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### SYNTHESIZED AND GEOMETRY OPTIMIZATION OF DIFFERENT SUBSTITUTED NITROGEN AND SULPHUR CONTAINING HETEROCYCLES

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#### ABSTRACT

A series of some novel 2-(5-methyl-1, 3, 4-thiadiazole-2-yl)-1H-Benzimidazole and 2-(1H-benzimidazol-2-yl)-1,3-benzothiazole derivatives were designed and synthesized under microwave irradiation via multistep reaction. The structures of substituted nitrogen and sulphur containing heterocycles were confirmed by <sup>1</sup>H NMR, MS, IR. The antibacterial activities of substituted nitrogen and sulphur containing heterocycles were determined. The antibacterial activity results indicated that the compounds Ib, Ie, and Id exhibited good activity against *Staphylococcus aureus*, and the compounds Ic and If displayed good activity against *Escherichia coli*. Theoretical calculation of the synthesized compounds was carried out with B3LYP/6-31G (d). The full geometry optimization was carried out using 6-31G(d) basis set, and the frontier orbital energy and HOMO and LUMO were discussed.

**Keywords:** *Substituted nitrogen and sulphur, Benzimidazole, Antibacterial activities, Geometry optimization.*

#### I. INTRODUCTION

Nowadays, nitrogen and sulphur containing substituted heterocycles became a research hot spot because they displayed excellent activities. Substituted heterocycles derivatives, especially benzimidazole compounds, exhibited diverse activities, such as the pharmacological activity like antibacterial and geometry optimization of different compounds. Many references reported that amides and sulfonamides derivatives showed other interesting activities, including antimicrobial<sup>1-5</sup>, antioxidant activities<sup>6,7</sup>, anticancer activity<sup>8,9</sup> and anti-inflammatory activity<sup>10</sup>. We have synthesized twelve novel benzimidazole derivatives under microwave irradiation. Their chemical structures were confirmed by <sup>1</sup>H NMR, IR, MS. The antibacterial activity of substituted nitrogen and sulphur containing heterocycles was determined in vivo. In this paper we are discussing about their Geometry optimization using computational activity.

This paper pledge with the geometry optimization of newly synthesized compounds. The density functional theory (DFT) deals with the relevancy of atoms, molecules and solids to nuclei that with success approach to calculate the electronic structure of molecules. The DFT usually deals with type of multicomponent systems, molecular properties, spin polarized system, superconductors, atomization energies, time dependent phenomena, ionization energies, electrical and magnetic properties, molecular dynamics etc. It provides data for molecular structure, thermodynamics stabilities and chemical reactivity of the molecules. It additionally maintains reliable data of molecules having little system, freelance of limitations inherent within the experimental approach. Numerous strategies and physical theory level of various compounds.<sup>11</sup>

DFT strategies area unit comparatively new and advanced can manufacture sensible geometries, energies and vibrational spectra of various synthesized compounds.<sup>12</sup> The vital methodology Becke–Perdew non-local functional (BP86) is found higher as compare to the hybrid B3LYP functional, particularly once used with numeric orbital basis sets. Liddell et.al has reported that numerous non-local density functional theory methods are very correct for figure out the geometries and corresponding energies of Mn<sub>2</sub> (CO)<sub>10</sub> and iron carbonyl compounds.<sup>13</sup> Various analysis has been done using ab initio calculations at the SCF and MP2 level with 6-311++G(d,p) basis set and B3LYP calculations with 6-31G(d,p) and 6-31+G(d,p) basis sets. Additionally, it's been considered that the efficiency of the various strategies of calculations are calculable by scrutiny between the predicated value of vibrational frequencies and infrared intensities and therefore the experimental information.<sup>14</sup>

This methodology is applicable for analysed completely different molecules on the idea of relative rates, stereo and regioselectivity. Activation energy for cycloaddition were dependent on the computation level, HF value shows large barriers, DFT calculation proved reasonable values among all and analysis of geometries of the cycloaddition structures showed strong mechanism. The frontier molecular orbitals showed that the reaction was controlled by charge transfer analysis.<sup>15</sup>

## II. RESULTS AND DISCUSSION

### Molecular Orbital Study

The most generally used approach by chemists is the molecular orbital (MO) theory. The frontier molecular orbitals assumes a vital part in the electronic and optical properties, and also in chemical reactions [16]. In the present investigation, we have synthesized nitrogen and sulphur containing heterocyclic compounds. Molecular Orbital studies have been effectively performed to molecular orbital (MO) energy levels for all incorporated molecules. With this method, the ability of molecules to donate or accept electrons can be anticipated with analysis of global reactivity parameters for example energy of highest occupied molecular orbital ( $E_{HOMO}$ ), energy of lowest unoccupied molecular orbital ( $E_{LUMO}$ ), energy gap ( $\Delta E$ ), dipole moment ( $\mu$ ) and the total energy (TE) and Mulliken atomic charges. The computed quantum chemical properties are given in Table 1.

**Table 1: Computed Quantum Chemicals Parameters**

COMPOUNDS	QUANTUM CHEMICALS PARAMETER				
	$E_{HOMO}$	$E_{LUMO}$	$\Delta E_{(LUMO-HUMO)}$	Dipole Moment( $\mu$ )	Total EnergyTE
Compound 1	-5.6743ev	-0.00010 ev	5.67389 ev	1.50 Debye	-71.55au
Compound 2	-6.6411 ev	-0.00016 ev	6.64094 ev	1.85 Debye	-83.23au

All the calculations were performed with Argus lab. The molecular structures of these compounds were completely and geometrically optimized using the functional hybrid B3LYP (Becke, three-parameter, Lee-Yang-Parr exchange-correlation function).<sup>16</sup> Density function theory (DFT) formalism with electron basis set 6-31G (d) for all atoms. This approach is shown to yield good geometries for a wide variety of frameworks. This basis set gives great geometry optimizations. The frontier molecular orbital energies of these compounds are shown in Figures 1-2 Figures demonstrate the optimized structures and HOMO and LUMO densities of all molecules. It is seen from the figures 1 to 2 that the HOMO and LUMO densities vary from each other for all the compounds. The HOMO and LUMO energy orbitals are the most part possessed on the heteroatom. The energy gap between HOMO and LUMO is a basic parameter in deciding molecular electrical transport properties. The frontier orbital (highest occupied molecular orbital-HOMO and lowest unoccupied molecular orbital-LUMO) of a chemical species are most important in defining its reactivity.

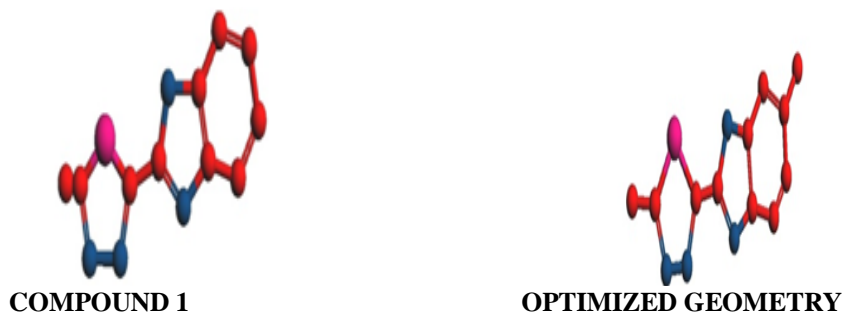




Figure 1: Optimized, HOMO, LUMO of compound1: 2-(5-methyl-1,3,4-thiadiazol-2-yl)-1H-benzimidazole

In this study we have located the lowest unoccupied molecular orbital (LUMO) energy is -12.6979 eV and the highest occupied molecular orbital (HOMO) energy is -13.5856 eV. The energy gap ( $\Delta E$ ) of HOMO–LUMO clarifies a definitive charge transfer interaction inside the molecule, and the frontier orbital energy gap of title compound is found to be 0.8877 eV obtained at DFT method using 6-31G(d) basis set. Lower the HOMO–LUMO gap explains the eventual charge transfer interactions taking place within the molecule, which influences the biological activity of the molecule. Increasing values of  $E_{\text{HOMO}}$  and decreasing value of  $E_{\text{LUMO}}$  increase the reactivity of the synthesized compounds and decrease their activity against the tested microorganisms.<sup>17</sup>

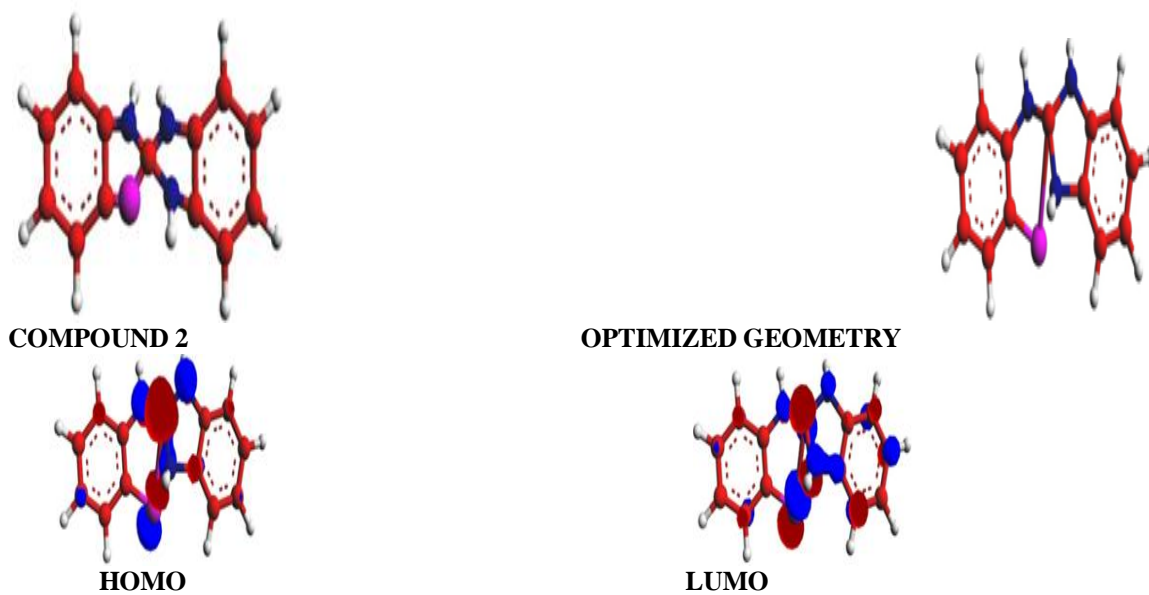


Figure 2: Optimized, HOMO, LUMO of compound2: 2-(1H-benzimidazol-2-yl)-1,3-benzothiazol

### Energy Gap ( $\Delta E$ )

$\Delta E$  (energy gap  $\Delta E = E_{\text{LUMO}} - E_{\text{HOMO}}$ ) is an imperative parameter gives a measure for the stability of the formed complex. The lower value of  $\Delta E$  has, the higher stability is for the formed complex. The value of  $\Delta E$  for compound 1 and compound 2 are 5.673 and 6.640 eV respectively; the values of total energies are -71.55 au and -83.23 au. The values of  $\Delta E$  and total energy are proportional to the biological activity.

### Total Energy (TE)

The total energy (TE) figured by quantum chemical techniques is an important parameter. The total energy of a system is composed of the internal, potential, and kinetic energy. The calculations indicate that compound 2 has the more negative total energy (-83.23au) as compared to compound 1(-71.55au), showing its high stability over the other molecules. The most reactive derivative, for compound 1 is Ib and for compound 2 is Je, showed the lowest

activity against the tested microorganism, while the most stable for compound 1 is If and for compound 2 is Jb showed the best activity against the tested microorganism.

### Dipole Moment ( $\mu$ )

Dipole moment can be applied to talk about the molecule structure of the compounds and measure of polarity of a polar covalent bond. The volume of compounds also increases with the increase of dipole moment ( $\mu$ ). In the present study, the value of dipole moment for synthesized compounds 1 is 1.50 D and for compound 2 is 1.85 D. The compound 2 have similar values as that of H<sub>2</sub>O. The value of dipole moment for synthesized derivatives Ic, Id, Ie, If is 4.17, 4.72, 817.42, 382.89 Debye respectively, and for compound 2 derivatives Ja, Jb, Jc, Je, Jf is 2.22, 2.07, 4.35, 2.98, 2.40 respectively which is higher than that of H<sub>2</sub>O ( $\mu = 1.85$  D). The high dipole moment value of these compounds probably indicates strong dipole–dipole interactions.

### Mulliken Atomic Charges

The Mulliken charge distributions of all studied molecules are shown in Table 2 respectively. Mulliken atomic charge calculation has an important role in the application of quantum chemical calculation to molecular system because of atomic charges effect dipole moment, molecular polarizability, electronic structure and more a lot of properties of molecular systems. The charge distributions over the atoms suggest the formation of donor and acceptor pairs involving the charge transfer in the molecule. The Mulliken charge distribution of the molecule is calculated on B3LYP at 6-31G(d) level theory. The calculated values of title molecules are shown in Table 2.

The charge distribution of the title compound shows that all the nitrogen and oxygen atoms have maximum negative charges and Mulliken charges are less compared with natural charges. In addition negative charge spread over the some of the carbon atoms. This is due to the position of the atoms attachment with the molecule. From the above, we conclude that our designed candidate ready to nucleophilic substitution reactions.

*Table 2: Mulliken Atomic Charges (Compound 1)*

S.NO.	ATOMS	MULLIKEN ATOMIC CHARGES
1	C	-0.8099
2	S	0.3805
3	N	0.1206
4	C	-0.1672
5	N	0.0446
6	C	-0.0380
7	N	-0.0496
8	N	0.0001
9	C	0.0751
10	C	0.0488
11	C	-0.0936
12	C	0.0278
13	C	-0.0774
14	C	0.0157
15	C	0.5224

*Table 2.3: Mulliken Atomic Charges (Compound 2)*

S.NO.	ATOMS	MULLIKEN ATOMIC CHARGES
1	C	-0.2297
2	C	-0.0526
3	C	-0.2670
4	C	-0.1490
5	C	-0.2261
6	C	-0.1114
7	H	0.1987

8	H	0.1911
9	H	0.1986
10	H	0.2100
11	N	0.1315
12	S	-0.1130
13	C	-0.5815
14	N	0.1271
15	N	0.5359
16	H	0.1141
17	H	0.1157
18	H	0.1429
19	C	-0.2129
20	C	-0.1275
21	C	-0.2374
22	C	-0.0556
23	C	-0.3336
24	C	-0.0860
25	H	0.2109
26	H	0.1917
27	H	0.2033
28	H	0.2119

### III. CONCLUSION

The DFT calculations indicated that the calculated chemical reactivity descriptors of the molecules correlated well with antibacterial activity. Reduction of  $E_{\text{HOMO}}$  and increase of  $E_{\text{LUMO}}$ , that is, a reduction in the reactivity and an increase in the stability of the synthesized compounds increased their activity against the tested microorganism. The most reactive derivative, showed the lowest activity, indicating that the most chemically stable compound had the best antibacterial activity. It could be concluded that these classes of compounds certainly hold promise towards good active leads in medicinal chemistry.

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