A quantum chemical study of 2-(Imidazol-1-yl)-4-Methylphenol

Abstract
The derivatives of imidazole like methotrexate, and omeprazole are important medicine available in pharmaceutical industries as anti-cancer, anti-microbial, and anti-inflammatory agents. In present communication geometry optimization of imidazole derivatives 2-(Imidazol-1 yl)-4 Methylphenolars has been done by using combination of DFT/B3LYP method and 6-311G(d,p) basis set. The optimized parameters of title molecules are compared with corresponding experimental data. The vibrational analysis, electronics properties of title molecule are calculated by using same level theory. The electronic properties of 2-(Imidazol-1-yl)-4-methylphenol are explained with the help of HOMO, LUMO and MESP. The calculated band gap of title molecule shows that title molecule is chemically inactive. We hope our study on title molecule provides new path way to researchers for further work on title molecule.

Keywords: Vibrational analysis, electronic properties, DFT, HOMO, LUMO.

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Introduction

The Quantum chemical calculations are very useful to know geometry vibrational spectra, electronic properties, UV spectra and polarizability of any unknown molecule [*WalbaH.et.al.1961,*]. Imidazol is an organic compound with the formula $C_3N_2H_4$. It is the colourless or white solid and soluble in water. It is an aromatic heterocycle. It is classified as a diazole and has non adjacent nitrogen atoms in meta substitution [Karitzky A.R.et.al.1984]. It has density 1.23 g/cm^3, and acidity falls upto 6.95.Imidazol having melting point 89 to 91^{0}c and boiling point 256^{0}c [*Grimmett et.al.1997*].It is most important biological compound, planer 5 membered ring like pyrrole ring that replace two equivalent tautomeric form because it can be bound to one or another nitrogen atom [*Brown, E. G.et.al.1998*]. Imidazole was first reported in 1858 by the German chemist Heinrich Debus. It was shown that glyoxal, formaldehyde and ammonia [*Pozharskii, A. F.et al. 1997*].This pyrrole ring consists of three carbon, two nitrogen and three hydrogen atoms and two double bond . It is also known as 2-Imidazole [Gilchrist, TL et.al.1995].It beard two nitrogen atom in which one nitrogen sheared hydrogen atom and other is called pyrrole type nitrogen [Rosemeyer, H.et.al. 2004]. The nitrogen-based heterocycles ring imidazole was discovered in 1840. After discovery of imidazole attracts many researchers due to their promising anti-cancer, anti-microbial, and anti-inflammatory activities[Sherer C.et.al.2014]. The geometry of imidazole provides advantage to interact with ligand by nonbonding interactions. The natural derivatives of imidazole such as histamine, histidine, biotin, alkaloids, and nucleic acid are approved as drug by FDA. The specific charter of imidazole in therapeutics the fused imidazole derivatives played important role in pharmaceutical industries.

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The derivatives of imidazole like methotrexate, and omeprazole are important medicine available in pharmaceutical industries as anti-cancer, anti-microbial, and anti-inflammatory agents. These drug of derivatives of imidazole shows some side effect [Gaba M.et.al.2016]. The researchers are trying to search potential candidate for better treatment under these desease by using Imidazole-based compounds. In this continuation [Pandey A.K.et al,2012,2015,2013,2017,2019,2020] we have selected fused imidazole derivative2-(Imidazol-1-yl)-4-Methylphenol for quantum chemical study. The Geometry optimization vibrational analysis electronic properties of 2-(Imidazol-1-yl)-4-Methylphenol is calculated by using combination of DFT/B3LYP method and 6-311G(d,p) method. We hope our study provides to calculate new biological active sites which is very useful to researchers for searching new drug with minimum side effect. In best of our knowledge no such quantum chemical study reported till now.

Computational methods

The entire calculation on title molecule have been done on personal laptop by using Gaussian 16 program package. The geometry optimization of title moleculehas been done without any symmetry constrain. Initial geometry of title moleculeis modelled by using Gauss View 6.0 program package.[Frisch A.,20016] The entire calculations on title molecule carried out by using combination DFT/B3LYP method and 6-311G (d,p) basis set. The whole calculations are carried by Gaussian 16 program package [M.J. Frisch, et. al. 2016].The vibrational analysis on title molecule is carried on Gauss View 6.0 program.The HOMO LUMO MESP are plotted by using Gauss veiw6.0

RESULTS AND DISCUSSION

Optimization

 The molecule having energy -2341.23a.u. with no symmetry so C_1 symmetry. The optimized geometry of title molecule along with bond length and bond angles are presented in fig-1.The synthesis crystal structure of title molecule is reported by Yoshinori Narutaetal. The crystal geometry of title molecule is monoclinic with $P2_1/n$ space group symmetry. The crystal having a=6.352A^0, b= 10.44A^0, c =13.52A^0 with β=97.199^0. [NarutaY, et.al,2001].The animated gauss view shows that the molecule having phenolic and imidazolylrings connected C1-N15 with bond length 1.427A^0 is well matched with calculated bond length 1.439A^0.In title molecule both ring phenolic and imidazolyl rings are slightly displaced from planarity. The calculated dihedral between both rings are 44.10^{0}are well matched with observed dihedral 42.21^0. The calculated -OH bond length placed on ortho position of phenolic ring is 1.385A^0 is well matched with observed -OH bond length 1.352A^0.

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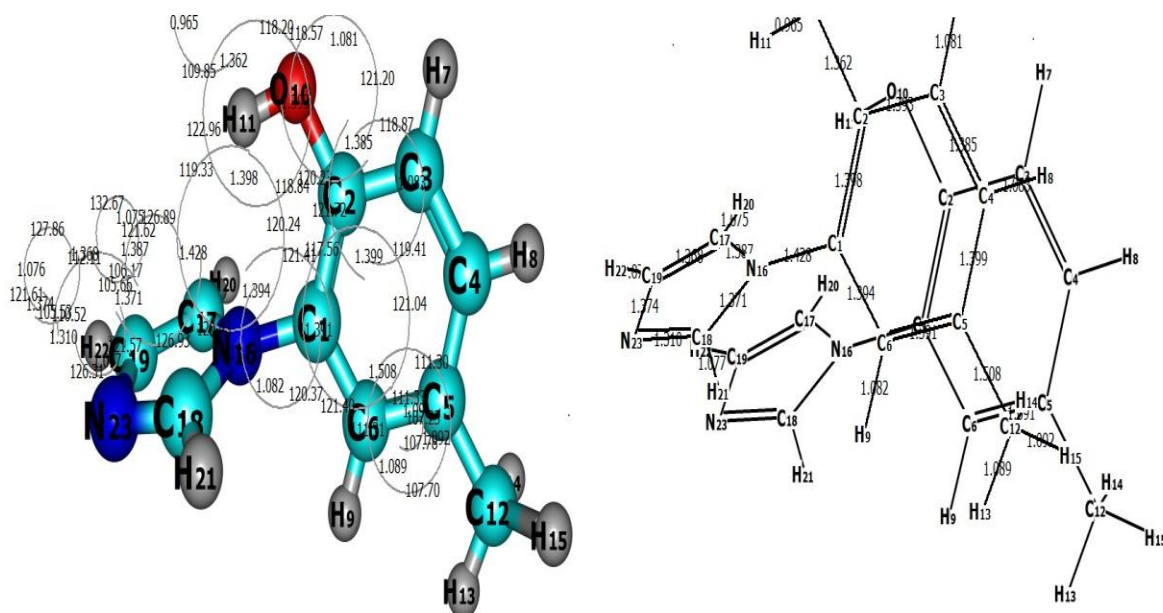
Fig .1Modal molecular structure of 2-(Imidazole-1-yl)-4-methylphenol

The chemical reactivity of any molecule is determined by nature of HOMO and LUMO molecular orbitals. The energy gap in between HOMO and LUMO are known as band gap and is important parameter to determine chemical reactivity of any system. The energy band gap is directly related to chemical reactivity of system. Any system having higher energy gap means less polarize high kinetic stability.[Gutowski M. et.al.1993, Bose SC.2011] The HOMO LUMO plot of title molecule is shown in fig-2. The HOMO is distributed over whole molecule however LUMO is distributed over carbmide ring. The transfer of electron HOMO → LUMO means shift means electron transfer from imidazolyl rings phenolic The MESP plot is very important to determine nature of electron density in term of color coding [Murray JS et.al.1996)]. The red color indicate more electronegative surface means better electronegative charge centre blue color represent more electropositive surface means better nucleophilic charge centre and yellow color means electrical neutral centre. The MESP plot of title molecule shown in fig-2. The O_{10} atom of title molecule is encircled with red color however N_{16} atom encircled with blue color which indicate that O_{10} is most electrophilic charge centre however N_{16} represent most nucleophilic charge centre.

Several electronic parameters are calculated by using HOMO and LUMO and listed in table-1. The chemical hardness is two times energy band gap. The negative eigenvalue of HOMO and LUMO are known as ionization potential and electronegativity.

IA=-ε_{HOMO}EA=- ε_{LUMO}------(1)

The value global hardness $\eta = \frac{1}{2}(\varepsilon_{LUMO}-\varepsilon_{HOMO})= (\frac{IA-EA}{2})$------- (2)

The electronegativity (χ) [Parr R.G. et al.1989, 1983, Pearson R.G.1989,Geerlings P.,et.al.2003]is given by

χ = - $\frac{1}{2}(\varepsilon_{LUMO}+\varepsilon_{HOMO})=(\frac{IA+EA}{2})$------(3)

The negative Eigenvalue of electronegativity is known as chemical potential

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$$(\mu = -\chi) \text{-------}(4)$$

The softness parameter is given by

$$S = \frac{1}{2\eta} = \frac{1}{\varepsilon LUMO - \varepsilon HOMO} \text{-------}(5)$$

The global electrophilicity index

$$(\omega = \mu^2/2\eta) \text{-----------}(6) \quad [22]$$

Table-1 Several electronic properties of title molecule

S.N.	H(eV)	L(eV)	ΔEgap(eV)	χ(eV)	μ(eV)	η(eV)	S(eV)$^{-1}$	ω(eV)	ΔN max
Imidazole	-6.505	-1.019	5.486	3.762	--3..762	2.743	0.1822	2.579	1.371
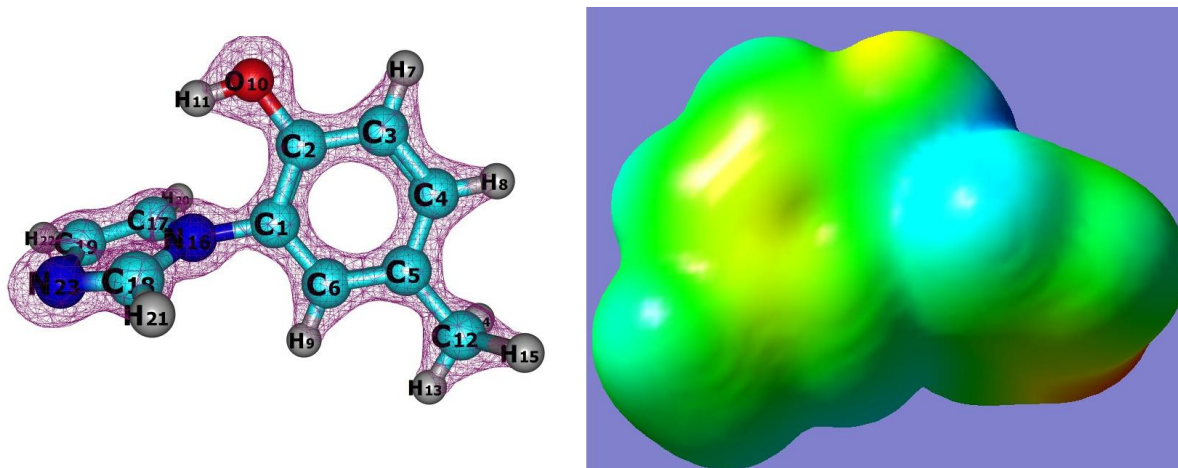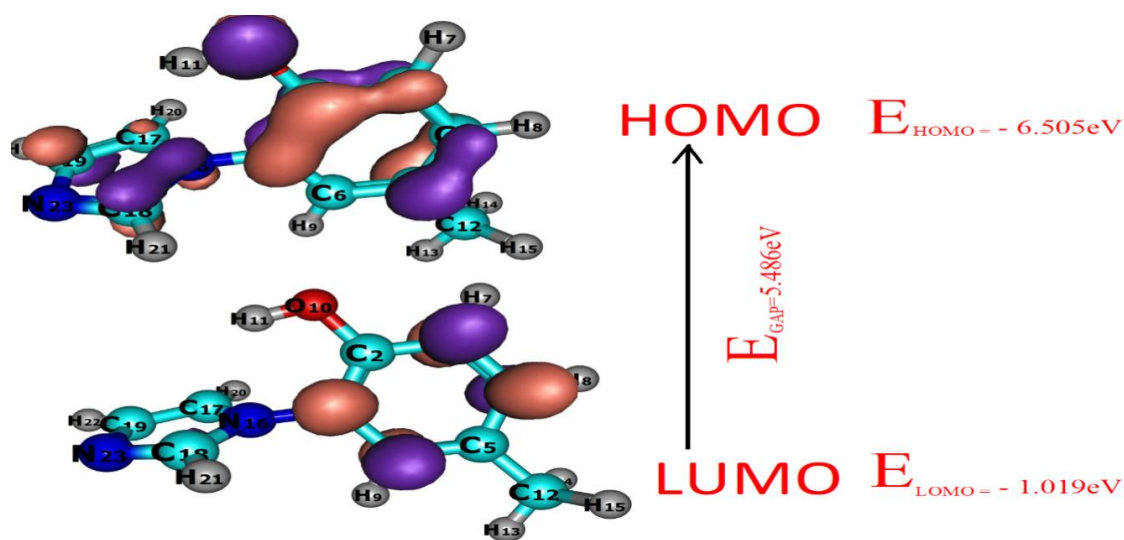
Fig-2 HOMO LUMO MESP plot of title molecule

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Vibrational Analysis

The title molecule having 23 atom so having 3N-5 modes of vibration so 110 modes of vibration. Out of 115 modes of vibration 114 are stretching and rest are bending modes. The whole spectra are divided in two part above 1000 are called functional group region however below 1000 modes are called finger print region. The calculated vibrational frequencies are lies some higher frequency region than observed IR spectra. The calculated IR spectra does not include molecular interaction anhormonicity electron electron correlation. To compensate these effect calculated IR frequencies are scaled by 0.96[**SunderganesanN.et.al.,2005**] The calculate IR frequencies scaled frequencies IR intensity and corresponding modes of vibrations are listed in table-2. Some important modes of vibrations are discussed below.

VIBRATIONAL MODES DISCRIPTION

The shift of O-H modes of vibrations generally related with power of hydrogen bond it normally seen at high frequency ranges from 3600 to 3400 cm[-1][Krishnakumar V. et.al., 2003]. In this study strong peak obtained at 3403 cm^{-1} which is due the stretching vibration. It observed different experimental at which low stretching for hydrogen atom and intermolecular interaction are occurring in stretching mode.In present study -CH group present and C-H vibration in the range 2800-3100 cm[-1][Krishnakumar V. et.al., 2005]. The molecules are identification C-H stretching vibration. Stretching vibrations are molecule obtained at 3108 to 3033 cm^{-1}Which are support by literature [Krishnakumar V. et.al., 2005]. At 1554,667 two mixed medium intense modes of vibration appears due to banding vibration in C-H molecule**.** On the lower side of spectra, two intense peaks due toscissoring modes of vibration, occur at 1612 cm^{-1}and 1460 cm^{-1}. The C-C rings are aromatic stretch known as semicircle stretching vibrations are calculated at 1644, 1281,1269,1114,1111 cm^{-1} etc. It supports literature [Krishnakumar V. et.al., 2005]. The C-C modes are torsional mode have been recorded spectral value from literature.The stretching vibration of C≡N are present having frequency 1551cm^{-1} to 1568cm^{-1} which agrees with the literature.

Table-2 Calculated IR frequencies along with respective intensity and assignment of title molecule

S.N.	Cal.Fre	Scaled Fre	Infra. Inte	Assignment
1	411.66	370.49	70.70	α ($O_{10}H_{11}$)
2	677.65	609.89	20.73	μ (C18H23N16) + μ ($C_{19}H_{22}$)
3	741.87	667.68	26.79	α ($C_{17}H_{20}$) + α ($C_{19}H_{22}$)
4	783.66	705.29	26.014	β ($C_5C_6C_{12}$) + μ (C_6H_9) +β ($C_2C_1O_{10}$)
5	831.40	748.26	22.09	α ($C_{18}H_{21}$) +α ($C_{19}H_{22}$)
6	841.78	757.53	31.34	α (C_4H_8)+ α (C_3H_7) +γ ($C_{12}H_{14}H_{15}$)
7	916.97	825.27	10.78	β ($N_{23}C_{19}C_{18}$) +μ ($C_{19}H_{22}$) +ψ ($C_{18}N_{16}$)
8	996.81	897.13	12.54	α ($C_{12}H_{13}H_{14}H_{15}$)+ψ (C_4C_5)+γ ($C_3C_4H_7$)+μ ($C_{19}H_{22}$)
9	1068.15	961.34	19.01	α ($C_{12}H_{13}H_{14}H_{15}$)+μ ($C_{17}H_{20}$)+μ ($C_{18}H_{21}$)

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10	1068.89	962.00	34.21	α $(C_{12}H_{13}H_{14}H_{15})$ + μ (C_6H_9)+ μ $(O_{10}H_{11})$+ψ $(N_{16}C_{18})$+ μ $(C_{17}H_{20})$+ μ $(C_{18}H_{21})$
11	1133.45	1020.11	13.94	ψ $(N_{23}C_{19})$+ μ $(C_{19}H_{22})$+ μ $(C_{18}H_{21})$+ψ (C_4H_8)
12	1204.54	1084.09	101.87	μ $(O_{10}H_{11})$+ψ (C_3C_2)+$\psi(C_4C_5)$+ μ (C_3H_7)+ μ (C_4H_8)+ μ (C_6H_9)
13	1217.56	1095.80	24.12	$\mu(C_{18}H_{21})R_1$ +ψ $(N_{23}C_{19})R_1$ + μ $(O_{10}H_{11})$+ μ (C_3H_7)+ μ (C_6H_9)+ψ $(C_{12}C_5)$
14	1261.73	1135.56	58.64	ψ (C_1C_6)+ μ (C_6H_9)+ μ (C_4H_8)+ μ (C_3H_7)+ψ $(N_{16}C_{18})$
15	1266.88	1140.19	13.34	μ $(C_{18}H_{21})$+ψ $(C_{18}N_{16})$+ μ $(C_{19}H_{22})$+ μ $(C_{17}H_{20})$
16	1300.30	1170.27	22.30	ψ $(N_{16}C_{18})$+ μ $(C_{18}H_{21})$+β $(N_{23}C_{18}C_{19})$+ψ $(N_{16}C_{17})$+ μ $(C_{19}H_{22})$+ μ (C_6H_9)
17	1335.41	1201.87	57.59	ψ $(N_{23}C_{19})$+ψ $(N_{16}C_{18})$+ μ $(C_{19}H_{22})$+ μ $(C_{17}H_{20})$+ψ (C_5C_6)+ψ (C_1C_2)
18	1366.71	1230.04	12.54	μ (C_6H_9)+ μ (C_4H_8)+ μ $(O_{10}H_{11})$
19	1393.49	1254.14	18.48	μ $(O_{10}H_{11})$+ψ $(N_{16}C_1)$+ψ $(N_{23}C_{18})$+ μ $(C_{19}H_{22})$
20	1502.34	1352.11	23.79	$\Psi_S(C_{12}H_{15}H_{14})$+ Ψ_S $(C_{12}H_{14}H_{13})$+ μ $(C_{18}H_{21})$+ μ $(C_{17}H_{20})$+ψ $(N_{16}C_{18})$
21	1512.71	1361.44	35.61	Ψ_S $(C_{12}H_{14}H_{15})$+ψ_{AS} $(C_{12}H_{13}H_{14})$+μ $(C_{17}H_{20})$+ ψ_{AS} $(N_{16}C_1C_{17})$
22	1531.08	1377.97	70.89	ψ $(N_{23}C_{18})$+ Ψ $(C_{17}C_{19})$+ $\Psi(C_{19}H_{22}N_{23})$+μ $(C_{18}H_{21})$+μ $(C_{17}H_{20})$
23	1543.45	1389.11	140.94	γ (C_3H_7)+ γ (C_4H_8)+ γ (C_6H_9)+ψ $(O_{10}C_2)$+$\psi_S(C_1C_2C_3)$+ ψ $(C_{17}C_{19})$
24	1628.65	1465.79	17.91	β $(O_{10}C_2H_{11})$+ψ (C_1C_2)+ ψ (C_5C_4)+β $(C_1C_6C_5)$+α $(C_2C_3C_4)$+β $(C_{12}C_5H_{13})$
25	3033.96	2730.56	33.15	Ψ_S $(C_{12}H_{13}H_{14})$+ Ψ_S $(C_{12}H_{14}H_{15})$
26	3078.64	2770.78	14.12	$\Psi_{AS}(C_{12}H_{14}H_{15})$
27	3108.78	2797.90	13.76	$\Psi(C_{12}H_{13})$+ Ψ_S $(C_{12}H_{14}H_{15})$
28	3780.99	3402.89	114.76	Ψ $(O_{10}H_{11})$

Where , ψ--stretching , β –scissoring , α—wagging , γ—rocking, μ -twisting

Conclusion

We have reported study of Imidazole through geometric parameters, vibrational frequency, electronic title molecules using DFT/B3LYP method and 6-311 G (d.p.) basis set. The calculated optimized parameters are well matched with corresponding observed value which shows that our calculation method well defined geometry of title molecule. The vibrational analysis of title molecule well represents its geometry. The calculated band gap shows that title molecule is chemically nonreactive molecule. We hope that our study provides new path for researcher for further work on title molecule.

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