

VIBRATIONAL SPECTRA OF 1,3-bis (marpholino/pepridino methyl)-5-oxyphenyl benzinidazoline-2-thiones: Antiviral and Antifungal

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ABSTRACT

The molecular structure and vibrational spectra of 1,3 bis(marpholino/pepridino methyl)-5-oxyphenyl benzinidazoline-2-thiones is calculated with the help of B3LYP density functional theory (DFT) using 6-31G as basis set and characterized by IR and RAMAN spectral studies. On the basis of B3LYP calculations, the normal coordinate analysis is performed to assign the vibrational fundamental frequencies. The full geometry optimization was carried out using a 6-31G basis set, and the frontier orbital energy. The calculated HOMO and LUMO energies show that charge transfer that charge transfer occurs within the molecule. Calculated bond lengths and bond angles were found to differ little bit from experimental values, and the compound exhibits antifungal and antiviral activity.

KEYWORDS: antifungal, antiviral, DFT, HOMO, LUMO

INTRODUCTION

Every drug has intrinsic chemical and physical properties which has been consider before development of pharmaceutical formulation. This property provides the framework for drugs combination with pharmaceutical ingredients in the fabrication of dosage form. Despite the diverse research and development (R&D) approaches adopted by pharmaceutical companies, the attrition rate is inadmissibly high. One of the factors contributing to the high attrition rates is an active compound with unacceptable absorption, distribution, metabolism, excretion, and toxicity (ADMET) adverse effects that thus needs to be withdrawn from development. This factor represents approximately 50% of all costly failures in drug development, and it has become widely appreciated that these areas should be considered as early as possible in the drug-discovery process. DFT is among the most popular and versatile methods available in condensed-matter physics, computational physics, and computational chemistry. In many cases the results of DFT calculations for solid-state systems agreed quite satisfactorily with experimental data. Also, the computational costs were relatively low when compared to traditional ways which were based on the complicated many-electron wave function, such as Hartree-Fock theory and its descendants. There is an important medical need for new antifungal agents with novel mechanisms of action to treat the increasing number of patients with life-threatening systemic fungal disease and to overcome the growing problem of resistance to current therapies.

Vibrational analysis of 1,3 Bis(marpholino/pepridino methyl)-5-oxyphenyl benzinidazoline-2-thiones by combining the experimental IR and Raman spectral data and theoretical information using scaled quantum chemical (SQM) technique based on density functional theory (DFT). The studies of HOMO, LUMO analysis have been used to elucidate information regarding charge transfer within the molecule.

METHOD, MATERIAL AND THEORY

Optimized geometrical structure of 1,3 Bis(marpholino/pepridino methyl)-5- oxyphenyl benzinidazoline-2-thiones.

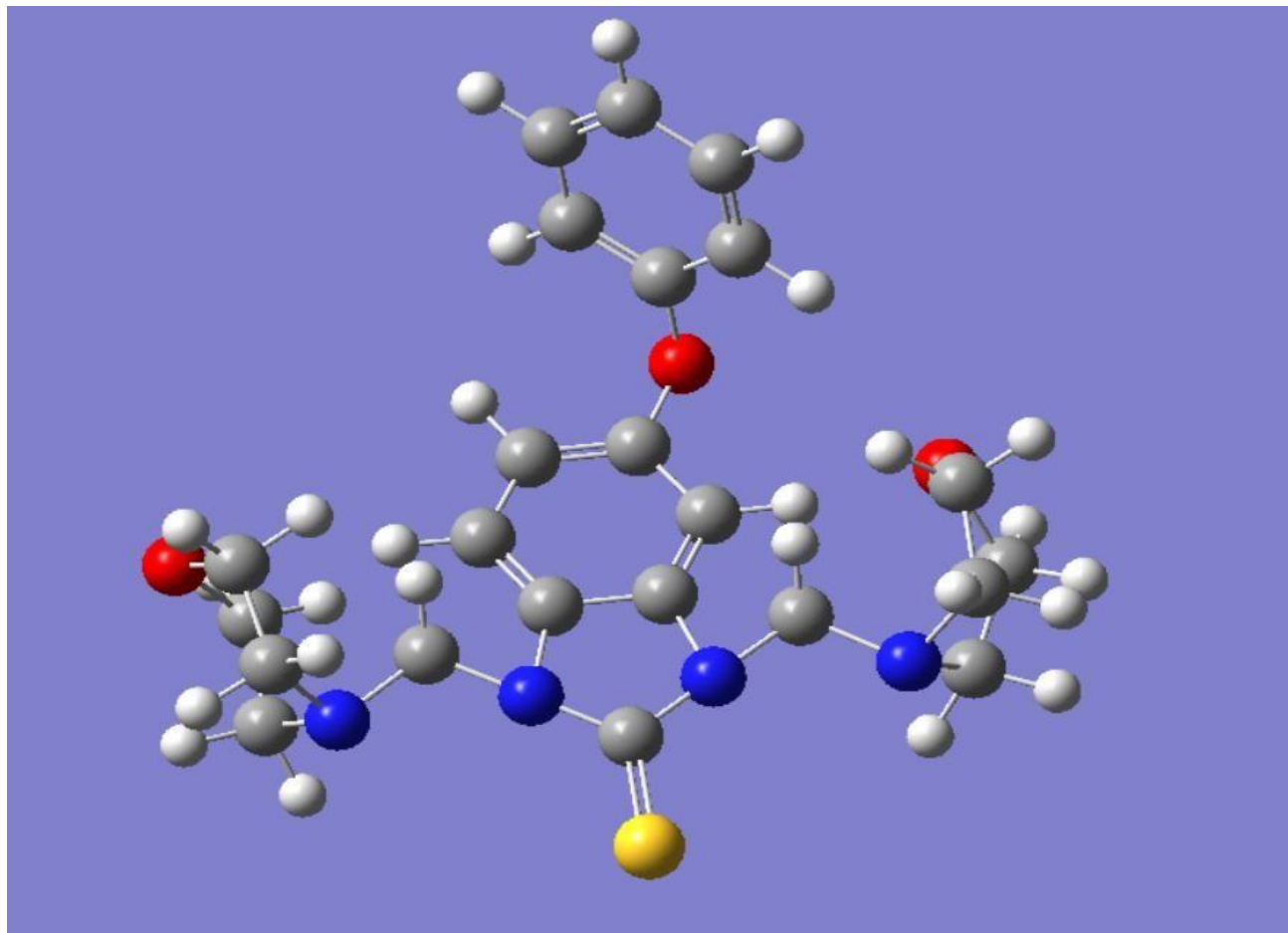


FIG-1

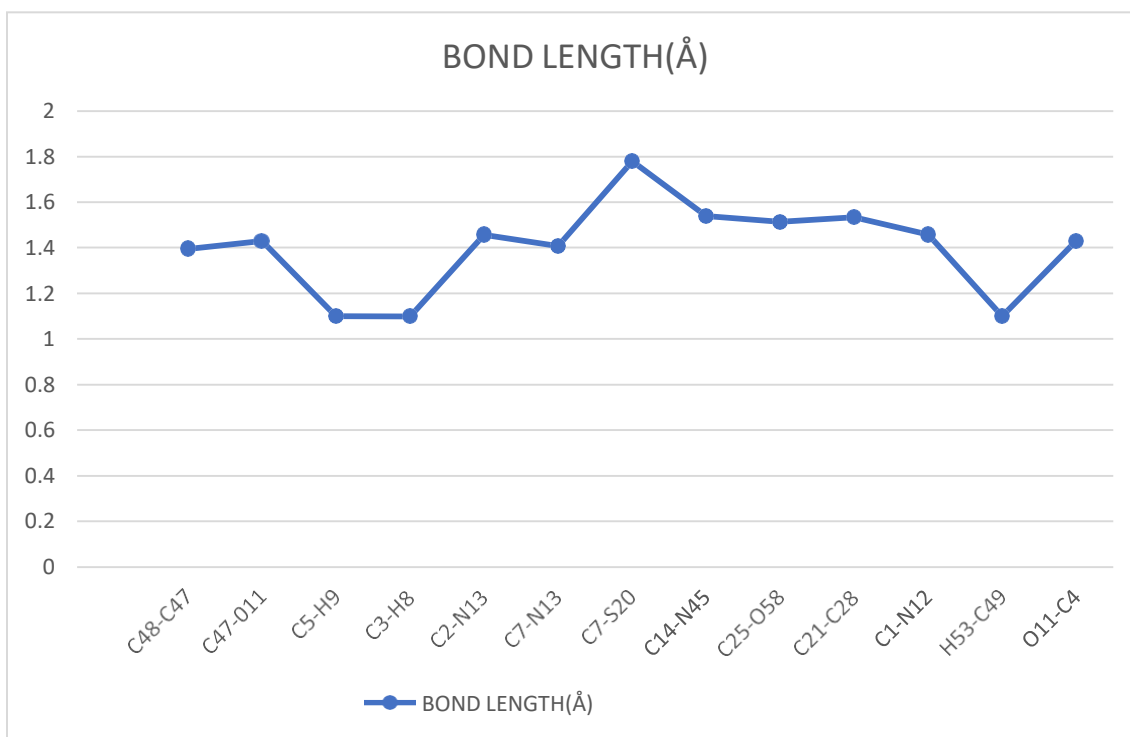
The molecular geometry optimization, energy and Vibrational frequency calculations have been performed for 1,3 Bis(marpholino/pepridino methyl)-5- oxyphenyl benzinidazoline-2-thiones using Gauss view 5.0 program package at the Becke3-Lee-Yang-Parr (B3LYP) level with standard 6-31G basis set. For plots of simulated IR spectra, pure Lorentzian band shapes were used. The Raman activity calculated by Gaussian program have been suitably adjusted by the scaling procedure with MOLVIB and subsequently converted to relative Raman intensity. DFT calculations allow the prediction and calculation of material behaviour on the basis of quantum mechanical considerations, without requiring higher order parameters such as fundamental material properties.

The optimized structural parameters such as bond lengths, bond angle were determined at B3LYP level theory with 6-31G basis set and are presented in Table given below-

ATOMS	BOND LENGTH(Å)
C48-C47	1.39516
C47-O11	1.43000
C5-H9	1.10025

C3-H8	1.09891
C2-N13	1.45750
C7-N13	1.40768
C7-S20	1.78000
C14-N45	1.54000
C25-O58	1.51386
C21-C28	1.53405
C1-N12	1.45766
H53-C49	1.09960
O11-C4	1.43000

TABLE-1

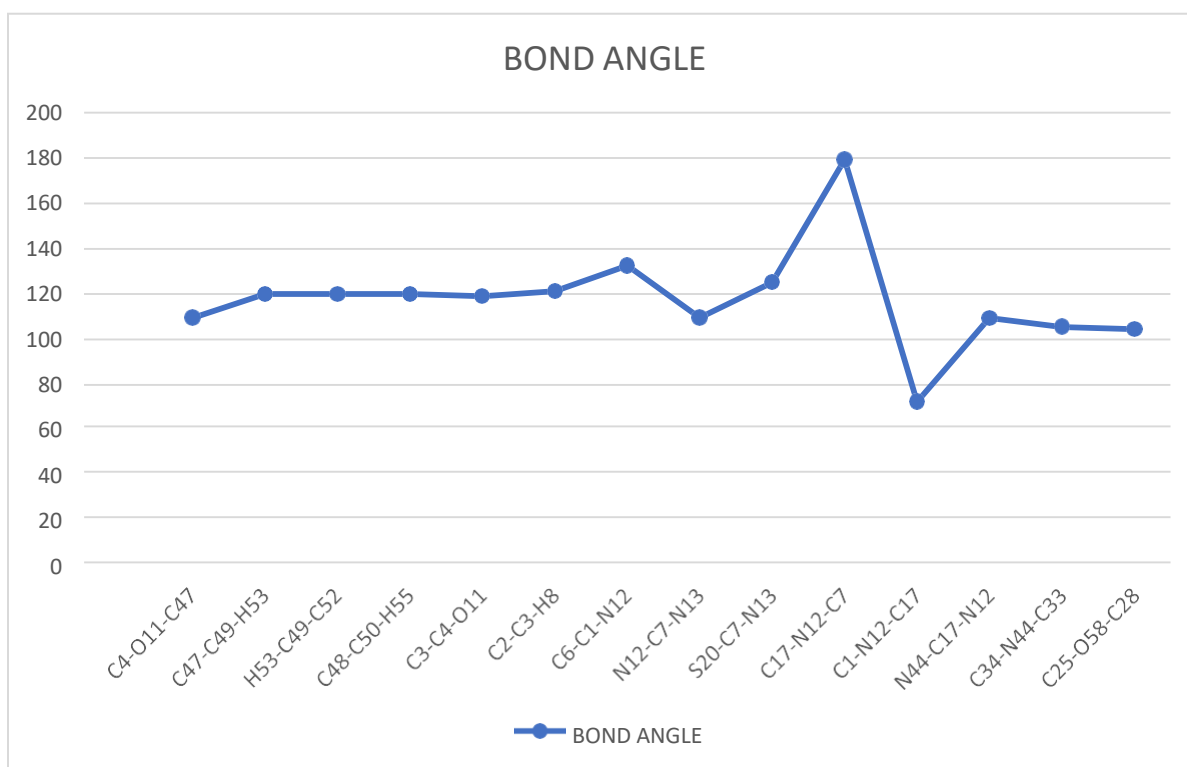


GRAPH-1

ATOMS	BOND ANGLE
C4-O11-C47	109.5
C47-C49-H53	120.008
H53-C49-C52	119.992
C48-C50-H55	120.013
C3-C4-O11	119.111
C2-C3-H8	121.271
C6-C1-N12	132.563

N12-C7-N13	109.573
S20-C7-N13	125.205
C17-N12-C7	179.250
C1-N12-C17	72.567
N44-C17-N12	109.471
C34-N44-C33	105.536
C25-O58-C28	104.558

TABLE-2



GRAPH-2

IR and Raman Frequencies

The vibrational spectral assignments have been carried out with the help of normal coordinate analysis. Non-redundant set of local symmetry coordinates constructed by suitable linear combinations of internal coordinates chosen according to the recommendations of Pulay. The computed wave numbers are selectively scaled according to the SQM procedure suggested by Rauhut and Pulay, the observed IR and Raman spectra are presented in Figs 2 and 3 respectively. These calculations were done by using B3LYP/6-31G.

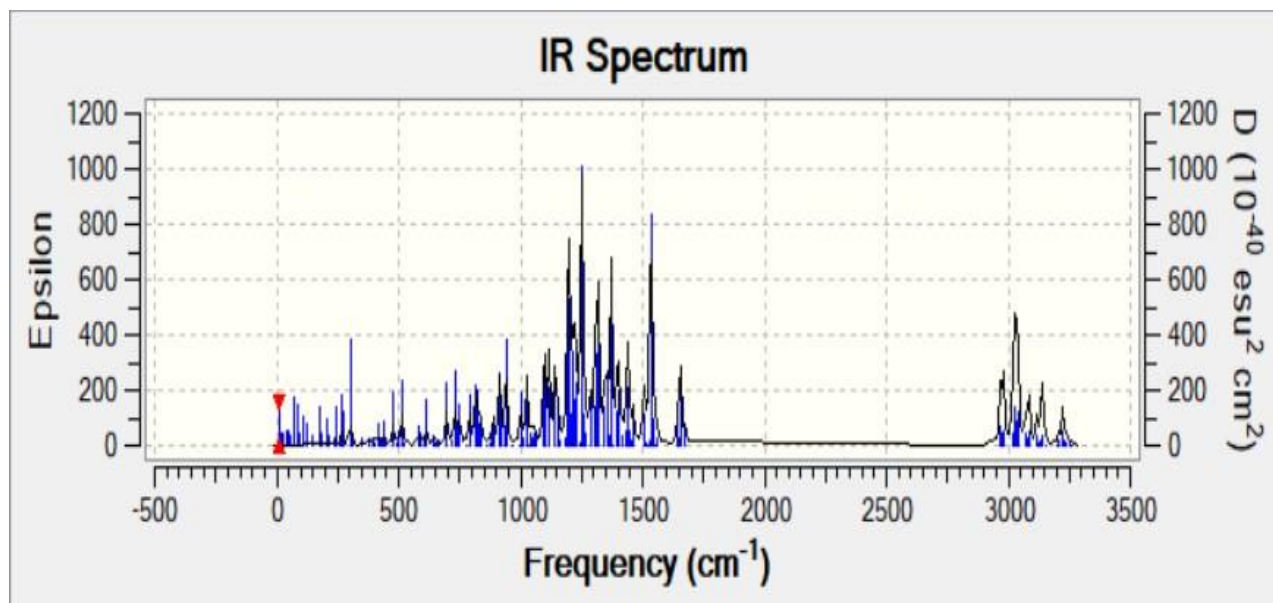


FIG-2

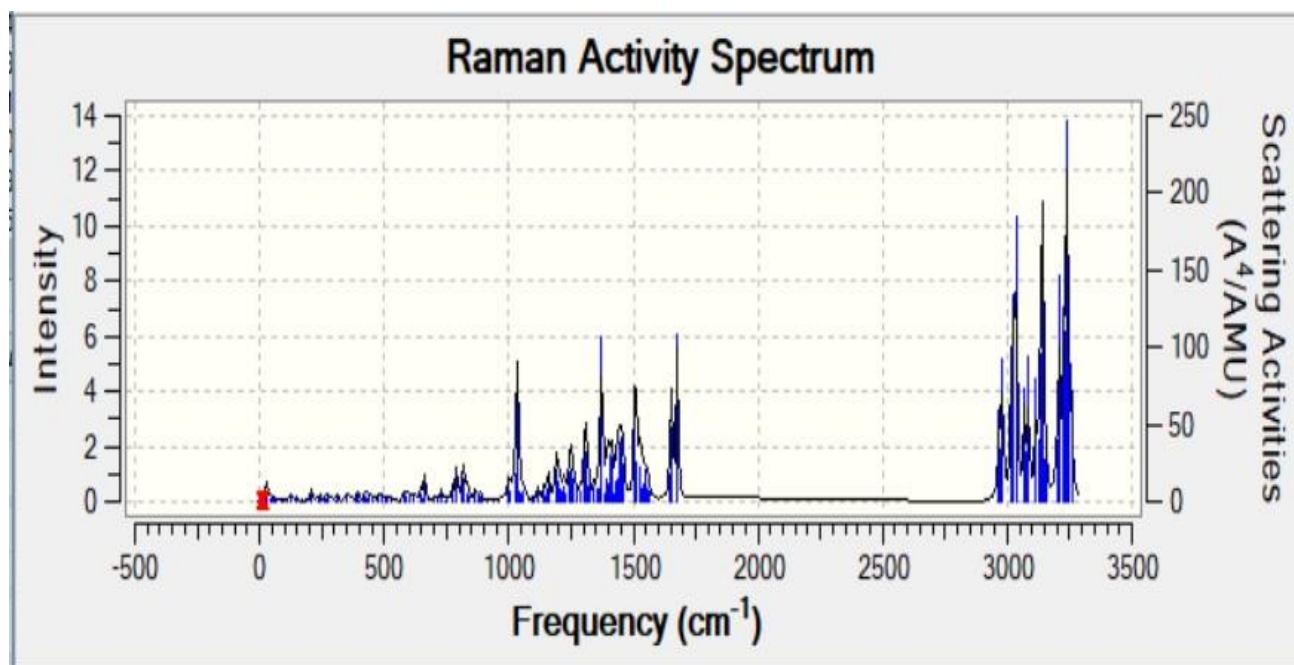


FIG-3

DEPOLARIZATION SPECTRA-

The depolarization ratio is the intensity ratio between the perpendicular component and the parallel component of the raman scattered light. Two polarization occur i.e. p- polarization and u- polarization. The optimised spectra of p-depolarization and u-depolarization is shown in the fig-4 and fig-5-

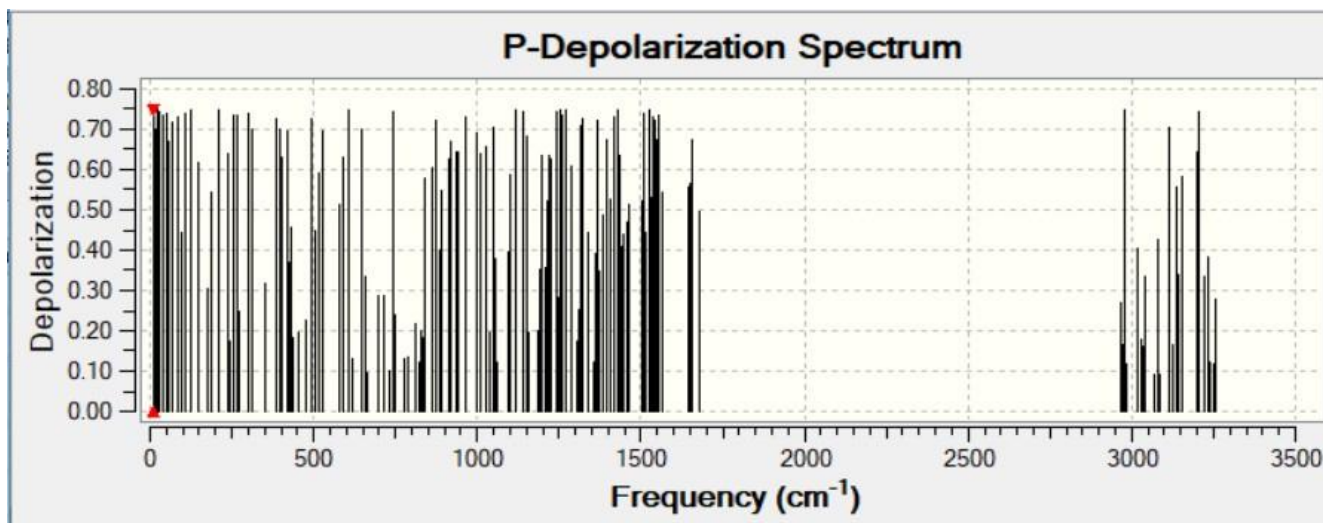


FIG-4

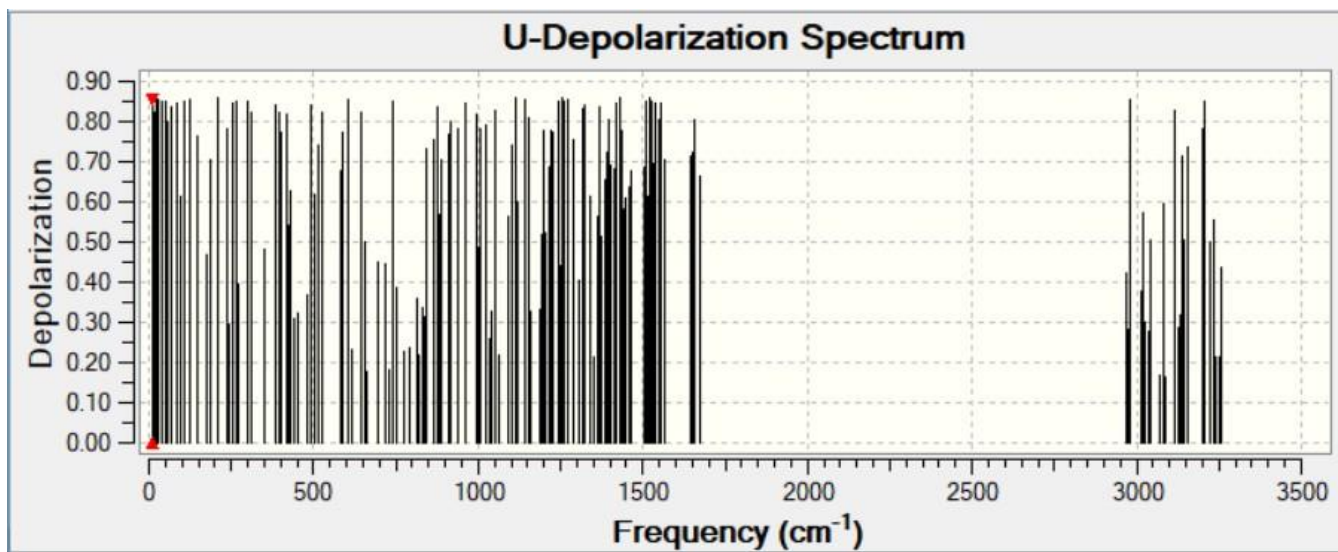


FIG-5

Molecular Orbital Energies

The most important orbitals in a molecule are the frontier molecular orbitals, called highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO). These orbitals determine the way the molecule interacts with other species. The frontier orbital gap helps characterize the chemical reactivity and kinetic stability of the molecule. A molecule with a small frontier orbital gap is more polarizable and is generally associated with a high chemical reactivity, low kinetic stability and is also termed as soft molecule.

The HOMO represents the ability to donate an electron, while LUMO as an electron acceptor represents the ability to obtain an electron. The electronic transition absorption corresponds to the transition from ground to the first excited state and is mainly described by one electron excitation from the highest occupied molecular orbital to the

lowest unoccupied molecular orbital. Consequently HOMO \rightarrow LUMO transition implies an energy transfer from the ring. The energy gap between HOMO and LUMO has been used to prove the bioactivity from intramolecular charge transfer. The energy gap measures the kinetic stability of the molecules.

The HOMO and LUMO energy calculated by B3LYP /6-31G method	
HOMO energy	-0.19897 a.u
LUMO energy	-0.03329 a.u
ENERGY GAP (HOMO-LUMO)	0.16568 a.u

The HOMO and LUMO energy gap explains the eventual charge transfer interactions taking place within the molecule. The HOMO and LUMO density plots of title compound are shown in Fig. 6 and fig.7

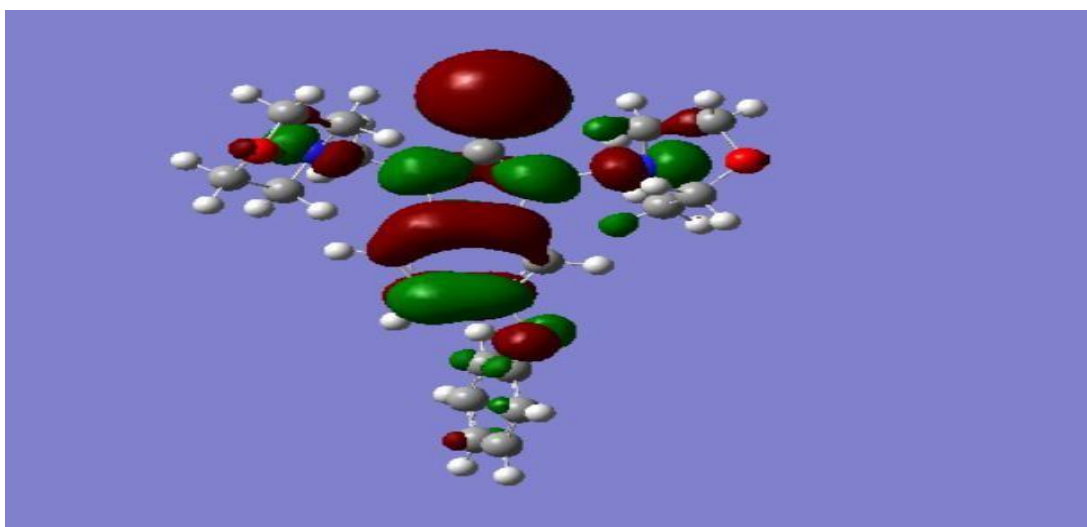


FIG-6

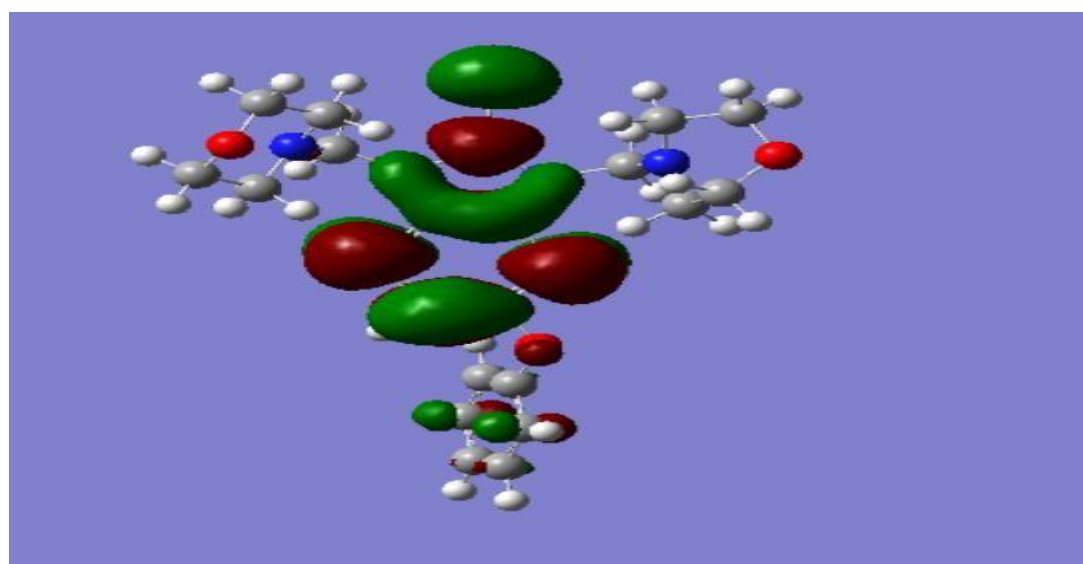


FIG-7

The IR and Raman Spectra have been recorded and the detailed vibrational assignments' are presented for 1,3 Bis(marpholino/pepridino methyl)-5- oxyphenyl benzinidazoline-2-thiones. The equilibrium geometries, IR and Raman spectra, HOMO and LUMO analysis of the title compound are determined and analyzed by B3LYP /6-31G level of theory . The lowering of HOMO and LUMO gap clearly explains the charge transfer interactions taking place within the molecule.

CONCLUSION: Thus the simulation report of 1,3 Bis(marpholino/pepridino methyl)-5- oxyphenyl enzinidazoline-2-thiones will be reported soon , work is under process.

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