A Theoretical Investigation of Molecular Structure, HOMO-LUMO, Spectroscopic Properties (IR and UV/Visible), First Order Hyperpolarizability, NBO Analysis and Fukui Function Analysis of Series of Benzo[d]isoxazole Isomers: A HF, DFT and TD-DFT Study

By

Ashutosh Kumar, Anjali Pandey and Anil Mishra
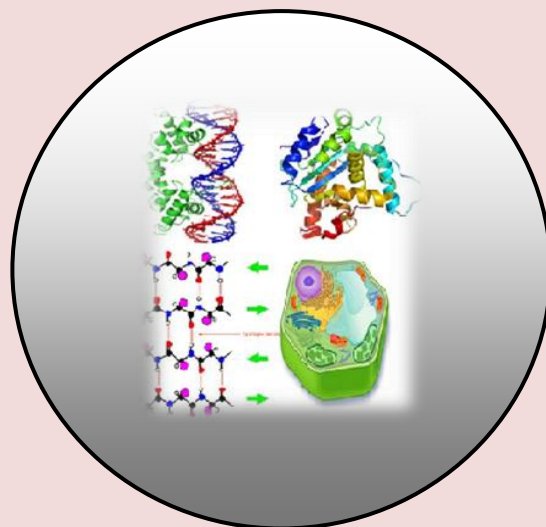
Journal of Biological and Chemical Research

An International Peer Reviewed / Referred Journal of Life Sciences and Chemistry

Indexed, Abstracted and Cited in various International and National Scientific Databases

Ashutosh Kumar
http:// www.sasjournals.com
htfp:// www.jbcr.co.in
jbiolchemres@gmail.com

RESEARCH PAPER

A Theoretical Investigation of Molecular Structure, HOMO-LUMO, Spectroscopic Properties (IR and UV/Visible), First Order Hyperpolarizability, NBO Analysis and Fukui Function Analysis of Series of Benzo[d]isoxazole Isomers: A HF, DFT and TD-DFT Study

Ashutosh Kumar, Anjali Pandey and Anil Mishra

Department of Chemistry, Faculty of Science, Central Facility for Computational Research (CFCR) (Computer Cluster), University of Lucknow, Lucknow- 226007, India
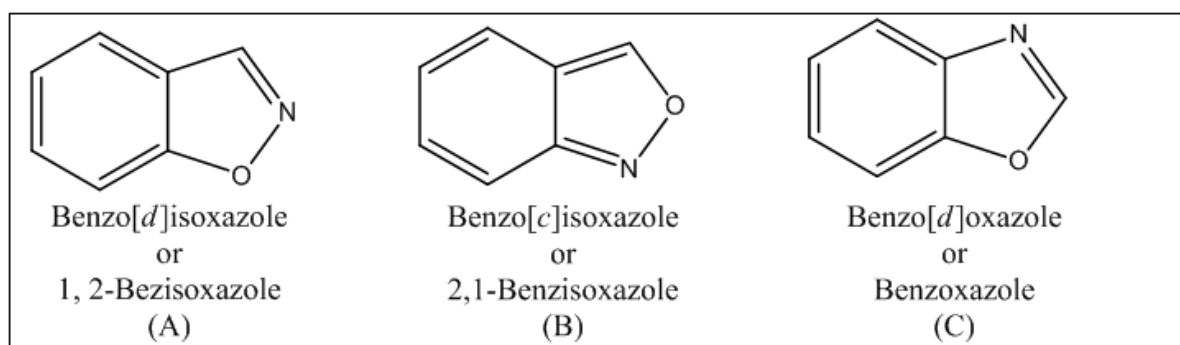
ABSTRACT
In this work, the molecular structure optimization, electronic properties like global chemical reactivity descriptors and local chemical reactivity descriptors (fukui function analysis for reactive site prediction of isomers), nonlinear optical property analysis, spectroscopic study (IR) and absorption spectrum analysis (UV/Visible) of benzo[d]isoxazole derivatives were theoretically computed in gas phase (SCF theory) and different solvents. Also, the solvent effect on geometry, electronic structure, frontier molecular orbital energies, UV-Visible absorption study (in vacuum, water, ethanol, DMSO, THF and aniline solvent (SCRF theory)) and vibrational frequencies (IR spectroscopic analysis in gas phase and water solvent) of benzo[d]isoxazole derivatives has been carried out based on IEF-PCM model. The results of benzo[d]isoxazole derivatives indicate that the polarity of solvents has played a significant role on the structures and properties. The reactive site prediction and hydrogen bond interaction analysis were determined by using fukui function analysis and natural bond orbital (NBO) method. The nonlinear optical property (NLO) related to polarizability (a), anisotropic polarizability (Δa) and dipole moment (μ) and first-order hyperpolarizability (β_{tot}) based on the finite field approach is also discussed. In this study, the HF/6-31+G (d, p), DFT/B3LYP/6-31+G (d, p) and TD-DFT/B3LYP/6-31+G (d, p) methods were used. Reasonable agreement has been found between the theoretically calculated data in gas phase and solvent phase.
Key words: Benzo[d]isoxazole isomers, FMO energies, Spectroscopic properties, Fukui function and NLO properties analysis.

INTRODUCTION
Benzofused five-membered heterocycles is essential to biology, medicine, different area of pharmaceutical research and useful reactants in the organic synthesis. It is not say that we are living in the age of heterocyclic chemistry. Benzofused isoxazoles/oxazole containing carbon, nitrogen and oxygen atoms with molecular formula C_7H_5NO. The chemical structures (isomeric form) of benzo-fused isoxazoles/oxazole are shown in scheme-1.

| Benzo[d]isoxazole or 1, 2-Bezisoxazole (A) | Benzo[c]isoxazole or 2,1-Benzisoxazole (B) | Benzo[d]oxazole or Benzoxazole (C) |

Scheme 1. The chemical structures of isomers (A to C) consider for this study.

The functionalized benzo [d] isoxazole have variety of uses, including pharmaceutical drugs such as some antipsychotics (including risperidone, paliperidone, ocaperidone and iloperidone) (Jain, et.al. 1988) and the anticonvulsant zonisamide. The substituted benzoxazole (benzo[d]oxazole) is found within the chemical structures of pharmaceutical drugs such as flunoxaprofen. Benzoxazole derivatives are also of interest for optical brighteners in laundry detergents (Smulders, et. al. 2012). Benzoxazoles belongs to the group of well known antitumoral, antioxidant, antiparasitic and antiallergic activity (Şener, et. al. 1991). Benzofused isoxazole and oxazole are another class of compounds well known to posses various kinds of biological activities. They have been used as a starting material for various chemical reactions for the preparation of heterocycles displaying useful activities. The vast range of pharmacological applications of these classes of compounds encouraged us for theoretical study of nucleophilic and electrophilic sites of the compounds which is almost a new topic for work to researchers for these isomers. At the present time, the computer simulation is one of the main tools to identify the regularities of behavior of the molecular system under various external influences (Glukhova, et. al. 2014). Molecular modeling is the computer simulation of molecular structures, which concerns the bond distance and bond angles in chemical compounds, also the results of insertion and substitutions of atoms or groups of atoms in the molecules or compounds. Molecular modeling is the sum of theoretical methods and computational techniques that used to predict or identify molecular behaviors specifically interactions between molecules (V. Jahed, et. al. 2014). Molecular modeling has been introduced as a valuable methodology for scientific research providing useful tools for the analysis and estimate of the physicochemical parameter and /or biological activity (Ho ltje, et. al. 1996). Theoretical studies on biologically active compounds are of interest in order to gain a deeper insight on their action and thus helping in the design of novel compounds with therapeutic effects. The knowledge of physico-chemical properties and sites of reaction of investigated isomeric compounds will provide a deeper insight of its probable action. Particularly, Mulliken atomic charges and NBO charges is related to the electronic density and is a very useful descriptor in understanding sites for electrophilic attack and nucleophilic reactions as well as hydrogen bonding interactions. In this paper, aim to study their properties and predict their applications, we give a complete description of molecular geometry, natural bond orbital (NBO), solvent effect on spectroscopic properties (IR and UV-Visible), nonlinear optical (NLO) properties, first static hyperpolorizability, local chemical reactivity indices such as local softness, Fukui function analysis and global chemical reactivity such as HOMO-LUMO energy gap (ΔE), ionization potential (I), electron affinity (A), chemical hardness (η), chemical potential (μ), electronegativity (χ) dipole moment (μ), chemical softness (S), electrophilicity index (ω), ΔN_{max} (is the maximum number of electron that an electrophile can acquire) of a series of benzo[d]isoxazole, benzo[c]isoxazole and benzo[d]oxazole.

MATERIAL AND METHODS
Benzo [d] isoxazole derivatives (isomers) was chosen as a model compound to study of the molecular structure, reactivity, NBO, solvent effect on (UV-Visible) and spectral property (IR), fukui function analysis for electrophilic and nucleophilic site prediction and NLO property calculations.

In the present study Hartree- Fock method (HF) and density functional theory (DFT) with B3LYP (Becke three parameter Lee-Yang-Parr) correlation functional (A.D. Becke, 1993) level of theory were performed on personal computer Intel (R) core (TM) i3-2370M CPU @ 2.40GHz using Gaussian 09W (Frisch, et al. 2009) program package developed by Frisch and coworkers. All the structures were fully optimized at DFT/B3LYP/6-31+G (d, p) and HF/6-31+G (d, p) level in gas phase employing the self-consistent field (SCF) theory and water solvent (SCRF theory) using IEF-PCM model. The optimized structures were subjected by vibrational analysis using DFT/B3LYP/6-31+G (d, p) level in gas phase and water solvent. All the global reactivity parameter calculations were performed using HF/6-31+G (d, p) and DFT/B3LYP/6-31+G (d, p) level in gas phase and water solvent and NBO study, local reactivity parameter were calculated by using DFT/B3LYP/6-31+G (d, p) level in water solvent. The oscillator strengths excited state energies and wavelength were investigated using TD-DFT/B3LYP/6-31+G (d, p) level in gas phase and using various solvents such as water, ethanol, DMSO, THF and aniline. The non linear optical (NLO) property calculations were using DFT/B3LYP/6-31+G (d, p) method in water solvent. In this work, the integral equation formalism polarizable continuum model (IEF-PCM) (M. Cossi, et. al. 2001, C. Adamo, et. al. 2001) was used for the solvent polarity which affects the chemical properties and geometry of chemical compounds. Gaussian output files were visualized by means of GAUSSIAN VIEW 05 software. All the structure of isomers was designed by Chem Draw Ultra 12.0 program (Cousins, 2011).

RESULTS AND DISCUSSION
Molecular Geometry
DFT studies have been performed to compare the geometric parameter with those obtained from Hartree- Fock method (HF/6-31+G (d, p) in gas phase and water solvent (ε=78.39 at 298.15 K)) using IEF-PCM model. The geometric parameters of title compounds (isomers) A-C were optimized using Gaussian 09 program at DFT/B3LYP/6-31+G (d, p) level in gas phase and water solvent. Here we explained that solvent polarity strongly effects that an isotropic splitting constant (α_{iso}) of all isomers. In this paper, the molecular geometries values in gas phase are correlate with water solvent value of all isomers. Optimized geometries are shown in Figure-1 and comparison of simulated selected bond lengths, bond angles and dihedral angles of compounds A-C along with HF level values are listed in Tables 1-3, respectively (Kumar, et. al. 2019).
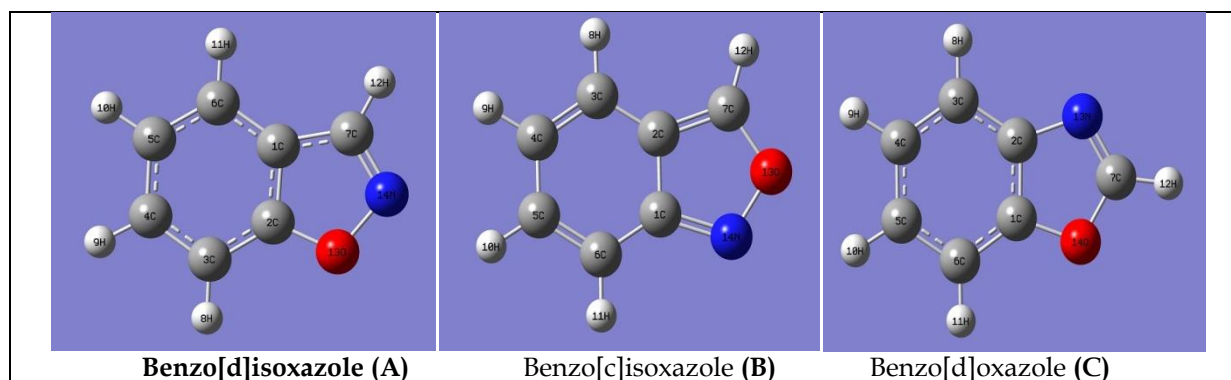
Figure 1. Optimized geometries of benzo[d]isoxazole isomers (**A to C**).

The results listed in tables-(1-3) show that comparative analysis of simulated bond length, bond angles and dihedral angles of all atoms in isomer A to C correlated nicely. Deviation in the bond lengths, bond angles and dihedral angles of isomer A was observed in range of 0.000-0.007 Å, 0.4-1.10° and 0.002-0.012° in HF method and 0.000-0.007Å, 0.04-0.38° and 0.01-0.0197° in DFT method respectively. Deviation in bond length was 0.007Å for O13-N14 in both methods, deviation in bond angle was 1.10° for C1-C2-C3 in HF method and 0.38° for C2-C1-C7 in DFT method and deviation in dihedral angle was 0.012° for C1-C7-N14-O13 in HF method and 0.0197 for C1-C2-O13-N14 in DFT method.

For isomer B deviations in selected bond lengths/ angles/dihedral angles was found in range 0-0.01Å/0.6-0.3-0.16°/0.01-0.093° in HF method and 0-0.02Å/0.02-0.34°/0-0.007° in DFT method. Similarly the deviation in bond lengths/angles/dihedral angles of isomer C was observed in the range 0-0.1Å/0.3-0.17°/0.0017-0.0047° in HF method and 0-0.003Å/0.02-0.69°/0-0.0005° in DFT method. Here negative torsion angle requires rotation in the opposite sense.

Table 1. Selected molecular parameters of isomer-A.

Bond Length	Benzo [d] isoxazole (A)			
	RHF/6-31+G(d, p)		RB3LYP/6-31+G(d, p)	
	Gas	Water	Gas	Water
	(Å)	(Å)	(Å)	(Å)
(C_1-C_2)	1.378	1.378	1.401	1.401
(C_1-C_6)	1.397	1.398	1.405	1.406
(C_2-C_3)	1.391	1.391	1.396	1.396
(C_2-O_{13})	1.333	1.337	1.356	1.360
(C_3-C_4)	1.377	1.378	1.392	1.393
(C_4-C_5)	1.408	1.409	1.413	1.414
(C_7-N_{14})	1.275	1.276	1.305	1.306
$(O_{13}-N_{14})$	1.371	1.378	1.412	1.419
(C_5-C_6)	1.375	1.376	1.390	1.390
Bond Angle	(°)	(°)	(°)	(°)
C2-C1-C6	120.48	120.61	119.97	120.07
C2-C1-C7	102.16	102.52	102.79	103.17
C1-C2-C3	122.98	123.08	123.20	123.24
C1-C2-O13	109.82	109.72	109.86	109.71
C1-C7-N14	111.28	111.24	112.23	112.13
H12-C7-N14	119.39	119.71	118.59	118.93
C2-O13-N14	108.83	108.64	108.29	108.14
C7-N14-O13	107.89	107.86	106.80	106.83
C1-C7-H12	129.32	129.04	129.17	128.92
Dihedral Angle	(°)	(°)	(°)	(°)
C6-C1-C2-C3	0.0067	0.0077	0.002	-0.0013
C6-C1-C2-O13	-180.00	-180.00	-180.00	-180.00
C7-C1-C2-C3	180.02	180.02	179.98	179.99
C7-C1-C2-O13	0.0086	0.0088	-0.025	-0.0111
C2-C1-C7-N14	-0.0103	-0.0112	0.0255	0.0226
C1-C2-C3-C4	-0.0232	-0.0226	0.0174	-0.0027
C1-C2-O13-N14	-0.0045	-0.0041	0.0171	-0.0026
C3-C2-O13-N14	179.98	179.98	-179.98	-180.00
C1-C7-N14-O13	0.0079	0.0091	-0.0159	-0.0245

Comparative analyses of geometric data of isomers A to C also indicate that the intermolecular hydrogen bonding affect the geometric parameters, particularly the O and N atoms of isomers A-C. From the geometric data of compounds A-C, it is clear that all the compounds act as good ligands for biologically active benzofused isoxazole/oxazole derivatives act as good drugs for human beings.

Frontier Molecular Orbital Analysis (FMO) and UV-Vis. Absorption Studies
The frontier molecular orbital determine the way in which the molecule interacts with other species. HOMO (highest occupied molecular orbital), which can be thought the outermost orbital containing electrons, tends to give these electrons such as an electron donor. On the other hand, LUMO (lowest unoccupied molecular orbital) can be thought the innermost orbital containing free places to accept electrons (Gece, 2008).

Table 2. Selected molecular parameters of isomer-B.

Benzo [c] isoxazole (B)				
Bond Length	RHF/6-31+G(d, p)		RB3LYP/6-31+G(d, p)	
	Gas	Water	Gas	Water
	(Å)	(Å)	(Å)	(Å)
(C_1-C_2)	1.43	1.42	1.44	1.442
(C_1-C_6)	1.44	1.44	1.42	1.429
(C_2-C_3)	1.43	1.43	1.42	1.427
(C1-N14)	1.29	1.29	1.32	1.331
(C2-C7)	1.35	1.35	1.37	1.376
(C7-O13)	1.31	1.31	1.33	1.339
(O13-N14)	1.36	1.37	1.39	1.404
(C7-H12)	1.06	1.06	1.08	1.080
(C4-C5)	1.45	1.45	1.43	1.439
Bond Angle	(°)	(°)	(°)	(°)
C2-C1-C6	120.17	120.11	120.37	120.33
C2-C1-N14	111.80	111.73	112.09	111.93
C6-C1-N14	128.02	128.14	127.52	127.72
C1-C2-C3	120.60	120.85	120.49	120.68
C1-C2-C7	102.31	102.65	102.95	103.29
C2-C7-O13	109.80	109.74	109.64	109.62
C7-O13-N14	110.93	110.87	110.87	110.74
C1-N14-O13	105.14	104.98	104.42	104.39
H12-C7-O13	116.59	116.86	116.05	116.25
Dihedral Angle	(°)	(°)	(°)	(°)
C6-C1-C2-C3	-0.002	0.0018	-0.0005	-0.0004
C6-C1-C2-C7	-180.0	180.00	-180.00	-180.00
C7-C2-C3-C4	180.0	-180.0	180.02	180.00
N14-C1-C6-C5	180.0	179.99	-179.99	-179.99
N14-C1-C6-H11	0.004	-0.0051	0.0015	0.0013
C7-C2-C3-H8	0.006	-0.0032	0.001	0.0008
C2-C7-O13-N14	0.095	0.0025	-0.0023	-0.0019
H12-C7-O13-N14	180.03	179.99	-180.00	-180.00
C7-O13-N14-C1	-0.101	0.0051	0.0	0.0

Therefore, while the energy of the HOMO is directly related to the ionization potential, LUMO energy is directly related to the electron affinity. Energy difference between HOMO and LUMO orbital is called energy gap (ΔE_{gap}) that is an important stability for structures (Lewis, et. al. 1994), in this case, the order of stability of the title compounds is C > A > B. HOMO-LUMO helps to characterize the chemical reactivity and kinetic stability of the chemical compounds (Uesugi, et. al. 1997). A molecule with small gap is more polarized and is known as soft molecule. Recently, the energy gap between HOMO and LUMO has been used to prove the bioactivity from intramolecular charge transfer (ICT) (Padmaja, et. al. 2009, Sudha, et. al. 2011) because it is a measure of electron conductivity. The frontier molecular orbital's HOMO and LUMO energies of compounds A-C, with B3LYP/6-31+G (d, p) method in gas phase and water solvent using IEF-PCM model is plotted in Figure 2 and given in Table-5.

The theoretical absorption studies were also carried out by using TD-DFT method at B3LYP/6-31+G (d, p) level of theory in gas phase, and integral equation formalism polarizable continuum model (IEF-PCM) was applied to account for solvent effect (for simulated UV-VIS spectra see figure-3-5). A comparison of characteristic theoretical UV-Vis. absorption wavelength (λ_{max}) of compounds A-C is given in table-4.

Table 3. Selected molecular parameters of isomer-C.

Benzo [d] oxazole (C)				
Bond Length	RHF/6-31+G(d, p)		RB3LYP/6-31+G(d, p)	
	Gas	Water	Gas	Water
	(Å)	(Å)	(Å)	(Å)
C1-C2	1.38	1.381	1.401	1.400
C1-C6	1.37	1.379	1.388	1.388
C2-C3	1.38	1.388	1.398	1.398
C1-O14	1.35	1.359	1.376	1.378
C2-N13	1.39	1.397	1.400	1.402
C7-O14	1.34	1.339	1.371	1.368
C7-N13	1.26	1.268	1.290	1.293
C7-H12	1.06	1.069	1.080	1.080
C4-C5	1.40	1.400	1.409	1.410
Bond Angle	(°)	(°)	(°)	(°)
C2-C1-C6	123.82	123.91	123.94	124.03
C2-C1-O14	107.21	107.14	107.41	107.35
C6-C1-O14	128.96	128.93	128.63	128.61
C1-C2-N13	108.10	107.99	108.64	108.50
C3-C2-N13	131.59	131.69	131.35	131.47
H12-C7-N13	127.26	127.39	127.89	128.00
H12-C7-O14	116.25	116.42	115.81	116.00
N13-C7-O14	116.48	116.17	116.29	115.98
C2-N13-C7	103.93	104.11	103.95	104.15
C1-O14-C7	104.26	104.57	103.68	104.00
Dihedral Angle	(°)	(°)	(°)	(°)
O14-C1-C2-N13	0.0084	0.0067	0.0032	0.0026
O14-C1-C6-H11	-0.0029	-0.0025	-0.0012	-0.0009
C2-C1-O14-C7	-0.0029	-0.0038	-0.0008	0.0001
C1-C2-C3-C4	-0.0005	-0.0004	-0.0001	-0.0001
C6-C1-O14-C7	-179.999	179.999	180.00	180.00
O14-C7-N13-C2	0.0096	0.0049	0.0041	0.0046
H12-C7-O14-C1	179.999	-180.001	-179.99	-179.99
N13-C7-O14-C1	-0.0045	-0.0008	-0.0022	-0.0031

The theoretical UV-Vis. spectrum of an isomer A showed increasing order of an absorption maximum at 306.39 nm > 295.39 nm > 248.30 nm > 248.15 nm > 248.03 nm > 247.86 nm, in water, gas phase, DMSO, ethanol, aniline and THF solvent, respectively. An isomer B showed increasing order of absorption maximum at 308.43 nm > 307.74 nm > 307.40 nm > 307.32 nm > 307.21 nm > 303.99 nm, in aniline, DMSO, THF, ethanol, water and gas phase, respectively. An isomer C showed increasing order of absorption maximum at 272.34 nm > 257.61 nm > 257.38 nm > 257.27 nm > 255.24 nm > 254.78 nm in gas, aniline, DMSO, ethanol, THF and water, respectively. The overall theoretical absorption maxima's order of compounds is B > A > C. The observed absorption maxima of compounds A to C can also be correlated with the HOMO-LUMO band gap. An isomer C and A have highest band gaps (Table-5) and this consistent with the UV results that these compounds have the highest energy of absorption (shorter absorption maximum). The band gap in isomer C is 5.66826 eV in gas phase and 5.68132 eV in water solvent is highest which corresponds to 272.34 nm in gas phase. Therefore, it can be concluded that the $\pi \rightarrow \pi^*$ transition in these compounds is a HOMO-LUMO transitions. It also interesting to note that isomers having intra-molecular hydrogen bonding (A-C) have the low molar absorptivity. In this paper, we are showing simulated UV-Visible spectrum of isomers-A to C shown in figure-3 to 5.
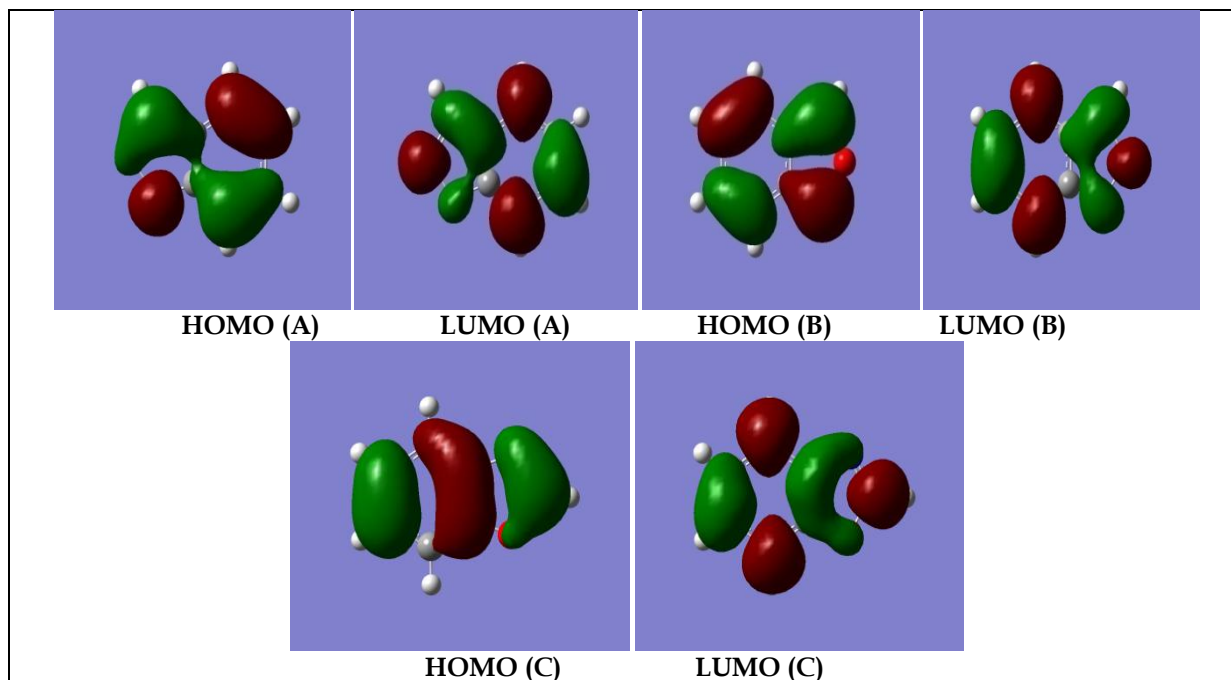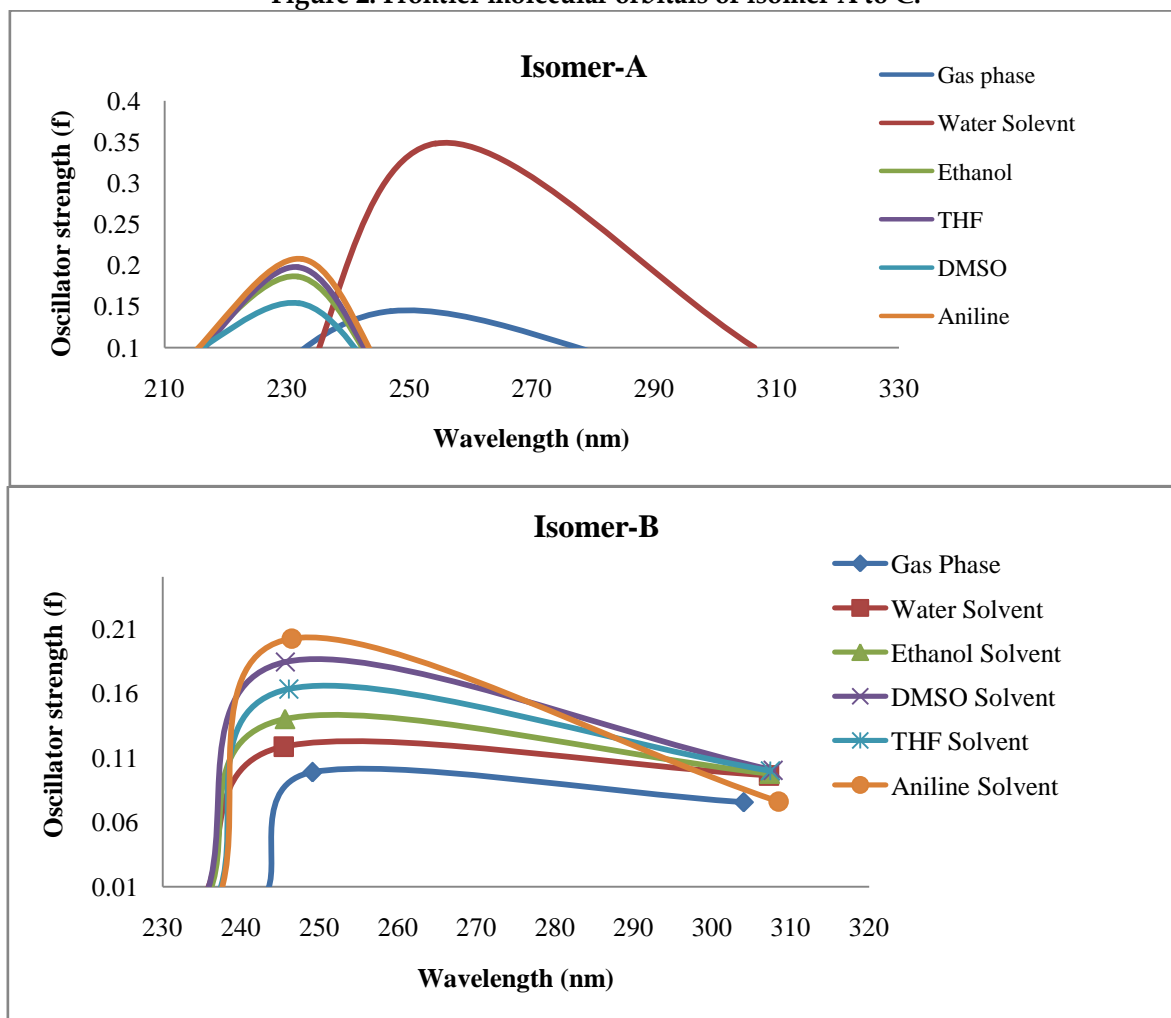
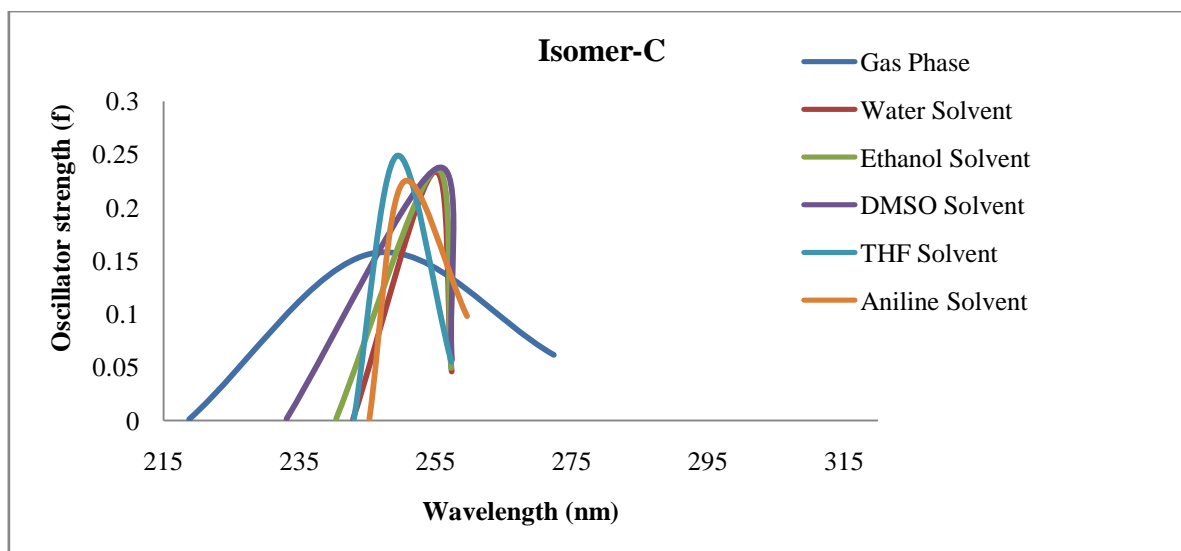Figure 2. Frontier molecular orbitals of isomer A to C.

Figure 3, 4 and 5. Simulated UV/Visible spectrum of isomer-A, B and C.

Table 4. Results of the absorption wavelength (λ$_{max}$), excitation energy and oscillator strength obtained by TD-DFT/B3LYP/6-31+G (d, p) for isomers A to C in different solvents.

Isomers/ solvent	Singlet Excited state	Excitation energy (eV)	Oscillator strength (f)	Calculated λ$_{max}$ (nm)
A/Gas	S$_1$	4.1973	0.0615	295.39
A/Water	S$_1$	4.0466	0.1309	306.39
A/Ethanol	S$_1$	4.9963	0.0314	248.15
A/DMSO	S$_1$	4.9932	0.0326	248.30
A/THF	S$_1$	5.0023	0.0328	247.86
A/Aniline	S$_1$	4.9988	0.0370	248.03
B/Gas	S$_1$	4.0786	0.0756	303.99
B/Water	S$_1$	4.0358	0.0962	307.21
B/Ethanol	S$_1$	4.0343	0.0976	307.32
B/DMSO	S$_1$	4.0288	0.1002	307.74
B/THF	S$_1$	4.0334	0.0998	307.40
B/Aniline	S$_1$	4.0198	0.1076	308.43
C/Gas	S$_1$	5.0425	0.1573	272.34
C/Water	S$_1$	4.8198	0.2337	254.78
C/Ethanol	S$_1$	4.8192	0.0493	257.27
C/DMSO	S$_1$	4.8172	0.0573	257.38
C/THF	S$_1$	4.8575	0.2385	255.24
C/Aniline	S$_1$	4.8129	0.0982	257.61

Global Reactivity Descriptors

The frontier molecular orbital's (HOMO and LUMO) of the chemical species are very important in defining its reactivity (Fukui, et. al. 1952, Mendoza-Huizar, 2011). Energies of HOMO and LUMO are popular quantum chemical descriptors. It has been shown (Zhou, et. al. 1990) that these orbital's play a major role in governing many chemical reactions, and are also responsible for charge transfer complexes (Franke, 1984). The energy of the HOMO is directly related to the ionization potential and characterizes the susceptibility of the molecule towards attack of electrophiles. The energy of LUMO is directly related to the electron affinity and characterizes the susceptibility of the molecule towards attack of nucleophiles. The concept of hard and soft electrophiles and nucleophiles has been also directly related to the relative energies of the HOMO and LUMO orbital's.

Hard nucleophiles have a low energy HOMO, soft nucleophiles have a high energy HOMO, and hard electrophiles have a high energy LUMO and soft electrophiles have a low energy LUMO (Fleming, 1976). HOMO-LUMO gap is an important stability index (Pearson, 1990). Molecular orbital energies are molecular properties whereas orbital densities are atomic properties, and provide useful information about donor acceptor interaction (Takahata, et. al. 1991). According to frontier electron reactivity theory, the chemical reaction takes place at a position where overlap of the HOMO and LUMO are the maximum (Fukui, 1975). In the case of donor molecule the HOMO density and in case of acceptor molecule the LUMO density is important for any reaction. Frontier orbital's densities can strictly be used to describe the reactivity of different atoms in the same molecule (Fukui, 1975). The electronegativity and hardness are of course used extensively to make predictions about chemical behavior. According to, the Koopmans theorem, ionization potential (IE), electron affinity (EA), Global electronegativity (χ), chemical potential (μ) chemical hardness (η), global softness (S), Global Electrophilicity index (ω) and ΔN_{max} can be expressed as follows (A. Kumar, et. al 2019):-

$IE = -E_{HOMO}$ Eq. 1
$EA = -E_{LUMO}$ Eq. 2
$\chi = (IE + EA)/2$ Eq. 3
$\mu = -\chi$ Eq. 4
$\eta = (IE - EA)/2$ Eq. 5
$S = 1/\eta$ Eq. 6
$\omega = \mu^2/2\eta$ Eq. 7

Besides, the maximum number of electron that electrophiles can acquire is given by the expression (Parr, et. al. 1999):

$\Delta N_{MAX} = -\mu/\eta$ Eq. 8

All the global chemical properties like total energies, HOMO energies, LUMO energies, ionization potential (IE), electron affinity (EA), electronegativity (χ), chemical potential (μ), hardness (η), softness (S), Electrophilicity index (ω) and ΔN_{MAX} was calculated at DFT/B3LYP/6-31+G (d, p) level in gas phase and water solvent using IEF-PCM model. Representing the results of all global chemical properties is given in Table 5.

Table 5. Global reactivity parameter of isomers A to C.

Parameters	Benzo[d]isoxazole DFT/6-31+G(d, p)		Benzo[c]isoxazole DFT/6-31+G(d, p)		Benzo[d]oxazole DFT/6-31+G(d, p)	
	Gas Phase	Water Solvent	Gas Phase	Water Solvent	Gas Phase	Water Solvent
T. Energy (a.u.)	-399.70	-399.71	-399.68	-399.696	-399.746	-399.752
HOMO (eV)	-7.061176	-7.03287	-6.3885	-6.41165	-6.87505	-6.92104
LUMO (eV)	-1.630465	-1.64788	-2.0824	-2.10719	-1.20679	-1.23971
ΔE_{gap} (eV)	5.4307115	5.38499	4.3060	4.30446	5.66826	5.68132
I (eV)	7.0611766	7.03287	6.3885	6.41165	6.87505	6.92104
A (eV)	1.630465	1.64788	2.0824	2.10719	1.20679	1.23971
χ (eV)	4.345820	4.34037	4.2354	4.25942	4.04092	4.08038
μ (eV)	-4.345820	-4.34037	-4.2354	-4.25942	-4.04092	-4.08038
η (eV)	2.7153557	2.69249	2.1530	2.15223	2.83341	2.84066
S (eV^{-1})	0.368275	0.37140	0.4644	0.46463	0.35293	0.35203
ω (eV)	3.477658	3.49840	4.1645	4.21486	2.88152	2.93056
ΔN_{Max}	1.600460	1.61202	1.9672	1.97907	1.42616	1.43641

An electronic system with larger HOMO-LUMO gap should be less reactive than one having smaller gap (Kurtaran, et. al. 2007). The IE (ionization potential) energy can be expressed through HOMO energies and EA (electron affinity) can be expressed through LUMO energies (Zhan, et. al. 2003).

The hardness (η) corresponds to gap between the HOMO and LUMO orbital energies. The larger the energy gap, the harder the molecule or compound. The hardness has been associated with stability of the chemical system.

As shown in table-5, the compound that has the highest HOMO energy is the isomer B (E_{HOMO} = -6.3885 eV in gas phase and -6.41165 eV in water solvent). This higher energy allows it to be the best electron donor. The compound that has the lowest LUMO energy is the isomer B (E_{LUMO} = -2.0824 eV in gas phase and -2.10719 eV in water solvent) which signifies that it can be the best electron acceptor. The compound which have lowest energetic gap is the isomer B (ΔE_{gap} = 4.3060 eV in gas phase and = 4.30446 eV in water solvent) this lower gap allows it to be the softest molecule. The compound that have the highest energy gap is the isomer C (ΔE_{gap} = 5.66826 eV in gas phase and 5.68132 eV in water solvent). Isomer B has lowest value of the ionization potential (I = 6.3885 eV in gas and 6.41165 eV in water solvent), so that will be the better electron donor. Isomer B also has the largest value of the electron affinity (A = 2.0824 eV in gas and 2.10719 eV in water solvent), so it is the better electron acceptor. Isomer A possesses higher electronegativity value (χ = 4.345820 eV in gas and 4.34037 eV in water solvent), than all isomers so; it is the best electron acceptor. Electronegativity (χ) increasing order of isomers A > B > C. Chemical hardness (softness) value of isomer B (η = 2.1530 eV in gas and 2.1522 eV in water solvent) is lesser (greater) among all the molecules, isomer B is found to be more reactive than all the compounds. Good electrophiles are a species characterized by a high chemical potential (µ) value and a low hardness (η) value. The value of Electrophilicity index (ω) for isomer B (ω = 4.1645 eV in gas phase and 4.2148 eV in water solvent) indicates that it is the stronger electrophiles than all isomers, than the order of electrophilicity index (ω) of the isomers is B > A > C. Isomer B has the smaller frontier orbital gap, so it is more polarizable and is associated with a high chemical reactivity, low kinetic stability and is also termed as soft molecule.

Local Reactivity Descriptors

The Fukui function is among the most basic and commonly used reactivity indicators. The Fukui function is given as the change in the density function ρ (r) of the molecule as a consequence of changing the number of electrons N in the molecule, under the constraint of a constant external potential. The Fukui function is defined as:

$$F(r) = \left(\frac{\partial \rho(r)}{\partial N}\right)_r \qquad \text{Eq. 9}$$

Where ρ(r) is the density, N is the number of electrons and r is the external potential exerted by the nucleus. Fukui functions are introduced, which are advocated as local reactivity descriptor in order to identify the most reactive sites for electrophilic or nucleophilic reaction within a molecule. The Fukui function indicates the propensity of the electronic density to deform at a given position upon accepting or donating electrons (Parr, et. al. 1989, Ayers, et. al. 2000). Also, it is possible to define the corresponding condensed or atomic Fukui functions on the jth atom site as,

$f_j^+ = [q_j (N+1) - q_j (N)]$ (for nucleophilic attack)   Eq. 10

$f_j^- = [q_j (N) - q_j (N-1)]$ (for electrophilic attack)   Eq. 11

$f_j^0 = [q_j (N+1) - q_j (N-1)]/2$ (for free radical attack)   Eq. 12

For an electrophilic f_j^- (r), nucleophilic f_j^+ (r) and for free radical attack f_j^0 (r) on reference molecule, respectively. In these equation, q_j is the atomic charge (evaluated from Mulliken population analysis, electrostatic derived charge, etc.) at the jth atomic site in the neutral (N), anionic (N+1) or cationic (N-1) chemical species.

The condensed dual descriptor has been defined as $\Delta f (r)_j = f_j^+ - f_j^-$ Eq. 13 [29, 30]. From the interpretation given to the Fukui function, one can note that the sign of the dual descriptor is very important to characterize the reactivity of a site within a molecule towards a nucleophilic or an electrophilic attack. That is, if $\Delta f (r)_j > 0$, then the site is favored for nucleophilic attack, whereas if $\Delta f (r)_j < 0$, then the site may be favored for an electrophilic attack (Morell, et. al. 2006, Gazquez, 1997, Gazquez, 2009). In 1998, Roy (Roy, et. al. 1998) proposed the "relative electrophilicity" (s_k^+/s_k^-) and the "relative nucleophilicity" (s_k^-/s_k^+) descriptors for the study of the intermolecular reactivity. The electrophilic and nucleophilic local softness s_k^+ and s_k^- (Ayers, et. al. 2002) are given by the following equations:

$$s_k^+ = S f_k^+ \qquad \text{Eq. 14}$$
$$s_k^- = S f_k^- \qquad \text{Eq. 15}$$

Where S is the chemical softness and f_k^+ and f_k^- are the electrophilic and nucleophilic Fukui functions. Calculated values of above parameters for isomers A-C are presented in tables-6, 7 and 8.

In this study, gross charges were calculated by using Mulliken charges analysis in order to calculate the condensed Fukui function, condensed dual descriptor and local softness. The condensed Fukui functions, condensed dual descriptor and local softness for the isomers A-C are given in table 6, 7, 8.

Table 6. Condensed Fukui function ($f_{(r)}^+$, $f_{(r)}^-$, $f_{(r)}^0$ & $\Delta f_{(r)}$) and local softness (s+ & s-) indices for nucleophilic, electrophilic and radical attacks in benzo [d] isoxazol isomers calculated at B3LYP/6-31+G (d, p) level in water solvent using IEF-PCM model.

			Benzo [d] isoxazol (A)			
Atoms	$f_{(r)}^+$	$f_{(r)}^-$	$f_{(r)}^0$	$\Delta f_{(r)}$	s_k^+	s_k^-
1C	0.272673	0.277323	0.274998	-0.00465	0.101271	0.102998
2C	0.039583	0.04745	0.0435165	0.348338	0.0147012	0.017623
3C	0.145797	0.129223	0.13751	0.016574	0.0541493	0.047993
4C	-0.01253	0.089229	0.0383495	-0.101759	-0.004653	0.033139
5C	0.143789	-0.049421	0.047184	0.19321	0.0534035	-0.0183550
6C	-0.075654	0.008425	-0.0336145	-0.084079	-0.0280980	0.0031290
7C	0.00931	-0.013789	-0.0022395	0.023099	0.0034577	-0.0051212
13O	0084816	0.083613	0.0842145	0.001203	0.031500	0.0310540
14N	0.113341	0.200872	0.1571065	-0.087531	0.042095	0.0746043

Table 7. Condensed Fukui function ($f_{(r)}^+$, $f_{(r)}^-$, $f_{(r)}^0$ & $\Delta f_{(r)}$) and local softness (s+ & s-) indices for nucleophilic, electrophilic and radical attacks in benzo [c] isoxazol isomers calculated at B3LYP/6-31+G (d, p) level in water solvent using IEF-PCM model.

			Benzo[c]isoxazole (B)			
Atoms	$f_{(r)}^+$	$f_{(r)}^-$	$f_{(r)}^0$	$\Delta f_{(r)}$	s_k^+	s_k^-
1C	-0.338396	-0.117814	-0.228105	-0.220582	-0.15723	-0.0547404
2C	0.333142	0.167651	0.2503965	0.165491	0.15478	0.0778964
3C	0.038455	0.093023	0.065739	-0.054568	0.01786	0.0432216
4C	0.160154	0.074248	0.117201	0.085906	0.07441	0.0344981
5C	0.07625	0.064103	0.0323515	0.011547	0.03542	0.0300632
6C	0.335611	0.105168	0.052584	0.230443	0.15593	0.0488646
7C	0.051882	0.331862	0.165931	-0.27998	0.02410	0.1541944
13O	0.064289	0.061659	0.0308295	0.00263	0.02987	0.0286488
14N	0.278631	0.2195	0.10975	0.059131	0.12946	0.1019872

These table shows that the most reactive site of isomer A, B and C are the 1C, 6C and 3C, for the nucleophilic attack, and 1C, 7C and 7C respectively, for electrophilic attack and 1C, 2C and 7C respectively for radical attack.

Table 8. Condensed Fukui function ($f_{(r)}^+$, $f_{(r)}^-$, $f_{(r)}^0$ & $\Delta f_{(r)}$) and local softness (s+ & s-) indices for nucleophilic, electrophilic & radical attacks in benzo [d] oxazol isomers calculated at B3LYP/6-31+G (d, p) level in water solvent using IEF-PCM model.

			Benzo [d] oxazol (C)			
Atoms	$f_{(r)}^+$	$f_{(r)}^-$	$f_{(r)}^0$	$\Delta f_{(r)}$	s_k^+	s_k^{--}
1C	0.059652	0.009576	0.034614	0.050076	0.02099	0.00337
2C	-0.001679	-0.183532	-0.0926055	0.181853	-0.00059	-0.06460
3C	0.229325	0.22281	0.2260675	0.006515	0.08072	0.07843
4C	0.07777	-0.00515	0.0363135	0.082927	0.02737	-0.00181
5C	0.19471	0.11716	0.155935	0.07755	0.06854	0.04124
6C	0.089429	0.17178	0.1306045	-0.082351	0.03148	0.06047
7C	0.1208	0.381908	0.251354	-0.261108	0.042525	0.13444
13N	0.167019	0.201036	0.1840275	-0.034017	0.05879	0.07077
14O	0.062968	0.084411	0.0736895	-0.021443	0.02216	0.02971

In table 6, 7 and 8, the condensed local softness value for isomer A-C are shown. As expected, in almost all the cases the N-atom is found to the most preferred site for protonation since in these compounds there is intra molecular hydrogen bonding takes place.

From table-6, 7 and 8, the interpretation for the dual descriptor presented, that for isomer A are C1, C3, N14 and isomer B are C2, C7, C4 and isomer C are C7, C3, C6 are the preferred site for nucleophilic attack. From table-6, 7 and 8, note the presence of negative values of the Fukui function. Recently it was reported that a negative Fukui function value means that when adding an electron to the molecule, in spots, the electron density is reduced; alternatively when removing an electron from molecule, in some spots the electron density is increased. Ayres et al, has related this behavior with the reduction and oxidation of atomic centers into the molecule (Glendening, et. al. 1996).

Table 9. Second order perturbation theory analysis of Fock matrix on NBO of isomer-A.

Donor NBO (i)	Type	ED/e	Acceptor NBO (j)	Type	ED/e	E $^{(2)a}$ Kcal/mol	$(E_{(j)} - E_{(i)})^b$ a.u.	$F_{(i, j)}^c$ a.u.
C1-C2	π	1.96	C5-C6	π*	0.27	18.50	0.29	0.061
C1-C2	π	1.60	C7-N14	π*	0.24	24.99	0.26	0.075
C1-C6	σ	1.97	C1-C7	σ*	0.028	3.73	1.21	0.060
C1-C7	σ	1.97	C2-C3	σ*	0.020	4.94	1.24	0.070
C2-C3	σ	1.97	C1-C2	σ*	0.03	3.60	1.26	0.060
C2-O13	σ	1.99	C1-C6	σ*	0.20	2.26	1.49	0.052
C3-C4	π	1.97	C1-C2	π*	0.44	22.28	0.27	0.073
C4-C5	σ	1.98	C6-H11	σ*	0.01	2.41	1.16	0.047
C5-C6	π	1.97	C3-C4	π*	0.29	20.45	0.28	0.068
C7-N14	π	1.99	C1-C2	π*	0.44	7.49	0.35	0.051
C7-N14	σ	1.97	C1-C6	σ*	0.02	3.67	1.44	0.065
O13-N14	σ	1.98	C2-C3	σ*	0.02	4.41	1.36	0.069
LP(2)O13	n	1.97	C1-C2	π*	0.44	28.61	0.35	0.095
LP(2)O13	n	1.75	C7-N14	π*	0.24	15.68	0.33	0.066
LP(1)N14	n	1.96	C1-C7	σ*	0.02	4.74	0.97	0.061

Natural Bond Orbital Analysis (NBO)

The natural Bond Orbital (NBO) calculations were performed using NBO Version 3.1 program as implemented in the Gaussian 09 package at the B3LYP/6-31+G (d, p) level in the water solvent using IEF-PCM model in order to understand various second-order interactions between the filled orbital of one system and vacant orbital of another subsystem, which is a measure of intermolecular delocalization or hyper-conjugation. NBO analysis provides the most accurate possible percentage of electron density. A useful aspect of the NBO method is that it gives information about interactions of both filled and virtual orbital spaces that could enhance the analysis of intra and inter-molecular interactions. The second-order Fock-matrix was carried out to evaluate the donor-acceptor interactions in the NBO basis. The interactions result in a loss of occupancy from the localized NBO of the idealized Lewis structure into an empty non Lewis orbital. For each donor (i) and acceptor (j) the stabilization energy (E2) associated with the delocalization i → j is determined as (M. Jag, 2001):

$$E(2) = \Delta E_{ij} = q_i \frac{(F_{ij})^2}{(E_j - E_i)} \qquad \text{Eq. 16}$$

Where, q_i → donor orbital occupancy, E_i, E_j → diagonal elements and F_{ij} → the off diagonal NBO Fock matrix element.

In NBO analysis large E (2) value shows the intensive between electron-donors and electron acceptors, and greater the extent of conjugation of the whole system, the possible intensive interaction are given in table 9-11. The strongest interactions found in isomer-A are LP(2) (O13) → π*(C1-C2), π*(C7-N14); π(C1-C2) → π*(C7-N14), π*(C7-N14); π(C3-C4) → π*(C1-C2); π(C5-C6) → π*(C3-C4) and π(C7-N14) → π*(C1-C2), producing a total of 138 kcal/mol stabilization energy. The most intensive interactions found in isomer-B are LP(2) (O13) → π*(C2-C7), (C1-N14); π(C5-C6) → π*(C1-N14); π(C3-C4) → π*(C2-C7), π*(C5-C6) and π(C2-C7) → π*(C1-N14), π*(C3-C4)

leading to total stabilization energy of 150.28 kcal/mol. The strongest interactions found in isomer-C are: LP(2) (O14) → π*(C7-N13), π*(C1-C2); π(C5-C6) → π*(C1-C2), π*(C3-C4); π(C3-C4) → π*(C1-C2), π*(C5-C6) and π(C1-C2) → π*(C5-C6), resulting in total stabilization energy of 156.04 kcal/mol. The total stabilization energy order of intense NBO interactions in isomers are C > B > A, suggesting less electron delocalization found in isomer A.

Table 10. Second order perturbation theory analysis of Fock matrix on NBO of isomer-B.

Donor NBO (i)	Type	ED/e	Acceptor NBO (j)	Type	ED/e	E (2)[a] Kcal/mol	(Ei – Ej)[b] a.u.	Fij[c] a.u.
C1-C2	σ	1.95	C7-H12	σ*	0.01	4.82	1.12	0.066
C1-C6	σ	1.97	C5-H10	σ*	0.01	2.52	1.18	0.049
C1-N14	π	1.99	C5-C6	π*	0.19	9.09	0.36	0.052
C1-N14	π	1.87	C2-C7	π*	0.32	8.90	0.34	0.051
C2-C3	σ	1.97	C2-C7	σ*	0.02	4.21	1.27	0.066
C2-C7	π	1.98	C1-N14	π*	0.43	27.83	0.28	0.081
C2-C7	π	1.70	C3-C4	π*	0.19	16.58	0.31	0.066
C3-C4	π	1.98	C2-C7	π*	0.32	18.75	0.28	0.066
C3-C4	π	1.79	C5-C6	π*	0.19	16.60	0.30	0.063
C4-C5	σ	1.98	C3-H8	σ*	0.01	2.68	1.15	0.050
C5-C6	π	1.79	C1-N14	π*	0.43	24.41	0.26	0.076
C7-O13	σ	1.99	C2-C3	σ*	0.02	3.97	1.48	0.069
O13-N14	σ	1.98	C1-C6	σ*	0.02	5.07	1.35	0.074
LP(2)O13	n	1.97	C1-N14	π*	0.43	13.04	0.35	0.062
LP(2)O13	n	1.67	C2-C7	π*	0.32	33.07	0.36	0.098
LP(1)N14	n	1.97	C1-C2	σ*	0.03	5.15	0.96	0.063

Table 11. Second order perturbation theory analysis of Fock matrix on NBO of isomer-C.

Donor NBO (i)	Type	ED/e	Acceptor NBO (j)	Type	ED/e	E (2)[a] .Kcal/mol	(Ei – Ej)[b] a.u	Fij[c] a.u
C1-C2	π	1.975	C5-C6	π*	0.327	17.98	0.29	0.066
C1-C6	σ	1.978	C1-C2	σ*	0.038	3.90	1.27	0.063
C1-O14	σ	1.988	C7-H12	σ*	0.018	2.37	1.35	0.051
C2-C3	σ	1.977	C1-C2	σ*	0.038	3.12	1.25	0.056
C2-N13	σ	1.973	C7-H12	σ*	0.018	5.75	1.21	0.075
C3-C4	π	1.977	C1-C2	π*	0.449	19.67	0.27	0.067
C3-C4	π	1.700	C5-C6	π*	0.327	19.83	0.28	0.067
C4-C5	σ	1.981	C3-H8	σ*	0.012	2.36	1.16	0.047
C5-C6	π	1.973	C1-C2	π*	0.449	21.57	0.27	0.071
C5-C6	π	1.697	C3-C4	π*	0.309	18.43	0.28	0.065
C7-N13	σ	1.988	C2-C3	σ*	0.022	5.92	1.44	0.083
C7-N13	π	1.907	C1-C2	π*	0.449	14.58	0.35	0.071
C7-O14	σ	1.990	C1-C6	σ*	0.020	4.95	1.47	0.076
LP(1)N13	n	1.920	C7-O14	σ*	0.050	12.06	0.72	0.084
LP(2)O14	n	1.971	C1-C2	π*	0.449	23.38	0.36	0.086
LP(2)O14	n	1.722	C7-N13	π*	0.248	35.18	0.34	0.098

a E(2) means energy of hyper conjugative interactions (stabilization energy in Kcal/mol)
b Energy difference between donor and acceptor i and j NBO orbital's in a.u.
c F(ij) is the Fock matrix elements between i and j NBO orbital's in a.u.

Vibrational Analysis

Vibrational spectroscopy is a spectroscopic technique used for the identification of functional groups in order to elucidate the structure of a target molecule, kinetics of chemical reactions, etc. The theoretically calculated spectra at DFT/B3LYP/6-31+G (d, p) in gas phase and water solvent using IEF-PCM model.

The spectral assignments of vibrational modes of all isomers are done with the VEDA-4 program (G. Socrates, 2001). The comparative gas phase and water solvent IR spectra are shown in the Figure-6. The value of correlation coefficient (R^2=0.998 for isomer-A, R^2= 1.0 for isomer-B and R^2=1.0 for isomer-C using DFT method) showed that good agreement between calculated wavenumbers cm^{-1} in gas phase and water solvent calculated wavenumbers cm^{-1}. The correlation graph is shown in figure-7. Comparison of prominent frequencies of isomers A to C has given in Table 12 and 13.

C-H Stretching vibrations

An aromatic compound commonly shows multiple weak bands in the region of 3100-3000 cm^{-1} due to the asymmetric ν(C-H) stretching vibrations; they are not appreciably affected by the nature of the substituent (N.B. Colthup, et.al. 1990, F. R. Dollish, et.al. 1997, G. Varasanyi, 1969, M.H. Jomroz, 2004), while the symmetric stretch appear between 3000-2900 cm^{-1} which is the characteristic region for the identification of C-H stretching vibrations (Manohar et al. 2008). In the present study, the calculated C-H stretching vibrational modes of the isomers A to C were obtained at 3200-1334 cm^{-1} in gas phase and 3208-1333 cm^{-1} in water solvent for isomer-A, 3282-1500 cm^{-1} in gas phase and 3287-1497 cm^{-1} in water solvent for isomer-B and 3286-3190 in gas phase and 3291-3195 cm^{-1} in water solvent for isomer-C respectively.

Isomer-A (Gas phase)   Isomer-A (Water solvent)

Isomer-B (Gas Phase)   Isomer-B (Water solvent)

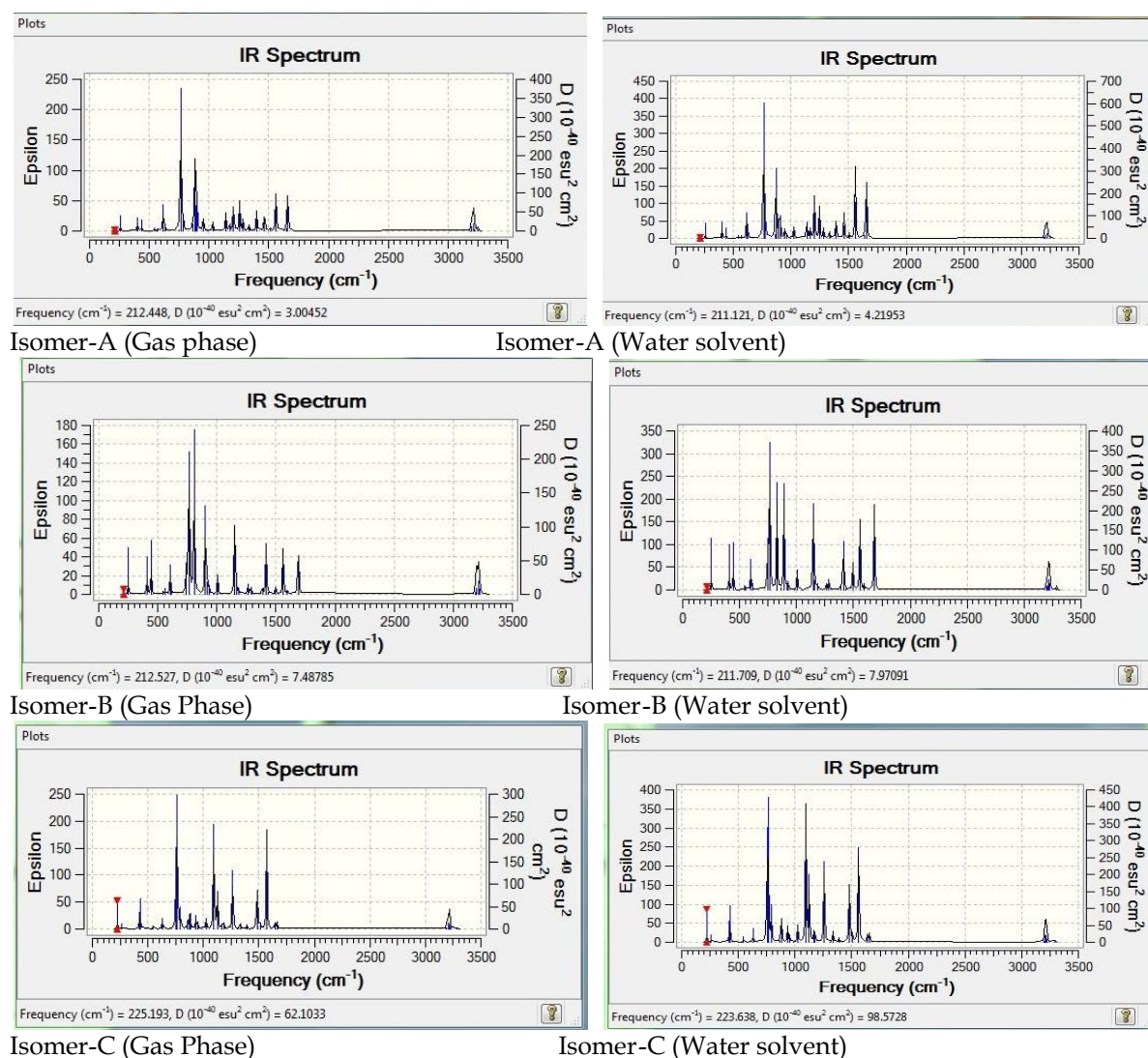Isomer-C (Gas Phase)   Isomer-C (Water solvent)

Figure 6. Simulated vibrational spectra of isomer A-C calculated at B3LYP/6-31+G (d, p) level in gas phase and water solvent.

C=C, C-N, C-O and N-O Stretching vibrations

In aromatic hydrocarbon, skeletal vibrations involving carbon-carbon stretching within the ring are absorbed in the region between 1600 – 1585 cm^{-1} (M. Karabacak, et.al. 2009). The wave number calculated at 3250-1284 cm^{-1} in gas phase and 3254-1281 cm^{-1} in water solvent for isomer-A, 3197-1287 cm^{-1} in gas phase and 3205-1285 in water solvent for isomer-B and 1662-1483 cm^{-1} in gas phase and 1658-1480 cm^{-1} in water solvent for isomer-C using DFT/B3LYP/6-31+G (d, p) method in the gas phase assigned to the C=C stretching vibration in benzene ring which shows good agreement with same level of calculation in water solvent The recognition of C-N vibrations is a difficult task, due to mixing of vibrations is possible in this region and however, with the help of force field calculations, the C-N stretching vibrations are pointing out and assigned. The bands established at 1560 cm^{-1} and 1393-1304 cm^{-1} in the gas phase and 1557 cm^{-1} and 1389-1304 cm^{-1} in water solvent for isomer-A and C respectively, for isomer-B stretching C-N vibrations are not observed. The C-O stretching vibration observed at 1464, 1385, 1333 cm^{-1} in gas phase and 1460, 1385, 1334 cm^{-1} in water solvent for isomer A-C respectively. The N-O stretching vibration of the isomer-A and B observed at 1643 and 3211 cm^{-1} in the gas phase and 1441 and 3217 cm^{-1} in water solvent in the same calculation, respectively. The N-O stretching vibrations for isomer-C are not observed at the same level of calculations.
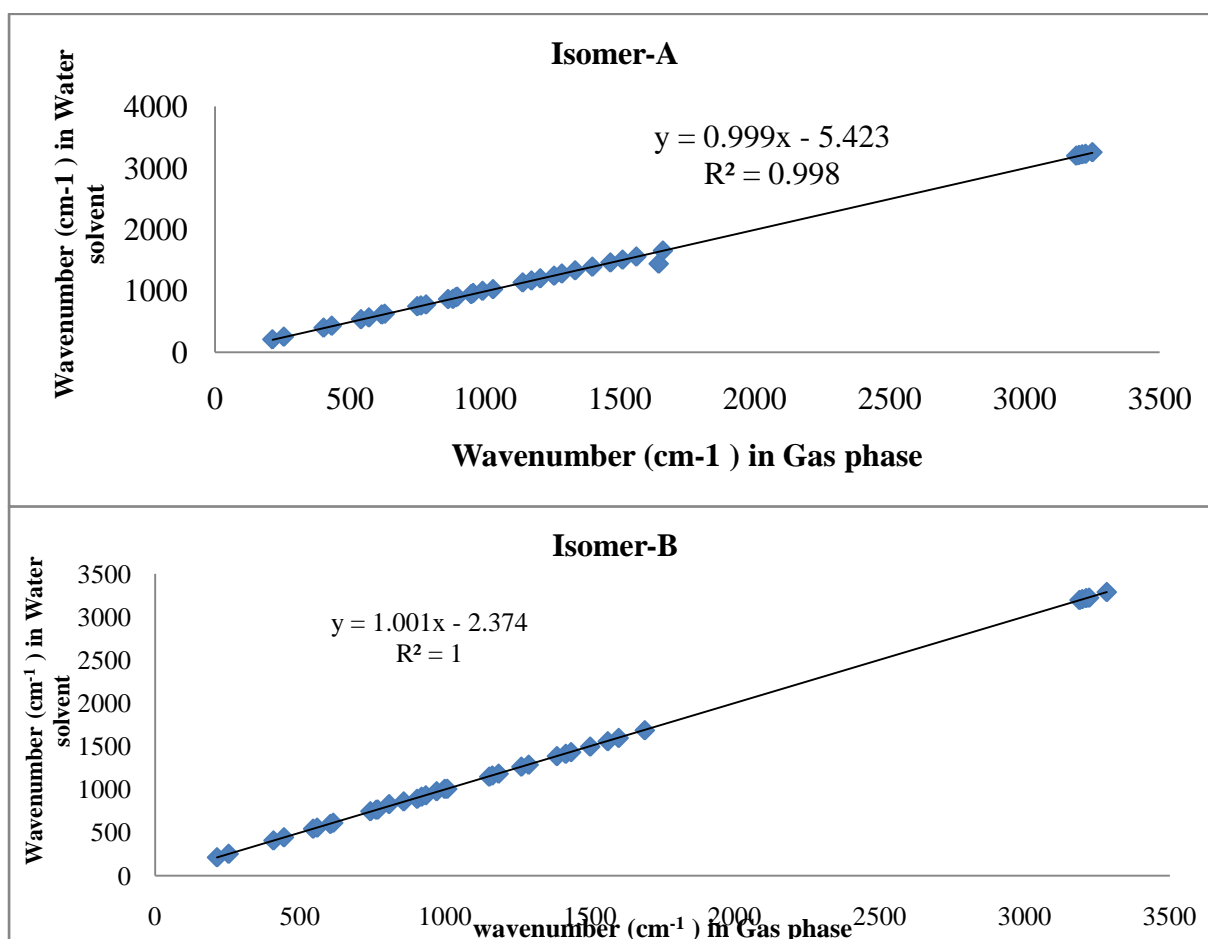
Bending, torsion and out-of-plane vibrations

In this paper, we are finding out the C-C-C bending vibrations of isomer-A to C obtained in region at 1256-863, 1262-856 and 1264-879 cm^{-1} in gas phase and 1246-866, 1262-859 and 1258-880 cm^{-1} in water solvent, respectively. The HCC bending vibrations for isomer-A, B and C are obtained in the region at 1029-891, 1162-902 and 1170-986 cm^{-1} in gas phase and 1026-994, 1159-889 and 1166-992 cm^{-1} in the water solvent, respectively.

Table 12. Calculated unscaled frequencies (cm^{-1}) and intensity of isomers A to C computed at DFT/B3LYP/6-31+G (d, p) in gas phase.

Modes NO.	A		B		C		Vibrational assignment of Isomer-A/B/C by VEDA-4 program
	Calculated Frequencies (cm^{-1})	IR Intensity	Calculated Frequencies (cm^{-1})	IR Intensity	Calculated Frequencies (cm^{-1})	IR Intensity	
1	212.44	0.1600	212.52	0.3989	225.19	3.5056	OCCC/CCCC/NCCC-OUT
2	254.82	2.5184	252.57	4.4207	259.90	0.7753	CCCC-TORS/CCCC-OUT/OCNC-TORS
3	402.04	3.4653	407.33	5.7658	421.39	3.9400	HCNO-TORS/CCCC-OUT/CNCC-TORS
4	432.36	3.2599	443.43	8.8812	430.39	7.3131	(HCCC)/(CCCC)/(CCCC) TORS
5	540.67	1.0454	544.06	0.6022	547.06	1.0414	(HCCC)/(HCCC)/(CCCC) TORS
6	569.90	0.7496	557.90	1.1998	584.18	0.0236	(CNOC)/(HCCC)/(CCCC) TORS
7	617.47	10.4978	603.65	6.6769	631.05	3.7221	(NOCC)/(CCCC)/(HCCC) TORS
8	628.40	3.0026	613.45	1.0624	632.06	0.9235	(HCCC)/(HCCC)/(HCCC) TORS
9	749.14	0.6405	741.66	8.6576	755.73	34.3536	(CCCC)/(CCCC)/((HCCC) TORS
10	762.47	71.6834	761.78	40.1400	764.77	57.2317	(HCCC)/(HCON)/(HCNC) TORS
11	781.64	6.8661	767.04	13.9658	795.01	9.8036	(CCCC)/(HCCC)/(HCCC) TORS
12	863.19	4.2307	806.21	49.4289	859.84	4.0923	(CCC)/(CCO)/(NCC)BEND
13	881.35	31.4493	856.70	0.0028	873.73	5.0160	(CHN)/(CCC)/(CNC) BEND
14	891.34	15.0621	902.91	29.6681	879.86	7.7416	(HCC)/(HCC)/(CCC) BEND
15	897.14	13.2416	918.10	4.3027	934.83	6.8642	(OCC)/(HCC)/(CCC) BEND
16	949.05	7.4658	932.85	2.5891	949.39	3.3956	(HCC)/(CCC)/(CCC) BEND
17	956.08	2.5395	970.22	0.3991	986.71	0.0008	(NOC)/(HCC)/(HCC) BEND
18	991.04	0.0007	998.01	0.0035	1025.60	5.4572	(HCC)/(CCC)/(HCC) BEND
19	1029.79	6.0851	1006.80	6.0847	1094.44	63.7172	(HCC)/(CCC)/(HCC) BEND
20	1139.71	8.5057	1151.52	29.5798	1126.42	23.6864	(CCC)/(HCO)/(HCN) BEND
21	1172.25	4.6242	1162.28	3.2669	1170.73	3.6282	(CCC)/(HCC)/(HCC) BEND
22	1204.92	16.3874	1183.92	1.3467	1183.36	3.2588	(CNO)/(CCC)/(OCN) BEND
23	1256.10	14.0734	1262.64	3.5504	1264.35	41.1254	(CCC)/(CCC)/(CCC) BEND
24	1284.80	7.4523	1287.66	3.4947	1304.78	0.0091	(CC)/(CC)/(NC) STRE
25	1334.16	3.1794	1385.24	3.2031	1333.34	4.0198	(CH)/(OC)/(OC) STRE
26	1397.74	9.7986	1415.71	15.6666	1393.37	1.9925	(CH)/(CC)/(NC) STRE
27	1464.73	13.2822	1434.06	0.8803	1483.28	31.9120	(OC)/(CC)/(CC) STRE
28	1509.74	2.1363	1500.05	3.8863	1511.06	4.6813	(CH)/(CH)/(CC) STRE
29	1560.83	23.5693	1560.58	17.8245	1571.07	52.9991	(NC)/(CH)/(CC) STRE
30	1643.68	2.1665	1598.20	2.1067	1644.31	3.8602	(ON)/(CC)/(CC) STRE
31	1659.17	24.0579	1688.35	22.5884	1662.76	5.4899	(CH)/CH)/(CC) STRE
32	3190.74	0.7818	3188.01	2.6098	3190.31	2.4350	(CC)/(CC)/(CH) STRE
33	3200.62	8.4055	3197.66	7.1141	3203.83	10.5706	(CH)/(CC)/(CH)STRE
34	3212.55	14.0030	3211.06	15.4316	3217.97	8.4120	(CC)/(ON)/CH) STRE
35	3225.12	3.0012	3221.20	5.6783	3222.73	3.8798	(CC)/(CH)/(CH) STRE
36	3250.37	1.5117	3282.16	0.3453	3286.72	0.4289	(CC)/(CH)/(CH) STRE

Some bending vibrations like C-N-O, N-O-C, C-H-N and O-C-C of isomer-A in gas phase and water solvent are obtained in the region at 1204/1203 cm⁻¹, 956/964 cm⁻¹, 881/868 cm⁻¹ and 897/904 cm⁻¹ respectively. Some selected tensional vibrations like CCCC, HCCC of isomer-A to C in gas/water solvent observed at 781-254/778-254 cm⁻¹, 741-212/745-211 cm⁻¹ and 795-631/791-628 cm⁻¹ and 762-432/761-432 cm⁻¹, 613-544/764-542 cm⁻¹ and 795-631/791-628 cm⁻¹ respectively. And the some selected out-of-plane vibrations OCCC of isomer-A in gas/water solvent is observed at 212/211 cm⁻¹ and in isomer-B out-of-plane vibration CCCC observed at 406-211/ 407-212 cm⁻¹ in gas/water solvent.

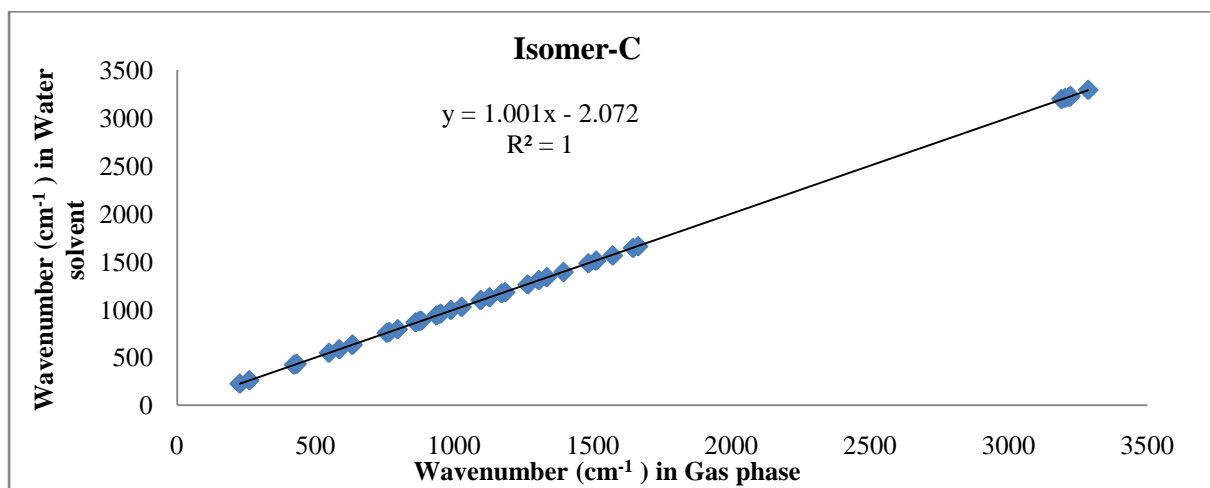**Figure 7. Correlation graph of isomer-A-C between calculated wavenumbers (cm⁻¹) in gas phase and calculated wavenumbers (cm⁻¹) in water solvent using DFT/B3LYP/6-31+G (d, p) method.**

Table 13. Calculated unscaled frequencies (cm⁻¹) and intensity of isomers A to C computed at DFT/B3LYP/6-31+G (d, p) in water solvent.

Modes NO.	A		B		C		Vibrational assignment of Isomer-A/B/C by VEDA-4 program.
	Calculated Frequencies (cm⁻¹)	IR Intensity	Calculated Frequencies (cm⁻¹)	IR Intensity	Calculated Frequencies (cm⁻¹)	IR Intensity	
1	211.12	0.2233	211.70	0.4230	223.63	5.5258	OCCC/CCCC/NCCC-OUT
2	254.31	4.2992	252.18	8.2768	259.17	1.4523	CCCC-TORS/CCCC-OUT/OCNC-TORS
3	401.54	7.2416	406.96	11.5848	421.49	6.5834	HCNO-TORS/CCCC-OUT/CNCC-TORS
4	432.28	4.9521	443.56	13.3363	429.01	11.7649	(HCCC)/(CCCC)/(CCCC) TORS
5	538.82	1.9096	542.85	1.2959	545.71	2.1346	(HCCC)/(HCCC)/(CCCC) TORS
6	567.07	1.6247	555.41	1.2731	583.09	0.0495	(CNOC)/(HCCC)/(CCCC) TORS
7	614.81	17.7157	597.94	11.3863	628.13	6.2652	(NOCC)/(CCCC)/(HCCC) TORS
8	626.45	6.1470	612.03	2.3985	631.14	1.2280	(HCCC)/(HCCC)/(HCCC) TORS
9	750.19	0.3902	745.59	24.4096	753.88	64.2571	(CCCC)/(CCCC)/((HCC) TORS
10	761.75	114.930	762.54	71.0391	762.95	82.0122	(HCCC)/(HCON)/(HCNC) TORS
11	778.40	14.9812	764.85	29.4252	791.26	21.8301	(CCCC)/(HCCC)/(HCCC) TORS
12	866.18	3.5925	828.15	55.8633	864.04	1.4345	(CCC)/(CCO)/(NCC)BE

							ND
13	868.48	68.2432	859.45	0.9876	878.28	14.1002	(CHN)/(CCC)/(CNC) BEND
14	894.28	18.5614	889.57	59.8617	880.33	10.3199	(HCC)/(HCC)/(CCC) BEND
15	904.70	22.5476	913.45	3.0113	935.22	11.5530	(OCC)/(HCC)/(CCC) BEND
16	946.74	9.9614	929.87	5.0183	953.25	4.9689	(HCC)/(CCC)/(CCC) BEND
17	964.79	4.1411	977.67	0.8300	992.33	0.0031	(NOC)/(HCC)/(HCC) BEND
18	999.56	0.0001	1004.89	0.0029	1024.18	13.0166	(HCC)/(CCC)/(HCC) BEND
19	1026.96	13.2885	1005.48	12.8423	1095.82	105.3833	(HCC)/(CCC)/(HCC) BEND
20	1136.34	19.9088	1146.41	62.6546	1125.00	56.6488	(CCC)/(HCO)/(HCN) BEND
21	1167.87	8.4267	1159.33	7.2649	1166.61	7.0729	(CCC)/(HCC)/(HCC) BEND
22	1203.59	38.6281	1181.26	5.0623	1179.27	7.6436	(CNO)/(CCC)/(OCN) BEND
23	1246.07	27.1862	1262.61	4.4540	1258.34	75.6360	(CCC)/(CCC)/(CCC) BEND
24	1281.37	8.7374	1285.21	8.3220	1304.80	0.1733	(CC)/(CC)/(NC) STRE
25	1333.43	7.4660	1385.03	4.2703	1334.90	8.6047	(CH)/(OC)/(OC) STRE
26	1392.29	21.4049	1411.61	42.9711	1389.03	3.1248	(CH)/(CC)/(NC) STRE
27	1460.79	20.8083	1430.97	0.7237	1480.63	57.6060	(OC)/(CC)/(CC) STRE
28	1506.93	4.6880	1494.99	18.4446	1507.63	7.5336	(CH)/(CH)/(CC) STRE
29	1557.51	63.2705	1557.40	48.4327	1561.86	108.9111	(NC)/(CH)/(CC) STRE
30	1441.77	5.5008	1595.50	3.6378	1641.11	7.3447	(ON)/(CC)/(CC) STRE
31	1654.17	61.2106	1684.70	61.7969	1658.64	8.4114	(CH)/CH)/(CC) STRE
32	3198.36	2.3348	3195.13	5.3492	3195.51	2.7368	(CC)/(CC)/(CH) STRE
33	3208.82	11.5289	3205.44	7.5312	3207.20	14.2677	(CH)/(CC)/(CH)STRE
34	3220.03	18.3177	3217.88	20.3505	3217.06	17.3296	(CC)/(ON)/CH) STRE
35	3227.44	5.1111	3221.79	12.1784	3226.11	5.6597	(CC)/(CH)/(CH) STRE
36	3254.53	1.7813	3287.64	2.9313	3291.23	2.5497	(CC)/(CH)/(CH) STRE

STRE= Stretching, BEND = Bending, TORS = Torsional modes, OUT = Out-of-plane

Nonlinear optical properties and Dipole moment
The nonlinear optical (NLO) properties results due to the interactions of electromagnetic fields in various media to produce new fields which are the change in frequency, phase, amplitude and other propagation characteristics from the incident fields (Kleinman, 1962). The computational approach is inexpensive, yet an effective way to design molecules by analyzing their potential which helps to determine the molecule NLO properties. The first hyperpolarizability (β_{tot}) and its related properties (α and β) of isomer-A to C have been calculated using B3LYP/6-31+G (d, p) level of theory in the gas phase and water solvent using IEF-PCM model and are presented in table-14.

Table 14. The dipole moments (μ), Polarizability (α) and the first hyperpolarizability (β) of isomer-A-C calculated by B3LYP/6-31+G (d, p) level in gas phase and water solvent.

Parameter	A		B		C	
	Gas	Water	Gas	Water	Gas	Water
μ_{tot} (Debye)	3.3783	4.5691	3.3860	4.6739	1.3892	1.9398
Polarizability (α_{tot})						
α_{xx}	118.459	163.581	119.541	166.339	118.915	160.690
α_{xy}	-2.522	-2.476	2.747	2.700	0.636	1.012
α_{yy}	94.199	129.846	97.949	136.890	91.985	127.288
α_{xz}	-0.001	0.006	-0.006	-0.009	-0.008	-0.011
α_{yz}	0.001	0.001	-0.003	-0.005	-0.004	-0.006
α_{zz}	48.455	64.028	48.887	64.726	48.345	64.047
α_{tot} (esu) × 10⁻²⁴	12.8984	17.6582	13.1590	18.1769	12.8067	17.3900
First Hyperpolarizability (β_{tot})						
β_{xxx}	29.8428	40.4056	-12.2367	-19.5813	18.5677	18.2203
β_{xxy}	7.9735	10.0777	12.8953	16.1713	-6.5794	-8.1767
β_{xyy}	-0.2512	1.1010	-1.6768	-3.4014	-14.1563	-16.5529
β_{yyy}	1.9168	4.9887	9.7167	14.9108	-9.0115	-11.4753
β_{xxz}	0.0095	-0.0020	0.0019	0.0023	0.0009	0.0011
β_{xyz}	0.0005	0.0019	-0.0005	-0.0006	0.0028	0.0032
β_{yyz}	0.0012	-0.0014	-0.0003	-0.0004	0.0023	0.0027
β_{xzz}	-6.4599	-5.8074	7.5995	7.1419	7.2585	7.2015
β_{yzz}	-2.3172	-1.9047	-0.6974	0.0942	-1.8316	-2.2217
β_{zzz}	0.0025	-0.0017	-0.0020	-0.0020	-0.0020	-0.0018
β_{tot} (esu) × 10⁻³³	2.10276	1.04042	0.06240	0.03022	0.1814	0.2046

To calculate all the electric dipole moment and first-order hyperpolarizability tensor components for a given system will depend on the choice of the Cartesian coordinate system (x, y, z) = (0, 0, 0) was chosen at own center of mass of the molecule. For molecular system with spherically symmetrical electron density polarizability is isotropic. The Polarizability of the novel molecular system for which $\alpha_{xx} \neq \alpha_{yy} \neq \alpha_{zz}$ (P) will no longer have the same direction as (E).

The energy of a system is a function of the electric field in the presence of an applied electric field. The first order hyperpolarizability is a third rank tensor that can be described by 3×3×3 matrices. The 27 component of the 3D matrix can be reduced to 10 components because of the Kleinman symmetry (Kleinman, 1962). The components of β are defined as the coefficients in the Taylor series expansion of energy in an external electric field. If the external electric field is homogeneous and weak, then expansion becomes,

$E = E^0 - \mu_i F_i - \frac{1}{2} \alpha_{ij} F_i F_j - \frac{1}{6} \beta_{ijk} F_i F_j F_k + \ldots\ldots.$ Eq 17

Where E^0 is the energy of the unperturbed molecule, F_i is the field at the origin and μ_i, α_{ij} β_{ijk} and γ_{ijkl} are the components of dipole moments, polarizability and the hyperpolarizability, respectively. The total static dipole moments (μ_{tot}), the mean polarizability (α_{tot}) and the first order hyperpolarizability (β_{tot}), using the x, y, z components can be calculated using the following equations:

$\mu_{tot} = [\mu_x^2 + \mu_y^2 + \mu_z^2]^{1/2}$ Eq. 18

$\alpha_{tot} = (\alpha_{xx} + \alpha_{yy} + \alpha_{zz})/3$ Eq. 19

$\beta_{tot} = (\beta_x^2 + \beta_y^2 + \beta_z^2)^{1/2}$ Eq. 20

$\beta_x = \beta_{xxx} + \beta_{xyy} + \beta_{xzz}$ Eq. 21

$\beta_y = \beta_{yyy} + \beta_{xxy} + \beta_{yzz}$ Eq. 22

$\beta_z = \beta_{zzz} + \beta_{xxz} + \beta_{yyz}$ Eq. 23

Since the values of the polarizabilities (α_{tot}) and the hyperpolarizabilities (β_{tot}) of the GAUSSIAN 09 output are obtained in atomic units (a.u.), the calculated values have been converted into electrostatic units (e.s.u.) (for α; 1 a.u. = 0.1482×10⁻²⁴ e.s.u., for β; 1 a.u. = 8.6393×10⁻³³ e.s.u.).

The calculated value of dipole moment (μ) for the isomer-A to C in gas phase and solvent phase were found to be 3.3783 D and 4.5691 D, 3.3860 D and 4.6739 D and 1.3892 D and 1.9398 D respectively, which are approximately greater than to the common value of urea, if we compare. Urea is one of the prototypical molecules used in study of the NLO purpose. The calculated values of polarizability (α) of the isomer-A to C in gas phase and water solvent are 12.8984 and 17.6582 × 10^{-24} e.s.u., 13.1590 and 18.1769 × 10^{-24} e.s.u. and 12.8067 and 17.3900 × 10^{-24} e.s.u. respectively. The magnitude of the hyperpolarizability (β) is one of important key factors in NLO system and useful as this clearly indicates the direction of charge delocalization. The B3LYP/6-31+G (d, p) level of theory calculated first static hyperpolarizability value for isomer-A to C in gas phase and water solvent is 2.10276 × 10^{-33} and 1.04042 × 10^{-33} esu, 0.06240 × 10^{-33} and 0.03022 × 10^{-33} esu and 0.1814 × 10^{-33} and 0.2046 × 10^{-33} esu respectively. The first static hyperpolarizability result explore that, the title compounds are able to generate the second order harmonic generation with more amplitude because largest β_{xxx} value of isomer-A and C and β_{xxy} value of isomer-B indicates charge delocalization is along the bond axis and involvement of σ orbitals in intra-molecular charge transfer process (Sinha, et. al. 2014). So, the present isomers- A-C can be used to prepare the NLO crystals for electronic applications. In addition to that, due to its elevated values of polarizability and first static hyperpolarizability, the present isomer A-C are able to bind with other molecules with fewer amounts of binding energy and an efficacious candidate for NLO material.

CONCLUSION

In the present work, we are used DFT/B3LYP and HF method to investigate theoretical analysis on geometries of benzo [d] isoxazole derivatives using 6-31+G (d, p) basis set in gas phase and water solvent using IEF-PCM model for both methods. All the electronic properties calculated at DFT/B3LYP/6-31+G (d, p) in gas phase and good agreement with in water solvent. The HOMO-LUMO band gap of isomer-A-C are in the order C > A > B and other electronic properties likes ionization potential, electron affinity, chemical hardness, softness, electronegativity and electrophilicity index of isomer-A-C have been calculated. The UV-Vis absorption property and solvent effects on isomers- A-C have been obtained by using TD-DFT/B3LYP/6-31+G (d, p) in gas phase, water, ethanol, DMSO, THF, aniline. The obtained absorption maximums are in the range of 306.39-247.86 nm for isomer-A, 308.43-303.99 nm for isomer-B and 272.34-245.88 nm for isomer-C. The vibrational frequencies and infrared intensities of isomer-A-C have been calculated by using DFT/B3LYP/6-31+G (d, p) in gas phase and show good agreement with water solvent. FMOs analysis reveals the presence of ICT within molecule. The possible electrophilic and nucleophilic reactive sites of the molecule wear predicted and the intramolecular interactions of the molecule wear also confirmed through NBO analysis, Fukui function also helps to identifying the electrophilic and nucleophilic nature of a specific site within a molecule, NBO and Fukui function both calculated by using DFT/B3LYP/6-31+G (d, p) in water solvent. The first hyperpolarizability analysis of all compounds was performed and isomer-A showed the highest value compared to B and C. This indicates that isomer-A may have a very good nonlinear optical response. Benzo fused isoxazole derivatives have very wide applications not only in clinical field but also in other areas of chemistry and hopefully the results of this study will increase the interest of researchers working in this field.

ACKNOWLEDGEMENTS

REFERENCES

Jain, A.K., Kelwala, S. and Gershon, S. (1988). Antypsychotic Drugs in Schizophrenia: Current Issues. *International Clinical Psychpharmacology*, 3. 1-30.

Smulders, E. and Sung, E. (2012). "Laundry Detergents, 2. Ingredients and Products" in Ullmann's Encyclopedia of Industrial Chemistry, Wiley-VCH, Weinheim. doi:10.1002/14356007.o15_013.

Şener, E., Yalçin, İ. and Sungur, E. (1991). QSAR of some antifungal benzoxazoles and oxazolo (4, 5-b)pyridines against C. Albicans. *Quant. Struct. Act. Relat*. 10. 223-228.

Glukhova, O.E., Savostyanov, G.V. and Slepchenkov, M.M. (2014). A new approach to dynamical determination of the active zone in the framework of the hybrid model (quantum mechanics/ molecular mechanics). *Procedia Material Science*. 6. 256-264.

Jahed, V., Zarrabi, A., Bordbar, A. and Hafezi, M.S. (2014). NMR (1H, ROESY) spectroscopic and molecular modeling investigation of supramolecular complex of β-cyclodextrin and curcumin. *Food Chemistry*. 165. 241-246.

Ho ltje, H.D., Folkers, G. in Manhold, R., Kubinyi, H. and Timmerman, H. (1996). (Eds), Methods and Principles in Medicinal Chemistry. Wiley-VCH. *Weinheim*. 23.

Becke, A.D. (1993). Density-functional thermochemistry.III. The role of exact exchange. *Journal of Chemical Physics.* 98. 5648-5652.

Frisch, M.J., et al. (2009). Gaussian 09, Revision A.1, Gaussian, Inc., Wallingford CT.

Cossi, M. and Barone, V. (2001). Time-dependent density functional theory for molecules in liquid solutions. *J. Chem. Phys.* 115 (10). 4708-4717.

Adamo, C. and Barone, V. (2001). A TD-DFT study of the electronic spectrum of s-tetrazine in gas - phase and in aqueous solution. *Chem. Phys. Lett.* 330 (1). 152-160.

Cousins, K.R. (2011). Computer Review of Chem Draw Ultra 12.0. *J. Am. Chem. Soc.* 133 (21). 8388–8388. DOI: **10.1021/ja204075s**.

Kumar, A., Pandey, A. and Mishra, A. (2019). Quantum chemical studies for inhibitory action of 3-hydroxybenzo[d] isoxazole tautomers on steel and thermodynamic, non-linear optical properties (NLO) using of density functional theory method (DFT). *J. Biol. Chem. Research*. Vol. 36 (1). 1-13.

Gece, G. (2008). The Use of Quantum Chemical Methods in Corrosion Inhibitor Studies. Corrosion *Science Corros. Sci.* 50. 2981-2992.

Lewis, D.F.V., Ioannides, C. and Parke, D.V. (1994). Interaction of a series of nitriles with the alcohol-inducible isoform of P450: Computer analysis of structure−activity relationships. *Xenobiotica*. 24. 401-408.

Uesugi, Y., Mizuno, M., Shimojima, A. and Takahashi, H. (1997). Structure and Dynamics of Electronic Excited States. *J. Phys. Chem*. 101. 268.

Padmaja, L., Ravi Kumar, C., Sajan, D., Joe, I.H., Jayakumar, V.S. and Pettit, G.R. (2009). Density functional study on the structural conformation and intramolecular charge transfer from the vibrational spectra of the anticancer drug combretastatin-A2. *Journal of Raman Spectroscopy*. 40. 419-428.

Sudha, S., Sundaraganesan, N., Kurt, M., Cinar, M. and Karabacak, M. (2011). FT-IR and FT-Raman spectra, vibrational assignments, NBO analysis and DFT calculations of 2-amino-4-chlorobenzonitril. *Journal of molecular structure*. 985. 148-156.

Fukui, K., Yonezawa, T. and Singu, H. (1952). A Molecular Orbital Theory of Reactivity in Aromatic Hydrocarbons. *J. Chem. Phys.* 20. 722.

Mendoza-Huizar, L.H. and Rios-Reyes, C.H. (2011). Chemical Reactivity of Atrazine Employing the Fukui Function. *J. Mex. Chem. Soc.* 55 (3). 142-147.

Zhou, Z. and Parr, R.G. (1990). Activation hardness: new index for describing the orientation of electrophilic aromatic substitution. *J. Am. Chem. Soc.* 112 (15). 5720-5724.

Franke, R. (1984). Theoretical Drug Design Methods, Elsevier Science Ltd. London.

Fleming, I. (1976). Molecular Orbital's and Organic Chemical Reactions. John Wiley and Sons. London.

Pearson, R.G. (1990). Hard and soft acids and bases−the evolution of a chemical concept. *Coord. Chem. Rev.* 100. 403-425.

Takahata, Y. and Prabhakar, Y.S. (1991). Quantum QSAR of the antirhinoviral activity of 9-benzylpurines. Drug Des. Delivery. 7. 227.

Fukui, K. (1975). Theory of Orientation and Stereo selection. Springer-Verlag. New York.

Kumar, A., Pandey, A. and Mishra, A. (2019). Theoretical study of triphenyl amine-based dyes with different linker groups for dye-sensitized solar cells. Vol. 36 (1). 102-110.

Parr, R.G., Von Szentpaly, L. and Liu, S. (1999). Electrophilicity index. J. Am. Chem. Soc. 121 (9). 1922-1924.

Kurtaran, R., Odabasioglu, S., Azizoglu, A., Kara, H. and Atakol, O. (2007). Experimental and computational study on [2, 6-bis (3, 5-dimethyl-N-pyrazolyl) pyridine]-(dithiocyanato) mercury (II). Polyhedron. 26 (17). 5069-5074.

Zhan, C.G., Nicholos, J.A. and Dixon, D.A. (2003). *J. Phys. Chem*. A. 107 (20). 4184-4195.

Parr, R.G., Yang, W. (1989). Functional Theory of Atoms and Molecules. Oxford University Press. New York.

Ayers, P.W. and Parr, R.G. (2000). Variational Principles for Describing Chemical Reactions: The Fukui Function and Chemical Hardness Revisited. J. Am. Chem. Soc. 122 (9). 2010-2018.

Morell, C., Grand, A. and Toro-Labbe, A. (2006). Theoretical Support for using the Δf (r) Descriptor, *Chemical Physical Letters*. 425 (4-6). 342-346.

Gazquez, J. (1997). The Hard and Soft Acids and Bases Principle, *Journal of Physical Chemistry* A. 101. 4657-59.

Gazquez, J.L. (2009). Chemical Reactivity Concepts in Density Functional Theory in Chattaraj, P.K. (Ed.). Chemical Reactivity Theory: A Density Functional View, CRC Press-Taylor and Francis Group, Boca Raton, Fl, Ch.2 pp. 7-21.

Roy, R.K., Krishnamurti, S., Geelings, P. and Pal, S. (1998). Local softness and hardness based reactivity descriptor for predicting intra and intermolecular reactivity sequences: Carbonyl compounds, *J. Phys. Chem. A.* 102. 3746-3755.

Ayers, P.W., Morrison, R.C. and Roy, R.K. (2002). Variational principles for describing chemical reactions: Condensed reactivity indices. *J. Chem. Phys.* 116. 8731-8734.

Glendening, E.D., Badenhoop, J.K., Reed, A.D., Carpenter, J.E. and Weinhold, F.F. (1996). Theoretical Chemistry Institute, University of Wisconsin, Madison, WI.

Jag, M. (2001). In Organic Spectroscopy-Principles and Applications 2nd edn, Narosa Publishing House. New Delhi.

Socrates, G. (2001). Infrared and raman characteristic group frequencies. Tables and charts. 3rd ed. John Wiley. New York.

Colthup, N.B., Daly, L.H. and Wiberley, S.E. (1990). Introduction to infrared and raman spectroscopy. Academic Press. New York.

Dollish, F.R., Fateley, W.G. and Bemteley, F.F. (1997). Characteristics Raman Frequencies of Organic compounds. Wiley. New York.

Varasanyi, G. (1969). Vibrational Spectra of Benzene Derivatives. Academic Press, New York.

Jomroz, M.H. (2004). Vibrational energy distribution analysis, VEDA4. Warsaw.

Manohar et al. (2008). Crystal growth and characterization of *N*-hydroxyphthalimide ($C_8H_5NO_3$) crystal. *Spectrochem Acta* Part A. 71. 110**.**

Karabacak, M., Kurt, M. and Atac, A. (2009). Experimental and theoretical FT-IR and FT-Raman spectroscopic analysis of N1-methyl-2-chloroaniline**.** *J. Phys. Org. Chem*. 22. 321-330.

Kleinman, D.A. (1962). Nonlinear Dielectric Polarization in Optical Media. Phys. Rev. 126: 1977.

Sinha, L., Prasad, O., Karabacak, M., Mishra, H.N., Narayan, V., Asiri, A.M. (2014). Quantum-chemical (DFT, MP2) and spectroscopic studies (FT-IR and UV) of monomeric and dimeric structures of 2(3H)-Benzothiazolone. Spectrochimica Acta Part A. *Molecular and Biomolecular Spectroscopy*. 120. 126–136.

Corresponding author: Ashutosh Kumar, Department of Chemistry, Faculty of Science, Central Facility for Computational Research (CFCR) (Computer Cluster), University of Lucknow, Lucknow- 226007, India
Email: mishraanil101@hotmail.com, ashutosh.chemist@gmail.com