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QUANTUM CHEMICAL STUDY ON TWO BENZIMIDAZOLE DERIVATIVES

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Abstract

A quantum chemical study was done on two of benzimidazole derivatives (1-(2-methoxyethyl)-7-methyl-2-[4-(propan-2-yl)phenyl]-1H-1,3-benzodiazole), and (4,7-dibromo-1-(2-methoxyethyl)-2-[4-(propan-2-yl)phenyl]-1H-1,3-benzodiazole) in gas phase. DFT/B3LYP method was considered to calculate the energetic behavior and the quantum chemical descriptors such as the energy gap between HOMO and LUMO, the total energy for various orbital transitions, chemical hardness, softness, electrophilicity index, electro-negativity. Besides, a theoretical study was done for the compounds, which were in gas-phase, in order to study and examine the effect of changing the temperature of the molecule which was from (200K to 1000K) on thermodynamics properties (Enthalpy, Entropy, Heat capacity and correlation properties).

Key Words: Benzimidazole derivatives; HOMO; LUMO; DFT; thermodynamics.

Özet

İki benzimidazol türevinin (1- (2-metoksietil) -7-metil-2- [4- (propan-2-il) fenil] -1H-1,3-benzodiazol) ve (4,7-dibromo-1- (2- metoksietil) -2- [4- (propan-2-il) fenil] -1 H-1,3-benzodiazol) gaz fazında DFT/B3LYP yönteminin enerjik davranışı ve HOMO ve LUMO arasındaki enerji boşluğu, çeşitli yörünge geçişleri için toplam enerji, kimyasal sertlik, yumuşaklık, elektrofiliklik indeksi, elektro-negatiflik gibi kuantum kimyasal tanımlayıcıları hesapladığı düşünülmüştür. Ayrıca, gaz fazında olan bileşikler için (200 K ila 1000 K) arasındaki molekülün sıcaklığının termodinamik özellikler (Entalpi, Entropi, Isı kapasite ve korelasyon özellikleri) üzerindeki etkisini incelemek ve incelemek amacıyla teorik bir çalışma yapılmıştır.

Anahtar Kelimeler: Benzimidazol türevleri; HOMO; LUMO; DFT; termodinamik

1. Introduction

Benzimidazole is a bicyclic compound consists of a fusion of benzene, which provides a privileged structure (Palit et al., 2017). Because of the pharmacophore functions of this compound, in healthcare chemistry, and in the medical specialty, these important groups of benzimidazole substances have been found active applications in many fields also it got the attention of pharmacists and chemists for the last few decades (Wright, 1951).

Benzimidazole possesses has a lot of biological activities, like antimicrobial, anti-fungal, anti-histaminic, medication, antiviral, anti-cancer, anti-oxidant, anti-ulcerative, etc., because of that, benzimidazole derivatives can be considered as a vital moiety of the molecules of “pharmaceutical interest“ (Pathak et al., 2010). Benzimidazole gives a very wide range of uses in Osteoporosis medications according to its and his derivative's ability to combine with the calcium-sensing receptor (CaSR) located on the cell surface (Wolf et al., 2010; Gerspacher et al., 2010), this reason gives a huge interest to investigate such compound.

Mohamod et al. synthesized some (bis benzimidazole derivatives), and they evaluated antibacterial activity for most of the target compounds against four

strains of bacteria including (E.coli, P. aeruginosa) as gram-negative bacteria and (B. subtilis, S. aureus) as gram-positive bacteria, and reported that the tested compounds had shown various activity against both gram-negative and gram-positive bacteria used (Mahamod et al., 2019).

The Density functional theory DFT became a regular tool for the first principles of quantum chemical calculations on the electronic structure, and the properties of many molecular systems where no other first-principles methods can achieve similar accuracy at the same low cost especially in the principles (Raja, Muhamed, Muthu, Suresh, 2017), DFT replaces the usual (ab ignition) wavefunctions, which depend on spatial variables by the electron density which depends only on three spatial variables as a means to reach for a solution to the Schrodinger's equation.

With the exact exchange-correlation functional (Kanungo et al., 2019), DFT can take into full account of all complexes effect were unlikely the exact exchange-correlation functional is unknown which making it so essential to follow more and more accurate and reliable approximate functionals (Kanungo et al., 2019).

There are almost three categories of density functional methods, first method: Local density approximation (LDA), which assumes that the density of the molecule is uniform throughout the molecule, and is typically not a very popular method. The second method is the gradient corrected (GC) methods look to account for the non-uniformity of the electron density. The last category is the hybrid methods, which attempt to incorporate some of the more useful features from ab initio methods (specifically Hartree-Fock methods) with some of the improvements of DFT mathematics. Hybrid methods, such as B3LYP, tend to be the most generally used methods for computational chemistry practitioners (Al-Sawaff, Kandemirli, Evecen, 2019).

2. Materials and Methods

Computational Method:

A three-dimensional analysis was performed to estimate the effect of substitution groups in Benzimidazole ring in positions para, meta, and ortho, to produce new derivatives compounds which consider as an ionic monomer and dimer contrast agent, respectively (Bielecki & Lipiec, 2016).

The geometries of these molecules (1-(2-methoxyethyl)-7-methyl-2-[4-(propan-2-yl)phenyl]-1H-1,3-benzodiazole), and (4,7-dibromo-1-(2-methoxyethyl)-2-[4-(propan-2-yl)phenyl]-1H-1,3-benzodiazole) were fully optimized in gas phase by using (Lee-Yang-Parr correlation functional (B3LYP)), and (gradient corrected DFT) with "Becke's three-parameter hybrid exchange functional", and with the B3LYP/6-311G(d,p) basis set.

The High Occupied Molecular Orbitals (HOMO) and Low Unoccupied Molecular Orbital (LUMO) energies and molecular properties related to E_{HOMO} and E_{LUMO} including the hardness(η), softness(s), electronegativity(χ), chemical potential(μ), electrophilicity index(ω), nucleofugality △En and electrofugality △En were calculated, in addition, the change of temperature was investigated to see the final results of heat on the compounds. These parameters were calculated by using the following information (Sharma et al., 2019; Tokay et al., 2008; Kandemirli et al., 2014). The hardness is a half of the energy gap between HOMO and LUMO that:

$$\eta \cong \frac{1}{2}(\varepsilon_{HOMO} - \varepsilon_{LUMO}) \cong \frac{1}{2}(I - A) \quad (1)$$

Where A and I are the electron affinity and the ionization potential of the compounds. The softness can be calculated from hardness:

$$S = \frac{1}{2\eta} \quad (2)$$

Electronegativity can be calculated from E_{HOMO} and E_{LUMO} using the following equation:

$$\chi = -\frac{1}{2}(E_{HOMO} + E_{LUMO}) \quad (3)$$

From electronegativity, chemical potential can estimated that μ = -χ

$$\mu = \frac{1}{2}(E_{HOMO} + E_{LUMO}) \quad (4)$$

Electrophilicity index (ω) and nucleofugality (ΔEn) and electrofugality (ΔEe) can be taken from the chemical potential μ, and hardness η by the following equations respectively (Chattaraj, Sarkar, Roy, 2006; Matić et al., 2017).

Nucleofugality; $\Delta En = (\mu + \eta)^2/2\eta$ (5)

Electrophilicity index; $\omega = \frac{\mu^2}{2\eta}$ (6)

Electrofugality; $\Delta E_e = \frac{(\mu-\eta)^2}{2\eta}$ (7)

The quantum chemical calculations were performed by employing the density functional theory with Becke3-Lee-Yang-Parr (B3LYP) levels and 6-311G(d,p) basis set by applying it to "Gaussian 09W" program packages"(Frisch et al., 2013), and the visual images of the structure, where these properties spectroscopically and electronically, along with the molecular optimization were accomplished by (GaussView 5) software package (Dennington, 2009).

3. Results and Discussion

3.1. Electronic Properties

The diagram of compounds in vitro activity is shown in Figure 1. The derivatives of benzimidazole moiety will show very strong antioxidant properties when benzimidazole was substituted with hydrogen and barium substances. Derivative 2 substituted with Br (R1, R2 = Br) was more active (Anastassova et al., 2018; Fei et al., 2013; Khanna et al., 2011). In here two compounds, benzimidazole derivatives were studied (Table 1). A chemical diagram of (1) and (2) compound is given in Figure 2.

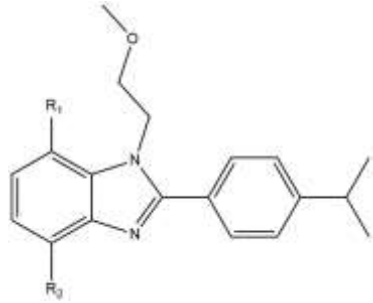

Figure 1. The diagram of compounds in vitro activity

Table 1. Investigated (1) and (2) compound.

Compound	Chemical Formula	Name	R1	R2
1	$C_{20}H_{24}N_2O_2$	1-(2-methoxyethyl)-7-methyl-2-[4-(propan-2-yl)phenyl]-1H-1,3-benzodiazole	Methoxy	H
2	$C_{19}H_{20}N_2OBr_2$	4,7-dibromo-1-(2-methoxyethyl)-2-[4-(propan-2-yl)phenyl]-1H-1,3-benzodiazole	Br	Br

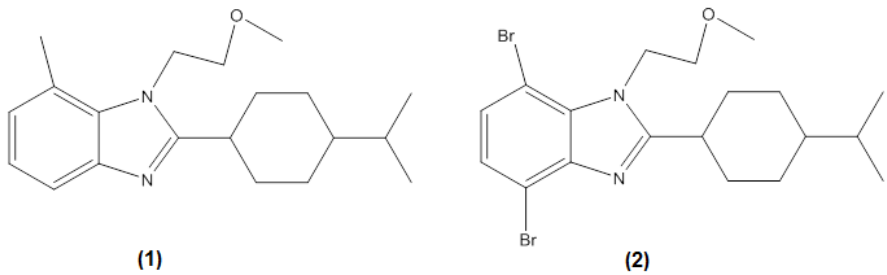

Figure 2. Chemical diagram of (1) and (2) compound.

Chemical stability is mainly influenced by the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). HOMO and LUMO play an important role in the electrical properties (Joshi et al., 2014). The LUMO represents electron accepting ability, while the HOMO represents electron-donating ability. The HOMO and LUMO energies give a lot of important quantities. Optimized structure, HOMO, LUMO and electron density of compound (1) and compound (2) in gas phase calculated at DFT/B3LYP level with 6-311G(d,p) basis set are given in Figure 3.

LUMO was mainly localized on benzimidazole and phenyl rings for the studied two compounds, on the other hand, HOMO was mainly localized in benzimidazole ring.

The potential increases in the order of red < orange < yellow < green < blue (Lu 2014). From the result given in the mapped (ESP) have been plotted for the title molecules in the 6-311G(d,p) basis set using the computer software Gauss View.

According to red regions are generally localized on the benzimidazole ring in the molecules studied.

The energy gap (△E) between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) considered as a particularly interesting property for the molecules under study.

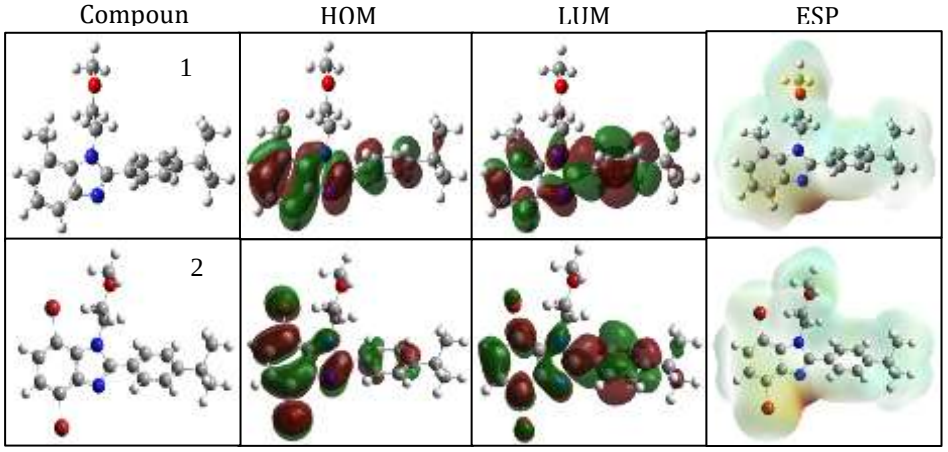

Figure 3. Optimized structure, (HOMO), (LUMO), and electron density (ESP) for compound (1) and

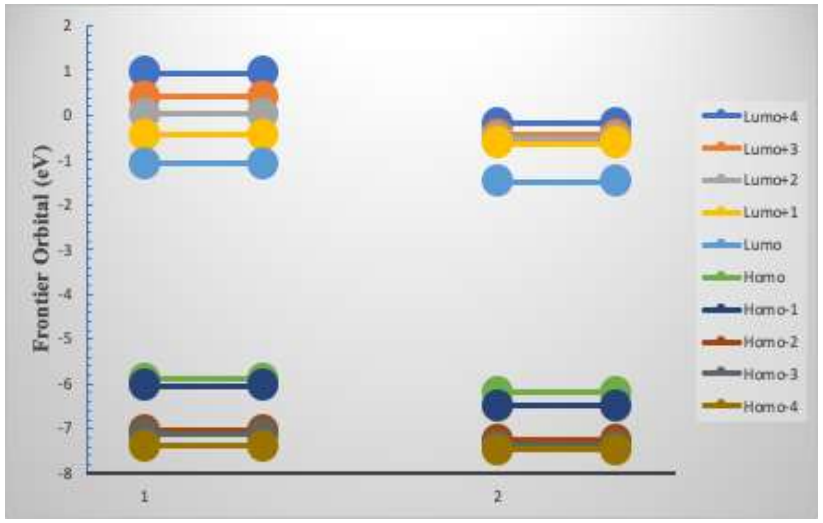

Figure 4. Energy gap between HOMO and LUMO for the two compounds

The chemical activity of the molecules is related to the energy gap where Table 2 shows the quantum chemical parameters such as E_{HOMO}, E_{LUMO}, polarizability, hardness, softness, chemical potential, and electrophilicity index for compound (1) and compound (2), using B3LYP/6-311G(d,p) in the gas phase.

Table 2. Some quantum chemical parameters

	E_{Homo}	E_{Lumo}	X (electro negativity)	η (hardness)	S (softness)	μ (chemical potentia)	ω (electrophilicity index)	ΔEn	ΔEe
1	-1.086	4.80	3.486	2.400	0.208	-3.486	2.532	0.246	7.219
2	-1.492	4.69	3.837	2.345	0.213	-3.837	3.140	0.474	8.150

The two molecular orbital energies of molecules close to E_{HOMO} and E_{LUMO} energy values have been presented in Figure 3. These values show E_{HOMO} and E_{LUMO} energy values changes with the changing R1 and R2 groups.

The electron-withdrawing or donating groups influence the E_{HOMO} and E_{LUMO} energies. In compound (1) (R1=methoxy and R2=H group) energy gap is -5.88 eV and less than compound (2).

The 2nd compound has more electronegativity than the 1st compound due to the presence of bromine groups in (R1, R2), on the other hand, the 1st compound can be considered harder than the 2nd compound according to the presence of hydrogen in R1 where the values were equal to η =2.345. On the other hand, the chemical potential seems to be greater in the 1st compound than the 2nd compound where the amount was -3.837, this result was because of the presence of (Me, and H) at (R1 and R2) respectively. As well as the electrophilicity index and electro-negativity had a bigger amount in the 2nd compound (0.474 and 8.150) respectively which were affected by the presence of (Br) at R2.

3.2. Thermodynamic properties

The full energy amount of the molecule can be shown through the total amount of the translation, rotational, electronic energies, and vibrational show where the less amount of energy has been calculated (SCF energy) was agreed with the optimized construction of the molecule (Fogolari et al., 2015).

Zero-point vibrational energy is the lowest acceptable amount of energy at the quantum mechanical system, and the desired amount of heat used to make the

temperature of any substance higher than the natural amount for one grade is "the capacity of heat" where The quantitative measurement of randomness in any system can be described as the entropy (Fogolari et al., 2015).

By using B3LYP/6-311G(d,p) basis set, the parameters of the ordinary statistical thermodynamic properties like enthalpy (H), heat capacity (C) and entropy (S), for the Benzimidazole derivatives were calculated from the theoretical coordination of the frequencies at the range of temperature 200-1000 K in a scale factor of 0.96 (Babu et al., 2011), as a standard range (Ford, 2016). Furthermore, following the equipartition theorem, the translational energy, rotational energy, and molecular vibrational intensities increase with increasing temperature, as a result, the thermodynamic functions increase with increasing temperature ranging from 200 to 1000 K as shown in tables (Chodera & Mobley, 2013). The linking equations between heat capacity, enthalpy, entropy, and temperature values changing were done by linear and quadratic formulas and the matching suitable factors (R2) for these thermodynamic properties as for (1) and (2) compounds, respectively, so by using these equations, without any further computational procedures, was clearly concluded that the characteristics of these compound at any change in any point of temperature, the thermodynamical parameters are linearly dependent on the temperature value (Wright, 1951; Sachin et al., 2011). The figures below illustrate the thermodynamic properties change due to the temperature changes with the correlation values for all compounds.

The correlation equations of (1) are as follows:

$$H= -6.39474+0.0456T +9.01951x10^{-5}T^2 ; (R^2 = 0.99972)$$

$$S= 65.66912+ 0.347T -6.86782x10^{-5}T^2 ; (R^2 = 0.99999)$$

$$C= -5.5146+ 0.36129T -1.50086x10^{-4}T^2 ; (R^2 = 0.99974)$$

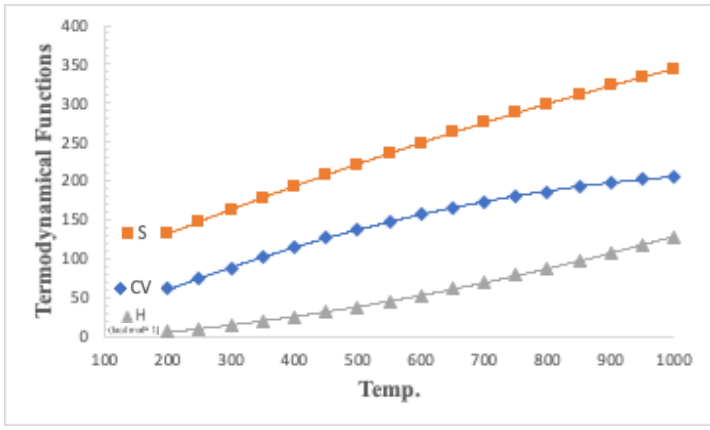

Figure 5. Correlation graphics of thermodynamic properties and temperatures for (1) compound.

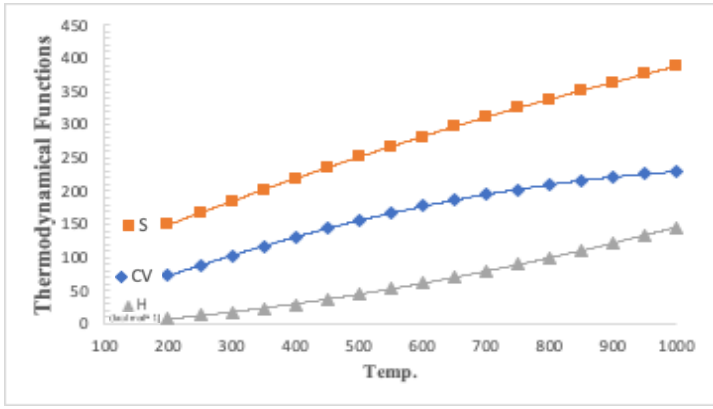

Figure 6. Correlation graphics of thermodynamic properties and temperatures for

(2) compound.

The correlation equations of (2) are as follows:

$$H = -6.71624 + 0.05271T + 8.16403 \times 10^{-5} T^2 \; ; (R^2 = 0.99973)$$

$$\text{“}S = 76.49348 + 0.35947T - 8.21179 \times 10^{-5} T^2 \; ; (R^2 = 1)$$

$$C = 3.65236 + 0.33617T - 1.43142 \times 10^{-4} T^2 \; ; (R^2 = 0.9997)$$

4. Conclusion

Through the optimization of benzimidazole derivates by using Lee-Yang-Parr correlation functional (B3LYP) and, our calculations indicated that the energy gaps values of HOMO vs LUMO in benzimidazole increased by Br substitution and were affected by the presence of the benzene ring in case of the second compound, these

changes led to modifications in the other chemical calculation that depends on energy gap values such as electrofugality ΔEe and nucleofugality ΔEn, chemical potential, chemical hardness, electrophilicity index, and electronegativity.

Density functional theory (DFT) B3LYP/6-311G (d,p) calculations were executed for further study on the properties of thermodynamic for the molecule, on the other hand, the parameters of thermodynamic properties like enthalpy, entropy, and heat capacity, were found to be increased with the increasing of the temperature, where the was raised from 200 K to 1000 K.

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