

## Molecular structure, vibrational spectroscopic studies and nonlinear optical analysis of Thiacetazone

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### Abstract

In this work, theoretical study by using the DFT method on thiacetazone (TCZ) is reported. The FTIR and FT-Raman spectra of TCZ were noted in the regions 4000–400cm<sup>-1</sup>; The HOMO, LUMO and Gap energy of these compounds have been calculated and reported in this paper. The theoretical study of such compound has not been reported as we know. Thus, our aim to explain the spectroscopic properties on the basis of the DFT quantum chemical calculations and we are interested to explain the nonlinear optical analysis. The study of structural, vibrational spectroscopic studies and nonlinear optical properties for these compounds could help to design more efficient functional photovoltaic organic compounds.

**Keywords:** FTIR, FT-Raman, DFT, TCZ,NLO

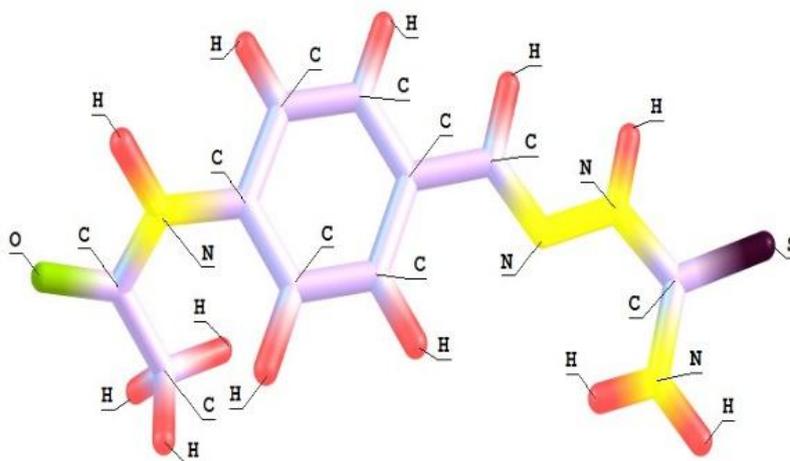


Figure1: Optimized structure of Thiacetazone

## Introduction

TCZ is an inexpensive, antitubercular, bacteriostatic drug that has been widely used in combination with isoniazid in Africa and South America<sup>1</sup>. Chemical analogues of TCZ, SRI-224 and SRI-286, have been synthesized and tested against *Mycobacterium avium* and found to be more effective than TCZ in vitro and in mice<sup>2</sup>. We and others have recently shown that TCZ is a prodrug that is activated by the mycobacterial monooxygenase EthA, which is also the activator of two other anti-tuberculosis drugs, ethionamide (ETH) and isoxyl (ISO)<sup>3,4,5</sup>. However, the mechanism of action of TCZ remains an enigma. Our first observation on effects of TCZ on *M. bovis* BCG was that it affects mycolic acid synthesis<sup>3</sup>. Therefore the vibrational studies of such a compound is very important for further applications.

The present work deals with the theoretical analysis of FT-IR, FT-Raman spectroscopic investigation of TCZ utilizing DFT (B3LYP) method with 6-311+G (d,p) as basis sets. Vibrational spectral analysis has been done. On the basis of vibrational analysis, the nonlinear optical analysis and thermodynamic properties of the title compound have been calculated. The HOMO and LUMO analysis have been used to elucidate information regarding charge transfer within the molecule.

## Materials and Methods

### Computational details

The DFT with the Becke's three-parameter hybrid functional (B3)<sup>6,7</sup> for the exchange part and the Lee–Yang–Parr (LYP) correlation function<sup>8</sup>, accepted as a cost-effective approach has been used to compute optimized structural geometrical parameters, vibrational frequencies FT-IR and FT-Raman of the heading molecule. For all calculations are performed tandem with Gaussian 09 suite of quantum chemical codes<sup>9</sup>. The structural parameters after optimized were employed calculations of the vibrational frequencies, isotropic chemical shifts and electronic properties by using B3LYP with 6-311+G(d,p) basis set.

## Results and discussion

### Geometrical structure

The optimized structure of Thiacetazone are shown in the following Fig 1. The corresponding minimum energy obtained by B3LYP/6-311+G(D,P) method were fall on -1080.9369747. From the optimized geometry the optimized structural parameters are tabulated on Table 2 & 2a.

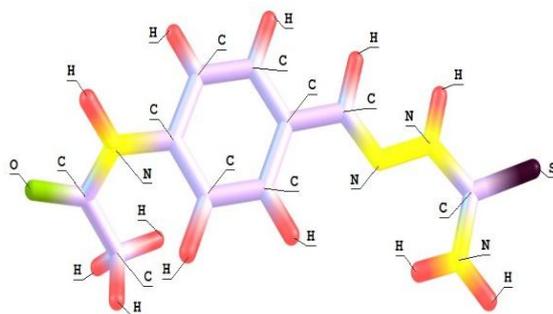


Figure1: Optimized structure of Thiacetazone

Atom. No	Atom
1	S
2	O
3	N
4	N
5	N
6	N
7	C
8	C
9	C
10	C
11	C
12	C
13	C
14	C
15	C
16	C
17	H
18	H
19	H
20	H
21	H
22	H
23	H
24	H
25	H
26	H
27	H
28	H

Table 2: Atom Number from the optimized figure of Thiacetazone

Bond Angle		Bond Length	
A(1-16-5)	120.1	R(1-16)	1.674
A(1-16-6)	124.8	R(2-14)	1.218
A(2-14-3)	119.0	R(3-7)	1.409
A(2-14-15)	121.9	R(3-14)	1.388
A(7-3-14)	131.9	R(3-21)	1.013
A(7-3-21)	116.3	R(4-5)	1.355
A(3-7-9)	118.6	R(4-13)	1.285
A(3-7-10)	122.7	R(5-16)	1.373
A(14-3-21)	111.4	R(5-26)	1.016
A(3-14-15)	119.1	R(6-16)	1.347
A(5-4-13)	117.7	R(6-27)	1.009
A(4-5-16)	122.2	R(6-28)	1.005
A(4-5-26)	121.8	R(7-9)	1.401
A(4-13-8)	122.8	R(7-10)	1.404
A(4-13-22)	120.6	R(8-11)	1.403
A(16-5-26)	116.1	R(8-12)	1.404
A(5-16-6)	115.1	R(8-13)	1.459
A(16-6-27)	120.4	R(9-11)	1.388
A(16-6-28)	118.3	R(9-17)	1.084
A(27-6-28)	121.3	R(10-12)	1.386
A(9-7-10)	118.6	R(10-18)	1.081
A(7-9-11)	120.6	R(11-19)	1.085
A(7-9-17)	119.5	R(12-20)	1.083
A(7-10-12)	120.5	R(13-22)	1.096
A(7-10-18)	120.0	R(14-15)	1.514
A(11-8-12)	118.0	R(15-23)	1.089
A(11-8-13)	119.2	R(15-24)	1.094
A(8-11-9)	121.1	R(15-25)	1.090
A(8-11-19)	119.7		
A(12-8-13)	122.7		
A(8-12-10)	121.1		
A(8-12-20)	119.2		
A(8-13-22)	116.6		
A(11-9-17)	120.0		
A(9-11-19)	119.2		
A(12-10-18)	119.4		
A(10-12-20)	119.7		
A(14-15-23)	107.3		
A(14-15-24)	109.9		
A(14-15-25)	113.1		
A(23-15-24)	107.8		
A(23-15-25)	110.1		
A(24-15-25)	108.4		

Table 2a : Bond Angle and Bond Length of Thiacetazone

### 3.2 Vibrational analysis

The FTIR and FT RAMAN spectrum of Thiacetazone is shown in Figure 2 & 3, Thiacetazone shows C=O<sup>10,11</sup> stretching vibration at lower wave number, 1748.7cm<sup>-1</sup> due to less nitrogen electron pair deralization. The N-H<sup>12</sup> bend bending modes are assigned to peaks at 1611.4, 1642.8 cm<sup>-1</sup>. The C-N<sup>13</sup> single bond stretching vibrations are positioned between 1200 and 1300 cm<sup>-1</sup>. The C=S stretching<sup>14,15</sup> vibrations are intense and sharp between 1500 and 1400cm<sup>-1</sup>. Above experimental data compared with computationally

calculated data, they were good agreement with each other. Vibrational parameters are tabulated in Table 3.

Frequency	IR intensity	Raman intensity	Assignment
942.6577	16.5945	8.3018	
969.8947	4.2765	4.8009	
984.4457	0.2211	1.4678	
1027.3082	39.0444	5.421	
1029.2858	24.9493	2.7326	
1054.5713	10.6865	0.6728	
1064.4353	33.3906	24.2031	
1126.603	175.2782	378.5144	
1149.4841	64.9408	89.5749	
1200.6882	49.3741	776.6804	C-N stretch
1251.1103	23.8161	56.2523	C-N stretch
1256.3099	19.6127	581.4493	C-N stretch
1278.5125	491.3925	45.1278	C-N stretch
1320.2474	504.9653	23.4176	
1331.5617	91.6578	272.3188	C-H rock
1337.2286	72.0468	177.8181	C-H rock
1388.4765	160.0418	181.4324	
1401.0941	92.573	9.2019	C-H bend
1435.828	8.3086	419.156	
1448.1209	73.7145	5.4051	C-H bend
1476.4314	23.634	5.3463	
1487.8138	11.6301	12.2342	
1492.829	11.1626	1.5443	
1528.1261	782.3795	11.1877	C=S Stretch
1553.3907	21.0961	75.756	
1603.6121	0.3092	1373.9404	
1611.3756	225.3276	203.7576	N-H bend
1642.8191	78.4535	7257.33	N-H bend
1662.4465	79.6983	1442.4766	-C=C- stretch
1748.7072	700.8205	195.4787	C=O stretch
3042.0265	45.7271	64.2132	=C-H stretch
3047.0717	2.4527	177.978	

Table 3: vibrational parameters of Thiacetazone

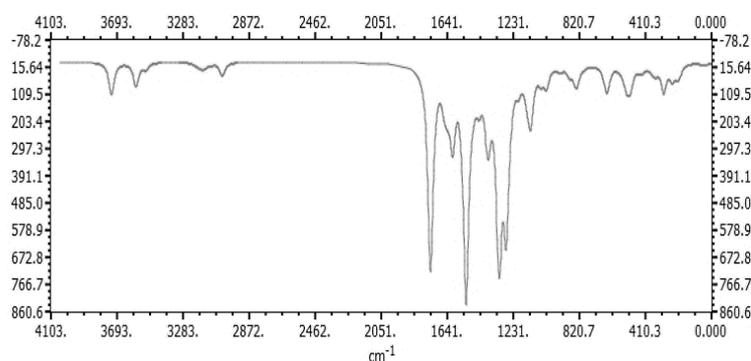


Figure: 2 FTIR Theoretical spectrum of thiacetazone

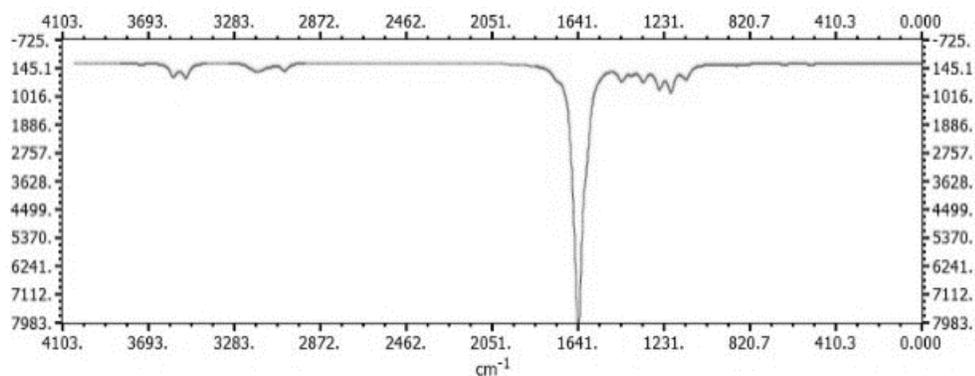


Figure: 3 FT – RAMAN Theoretical spectrum of Thiacetazone

### HOMO-LUMO analysis

To explain several types of reactions and for predicting the most reactive position in conjugated systems, molecular orbitals and their properties such as energy are used. The highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) are the most important orbitals in a molecule. The eigen values of HOMO and LUMO and their energy gap reflect the biological activity of the molecule. A molecule having a small frontier orbital's gap is more polarizable and is generally associated with a high chemical reactivity and low kinetic stability. HOMO, which can be thought as the outer orbital containing electrons, tends to give these electrons as an electron donor and hence the ionization potential is directly related to the energy of the HOMO. On the other hand LUMO can accept electrons and the LUMO energy is directly related to electron affinity. Two important molecular orbitals (MO) were examined for the title compound, the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) which are given in Figs. 4 & 5. In the title compound, the HOMO of  $\pi$  nature is delocalized over the whole C–C bonds of the phenyl ring, and carbonyl group and C=S groups. By contrast, LUMO is located over the carbonyl group and C=S groups. Accordingly, the HOMO–LUMO transition implies an electron density transfer from the phenyl ring to the carbonyl group through the C=S group. For understanding various aspects of pharmacological sciences including drug design and the possible ecotoxicological characteristics of the drug molecules, several new chemical reactivity descriptors have been proposed. Conceptual DFT based descriptors have helped in many ways to understand the structure of molecules and their reactivity by calculating the chemical potential, global hardness and

electrophilicity. Using HOMO and LUMO orbital energies, the ionization energy and electron affinity can be expressed as:  $I = E_{\text{HOMO}}$ ,  $A = E_{\text{LUMO}}$ ,  $n = (-E_{\text{HOMO}} + E_{\text{LUMO}})/2$  and  $\mu = 1/2(E_{\text{HOMO}} + E_{\text{LUMO}})$  proposed the global electrophilicity power of a ligand as  $\omega = \mu^2 / 2n$ .

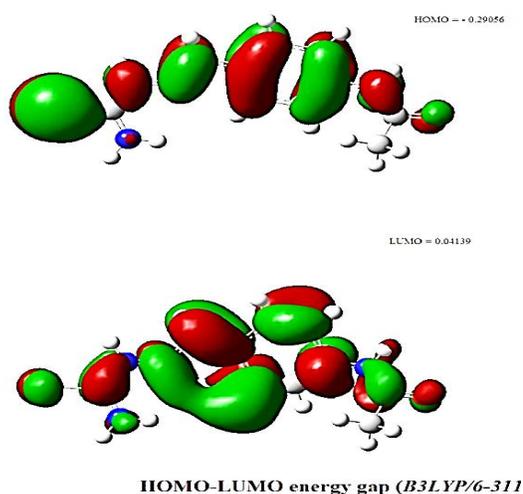


Figure 2: HOMO and LUMO plots of Thiacetazone

### Atomic charges:

The charge distribution of Thiacetazone shows that the S, O and C have negative charges whereas all the hydrogen atoms have positive charges. The maximum atomic charge is obtained for H when compared with other atoms. This is due to the attachment of negatively charged carbonyl group. Various atomic charges tabulated in table 4.

Mulliken atomic charges					
1	S	-0.554851	15	C	-0.433941
2	O	-0.316159	16	C	0.060794
3	N	-0.097821	17	H	0.119254
4	N	0.175734	18	H	0.122393
5	N	-0.014596	19	H	0.123996
6	N	-0.319912	20	H	0.115730
7	C	-0.416679	21	H	0.287721
8	C	0.714300	22	H	0.077025
9	C	-0.216007	23	H	0.186355
10	C	0.425395	24	H	0.185593
11	C	-1.016328	25	H	0.150506
12	C	-0.104303	26	H	0.273572
13	C	-0.163049	27	H	0.248439
14	C	0.093462	28	H	0.293377

Table 4: Atomic charges of Thiacetazone

### Thermodynamic properties

On the basis of vibrational analyses and statistical thermodynamics, the standard thermodynamic functions: heat capacity ( $C_{p,m}^0$ ), entropy ( $S_m^0$ ) and enthalpy ( $H_m^0$ ) were calculated using perl script THERMO.PL<sup>16</sup> and are listed in Table 5. As observed from Table 5, the values of  $C_{p,m}^0$ ,  $S_m^0$  and  $H_m^0$  all increase with the increase of temperature from 100 to 1000 K, which is attributed to the enhancement of the molecular vibration as the temperature increases.

$T$ (K)	$S$ (J/mol.K) [ $S_m^0$ ]	$C_p$ (J/mol.K) [ $C_{p,m}^0$ ]	$ddH$ (kJ/mol) [ $H_m^0$ ]
100.00	362.11	115.18	7.67
200.00	463.96	187.11	22.77
298.15	551.63	255.95	44.55
300.00	553.22	257.20	45.03
400.00	636.10	320.57	73.99
500.00	713.55	373.78	108.80
600.00	785.65	416.91	148.41
700.00	852.63	451.86	191.91
800.00	914.90	480.55	238.57
900.00	972.93	504.50	287.86
1000.00	1027.16	524.75	339.35

Table 5: Thermodynamic properties

### NLO properties

Non-linear optical (NLO) is at the forefront of current research because of its importance in providing key functions of optical modulation, optical switching, optical logic and optical memory for the emerging technologies in areas such as telecommunications, optical interconnections and signal processing. The first hyperpolarizability ( $\beta_0$ ) of this molecular system is calculated using the **B3LYP/6-311+G(D,P)** method, based on the finite field approach. In the presence of an applied electric field, the energy of a system is a function of the electric

$$E = E_0 - \sum_i \mu_i F^i - \frac{1}{2} \sum_{ij} \alpha_{ij} F^i F^j - \frac{1}{6} \sum_{ijk} \beta_{ijk} F^i F^j F^k - \frac{1}{24} \sum_{ijkl} \gamma_{ijkl} F^i F^j F^k F^l + \dots$$

field. First hyperpolarizability is a third rank tensor that can be described by a  $3 \times 3 \times 3$  matrix. The 28 components of the 3D matrix can be reduced to 10 components due to the Kleinman symmetry. The components of  $\beta$  are defined as the coefficients in the Taylor series expansion of the energy in the external electric field. When the electric field is weak and homogeneous, this expansion becomes. where  $E_0$  is the energy of the unperturbed molecule,  $F^1$  is the field at the origin,  $\mu_i$ ,  $\alpha_{ij}$ ,  $\beta_{ijk}$  and  $\gamma_{ijkl}$  are the components of dipole moment, polarizability, the first hyper polarizabilities, and second hyperpolarizabilities, respectively. The calculated first hyperpolarizability of the title compound is 8526.837586 esu.

The polar and hyperpolar values of title compound are tabulated (Table 6).

	Polar for au	Polar for esu
$\alpha_{xx}$	195.5255561	28.97688741
$\alpha_{xy}$	74.2771709	11.00787673
$\alpha_{yy}$	373.9484907	55.41916632
$\alpha_{xz}$	-9.7708737	-1.448043482
$\alpha_{yz}$	-7.5593467	-1.120295181
$\alpha_{zz}$	102.322426	15.16418353
	HyperPolar for au	HyperPolar for esu
$\beta_{xxx}$	107.530251	928.9860975
$\beta_{xxy}$	-129.9054739	-1122.292361
$\beta_{xyy}$	-413.5801784	-3573.043235
$\beta_{yyy}$	-886.040121	-7654.766417
$\beta_{xxz}$	45.3758342	392.0154444
$\beta_{xyz}$	73.6860437	636.5958373
$\beta_{yyz}$	42.6927817	368.8357489
$\beta_{xzz}$	19.0862792	164.8920919
$\beta_{yzz}$	75.4452301	651.7939764
$\beta_{zzz}$	-2.9492337	-25.4793147

Table 6: Polar and Hyper polar coordinates

## Conclusion

This paper we investigated theoretical spectroscopic study performed FT-IR, FT-Raman spectra of Thiacetazone molecule. To have more information on the structural parameters, the optimized geometric parameters were determined theoretically at B3LYP/6-311+G(d,p) level of theory. The HOMO LUMO energy strongly supports the presence of intramolecular energy transfer with the molecule and chemical potential, global hardness and electrophilicity are also calculated. The statistical thermodynamics properties were also obtained according to variation temperature. It is seen that statistical thermodynamics properties increase with the increasing temperature. The calculated value of  $b$  for the title compound is relatively higher than that of urea and therefore the title compound possesses considerable NLO properties.

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