Yuzuncu Yil University
Journal of the Institute of Natural & Applied Sciences
https://dergipark.org.tr/en/pub/yyufbed

Research Article

Theoretical Investigation of Some Synthesized 3-Arylamino-5-[2-(Substituted 1-imidazole) Ethyl 1]-1,2,4-Triazole Derivatives

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Article Info

Received: 30.05.2022
Accepted: 12.09.2022
Online April 2023

DOI:10.53433/yyufbed.1123076

Keywords
Antimicrobial,
Chemical Parameters,
DFT,
Imidazole,
Nonlinear Optical Properties,
1,2,4-triazole

Abstract: In this study, quantum chemical calculations were made and interpreted to obtain chemical, nonlinear optical properties and antibacterial activity parameters of eight 1,2,4-triazole derivatives. In addition, the most stable structure was found in the B3LYP/6-311++G(d,p) method by optimizing the density functional theory of eight compounds. Based on the results of optimized molecules, HOMO-LUMO energies and chemical parameters calculated from these energy values (I.ionization potential, A: electron affinity, ΔE energy gap, χ: electronegativity, σ: molecular softness, η: molecular hardness, ω: electrophilic index, ε: nucleophilic index, μ: chemical potential) values were determined.

Bazı Sentezlenmiş 3-Arilamino-5-[2-(Sübstitüe Edilmiş 1-İmidazol) Etil 1]-1,2,4-Triazol Türevlerinin Teorik İncelenmesi

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Makale Bilgileri

Geliş: 30.05.2022
Kabul: 12.09.2022
Online Nisan 2023

DOI:10.53433/yyufbed.1123076

Anahtar Kelimeler
Antimikrobiyal,
DFT,
Doğrusal olmayan optik özellikler,
İmidazol,
Kimyasal parametreler,
1,2,4-triazole

Öz: Bu çalışmada, sekiz adet 1,2,4-triazol türevinin kimyasal, doğrusal olmayan optik özellikleri ve antibakteriyel aktivite parametrelerini elde etmek için kuantum kimyasal hesaplamaları yapılmış ve yorumlanmıştır. Ayrıca, sekiz bileşiğin en kararlı yapıları, yoğunluk fonksiyonel teorisinde B3LYP/6-311++G(d,p) kullanılarak optimize edilerek bulunmuştur. Optimize edilmiş moleküllere ait sonuçlardan yola çıkarak HOMO-LUMO enerjileri ve bu enerji değerlerinden hesaplanan kimyasal parametreler (I.iyonizasyon potansiyeli, A: elektron ilgisi, ΔE enerji aralığı, χ: elektronegatiflik, σ: moleküler yumuşaklık, η: moleküler sertlik, ω: elektrofilik indeks, ε: nükleofilik indeks, μ: kimyasal potansiyel) değerleri belirlendi.

1. Introduction

Heterocyclic compounds and their derivatives are widely found in nature. These molecules are used extensively in many fields such as paint industry, medicine and cosmetics. The triazole molecule and its derivatives, which is an important heterocyclic group, have been included in a comprehensive study area in recent years. Heterocyclic molecules containing a five-membered 1,2,4-triazole skeleton and their derivatives have attracted particular attention due to the increase in the study area. Scientific studies have shown that molecules containing 1,2,4-triazole ring in their structure have different biological properties such as antibacterial, antimicrobial, analgesic, antifungal, anti-inflammatory, antihypertensive, antiviral, anticancer and antioxidant (Malbec et al., 1984; Holla et al., 2003; Shaker et al., 2005; Salgın Gökşen et al., 2007; Amir et al., 2008; Bagihalli et al., 2008; Kuş et al., 2008; Eswaran et al., 2009; Ahmad et al., 2017; Gundlewad & Patil, 2018; Yüksek et al., 2020; Acosta et al., 2021).

Schiff bases can be synthesized from the triazole molecule and its derivatives. This groups of compounds have a wide range of uses in antifungal, antibacterial, anticancer, antiviral and many other biological fields (Chou & Talalay, 1984; Fletcher et al., 1986; Mishra et al., 1989; Invidiata et al., 1996; Singh et al., 2007; Mohamed et al., 2007; Rejhova et al., 2018).

In addition, highly selective fluorescent and colorimetric sensors, highly optically selective and electrochemically active chemosensors and similar studies have been carried out (Beytur et al., 2019; Irak & Beytur, 2019).

In this study, the optical properties of the 3-arylamino-5-[2-(substituted 1-imidazole)ethyl 1]-1.2.4-triazole molecule, which was previously synthesized experimentally, were calculated with the help of theoretical chemistry and antibacterial activity was calculated based on these properties.

2. Material and Methods

2.1. Material

Molecules in this study have entered the literature with an experimental study conducted by Demirayak et al. (2000). The synthesis route of 8 compounds used in the calculations is given in Figure 1.

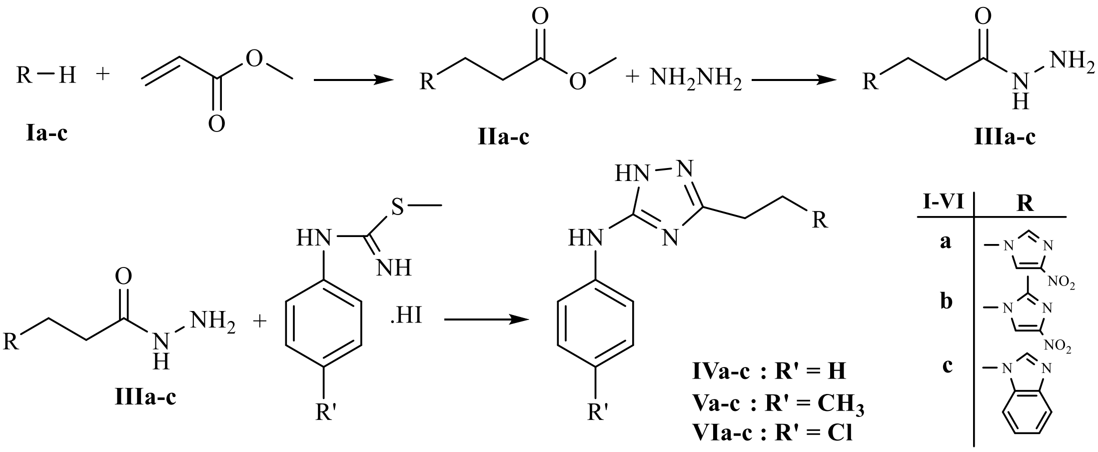


Figure 1. Synthesis scheme of calculated molecules is given (Demirayak et al., 2000).

2.2. Method

All molecules were plotted in GaussView5.0 molecular imaging software (Dennington et al., 2009); calculated with the help of Gaussian09W package program (Foresman & Frisch, 1996; Frisch et al., 2009). Ground state or excited states of molecules or atoms can be used in the theoretical calculation processes (Gümüş et al., 2015; Turhan Irak & Gümüş, 2017). Geometry optimizations of all molecules were carried out first with the MM2 method and then with the semi-experimental PM3, SCF molecular orbital (MO) method. Further geometric optimizations were calculated by selecting RHF and B3LYP/6-

31++G(d,p). The calculation results did not yield any negative frequency results (Turhan Irak & Gümüş, 2017; Manap & Medetalibeyoğlu, 2018).

The HP420WS desktop computer with Intel Xeon ® CPU E5–1650 v2Q 3.50 GHz X 12 64–bit 48 GIB is used in the calculations. Calculations were carried out on the WINDOWS operating system, with high-performance server systems (workstations).

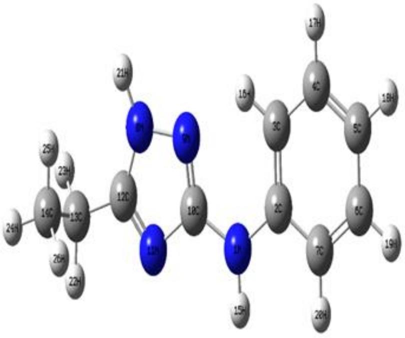
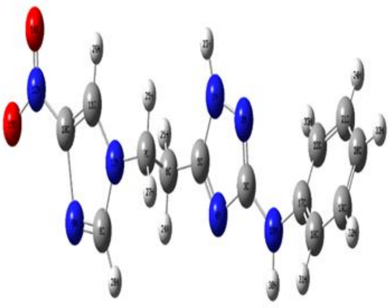
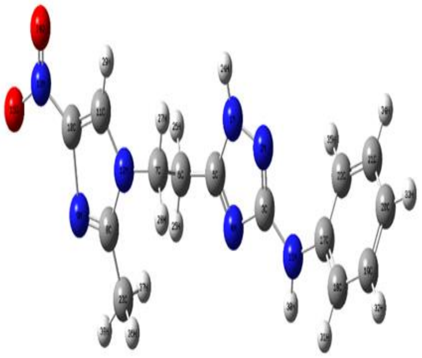
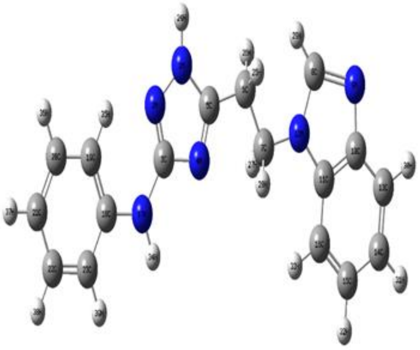
3. Results

With the development of modern computational simulation methods, specific features such as some orbital, optical, and structural, were able to be calculated accurately, and in many cases results comparable to experimental data were obtained (Zhou et al., 2013; Sebastian et al., 2013). HOMO-LUMO energies calculated from the optimized structures, energy differences and electronic data obtained from HOMO-LUMO energies “(I; Ionization potential, A; electron affinity, ΔE; Energy Gap, χ; electronegativity, σ; molecular softness, ω; Electrophilic Index, ε; Nucleophilic Index, μ; Chemical Potential)” values were determined. In the last step, the antimicrobial activity parameters of the molecules were calculated theoretically and compared with the experimental data by calculating the volume.

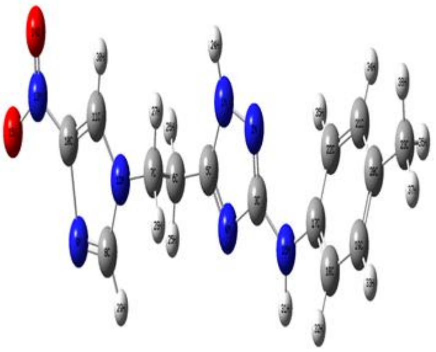
3.1. Calculated geometric optimization and energy results of molecules

As a result of the calculations, the IR and NMR values calculated from the optimized structure obtained for the AY-IVA molecule were compared with the available experimental data, and the most appropriate method and base set correlation coefficients were taken into consideration. The ground state optimized structures are given in Table 1.

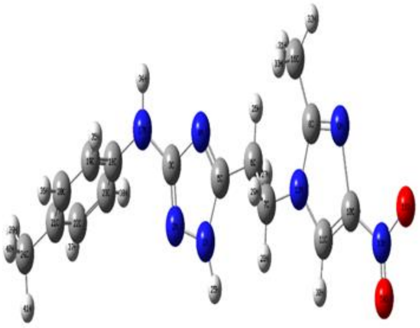
Table 1. Optimized structures using 6–311++g(d,p) basis set at DFT/B3LYP theory level in gas phase

AY	AY-IVA
	
AY-IVB	**AY-IVC**
	

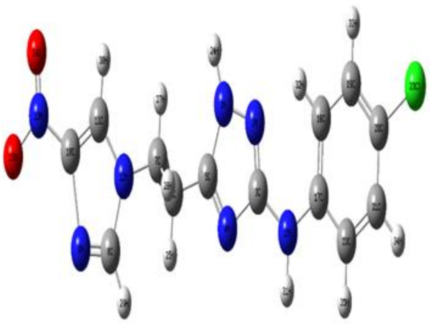
AY-VA



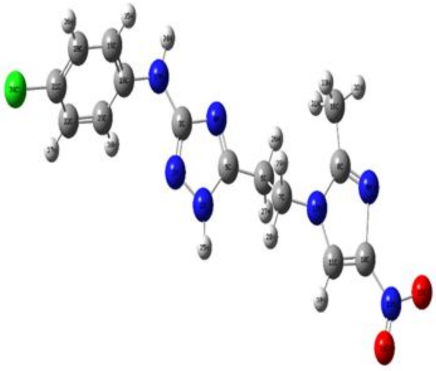
AY-VB



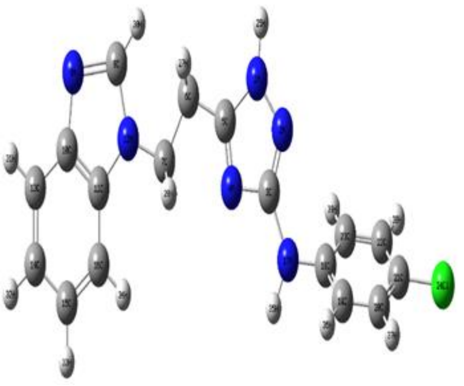
AY-VIA



AY-VIB



AY-VIC



In Table 2, the values recorded in the literature calculated in the gas phase "*3-Phenylamino-5-[2-(4-nitroimidazol-1-yl)-ethyl]1,2,4-triazole* **(IVa),** *3-Phenylamino-5-[2-(2-methyl-4-nitroimidazol-1-yl)-ethyl]1,2,4-triazole* **(IVb),** *3-Phenylamino-5-[2-(benzimidazol-1-yl)-ethyl]1,2,4-triazole* **(IVc),** *3-(4-Methyl)phenylamino-5-[2-(4-nitroimidazol-1-yl)-ethyl]1,2,4-triazole* **(Va),** *3-(4-Methyl)phenylamino-5-[2-(2-methyl-4-nitroimidazol-1-yl)-ethyl]1,2,4-triazole* **(Vb),** *3-(4-Chloro)phenylamino-5-[2-(4-nitroimidazol-1-yl)-ethyl]1,2,4-triazole* (**VIa**), *3-(4-Chloro)phenylamino-5-[2-(2-methyl-4 -nitroimidazol-1-yl)-ethyl]1,2,4-triazole* (**VIb**), *3-(4-Chloro)phenylamino-5-[2-(benzimidazol-1-yl)-ethyl]1,2,4-triazole* (**VIc**)" the energy values of the molecules calculated using the 6-311++g(d,p) basic set at the DFT/B3LYP theory level are given.

Table 2. Total energy values of the molecules calculated in the gas phase at the DFT/B3LYP theory level using the 6–311++g(d,p) basic set

Molecule	E_{total} (au)
AY	-607.46488
AY-IVA	-1037.0977
AY-IVB	-1076.4309
AY-IVC	-986.2213
AY-VA	-1076.4247
AY-VB	-1115.7578
AY-VIA	-1496.7201
AY-VIB	-1536.0533
AY-VIC	-1445.8439

When Table 2 is examined, it can be said that the energy decreases with the addition of the substituent and thus becomes more stable. The energy ranking is as follows:

$\mathbf{E_{total}}$: AY > AY-IVC > AY-IVA > AY-IVB = AY-VA > AY-VB > AY-VIC > AY-VIA > AY-VIB

Considering the above order, the addition of substituent according to the AY molecule has a positive effect on the energy.

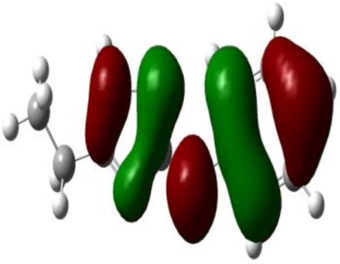
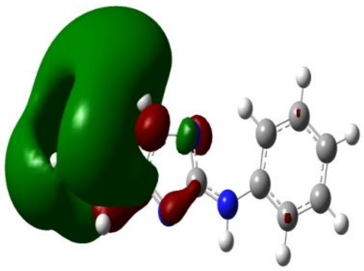
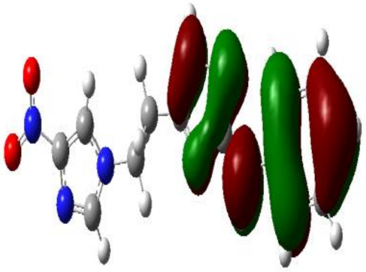
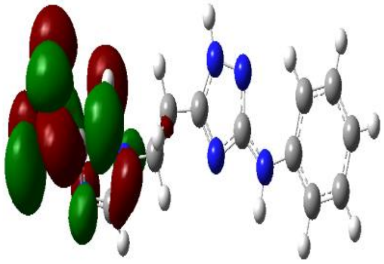
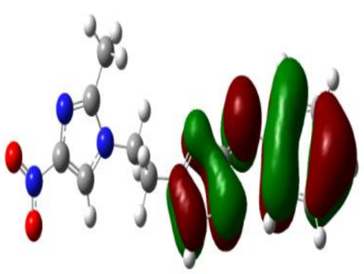
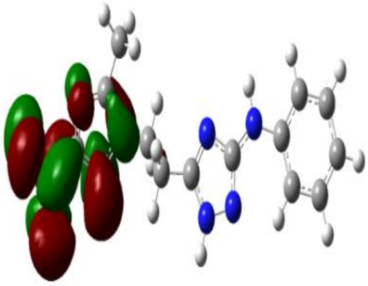
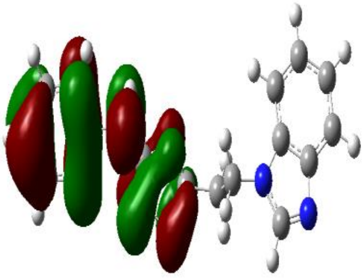
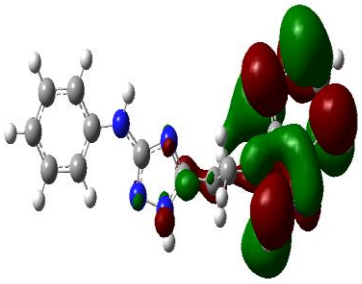
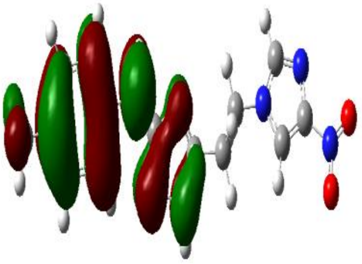
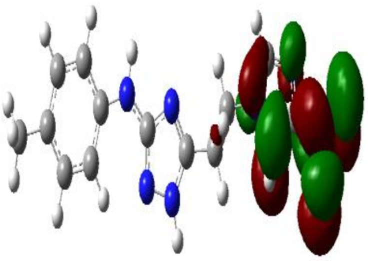
3.2. Frontier orbitals

The optimized ground state geometries and 3D boundary MO energy diagrams of the compounds are given in Table 2. Boundary molecular orbitals (MO) energy diagrams provide information about the reactivity of compounds. The highest occupied molecular orbital (HOMO) gives information about the basicity of the compound; The lowest unoccupied molecular orbital (LUMO) provides information about the acidity of the system. Therefore, it is important to investigate the boundary MOs of a molecule and to know which atoms contribute to these orbitals. The most important reason for this is; reactivity centers are determined by these energy schemes (Turhan Irak et al., 2019; Fukui, 1982).

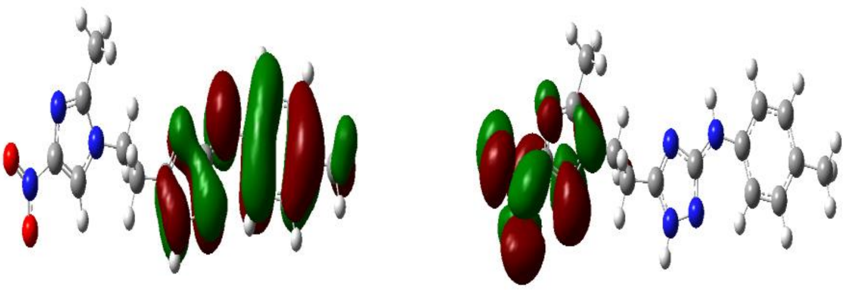
The HOMO and LUMO representations calculated by the 6-311++G(d,p) polarized basis set B3LYP method for the molecules whose structures were examined theoretically are given in Table 3.

As seen in the diagrams of IVA-VIB molecules in Table 3, HOMOs and LUMOs are separated from each other. The separation of HOMO-LUMO gives small exchange energies (Nakagawa et al., 2012; Mehes et al., 2012; Nasu et al., 2013; Gümüş & Gümüş, 2017). In the main structure (AY), HOMO-LUMO is dispersed into alkyl and Phenyl-(1H-[1,2,4]triazol-3-yl)-amine. When the HOMO-LUMO schemes of the other molecules in Table 3, which are formed by substitutions to the parent compound, are examined, it is seen that this distinction becomes more evident, as a result, it separates and is clearly dispersed.

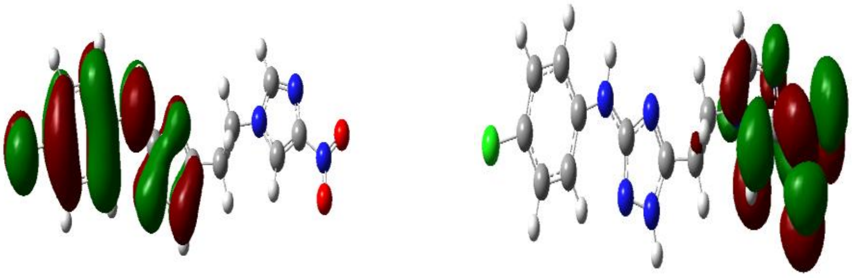
Table 3. HOMO and LUMO orbital surface views of molecules in the gas phase

Molecule	HOMO	LUMO
AY		
AY-IVA		
AY-IVB		
AY-IVC		
AY-VA		

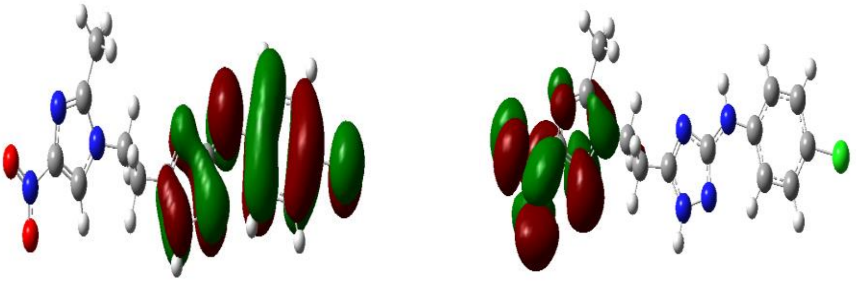
AY-VB



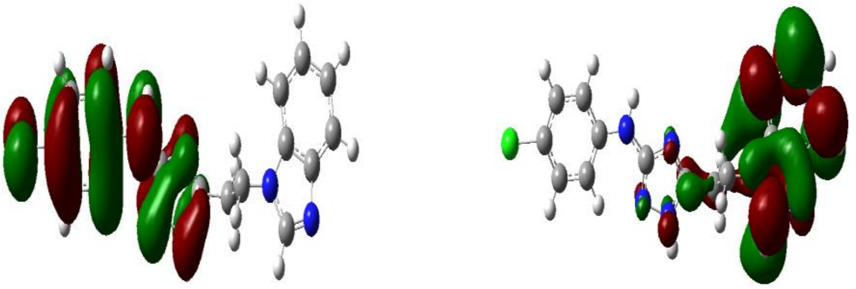
AY-VIA



AY-VIB



AY-VIC



3.3. Electronic structure identifiers

"Descriptors that depend on the electronic order and derive from the electronic structure of the compound are called electronic structure descriptors" (Koopmans, 1933). Some of them are "highest occupied molecular orbital energy (E_{HOMO}), lowest unoccupied molecular orbital energy (E_{LUMO}), LUMO-HOMO energy gap (ΔE), absolute hardness (η), absolute softness (σ), electronegativity (χ), chemical potential (μ), electrophilicity index (ω), nucleophilicity index (ε) and dipole moment (DM)". Of these descriptors, HOMO, LUMO and DM (Dipole Moment) are obtained from the Gaussian output file of the molecule.

Other descriptors can be calculated with the help of the equations found in the literature. According to Koopman's theorem, as seen from equations (1) and (2), the E_{HOMO} and E_{LUMO} values of any chemical species are related to its ionization energy and electron affinity values (Koopmans, 1933; Sastri & Perumareddi, 1997).

$$I = - E_{HOMO} \tag{1}$$

$$A = - E_{LUMO} \tag{2}$$

Energy gap (ΔE) (Jesudason et al., 2009), absolute hardness (η) (Gökçe & Bahçeli, 2011), absolute softness (σ) (Arivazhagan & Subhasini, 2012), electronegativity (χ) and chemical potential (μ) (Masoud et al., 2012) It can be calculated by equation 3-7.

$$\Delta E = E_{LUMO} - E_{HOMO} \tag{3}$$

$$\eta = I - A / 2 \tag{4}$$

$$\sigma = 1 / \eta \tag{5}$$

$$\chi = I + A / 2 \tag{6}$$

$$\mu = -\chi \tag{7}$$

R. G. Parr and colleagues proposed an identifier defined as the electrophilicity index (ω). According to Parr & Yang (1989) “electrophilicity index is a measure of the energy decrease due to the maximum electron flow between the donor and the acceptor” and is given as in equation 8.

$$\omega = \mu 2 / 2\eta \tag{8}$$

$$\varepsilon = \mu \, x \, \eta \tag{9}$$

Table 4. Some electronic structure descriptors calculated in gas phase for optimized molecules

	E_{HOMO}									

	E_{HOMO} (eV)	E_{LUMO} (eV)	ΔE (eV)	η (eV)	σ (eV^{-})	χ (eV)	μ (eV)	ω (eV)	DM (D)	ε (eV^{2})
AY	-5,49	-0,59	4,90	2,45	0,40	3,04	-3,04	1,89	3,62	-7,46
AY-IVA	-5,94	-2,56	3,38	1,69	0,59	4,25	-4,25	5,34	6,43	-7,18
AY-IVB	-5,92	-2,44	3,48	1,74	0,57	4,18	-4,18	5,02	6,57	-7,29
AY-IVC	-5,75	-1,00	4,74	2,37	0,42	3,37	-3,37	2,40	1,55	-8,01
AY-VA	-6,04	-2,81	3,22	1,61	0,61	4,43	-4,43	6,08	8,13	-7,16
AY-VB	-6,03	-2,67	3,35	1,67	0,59	4,35	-4,35	5,65	8,17	-7,31
AY-VIA	-6,04	-2,60	3,44	1,72	0,58	4,32	-4,32	5,43	4,26	-7,45
AY-VIB	-6,03	-2,48	3,55	1,77	0,56	4,26	-4,26	5,11	4,47	-7,57
AY-VIC	-5,87	-1,06	4,80	2,40	0,41	3,46	-3,46	2,49	1,11	-8,33

Electronic structure descriptors of 8 molecules registered in the literature, including the studied main structure and reference molecules, are given in Table 4.

3.4. HOMO and LUMO energies

According to Koopmans theorem, “HOMO energy is directly related to ionization potential and LUMO energy is directly related to electron affinity. If the HOMO is high-energy, such a molecule has a high tendency to donate electrons. If the LUMO is of low energy, such a molecule has a high tendency to gain electrons. In other words, HOMO water with high energy can be considered as a good Lewis base, and LUMO water with low energy can be considered as a good Lewis acid” (Sayın & Karakas, 2013).

The HOMO energies in Table 4 for the investigated compounds; $\mathbf{E_{HOMO}}$**:** AY > AY-IVC > AY-VIC > AY-IVB > AY-IVA > AY-VB ≅ AY-VIB > AY-VIA ≅ AY-VA while decreasing during: LUMO energies; $\mathbf{E_{LUMO}}$**:** AY-VA < AY-VB < AY-VIA < AY-IVA < AY-VIB < AY-IVB < AY-VIC <

AY-IVC < AY increases during. It has been observed that the addition of substituent changes the boundary orbital energies according to the main structure and is effective. When the compounds obtained during the addition reactions are evaluated among themselves, no significant changes are observed in the HOMO values; A great difference was observed in LUMO values. It was observed that LUMO energy values changed with the effect of the substituent.

3.5. Energy gap (ΔE)

The energy gap of a molecule depends on the LUMO and HOMO energies of the molecule and is calculated from the equation in equation 3 ($\Delta E = E_{LUMO} - E_{HOMO}$). The HOMO-LUMO energy gap is a parameter needed to explain molecular properties (Lewis et al., 1994). The energy gap value of a molecule is used to measure the activity of the molecule against another molecule. When the compounds are evaluated among themselves;

ΔE: AY > AY-VIC > AY-IVC > AY-VIB > AY-IVB > AY-VIA > AY-IVA > AY-VB > AY-VA decreases during.

When paying attention to the table; The energy gap values of the compounds decreased compared to AY. It has been observed that the addition of substituent changes the energy gap value as in the boundary orbitals. Since the gap between HOMO and LUMO energy values is defined as the chemical stability of the molecule, the closer this energy gap is to each other, the easier the interaction will be. Thus, the smaller the energy, the easier it will be for the reactants to interact and react. Among the results obtained, AY-VA compound has the lowest energy gap. This compound, respectively; Compounds AY-VB, AY-IVA and AY-VIA follow.

3.6. Hardness (η), softness (σ), electronegativity (χ), and chemical potential (μ)

Hardness is a measure of the polarizability of a chemical species. Lewis acids and bases can be classified as hard or soft. If the electron cloud of a chemical species is strongly attracted by the nucleus, it is soft if not by hard force. Therefore, hard species have low polarizability and soft species have high polarizability. According to the concept of hard and soft acids and bases (HSAB), hard acids interact more strongly with hard bases, and soft acids interact more strongly with soft bases (Sayin & Karakaş, 2017).

η: AY > AY-VIC > AY-IVC > AY-VIB > AY-IVB > AY-VIA > AY-IVA > AY-VB > AY-VA
σ: AY < AY-VIC < AY-IVC < AY-VIB < AY-IVB < AY-VIA < AY-IVA ≅ AY-VB < AY-VA

Mulliken electronegativity is the arithmetic mean of the ionization energy and electron affinity of the chemical species. Species with low electronegativity tend to donate more electrons. The chemical potential is defined as the partial molar Gibbs free energy, the opposite of electronegativity. In that case, it can be said that the efficiency of the substance with low chemical potential against other substances is low (Kaya et al., 2014).

χ: AY-VA > AY-VB > AY-VIA > AY-VIB > AY-IVA > AY-IVB >AY-VIC > AY-IVC > AY
μ: AY-VA < AY-VB < AY-VIA < AY-VIB < AY-IVA < AY-IVB < AY-VIC < AY-IVC < AY

In the light of this information, AY-5A compound has the highest η and χ values. Likewise, the compound with the lowest σ and μ values, respectively, is AY-VA. Compounds AY-VB and AY-VIA follow. It was determined that the AY-VA molecule was softer when compared with other molecules in terms of Hardness (η) and Softness (σ). This showed that this molecule can be polarized more easily. AY-VA (μ) indicates that the molecule with a low chemical potential has a lower effectiveness against other substances. In addition, the molecule with low electronegativity has a higher tendency to donate electrons AY (χ). Theoretical methods used to calculate the hardness and softness parameters, which cannot be found experimentally, give very good results. With the obtained data, the high hardness and low softness data of the molecules show that the chemical activity is low and the kinetic stability is high. This trend is quite consistent with the ΔE rank.

3.7. Electrophilicity (ω) and nucleophilicity (ε) index

The electrophilicity index is a descriptor proposed by Parr & Yang (1989). This descriptor is the numerical expression of the spherical electrophilic power of a molecule. The electrophilicity index of the molecule provides quantitative classification of its reactivity (Kiyooka et al., 2013).

ω: AY-5A > AY-5B > AY-6A > AY-4A > AY-6B > AY-4B > AY-6C > AY-4C > AY

When compared with other molecules, the electrophilic index of the AY-5A(ω) molecule was determined to be higher, which indicates that this molecule is more reactive. The nucleophilicity index is a numerical expression of the electron donating ability of the molecule (Erkan Kariper et al., 2014).

ε: AY-VA >AY-IVA>AY-IVB >AY-VB>AY-VIA>AY>AY-VIB>AY-IVC >AY-VIC

The decreasing electrophilicity index and increasing nucleophilicity index of the molecule play an important role in its efficiency. When Table 4 is examined, it is seen that there is a linear trend between the ω and ε values of the compounds and the ΔE η, σ, χ and μ values.

3.8. Dipole moment (DM)

The dipole moment, a measure of its polarity, is given in debye (D) units. The increase in polarity parallels the increase in dipole moment. The electronic structure parameters change according to the differences in the molecular structure, and the activities of the compounds can be correlated with these parameters.

DM: AY-VB>AY-VA>AY-IVB>AY-IVA>AY-VIB>AY-VIA>AY>AY-VIA>AY-IVC> AY-VIC

According to the results given above, it is possible to talk about high dipole interaction in the AY-VA molecule.

3.9. Non-linear optical (NLO) properties

Average linear polarizability (α), anisotropic polarizability (Δα) , primary hyperpolarizability (β_0) parameters are used to predict the NLO properties computationally. α; is the average linear polarizability (Govindarajan et al., 2012). Molecules with large polarizability in a given electric field have large induced dipole moments. The components of polarizability (Δα) in the direction of x, y and z coordinates are calculated with the following

Equation 10 from the outputs of the average linear polarizability calculation program as α_{xx}, α_{yy} and α_{zz}.

$$\alpha = 1/3(\alpha_{xx}+\alpha_{yy}+\alpha_{zz}) \tag{10}$$

Primary hyperpolarizability (β_0) is the first derivative of polarizability with respect to the applied electric field. Primary hyperpolarizability is calculated by equation 11 from the β_0 components obtained from the calculation methods.

$$\beta_0 = [(\beta_{xxx}+\beta_{xyy}+\beta_{xzz})^2 + (\beta_{yyy}+\beta_{xxy}+\beta_{yzz})^2 + (\beta_{zzz}+\beta_{xxz}+\beta_{yyz})^2]^{1/2} \tag{11}$$

The polarizability (α), and hyperpolarizability (β_0) values calculated using the molecule are given Table 5.

Table 5. NLO values calculated using the 6–311++G(d,p) basis set at the DFT/B3LYP theory level

	α ($x10^{-24}$ esu)	**$β_0$ ($x10^{-30}$ esu)**
AY	152.591	0.452
AY-IVA	221.703	0.787
AY-IVB	235.143	0.896
AY-IVC	250,373	0.508
AY-VA	237,456	0.732
AY-VB	250.660	0.864
AY-VIA	237.507	0.896
AY-VIB	250.995	0.982
AY-VIC	266.375	0.929

In organic-based materials, optical properties are defined by polarizability. Hyperpolarizability is a quantity that affects the performance of nonlinear optical properties of matter (Papadopoulos et al., 2006). In order for a molecule to show NLO properties, it is desired that polarizability, hyperpolarity and dipole moment are high, and the HOMO-LUMO energy difference is small.

When polarity is maximum, the HOMO-LUMO energy difference is minimum; At the point where the hyperpolarizability is maximum, the dipole moment should also be maximum. Looking at the polarizability and hyperpolarity values in Table 5, when the polarity is high, the HOMO-LUMO energy difference is low; It has been observed that the dipole moment is maximum when the hyperpolarizability is high. Urea is used as a reference in compounds with nonlinear optical properties. The hyperpolarity value of urea was calculated at the DFT/B3LYP theory level on the basis of 6–311++G(d,p) and was found to be 0.766x10-30 esu. When Table 5 is examined, it is seen that except AY AY-4C and AY-5A compounds have higher hyperpolarity values than urea. It can be said that molecules with a higher $β_0$ value of urea can be used as optical materials (Beytur & Avinca, 2021).

3.10. Antibacterial properties

Its antibacterial activity is described by the descriptive LUMO and density function. LUMO is a parameter that describes the electronegativity and reactivity of a molecule. Molecules with low capacity LUMO can accept electrons more than molecules with high capacity LUMOs and as a result show higher activity. Density indicates how tightly atoms are packed into a molecule; calculated as the ratio of molecular weight and molecular volume. Density is negatively correlated with reactivity hence activity. Thus, a molecule with a lower density will have higher activity (Khan et al., 2017).

Table 6. Antibacterial molecular descriptive parameters of the compounds calculated using the DFT/B3LYP/6-311++G(d,p) method

	E_{LUMO} (eV)	**m**	**v**	**d**
AY	-0.59	188.100	148.651	1.26
AY-IVA	-2.56	299.113	208.273	1.43
AY-IVB	-2.44	313.128	247.246	1.26
AY-IVC	-1.00	304.143	205.698	1.47
AY-VA	-2.81	313.128	201.300	1.55
AY-VB	-2.67	327.144	276.223	1.18
AY-VIA	-2.60	333.074	236.738	1.40
AY-VIB	-2.48	347.089	215.365	1.61
AY-VIC	-1.06	338.104	240.633	1.40

Total energy, LUMO, molecular weight and volume were calculated to examine the correlation between molecular properties (Table 6) and antibacterial activities to gain insight into the structure-activity relationship.

AY-VIA, AY-VB, AY-VA**;** it is thought that AY-VIA, AY-VB, AY-VA molecules show more antibacterial activity compared to other molecules.

Antibacterial activity is described on the basis of density and function of LUMO descriptors. Looking at the results in the table, it can be said that the compounds show antimicrobial activity as a result of theoretical calculations. The reason for this can be explained as follows: LUMO energy values of eight compounds formed by the addition of substituent to AY compound are lower than that of AY (-0.59 eV). Therefore, microbial activity can be considered in all molecules. In addition, when the density values are examined, it is observed that AY-IVB and AY-VB (1.26 g cm^{-3} and 1.18 g cm^{-3}) compounds are approximately equal to and lower than the density value of AY compound (1.26 g cm^{-3}). It is seen that the density values of other compounds are higher than that of AY. On the other hand, it is thought that AY-IVB and AY-VB molecules may show activity in this context. It is known that the membrane of bacteria is surrounded by an outer membrane containing lipopolysaccharides. Due to the high electrophilic and reactivity measured by LUMO, all the molecules studied seem to be able to associate with the lipophilic layer to increase the permeability. According to the theoretically calculated density results, AY-VB has the lowest concentration (1.18 g cm^{-3}) among the compounds, and therefore it can be expected to show higher antibacterial activity. Besides AY-VB, it can be said that AY-IVB may show higher activity compared to other molecules.

Experimental antimicrobial activities of IV(A-C), V(A-B), VI(A-C) compounds in the study conducted by Demirayak et al. (2000) using tube dilution technique, Staphylococcus aureus, Micrococcus luteus, Escherichia coli B, Pseudomonas aeroginosa, Candida albicans and Candida observed against glabrata fungi. They were tested against 6 microorganisms and their activities against Chloramphenicol succinate were evaluated. Considering the results, it was concluded that “some of the products tested had significant antibacterial activities. Most of the compounds have MIC values of 62.5 or 125 mg mL^{-1} against these microorganisms. However; unfortunately, no correlation could be detected between the substituents and biological activities of the compounds. The activities of the compounds against bacteria differed. As a result, it can be said that the antimicrobial activity results calculated theoretically are in harmony with the experimental studies.

4. Conclusion

Molecules with different functionalizations were calculated using the DFT/B3LYP/6-311++G(d,p) base set. The following results were obtained from the calculations made.

1. It can be said that the energy decreases and thus becomes more stable with different addition reactions such as hydrogen, methyl, 4-nitro imidazole, 2-methyl 4-imidazole and benzimidazole.
2. Addition reactions affect the total electronic energy. When looking at the HOMO-LUMO schemes, it is clearly observed that changes occur with the addition of the substituent.
3. It has been observed that some addition reactions change the boundary orbital energies with respect to the main structure and are effective. When the additions were evaluated among themselves, no great changes were observed between the HOMO values of the compounds, but significant differences were determined in the LUMO values. It can be said that the LUMO energy values changed with the effect of the substituent.
4. Energy gap (ΔE) values have decreased. However, it still showed that it is in a very stable form with wide energy band gap, low chemical activity, high kinetic stability.
5. With the data obtained, the high hardness and low softness data of the molecules show that the chemical activity is low and the kinetic stability is high. This trend is quite consistent with the ΔE rank. Likewise, ω and ε values of the compounds showed a linear trend with the results of ΔE, η, σ, χ and μ as a result of the calculations.
6. The electronic structure parameters change according to the differences in the molecular structure and the activities of the compounds can be correlated with these parameters. It can be said that the polarity increases with the substituent effect.
7. Considering the NLO properties, the α values are in agreement with the dipole moment values. It is seen that except AY-IVC, AY-VIC and AY-VIB compounds have higher

hyperpolarity values than urea. It can be said that molecules with a β_0 value of urea can be used as optical materials.

According to the theoretically calculated density results, AY-VB has the lowest concentration (1.18 g cm^{-3}) among the compounds, and therefore it can be expected to show higher antibacterial activity. This calculated value shows parallelism with the experimental result.

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