Electronic structure and vibrational analysis of Piperazine: 1- ((3- methylphenyl) piperazine- 1- yl)- 3-(oxy- phenyl) propane Anti- hypertensive drug

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Abstract

1- ((3- methylphenyl) piperazine- 1- yl)- 3-(oxy- phenyl) propane is an anti- hypertensive drug. Antihypertensives are a class of drugs that are used to treat hypertension (high blood pressure) including cardiovascular events. Antihypertensive therapy seeks to prevent the complications of high blood pressure, such as stroke and myocardial infarction.

The structure and the ground state energy of the molecules are analysed using DFT/B3LYP level under investigation. The optimised geometry and their properties like frontier orbital energy, vibrational frequencies have been used to understand the activity of the compund. Highest Occupied Molecular Orbital or HOMO and the Lowest Unoccupied Molecular Orbital or LUMO energies are calculated which shows the charge transfer within the molecule. The virational spectra of IR and Raman have been plotted with the help of B3LYP level of theory with the 6- 31G basis set from the Density function theory.

Keyword Vibrational spectra, IR and RAMAN spectrum, DFT, HOMO, LUMO, antihypertensive

Introduction

1- ((3- methylphenyl) piperazine- 1- yl)- 3-(oxy- phenyl) propane is a antihypertensive drung which is used in the treatment of hypertension or high blood pressure. Antihypertensive therapy seeks to prevent the complications of high blood pressure, such as stroke and myocardial infarction. Evidence suggests that reduction of the blood pressure by 5 mmHg can decrease the risk of stroke by 34% , of ischaemic heart disease by 21% , and reduce the likelihood of dementia, heart failure, and mortality from cardiovascular disease.

Depression and cardiovascular disease are major contributors to the global burden of disease. A bidirectional relationship is thought to exist between depression and heart disease due to the functional changes that underlie both conditions.

Bipolar disorder is associated with an increased risk of cardiovascular mortality and high blood pressure, whereas major depressive disorder is associated with an increased risk of high blood pressure.While there is growing evidence that the pathways that high blood pressure drugs target

may play a role in the development of mood disorders - suggesting implications in prescribing these drugs in hypertensive patients who may have an underlying mood disorder - results of the link between the two have been inconclusive. Still mental health is an under- recognized area in hypertension research.

Method, material and theory

Density functional theory (DFT) is among the most popular and versatile methods available in condensed- matter physics, computational physics, and computational chemistry.DFT calculations helps in the prediction and calculation of material behaviour on the basis of quantum mechanical considerations, without any requirement of higher order parameters such as fundamental material properties. By the use of DFT the energy of a molecule can be computed from the electron density instead of a wave function.

DFT is a computational quantum mechanical modelling method used in physics, chemistry and materials science in investigatation of the electronic structure (or nuclear structure) basically the ground state of many- body systems, in particular atoms, molecules, and the condensed phases. At present, the properties which can be determined or calculated by DFT are energies, Frontier orbital, geometries, spectrum, etc.

Density functional theory (DFT) calculations have been performed to predict the IR and Raman spectra for the molecule. Fourier transform infrared (FTIR) and Raman spectra of the compound have been obtained experimentally. All FTIR and Raman bands of the compound obtained experimentally were assigned based on the modeling results obtained at the B3LYP/6- 31G level.

In general, ab initio calculations give very good qualitative results and can yield increasingly accurate quantitative results as the molecules in question become smaller. The advantage of ab initio methods is that they eventually converge to the exact solution once all the approximations are made sufficiently small in magnitude.

DFT was applied using the B3LYP which is the keyword for the hybrid functional, which is a linear combination of the gradient functional proposed by Becke and Lee, Yang and Parr, together with the Hartree Fock local exchange function. Calculations were performed using the Gaussian 09. Gaussan is a general purpose computational chemistry software package. A basis set in theoretical and computational chemistry is a set of functions (called basis functions) that is used to represent the electronic wave function in the density- functional theory The DFT methods with 6- 31G basis set calculations were made first to optimize the structures. The vibrational frequencies and non- linear optical properties were calculated by means of DFT methods at the corresponding optimized geometries. All the calculations converged to an optimized geometry which corresponds to a true energy minimum as revealed by the lack of imaginary values in the calculate vibration frequencies. Vibration frequencies are calculated using B3LYP/6- 31G .

Optimized geometrical structure of Piperazine is shown in fig 1

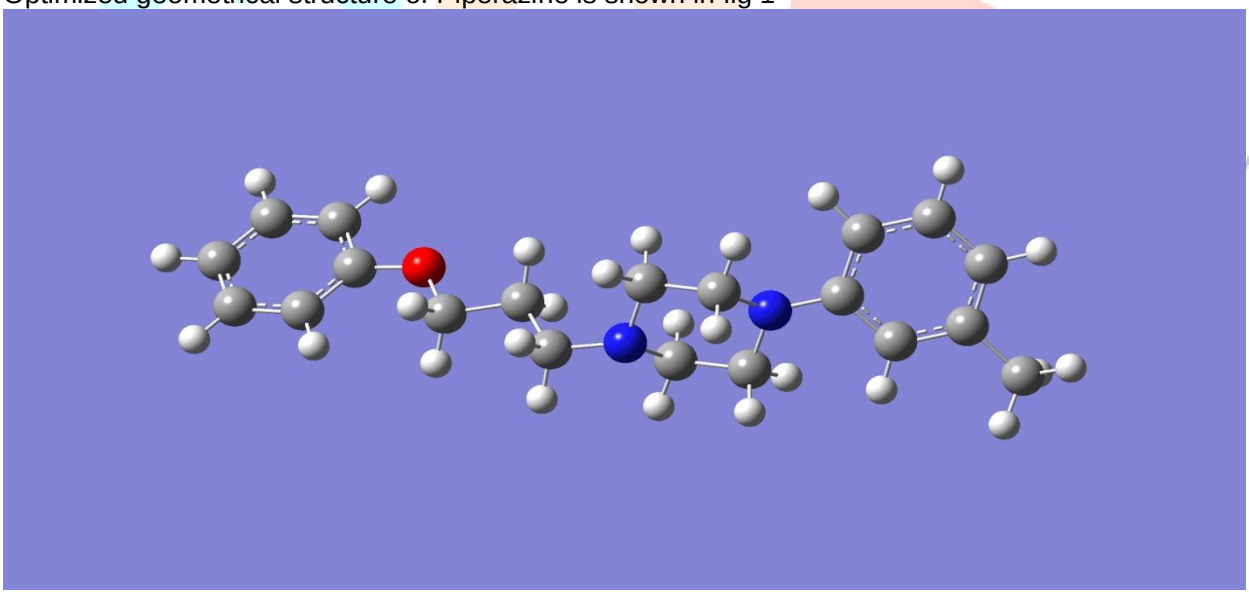


fig 1

IR and RAMAN Spectroscopy

Infrared spectroscopy (IR spectroscopy or vibrational spectroscopy) involves the interaction of infrared radiation with matter. It covers a range of techniques, mostly based on absorption spectroscopy. Infrared spectroscopy exploits the fact that molecules absorb frequencies that are characteristic of their structure. These absorptions occur at resonant frequencies, i.e. the frequency of the absorbed radiation matches the vibrational frequency. The energies are affected by the shape of the molecular potential energy surfaces, the masses of the atoms, and the associated vibronic coupling.

An IR spectrum can be visualized in a graph of infrared light absorbance (or transmittance) on the vertical axis vs frequency or wavelength on the horizontal axis. Optimized geometric structure of IR Spectra of Piperazine is shown in fig 2.

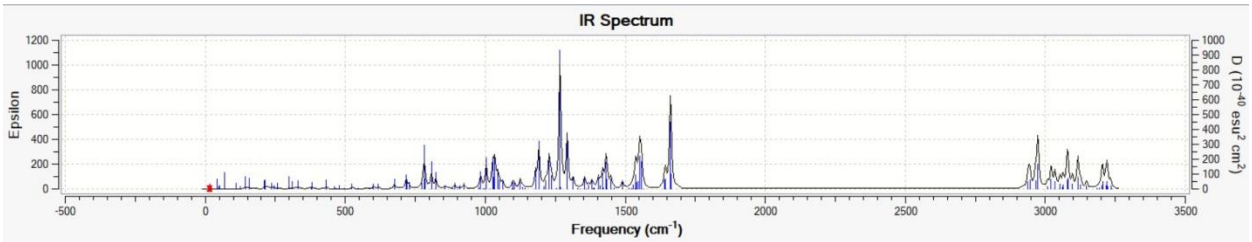


fig 2

A RAMAN spectrum is a plot of the intensity of the scattered light (y- axis) for each energy (frequency) of light (x- axis). The frequency is traditionally measured in a unit called the wavenumber (number of waves per cm, cm- 1).The plot on the x- axis frequencies is the shift in energy of the light that is of particular interest. The difference is called as RAMAN shift because in actual it is the difference value. Optimized geometric structure of Raman Spectra of Piperazine is shown in fig 3.

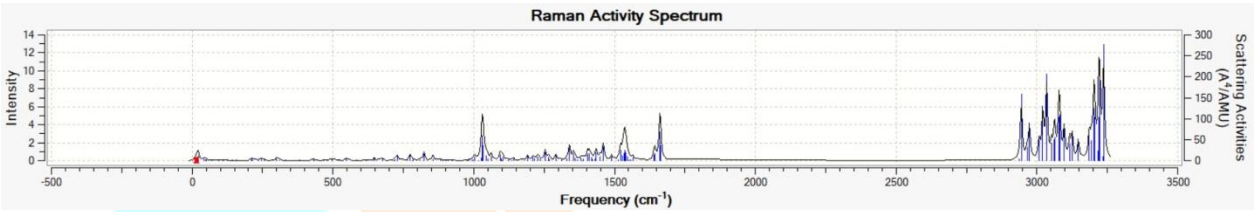


fig 3

Theoretically computed ground state optimized parameters

Parameters	(B3LYP/6-31G)
Energy (in a.u.)	- 962.24093616
Dipole moment (in Debye)	1.7464

1 Debye = 3.34*10 $^{-30}$ cm.

1a.u.of energy= 1hartree = 4.360 × 10 $^{-18}$ J. = 27.211eV= 2625kJ/mol = 627.5kcal/mol.

Molecular Orbital Energies

Frontier molecular orbital theory is an application of MO theory describing HOMO/LUMO interactions. There are two types of molecular orbitals namely HOMO and LUMO. The acronym stands for Highest Occupied Molecular Orbital(HOMO) and Lowest Unoccupied Molecular Orbital. The energy difference between the HOMO and LUMO is termed the HOMO –LUMO gap. HOMO and LUMO are sometimes called frontier orbitals in frontier molecular orbital theory. The difference in energy between these two frontier orbitals can be used to predict the strength and kinetic stability of transition metal complexes, as well as the colors they produce in solution the molecule which have small frontier orbital gap is more polarizable and high chemical reactivity. It has also low kinetic stability and

are known as soft molecules.

The density plot of the HOMO and LUMO of Piperazine is calculated at B3LYP/6- 31G level of theory and are shown in fig 4 and fig 5.

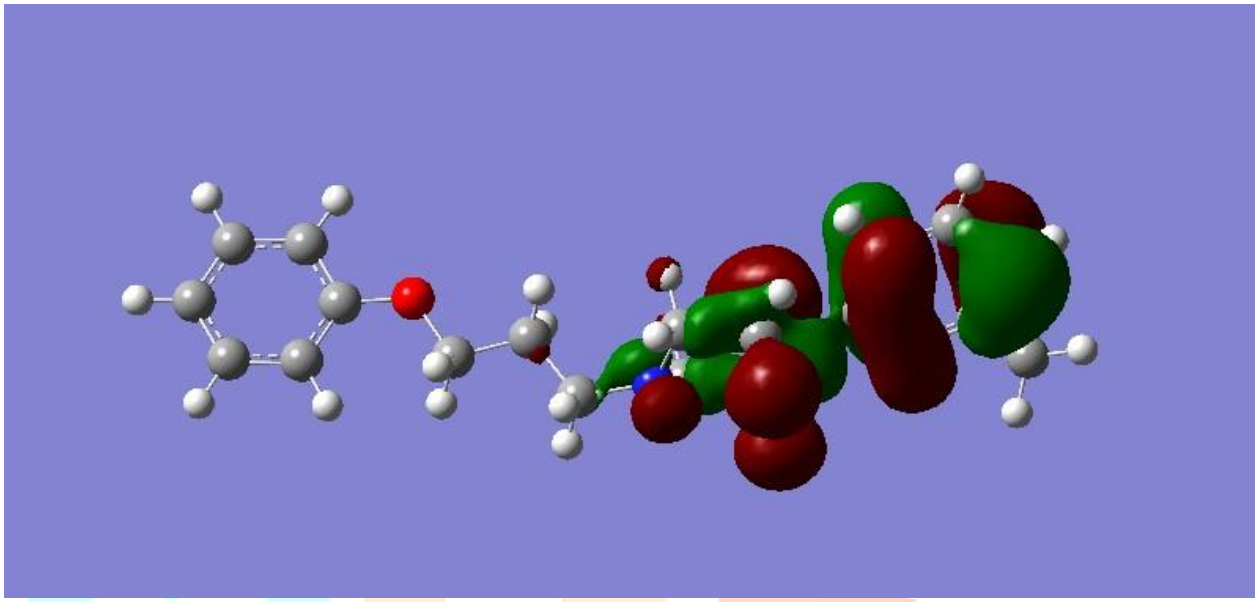


fig 4

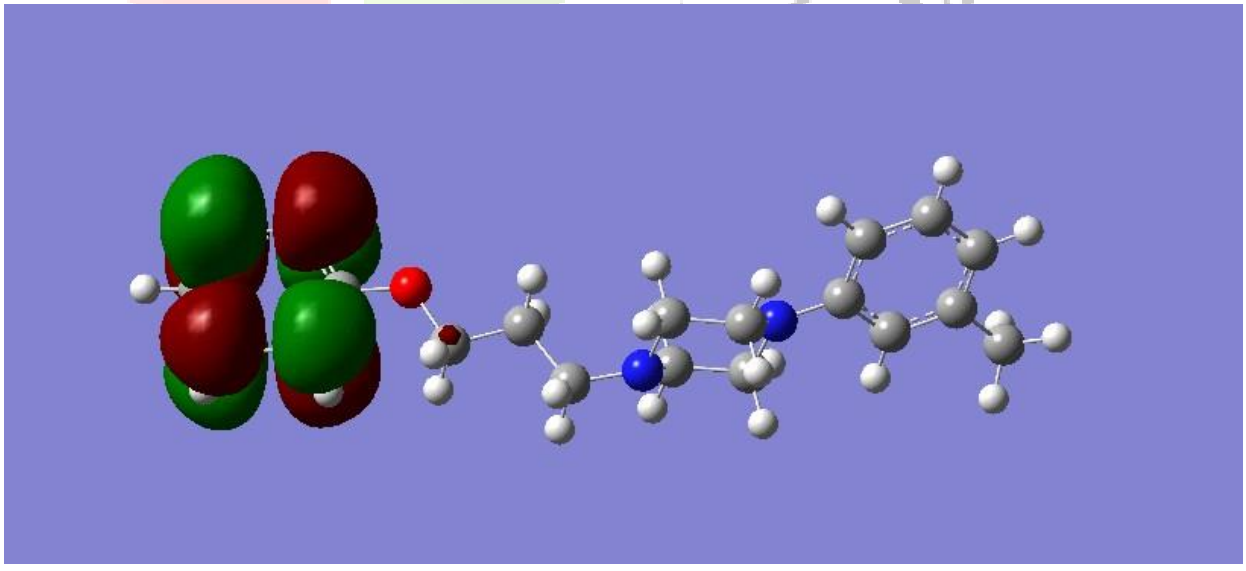


fig 5

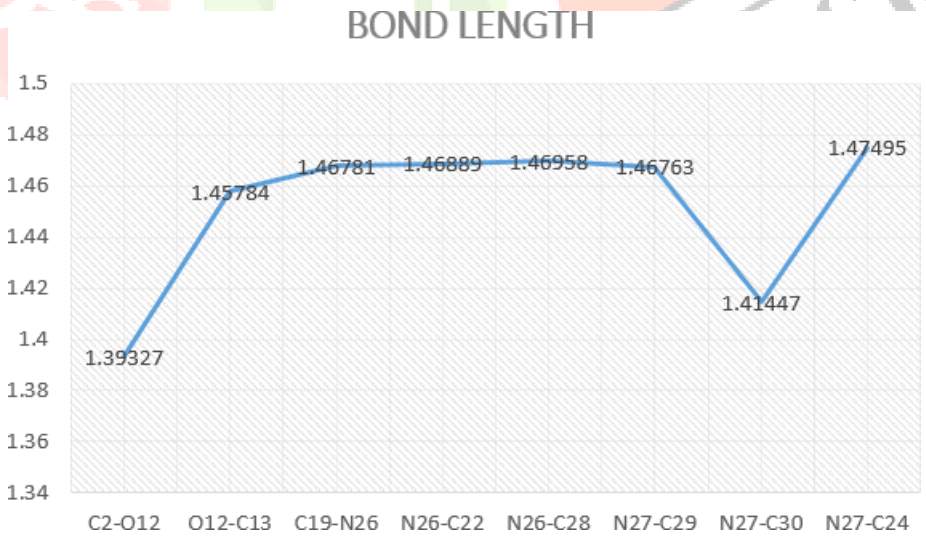
Homo **Lumo**	- 0 .18469 0 .00205
Frontier orbital energy gap	*0 .18674*

Bond length and Bond angle

The distance between the centers of two nuclei of atoms connected by a chemical bond is known as 'bond length. It is a transferable property of a bond between atoms of fixed types, relatively independent of the rest of the molecule. In other words, bond length is the distance between the nuclei (the center) of two atoms. Bond angle is the internal angle between the orbitals having bonded pair of electrons in the valency shell of the central atom in a molecule. Molecular geometries can be specified in terms of bond lengths and bond angles.Bond lengths and bond angle are the optimized structural parameters, so these were determined by B3LYP level theory with 6- 31G basis set.

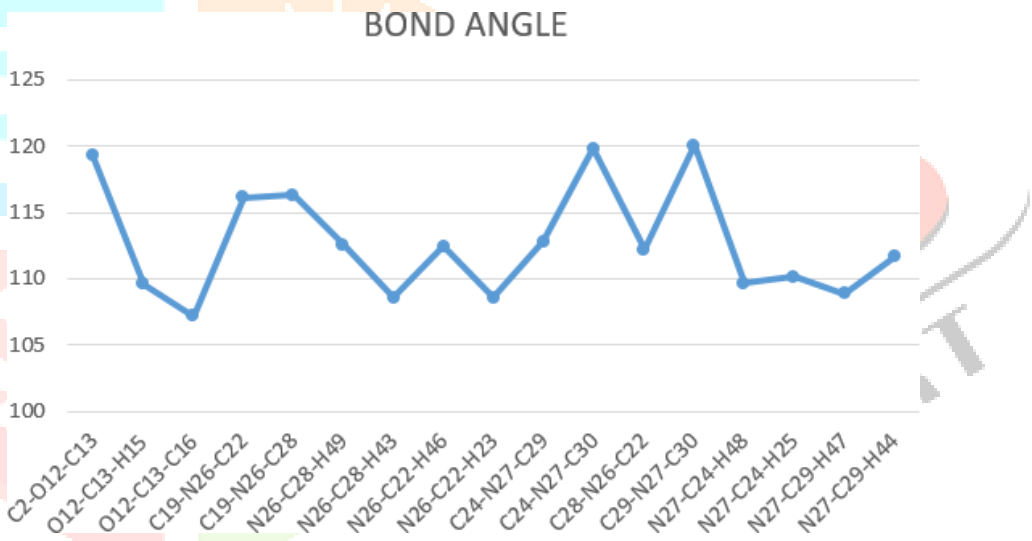
Bond angle table and graph of Piperazine is given below:

ATOM	BOND LENGTH
C2-O12	1.39327
O12-C13	1.45784
C19-N26	1.46781
N26-C22	1.46889
N26-C28	1.46958
N27-C29	1.46763
N27-C30	1.41447
N27-C24	1.47495



. Bond angle table and graph of Piperazine is given below:

ATOM	BOND ANGLE
C2-O12-C13	119.305
O12-C13-H15	109.624
O12-C13-C16	107.154
C19-N26-C22	116.1
C19-N26-C28	116.281
N26-C28-H49	112.54
N26-C28-H43	108.598
N26-C22-H46	112.419
N26-C22-H23	108.573
C24-N27-C29	112.827
C24-N27-C30	119.788
C28-N26-C22	112.222
C29-N27-C30	120.037
N27-C24-H48	109.652
N27-C24-H25	110.165
N27-C29-H47	108.898
N27-C29-H44	111.643



Conclusion: The simulation work is under progress. The results will be reported soon.

Acknowledgment: I am very thankful to the DSMNR University, Lucknow for the facility provided.

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