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ARTICLE

Molecular Structural and Vibrational Spectroscopic Assignments of 5-(4-Methoxyphenyl)-3-(1-methylindol-3-yl)-isoxazole using DFT Theory Calculations

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ABSTRACT

In an effort to evaluate and design fast, accurate density functional theory (DFT) methods for 5-(4-methoxyphenyl)-3-(1-methylindol-3yl)isoxazole compound was done using Gaussion' 09 program package using B3LYP method with the 6-31G basis set, which has been successfully applied in order to derive the optimized geometry, bonding features, harmonic vibrational wave numbers, NBO analysis and Mulliken population analysis on atomic charges in the ground state. Optimized geometries of the molecule have been described and collate with the experimental values. The experimental atomic charges demonstrates adequate concurrence with the theoretical prediction from DFT. The theoretical spectra values have been interpreted and compared with the FT-IR spectra. The calculated highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) energy gaps also confirm that charge transfer takes place within the molecule.

KEYWORDS

Indolyl isoxazole, Density functional theory, Mulliken.

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INTRODUCTION

The aromatic heterocyclic compounds are of a great chemical interest because they are present in the skeleton of biomolecules and macromolecules. They have been widely studied in chemistry from different points of view. These molecules currently present complex spectra due to large size [1]. The indole ring is found in many natural products such as the indole alkaloids, fungal metabolites and marine natural products. Syntheses and applications of indole based compounds have steadily increased in the last decades [2,3]. The computational quantum chemistry has become a powerful tool for the organic chemical community to analyze, elucidate their molecular structures and to carry out the assignment of the vibrational spectra. To gain further molecular information over many chemical processes, computational chemistry has emerged as an excellent tool. Indole and its derivatives have been the subject matter of different spectroscopic investigations due to their significance as drugs. Vibrational spectroscopy combined with quantum chemical computations have recently been considered as an effective tool in the vibrational analysis of indole molecules

[4]. In particular, the Kohn-Sham density functional theory (KS-DFT) has been a method of choice, mainly because it shows a good trade-off between accuracy and computational cost for treating large chemical systems [5]. The calculated value of HOMO-LUMO energy gap is used to interpret the biological activity of the molecule. Intramolecular hydrogen bonding interactions have received much attention from theoretical perspectives as they can determine the structures and activities of biological molecule. To our best of knowledge vibrational analysis and quantum chemical calculations of 5-(4-methoxyphenyl)-3-(1-methylindol-3yl)isoxazole has not been reported in literature. This scarcity seen in the literature inspired us to study this theoretical and experimental vibrational research cited on the structure of molecule to give an accurate assignment in experimental FT-IR spectrum [6,7].

As a result, the current consideration point to clarify the vibrational spectra of 5-(4-methoxyphenyl)-3-(1-methylindol-3yl)isoxazole molecule by applying the density functional theory (DFT) computations to acquire statistics about electronic effects and intramolecular charge transport accountable for biological activity.

EXPERIMENTAL

All the quantum chemical calculations have been carried out with Gaussian 09 program package [8] using DFT method, B3LYP functional and 6-31G (dip) basis set to predict the molecular structure, electronic transitions, electronic reactivity descriptors and first hyper polarizability. B3LYP invokes Becke's three parameter (local, non-local, Hartree-Fock) hybrid exchange functional (B3) [9], with Lee-Yang-Parr correlational functional (LYP) [10]. The basis set 6-31G with polarization functions on heavy atoms and polarization functions on hydrogen atoms are used for better representation of dipole moment of the molecule [11,12]. Time dependent density functional theory (TD).

Computational details

The DFT computation was carry out at the B3LYP/6-31G level of the theory to obtain optimized geometry and vibrations of normal modes of indolyl isoxazole using Gaussian 98 package [8]. The vibrational frequency assignments were made with a high degree of accuracy with the help of Chemcraft software program [13]. All the calculations were done for the optimized structures in gas phase GAUSSVIEW program [14]. DFT energy expression can be written as $E_{DFT}[\rho]-Ts[\rho] + E_{ne} + J[P] + E_{xc}[\rho]$ By equating E_{DFT} to the exact energy, this expression defines Exc, *i.e.* it is the part that remains after subtraction of the non-interacting kinetic energy and the E_{ne} and J potential energy terms. Molecular geometries were fully optimized by Berny's optimization algorithm using redundant internal coordinates. At the optimized form of the particle no imaginary frequency modes were acquired, providing that an accurate minimum on the potential energy surface was established. The optical geometry was resolved by reducing the energy relating to all geometrical parameters without striking molecular symmetry constraints. The scaling factor 0.903 was used to counteract the systematic error lead to neglecting anharmonicity and electron interaction. The TD-DFT method is based on the pragmatic observation that it is less computationally intensive than other methods with similar accuracy. The original theorem applied only to find out the ground-state electronic energy of a molecule using the TD-DFT method [15].

RESULTS AND DISCUSSION

Structure and geometrical properties: The optimized geometry parameters of at B3LYP level of computation are listed in Table-1. To understands the vibrational frequencies, it is important to study the compound geometry as structure based properties. The optimized geometrical parameters, the experimental and deliberated geometric values agree well with almost all values and structural behaviour of compound. The optimized structure of compound with numbering of the atoms are shown in Fig. 1. The molecule consists of three rings *viz.*, indole, isoxazole and phenyl rings.

Frontier molecular orbital studies: In 5-(4-methoxyphenyl)-3-(1-methylindol-3yl)isoxazole, HOMO is localized on indole ring, while LUMO orbitals of all compounds are localized on isoxazole. The HOMO and LUMO representations

TABLE-1
OPTIMIZED GOMETRICAL PARAMETERS OF 5-(4-METHOXYPHENYL)-3-(1-METHYLINDOL-3YL)ISOXAZOLE

Atom	Bond length (Å)	Atom	Bond angle (Å)	Atom	Dihedral angle (Å)
O_1N_2	1.4597	$N_2O_1C_3$	108.83	$O_1N_2C_4C_5$	0.6546
O_1C_3	1.3841	$O_1C_3C_4$	108.78	$N_2O_1C_3C_4$	0.3333
C_3C_4	1.3718	$C_3C_4H_{15}$	127.44	$O_1C_3C_4H_{15}$	177.64
C_4H_{15}	1.0758	$H_{15}C_4C_5$	126.46	$N_2C_5C_4H_{15}$	178.09
C_4C_5	1.4331	$C_4C_5N_2$	111.88	$N_2C_5C_6C_7$	21.169
C_5N_2	1.3407	$C_4C_5C_6$	128.25	$H_{15}C_4C_5C_6$	-0.3539
C_5C_6	1.4527	$C_5C_6C_7$	124.65	$C_{14}C_6C_7H_{16}$	179.59
C_6C_7	1.3831	$C_6C_7H_{16}$	128.57	$C_6C_7N_8H_{16}$	179.28
C_7H_{16}	1.0784	$H_{16}C_7N_8$	121.20	$H_{16}C_7N_8C_{31}$	0.0524
C_7N_8	1.3843	$C_7N_8C_{31}$	125.95	$C_7N_8C_{31}C_{13}$	179.37
N_8C_{31}	1.4566	$C_{31}H_{32}N_8$	110.92	$C_{31}H_{32}H_{33}H_{34}$	36.448
$C_{31}H_{32}$	1.0956	$C_{31}H_{32}H_{33}$	35.688	$C_{31}N_8C_{13}C_9$	179.29
$C_{31}H_{33}$	1.0957	$H_{32}H_{33}H_{34}$	59.926	$N_8C_{13}C_9H_{17}$	-0.5591
$C_{31}H_{34}$	1.0913	$C_{31}N_8C_{13}$	125.36	$H_{17}C_9C_{10}H_{18}$	-0.2799
N_8C_{13}	1.3941	$N_8C_{13}C_{14}$	107.76	$C_{13}C_9C_{10}C_{11}$	0.3990
$C_{13}C_9$	1.4001	$N_8C_{13}C_9$	129.74	$C_9C_{10}H_{18}C_{11}$	179.60
C_9H_{17}	1.0850	$C_{13}C_9H_{17}$	121.50	$C_{10}H_{18}C_{11}H_{19}$	0.4129
C_9C_{10}	1.3942	$C_{13}C_9C_{10}$	117.56	$C_{10}C_{11}C_{12}H_{19}$	179.64
$C_{10}H_{18}$	1.0851	$C_9C_{10}H_{18}$	119.52	$H_{19}C_{11}C_{12}H_{20}$	1.0895
$C_{10}C_{11}$	1.4120	$C_9C_{10}C_{11}$	120.98	$C_{11}C_{12}C_{14}H_{20}$	178.84
$C_{11}H_{19}$	1.0853	$H_{18}C_{10}C_{11}$	119.48	$C_3H_{21}C_{22}H_{27}$	-0.0211
$C_{11}C_{12}$	1.3939	$C_{10}C_{11}H_{19}$	119.24	$C_{21}C_{22}H_{27}C_{23}$	-179.97
$C_{12}H_{20}$	1.0841	$C_{19}C_{11}C_{12}$	119.52	$H_{27}C_{22}C_{23}H_{28}$	0.0105
$C_{12}C_{14}$	1.4073	$C_{11}C_{12}H_{20}$	119.97	$C_{22}C_{23}H_{28}C_{24}$	179.99
$C_{14}C_6$	1.4507	$H_{20}C_{12}C_{14}$	120.83	$H_{28}C_{23}C_{24}O_{35}$	-0.0169
C_3C_{21}	1.4556	$C_{12}C_{14}C_6$	134.78	$C_{23}C_{24}O_{35}C_{36}$	-0.0762
$C_{21}C_{22}$	1.4060	$C_3C_{21}C_{22}$	120.73	$C_{24}O_{35}C_{36}H_{37}$	-0.1975
$C_{22}H_{27}$	1.0835	$C_{21}C_{22}H_{27}$	119.12	$C_{36}H_{37}H_{38}H_{39}$	34.932
$C_{22}C_{23}$	1.3967	$H_{27}C_{22}C_{23}$	119.88	$C_{23}C_{24}C_{25}H_{29}$	179.99
$C_{23}H_{28}$	1.0827	$C_{22}C_{23}C_{24}$	119.61	$C_{24}C_{25}C_{26}H_{29}$	179.97
$C_{23}C_{24}$	1.4015	$H_{28}C23C_{24}$	121.11	$C_{25}C_{26}H_{29}H_{30}$	-0.0354
$C_{24}C_{25}$	1.4051	$C_{23}C_{24}O_{35}$	27.61	$C_{24}C_{25}C_{26}C_{21}$	-0.0238
$C_{25}H_{29}$	1.0834	$C_{24}O_{35}C_{36}$	118.95	$C_{25}C_{26}C_{21}H_{30}$	179.96
$C_{25}C_{26}$	1.3882	$O_{35}C_{36}H_{37}$	105.11	$H_{30}C_{26}C_{21}C_3$	0.0588

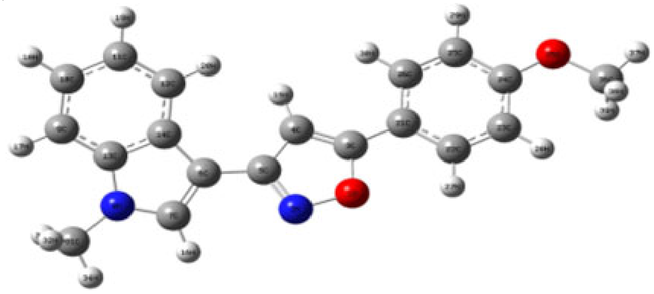


Fig. 1. Optimized structure of 5-(4-methoxyphenyl)-3-(1-methylindol-3yl)isoxazole

of 5-(4-methoxyphenyl)-3-(1-methylindol-3yl)isoxazole are shown in Fig. 2. The HOMO–LUMO energy gap, electron affinity, ionization potential and electronegatvity of 5-(4-methoxyphenyl)-3-(1-methylindol-3yl)isoxazole calculated at B3LYP/6-31G level are shown in Table-2. According to Koopmans' theorem [16], the frontier molecular orbital energies are given by

$$-\varepsilon_{HOMO} = I \text{ and } -\varepsilon_{LUMO} = A \qquad (1)$$

where, I = ionization potential and A = electron affinity. The eqn. 1 states that, HOMO energy is the ionization potential and LUMO energy is the electron affinity. Literature survey reveals that, the absolute electro negativity (χ), absolute hardness (η) and softness (S) of a compound can be calculated using the HOMO and LUMO energies. The operational definitions for the electronic parameters are given in Table-2.

TABLE-2
ENERGIES OF HOMO-LUMO OF 5-(4-METHOXYPHENYL)-3-(1-METHYLINDOL-3YL)ISOXAZOLE

Parameters (a.u)	B3LYP/6-31G
HOMO	-0.2357
LUMO	0.0045
HOMO-LUMO	0.2312
I	0.2357
A	-0.0045
X	0.2357
H	0.1156
S	4.3252

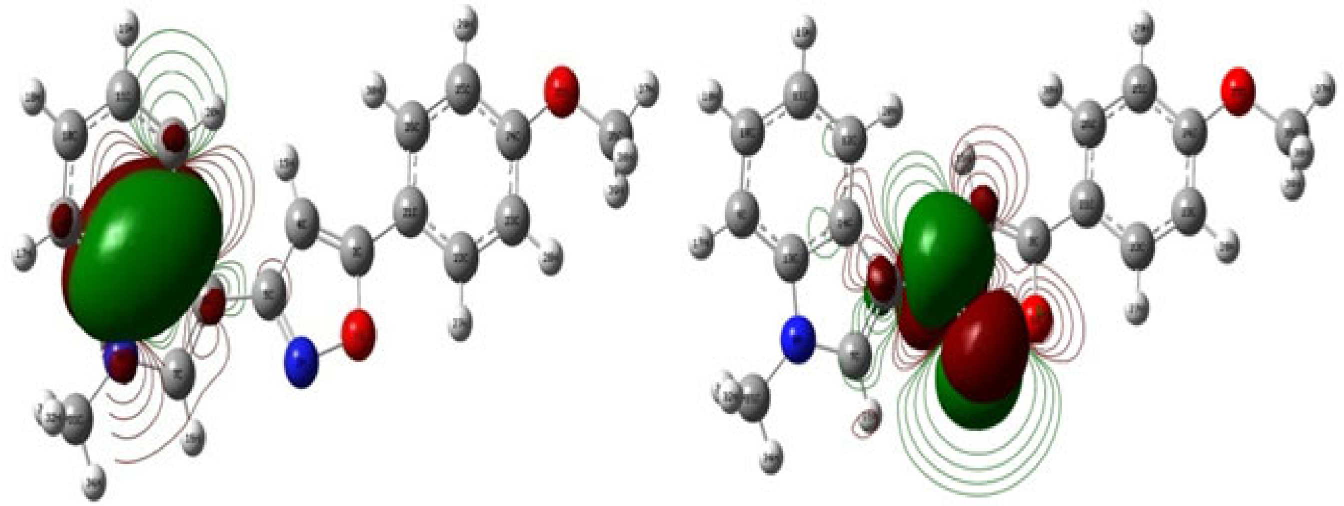
$$\chi = (I+A)/2,\ \eta = (I-A)/2 \text{ and } S = 1/2\eta \qquad (2)$$

Using the eqn. 2 we have calculated the electro negativity, hardness and softness. The obtained parameters listed in Table-2.

In case of present compound, HOMO = -0.2357, LUMO = -0.0045, energy gap = HOMO-LUMO = 0.2312, I = ionization potential = 0.2357; A = electron affinity = -0.0045; χ = electronegativity = 0.2357; η = hardness = 0.1156; S = softness = 4.3252. For proper understanding of various features of pharmacological sciences inclusive of drug design and the feasible eco-toxicological factors of the drug molecules, some novel chemical reactivity descriptors have been suggested. DFT depended descriptors have make possible in different ways to know the structure of molecules and by calculating the chemical effects to determines their reactivity, electrophilicity and global hardness.

Mulliken population analysis: Mulliken atomic charge calculation has an important role in the application of quantum chemical determination to molecular system as a result of atomic charges effect dipole moment of molecule, molecular polarizability, electronic structure of the compound and a lot of properties of molecular systems. The bonding capability of a molecule depends on the electronic charge on the chelating atoms. The atomic charge values have been obtained by Mulliken population analysis. To validate the reliability of present results, the Mulliken population analysis of 5-(4-methoxyphenyl)-3-(1-methylindol-3yl)isoxazole has been calculated using B3LYP/3-21G basis set. The bonding capability and molecular conformation was determined by electronic charge on an atom [17]. From the Mulliken population analysis atomic charge values were obtained (Fig. 3). The Mulliken atomic charges of component atoms of 5-(4-methoxyphenyl)-3-(1-methylindol-3yl)-isoxazole are presented in Table-3. The Mulliken atom charge of all hydrogen atoms are positive, oxygen and nitrogen atoms possess negative charge.

Vibrational assignments: The spectral data of 5-(4-methoxyphenyl)-3-(1-methylindol-3yl)isoxazole obtained experimentally by means of IR spectra and predicted theoretically by means of density functional theory (DFT) B3LYP/631G method. 5-(4-methoxyphenyl)-3-(1-methylindol-3yl)-



E = -0.2357 a.u. (HOMO)

E = -0.0045 a.u. (LUMO)

Fig. 2. HOMO and LUMO of 5-(4-methoxyphenyl)-3-(1-methylindol-3-yl)isoxazole

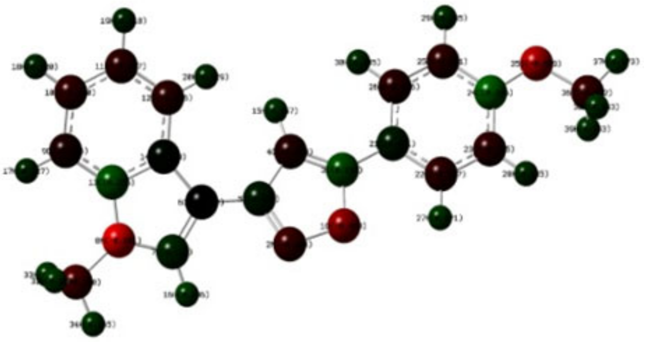


Fig. 3. Mulliken charge distribution of 5-(4-methoxyphenyl)-3-(1-methylindol-3yl)isoxazole

TABLE-3
MULLIKEN CHARGE DISTRIBUTION OF 5-(4-METHOXYPHENYL)-3-(1-METHYLINDOL-3YL)ISOXAZOLE

Atom	Mulliken atomic charges	Atom	Mulliken atomic charges	Atom	Mulliken atomic charges
O1	-0.458	C14	0.019	H27	0.171
N2	-0.188	H15	0.157	H28	0.135
C3	0.233	H16	0.186	H29	0.145
C4	-0.108	H17	0.127	H30	0.135
C5	0.078	H18	0.120	C31	-0.240
C6	-0.002	H19	0.118	H32	0.169
C7	0.119	H20	0.129	H33	0.164
N8	-0.691	C21	0.081	H34	0.165
C9	-0.086	C22	-0.147	O35	-0.559
C10	-0.150	C23	-0.145	C36	-0.172
C11	-0.137	C24	0.296	H37	0.173
C12	-0.136	C25	-0.141	H38	0.153
C13	0.256	C26	-0.126	H39	0.153

TABLE-4
VIBRATIONAL ASSIGNMENTS OF 5-(4-METHOXYPHENYL)-3-(1-METHYLINDOL-3YL)ISOXAZOLE

Mode	Calculated IR frequency (cm^{-1}) scaled	Intensity	Assignment	Type
111	3324	99	C_4-H_{15}	C-H Stretching
110	3304	99	C_7H_{16}	C-H Stretching
105	3219	98	C_9H_{17}	C-H Stretching
101	3184	90	$C_{36}H_{37}$	C-H Stretching
100	3164	86	$C_{31}H_{34}$	C-H Stretching
99	3110	100	$C_{36}H_{38}$	C-H Stretching
96	3067	86	$C_{36}H_{39}$	C-H Stretching
94	1673	42	C_3C_{21}	C-C Stretching
93	1642	59	C_3C_4	C-C Stretching
89	1565	17	$H_{27}C_{22}C_{23}$	H-C-C Bending
85	1531	16	$H_{20}C_{12}C_{14}$	H-C-C Bending
82	1503	12	$H_{37}C_{36}H_{38}$	H-C-H Bending
79	1477	18	$H_{27}C_{22}C_{23}$	H-C-C Bending
78	1446	10	C_4C_5	C-C Stretching
75	1385	52	C_9C_{10}	C-C Stretching
67	1228	58	$H_{28}C_{23}C_{24}$	HCC Bending
63	1177	10	N_8C_{31}	N-C Stretching
49	962	36	$C_3C_4C_5$	C-C-C Bending
40	807	10	$C_4C_3O_1$	C-C-O Bending
32	667	64	$C_{22}C_{23}C_{24}$	C-C-C Bending
29	613	17	$C_9C_{10}C_{11}$	C-C-C Bending

isoxazole consists of 39 atoms and hence 39 normal modes of vibrations were possible. For obtaining theoretical vibrational frequencies scaling factor of 0.903 is used. The deliberated vibrational frequencies are numbered from highest fundamental wave number to the lower [18]. The calculated wave numbers, intensity of vibrations and the corresponding vibrational assignments for fundamental modes of vibrations of title compound are shown in Table-4. Aromatic structure commonly shows the spectral region 3100-3000 cm^{-1} due to aromatic C-H stretching vibrations. The C-H stretching vibrations were observed at 3334-3067 cm^{-1} in the calculated data and 3068 cm^{-1} experimentally. The C–N stretching modes are observed at 1522 cm^{-1} experimentally and theoretically observed at 1177 cm^{-1}. The H–C–C in-plane bending vibration is observed as weak band at 1565, 1531 and 1228 cm^{-1}. The C–C–C in-plane bending vibration couples with mode 49, 32 and 29 and vibration showed bands in the range of 962, 667 and 613. The C–C-O bending vibrations (mode 40) are identified at 807 cm^{-1}.

Conclusion

The geometry optimization has been carried out using DFT level. The calculated values of DFT level, the vibrational wave numbers were in agreement with the experimental results. The simultaneous activation 5-(4-methoxyphenyl)-3-(1-methylindol-3yl)isoxazole was studied using FT-IR spectra, evidence for charge transfer interaction between the donor and the acceptor group through the system. This is responsible for the bioactivity of the molecule. The lowering of HOMO-LUMO band gap has higher biological activities of the molecule. The feasibilities of hydrogen bonding were explained by Mulliken charge analysis.

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