

HOMO LUMO STUDY , REACTIVITY DESCRIPTORS AND MULLIKEN CHARGES OF IMIDAZOLE DERIVATIVE

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Abstract – This study explains the theoretical justification and exploratory intent behind the specific evidence of nuclear structure, HOMO–LUMO gap, the molecular electrostatic potential, and mulliken charges utilising a density functional theory (DFT) system with a B3LYP/6-311++ basis set and the calculated Fukui and Parr functions have been used to locate the reactive electrophile and nucleophile centers in the molecule. The HOMO-LUMO essentialness levels' uniqueness chooses the molecule's engine steadfastness, substance reactivity, compound nonabrasiveness, and hardness. The molecular electrostatic potential (MEP) is a critical mechanical assembly in electrophilic and nucleophilic goals affirmation.

Key Words: Density Functional Theory, HOMO-LUMO Energy Band Gap, Chemical Potential, Electrophilicity

1.INTRODUCTION

Debus¹ made the initial discovery of the imidazole nucleus in the year 1859 by reacting glyoxal and ammonia to indicate its source, for which he offered the name glyoxalin. Hantzsch² coined the name "imidazole," which refers to a five-membered heterocyclic ring structure with an imino group and a tertiary nitrogen atom at positions 1 and 3, respectively. The extensive presence of imidazole and imidazolium compounds in biological and chemical systems has sparked interest in imidazole chemistry. A five-membered ring of three carbons and two nitrogens, with the nitrogens placed in the 1 and 3 positions, makes up the cyclic, planar molecule imidazole^{3,4,5,6}. The nitrogen at the first position is of the "pyrrole" kind.

Nucleobases and the hydrogen bonds between them in the Watson and Cricks model of DNA are actually responsible for the transmission of genetic information from generation to generation. In addition mononucleotides such as ATP and GTP are also important in regulating the cellular processes. Hence, more number of purines and pyrimidine compounds has been screened for a wide variety of biological targets than other heterocycles.⁷⁻⁹

Pyrimidines (cytosine, thymine and uracil) and their derivatives were found to possess a broad spectrum of pharmacological activities. In recent years, considerable attention has been directed towards synthesis of nucleic acid analogues in the hope of discovering new and more effective

antisense compounds. Many N-substituted uracil derivatives possess biological activity. The most prominent representatives are 5-fluorouracil, 5-thiouracil and their derivatives.

2. Ground State Structure Analysis^{10,11}

The minimum energy configuration of the 1A molecule was again optimized at B3LYP/6-311G++ (d, p) level. The optimized stable geometry and the scheme of atom numbering of the compound of 1,1'-(5-bromo-1H-imidazole-2,4-diyl)dipyrimidine-2,4(1H,3H)-dione¹² is represented in Fig.1. The optimized structural parameters bond length, bond angle and the dihedral angle for the more stable geometry of the title compound is determined at B3LYP with 6-311g basis sets are presented in Table 4.1. Structural parameter like bond distance, length or radius is the common distance between the nuclear of two bonded atoms in a molecule; it has values typically within the range less than 1 to 2 Å. This structural parameter influences the force of attraction binding such a molecule *i.e.* the smaller the bond length between the bonding atoms, the stronger is the force of attraction between them.

For disubstituted derivative **1A**, pyrimidine ring attached to second position of imidazole were coplanar with the imidazole ring. This result was confirmed by following torsional angles N2-C1-N9-C10 (-179.9) in **1A**. But the pyrimidine ring substituted at the 4th position of the imidazole ring were non-planar with the ring, because the high electronegativity of the bromine atom induces polarization both in σ – and π -frameworks of the imidazole moiety. In these compounds, due to interaction between bromogroup in imidazole and carbonyl group in pyrimidine ring, the pyrimidine ring (4th position of imidazole) is rotated out of the imidazole plane, making dihedral angles of 43.3° in **1A**.

2.1.Frontier Molecular Orbitals

The highest occupied molecular orbital, HOMO, and the lowest unoccupied molecular orbital, LUMO, of a molecule are called the frontier orbitals. It was Fukui¹³ who first noticed the prominent role played by HOMO and LUMO in governing chemical reactions. The positive phase is represented in red colour and the negative phase is represented in green colour. The energy gap of HOMO–LUMO explains the charge transfer interaction within the molecule. The HOMO–LUMO analysis for **1A** was conducted by B3LYP/6-311G (d, p) level of theory. Highly occupied molecular orbital (HOMO) and Lowest unoccupied molecular orbital (LUMO) are the main orbital that take part

in chemical stability. Molecular orbital's can provide insight into the nature of reactivity and some of the structural and physical properties.

The HOMO represents the ability to donate an electron, while LUMO as an electron acceptor represents the ability to obtain an electron. The one electron excitation from HOMO and LUMO mainly described the electronic transition absorption correspond to the transition from ground to first excited state⁴³. The energy gap between HOMO and LUMO has been used to prove the bioactivity from intermolecular charge transfer. The energy gap measures the kinetic energy stability of the molecules.

The gap between Homo & Lumo of 1A is 4.4871. This large gap indicates that charge transfer is taking place within the molecule. The energy gap measures the kinetic stability of the molecules. A large gap implies high stability and small gap implies low stability. The high stability in turn indicates low chemical reactivity and small gap indicates high chemical reactivity. A molecule having higher Soft value is more reactive than a molecule having smaller Soft value. In general, it can be said that the increase in softness increases chemical reactivity and increase in hardness decreases chemical reactivity.

The energy gap between HOMO and LUMO has been used to prove the bioactivity of the molecule. More gaps also indicate that the molecule is less polarised and is known as hard molecule and it implies high stability being less chemical reactivity. The different value of Homo and Lumo has mentioned on the above Table 1. The energy values of HOMO (E_{HOMO}) and LUMO (E_{LUMO}) are 6.2967 and 1.8096 for 6311-G respectively. In the studied compound the HOMO-LUMO energy gap (ΔE) is 4.4871 eV that reflects the chemical reactivity of the molecule.

hardness of the title molecule was observed to be 2.2449 eV which is similarly high. While its electro negativity value is nearly high uncovering that the compound is equipped for showing certain organic movement.

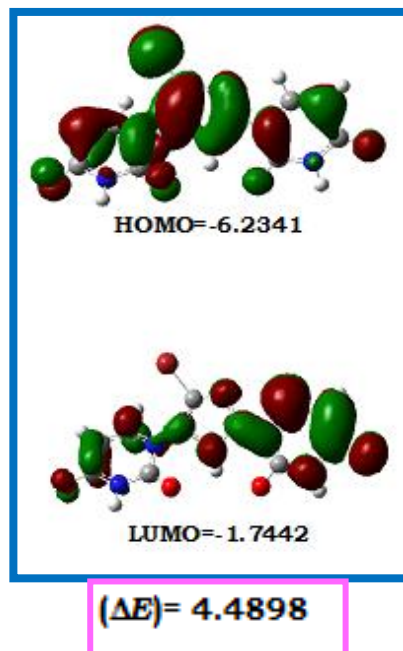


Fig -2: HOMO-LUMO pictures of compound 1A

2.2.. Mulliken charge distribution

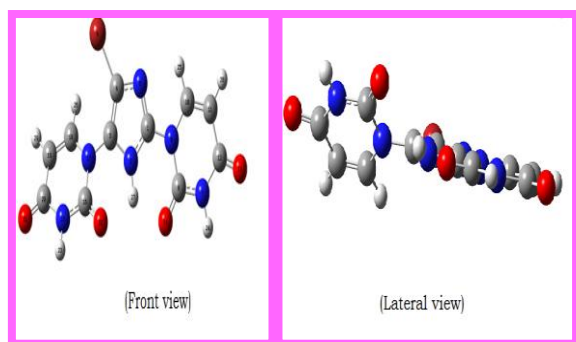


Fig -1: Optimized molecular geometries and atomic numbering of 1A

2.2. ELECTRONIC PROPERTIES

Electro negativity (A), hardness (η), softness (α), electrophilicity index (ω) are ordinarily utilized as worldwide reactivity parameters inside density functional theory. In the present examination, the HOMO and LUMO energies gap, absolute electronegativity, absolute hardness and electrophilicity index of the 1A molecule was registered by B3LYP/6-311+G(d,P). It has been found from the examination of the responsive descriptors that the chemical

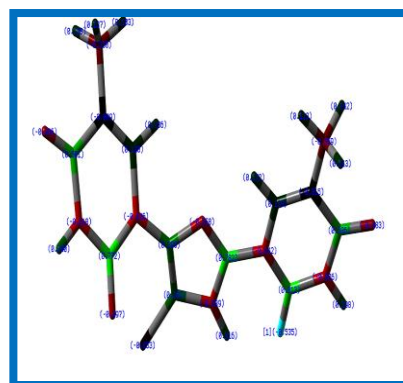


Fig - 3: MULLIKEN pictures of compound 1A

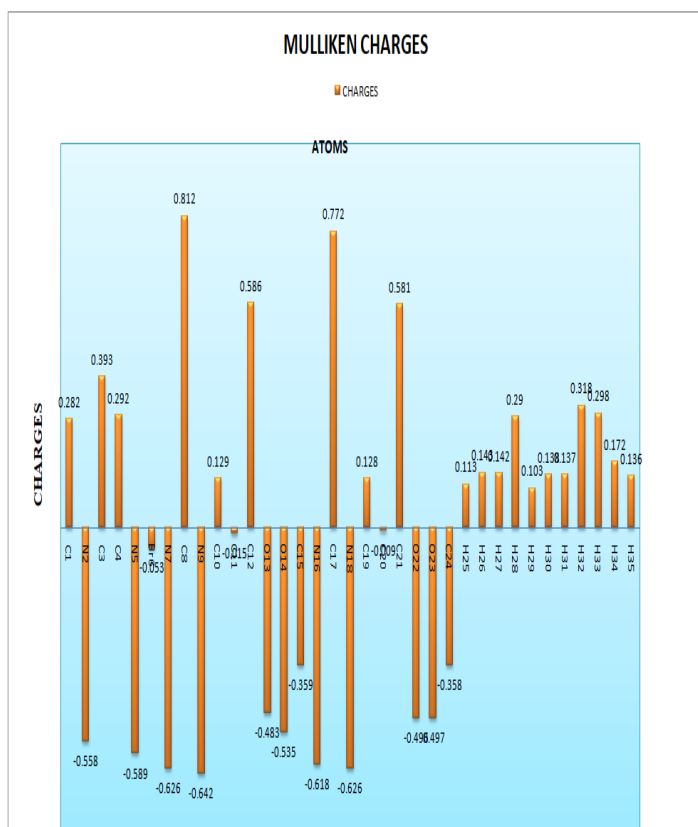
The calculation of atomic charges plays an important role in the application of quantum mechanical calculations to molecular systems. Mulliken charges¹⁴ are calculated by determining the electron population of each atom as defined in the basis functions. The charge distributions calculated by the Mulliken methods for the equilibrium geometry of 1A are given in Table 1. and the results can, however, better be represented in graphical form as depicted in Fig 4. In the 1A

compound, the distribution of Mulliken atomic charges shows the direction of delocalization and shows that the natural atomic charges are more sensitive to the changes in the molecular structure than Mulliken's net charge. Based on the charge distribution calculated by different basis set it can be concluded that all the hetero atoms showed significant electron density. The nitrogen atoms(N11,N12,N13) have more negative charges and this result suggest that the atoms bonded nitrogen atoms are electron acceptor. And more positive charge density has been found at C1 than that of other ring carbon atoms and this is 0.2630 for DFT.

In 1A an increased electron density(negative charge) can be also found at N2,C3,N5,C6,C7,C8,C9,C10,N11,N12,N13,N15C17,significantly positive charges were predicted for C4,C14,C16,H18,H19,H20,H21,H22,H23,H24,H25for,6311g basis set.

Fig -3: Graphical MULLIKEN charges of compound 1A

Table-1 MULLIKEN CHARGES



ATOMS	CHARGES
C1	0.282
N2	-0.558
C3	0.393
C4	0.292
N5	-0.589
Br6	-0.053
N7	-0.626
C8	0.812
N9	-0.642
C10	0.129
C11	-0.015
C12	0.586
O13	-0.483
O14	-0.535
C15	-0.359
N16	-0.618
C17	0.772
N18	-0.626
C19	0.128
C20	-0.009
C21	0.581
O22	-0.496
O23	-0.497
C24	-0.358
H25	0.113
H26	0.143
H27	0.142
H28	0.290
H29	0.103
H30	0.138
H31	0.137
H32	0.318
H33	0.298
H34	0.172
H35	0.136

3.

CONCLUSION

In this study work, we have performed the theoretical DFT analysis of a pharmaceutically important heterocyclic aromatic molecule, N-((1H-benzo[d]imidazol-2-yl) methyl) pyrimidin-4-amine for the first time. The optimized molecular geometry, energy gap between HOMO-LUMO and Molecular electrostatic potential of the N-((1H-benzo[d]imidazol-2-yl) methyl) pyrimidin-4-amine in the ground state have been calculated by using DFT (B3LYP) methods with 6-311++G (d, p) basis set. Furthermore, the absolute electro negativity (χ), the absolute hardness (η) ionization potential, electron affinity, hardness, potential, softness and electrophilicity index of the compound have been calculated in order to get insight into molecular structure of the compound.

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