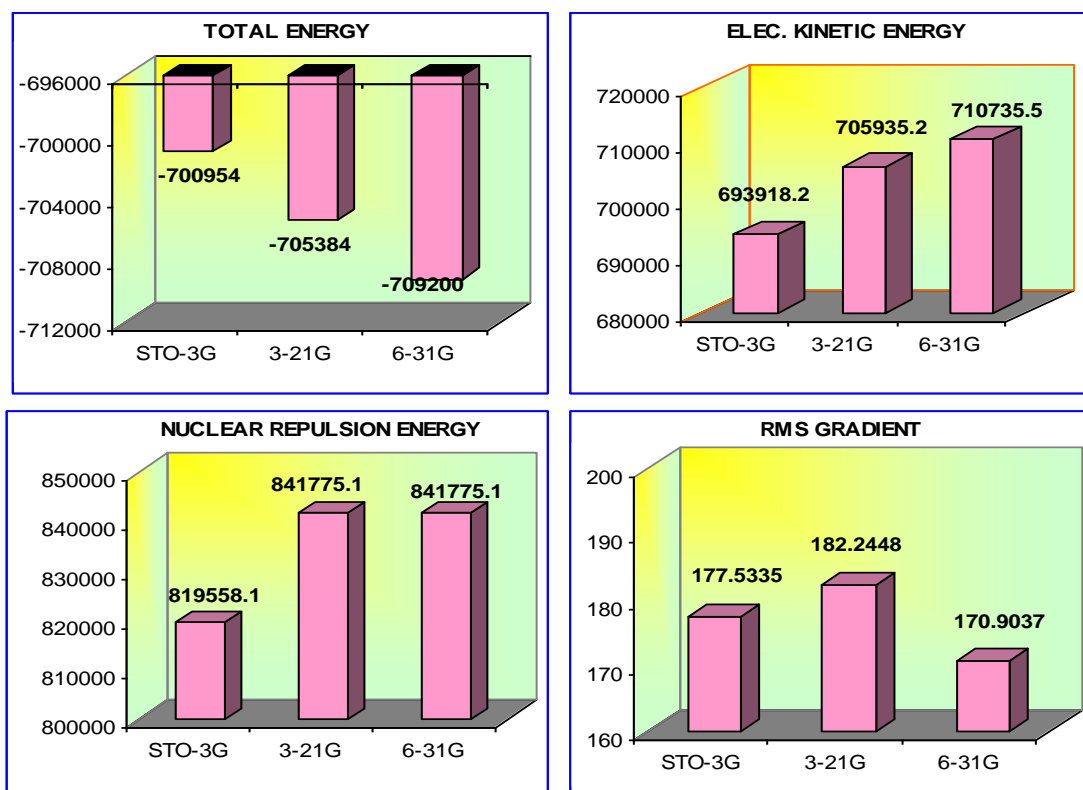


**Figure 5.** Graphical correlation between experimental and calculated fundamental vibrational frequencies obtained by *ab-initio* HF/STO-3G, HF/3-21G and HF/6-31G levels

**Thermodynamic Parameters :** The computed Total energy, Electronic Kinetic energy, Nuclear repulsion energy and RMS Gradient for Di-2 pyridyl ketone thiosemicarbazone by HF/STO-3G, HF/3-21G and HF/6-31G *ab-initio* levels are given in Table 6 and its graphical representations are presented in Figure 6. HF/6-31G gives highest electronic kinetic energy value of 710735.5469 and HF/STO-3G gives lowest electronic kinetic energy value of 693918.2067. HF/3-21G gives higher value of nuclear repulsion energy value of 841775.876 and HF/STO-3G gives lowest nuclear repulsion energy value of 819558.0873. The HF/3-21G gives higher value of RMS gradient value of 182.2448 and HF/6-31G gives lowest RMS gradient value of 170.9037.

**Table 6:** Computed Total energy, Electronic Kinetic energy, Nuclear repulsion energy and RMS Gradient obtained by *ab-initio* HF/STO-3G, HF/3-21G and HF/6-31G levels

PARAMETERS	HF/STO-3G	HF/3-21G	HF/6-31G
Total energy (kcal/mol)	-700954.0549	-705384.8593	-709200.2127
Electronic Kinetic energy	693918.2067	705935.1810	710735.5469
Nuclear Repulsion Energy	819558.0873	841775.8767	841775.07671
RMS Gradient	177.5335	182.2448	170.9037



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

## CONCLUSIONS

*Ab-initio* HF/STO-3G, HF/3-21G & HF/6-31G levels proved to be important auxiliary tools for geometry optimization and vibrational frequencies. In this regard, the correlation coefficients for bond lengths are 0.8763, 0.9977 and 0.8248 for HF/STO-3G, HF/3-21G & HF/6-31G levels respectively. Clearly, **HF/3-21G** method gives the maximum correlation (CC=0.9977) for bond lengths. The correlation coefficients bond angles are 0.7810, 0.3768 and 0.3866 for HF/STO-3G, HF3-21G and HF/6-31G levels respectively. It is obvious that HF/STO-3G level gives most satisfactory correlation (CC=0.7810). The correlation coefficients for vibrational frequencies are 0.9987, 0.9998 and 0.9997 for HF/STO-3G, HF/3-21G & HF/6-31G levels respectively. HF/3-21G levels give best linearity between experimental and calculated vibrational frequencies and hence are most satisfactory level. Atom electron densities and net atomic charges indicate the coordination sites in the molecule during complex formation with transition metal ions. It is clear that HF/STO-3G method give highest HOMO-LUMO gap and HF/6-31G lowest HOMO-LUMO gap energy. Negative value of HOMO energy is taken as ionization potential and thus HF/3-21G predicts largest value for IP while HF/STO-3G predicts smallest value for IP. 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 biological active compound.

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