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Structure reactivity analysis for Phenylalanine and Tyrosine

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Abstract

Phenylalanine (Phe) is one of the amino acids that cannot be produced in the body and must be ingested through diet. Tyrosine (Tyr) is also a non-essential amino acid and can be produced by Phe hydroxylation in the liver when the dietary intake of Tyr is low. Structure analysis is very important to know the correct synthesis and the reactivity of the molecule. In this study, the characterization of Phe and Tyr molecules were investigated using quantum chemical calculations. The molecular geometry for both molecules was determined using density functional theory (B3LYP) by handling the 6-311++G(d,p) basis set. The method of TD-DFT which is based on the B3LYP/6-31++G(d,p) level, was utilized in ethanol solvent to find the electronic absorption spectra. In addition, frontier molecular orbitals, electrostatic potential and molecular charge distributions analysis were carried out by B3LYP/6-311++G(d,p) theory. The energy differences between HOMO and LUMO for Phe were obtained as 0.19851 eV, which have a good argument with the reactivity compared with tyrosine, and energy band gap was 0.20501 eV.

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1. Introduction

The kinetics of Phe and Tyr were studied in humans [1]. The amino acids have been studied, to determine their biological and chemical properties. Additionally, in optoelectronic, they have a wide range of applications [2, 3]. In biology, Phe and Tyr are two organic compounds that have some fundamental differences in their structures. Both molecules have an NH2 group (amino), a COOH group (carboxylic acid), and a radical group (R-group) [4]. Generally, the amino acids family has been classified as polar and nonpolar, whereby Phe and Tyr belong to the nonpolar and the polar groups, respectively [5]. Tyr has one more hydroxide bonded with a phenyl ring compared to a Phe molecule Figure 1. In addition, they have some isomers with the same composition, but different geometry.

L-Phe is an isomer of Phe molecules that can be naturally found, while, D -Phe is an artificial product.

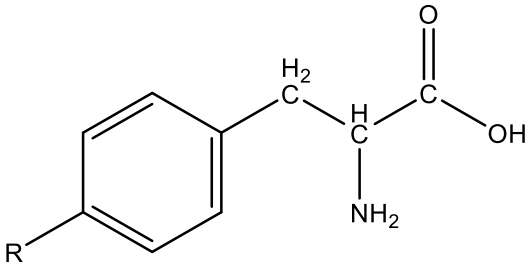

Figure 1. The chemical structure of phenylalanine (when R represents H) and Tyrosine (when R represents OH)

Similarly, Tyr has also L and D chemical structures. Amino acids are nonlinear optical biomolecules that can change the direction of electromagnetic radiation. Theoretical and experimental measurements, such as deuterium NMR [6], FT-IR, and Raman spectrometry [4, 7] have been carried out to determine structurally and some other properties of L-Phe and L-Tyr. Freire et al. [4] studied the vibrational behavior of all kinds of amino acids, includes L-Phe and L-Tyr, through the Raman spectrum.

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Density functional theory (DFT) is commonly used to study the electronic properties of organic compounds, molecular structure, chemical reactivity, and hydrogen bonding [8-11]. Among all of the approaches, the energy correlation is the main advantage in the DFT; accordingly, the estimated exchange nature energy coordination has a direct effect on the confidence. The DFT methods are creative exchange energy management, therefore, in many theoretical kinds of research DFT methods were used regularly [12, 13]. There are rare or no studies in which extensively make comparisons between L-Phe and L-Tyr molecules. Therefore, this study can cover these two amino acids from many points of view and it can make many contributions to the literature.

In this study, a theoretical computation based on the DFT technique has been carried out for Phe and molecules using the Gaussian 09W. The geometrical, charge distribution, and vibrational properties of these biomolecules have been compared in their ground states and the same conditions. The results have been compared to experimental results in the literature.

2. Computational Methods

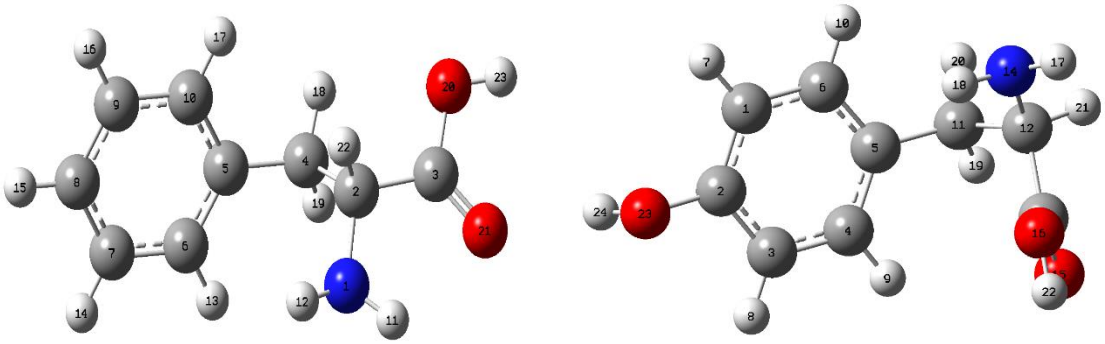
Gaussian 09W software package was used for computations based on DFT with a B3LYP hybrid functional and 6-311++G(d,p) basis set [14, 15]. The conformational and molecular energy profile was found by used B3LYP/6-311++(d,p) [16]. The molecular electrostatic potentials were assessed using the B3LYP/6-311++G(d.p) method to examine the reactive sites of our compounds. Also, frontier molecular orbitals parameters were performed for both compounds on the basis set of B3LYP/6-311++G(d,p).

3. Results and Discussion

3.1. Molecular geometry

The B3LYP/6-311++G(d,p) system acquires the best study for optimal geometry. Figure 2 shows the scheme of chemical composition and geometry of the L-Phe and L-Tyr molecules. Several molecular properties such as the dipole moment and spectroscopic transitions can be utilized by molecular symmetry. Both Phe and Tyr are aromatic due to the delocalization of the continued electrons in the benzene ring. The bond length for C-C and C=C in a benzene ring is equal to 1.54 and 1.40 Å, respectively, while the bond length for C=C (from ethylene) is equal to 1.34 Å [17]. For the DFT calculation using B3LYP/6-311++G(d,p), the bond length for C-C and C=C (in benzene ring) for our compounds was 1.51 and 1.39 Å, respectively. The bond length for C-N in both structures was 1.45 Å, which is consistent with the previous studies [18].

The C=O bond length for was equal to 1.231622 Å which is a little be smaller than C=O in Tyr equal to 1.233 Å. The bond length for C-O for both compounds is equal to 1.378 Å. It can be seen that in the geometrical structure in Figure 2. The result showed they are very different in the rotation of the atoms in a molecule, which means the bond angle and the dihedral were very different for both Phe and tyrosine. The values for the calculated geometric parameters are shown in Table 1.



(a) (b)

Figure 2. The theoretical geometrical structure of a) the phenylalanine and b) the Tyrosine with B3LYP/6-311++G(d,p).

Table 1. Geometrical parameters of Phenylalanine and Tyrosine by B3LYP/6-311++G(d,p).

phenylalanine		Tyrosine	
Parameters	6-311++G(d,p)	Parameters	6-311++G(d,p)
Bond Length		Bond Length	
N(1)-C(2)	145.487	C(1)-C(2)	139.381
C(2)-C(3)	151.182	C(2)-C(3)	139.418
C(2)-C(4)	156.092	C(3)-C(4)	139.676
C(4)-C(5)	151.385	C(4)-C(5)	140.584
C(5)-C(6)	140.397	C(1)-C(6)	139.746
C(6)-C(7)	139.847	C(5)-C(11)	151.573
C(7)-C(8)	139.779	C(11)-C(12)	155.857
C(8)-C(9)	139.854	C(12)-(13)	152.950
C(9)-C(10)	139.726	C12-N(14)	145.516
C(3)-O(20)	137.844	C(13)-O(15)	123.369
C(3)-O(21)	123.162	C(13)-O(16)	137.802
C(2)-O(23)		C92)-O(23)	141.725
Bond Angles (°)		Bond Angles (°)	
N(1)-C(2)-C(3)	10.871.990	C(1)-C(2)-C(3)	12.053.109
N(1)-C(2)-C(4)	11.171.210	C(2)-C(3)-C(4)	11.958.521
C(2)-C(4)-C(5)	11.211.240	C(3)-C(4)-C(5)	12.102.014
C(4)-C(5)-C(6)	12.112.410	C(2)-C(1)-C(6)	11.953.222
C(5)-C(6)-C(7)	12.078.110	C(4)-C(5)-C(11)	12.093.766
C(6)-C(7)-C(8)	12.021.650	C(5)-C(11)-C(12)	11.430.130
C(7)-C(8)-C(9)	11.957.120	C11-C12-C13	10.953.644
C(8)-C(9)-C(10)	12.008.260	C11-C12-N14	11.131.945
C(2)-C(3)-O(20)	11.223.110	C12-C13-O15	12.460.178
C(2)-C(3)-O(21)	12.577.080	C12-C13-O16	11.358.959
		C1-C2-O23	11.966.523
Dihedral Angles (°)		Dihedral Angles (°)	
C(3)-C(2)-C(4)-C(5)	6.387.876	C4-C5-C11-C12	-8.988.074
C(2)-C(4)-C(5)-C(6)	-9.329.010	C11-C12-C13-C16	12.689.600

3.2. Frontier molecular orbitals

The principle characterizing of the molecular orbital is the relationship between HOMO and LUMO with HOMO-1 and LUMO+1. In quantum chemistry, the frontier molecular orbital theory is critical [19]. The maximum straight-forward of such interactions, which helps to identify molecular qualities, is the one linked to the discrepancy between a natural system's highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) [20, 21].

The LUMO energy is associated with the affinity of the electrons and defines how sensitive the molecule to the nucleophilic attack. The HOMO energy is linked to the potential for ionization and defines how sensitive the molecule is to an electrophilic attacked [22, 23]. The chemical activity of the compound is generally indicated by the HOMO and LUMO energy values and the potential differences between them.

The small energy difference between HOMO and LUMO denotes a robust interaction and rapid reaction. Figure 3 shows the arrangement and energy levels of orbitals, including HOMO-1, HOMO, LUMO, and LUMO+1, which determined by a B3LYP/6-311++G(d,p) level for Phe and tyrosine. The results show that the higher energy level between HOMO and LUMO was appeared in Tyr molecule compared with

Phenylalanine, while the energy level between HOMO-1 and LUMO+1 for both compounds are closed to each other. The energy gap for Phe and Tyr are 0.19851eV and 0.20501 eV, which indicates that Phe molecule has more reactivity compared to Tyr molecule this is due to lower energy bandgap.

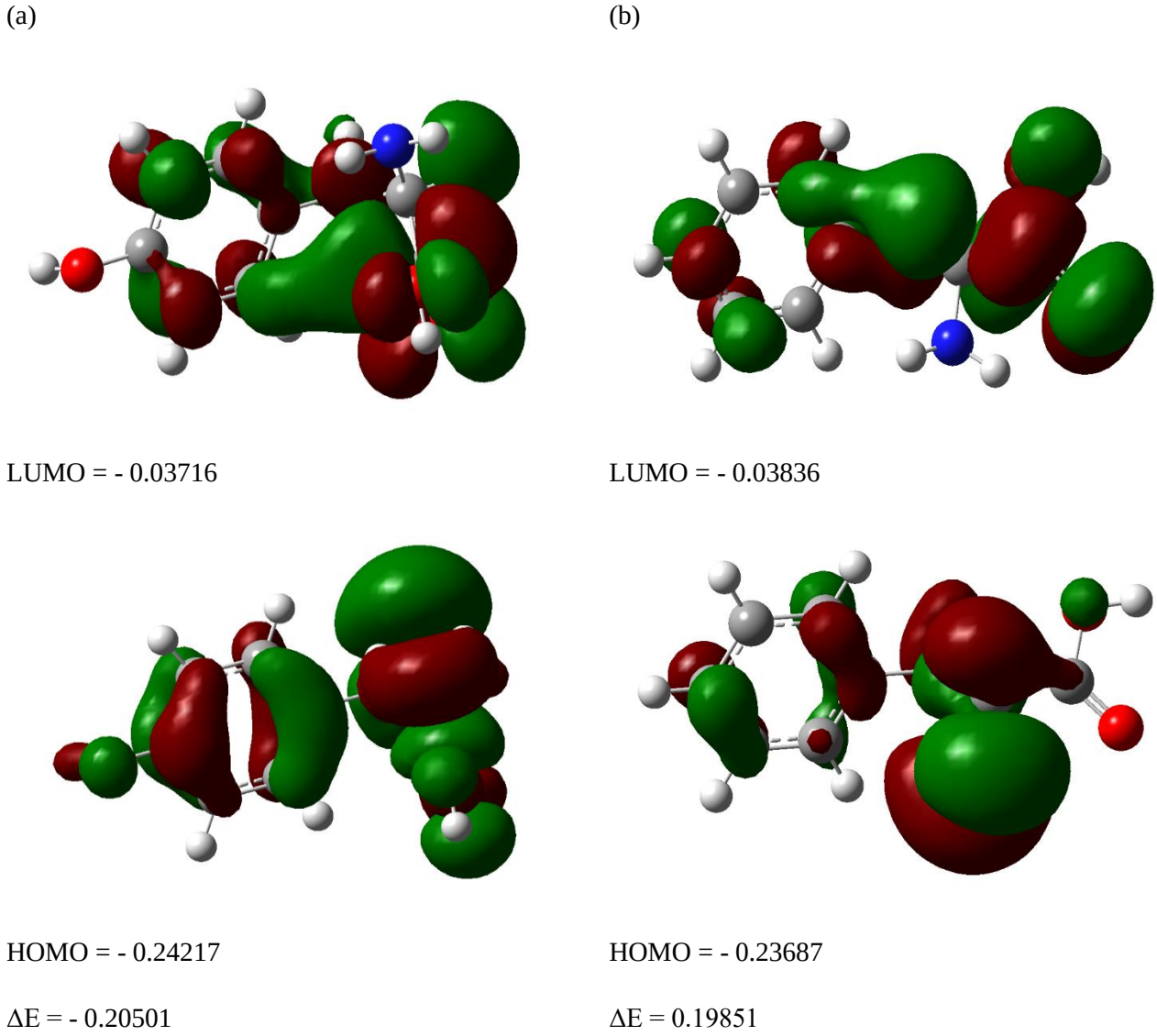


Figure 3. Molecular orbital surfaces and energy levels for the HOMO and LUMO analysis by B3LYP/6-311++G(d,p) a) Tyrosine b) phenylalanine

Various molecular parameters can be calculated based on the HOMO and LUMO energy values [24]. The minimum amount of energy required to eliminate an electron in a gaseous state from the atom or molecule is known as the ionization potential which is expressed as $I=-E_{HOMO}$, also the amount of energy expelled as a result of one electron being added to a gaseous molecule is called electron affinity ($A=-E_{LUMO}$) [25, 26]. The predilection of a nuclear to draw electrons is known as electronegativity (X) [27]. The prevention of weight transfer in a molecule is denoted by chemical hardness (η) [28]. Table 2 shows the electronic structure parameters, which determined using the B3LYP/6-311++G(d,p) technique. The results show that the hardness of Phe less than Tyr molecule.

Table 2. Electronic parameters for both Phe and Tyr.

In a Basis Set B3LYP/6-311++G(d,p)	Equations	Result of phenylalanine	Result of Tyrosine
E_{LOMO+1} (eV)	E_{LOMO+1} (eV)	-0.02107	-0.02444
E_{LOMO} (eV)	E_{LOMO} (eV)	-0.03836	-0.03716
E_{HOMO} (eV)	E_{HOMO} (eV)	-0.23687	-0.24217
E_{HOMO-1} (eV)	E_{HOMO-1} (eV)	0.25743	0.25444
$\Delta E = E_{HOMO} - E_{LOMO}$ (eV)	HOMO - LOMO	-0.19851	-0.20501
$\Delta E = E_{HOMO-1} - E_{LOMO+!}$ (eV)	(HOMO-1) – (LOMO+1)	-0.23636	-0.23000
I (eV)	$I= - E_{HOMO}$	0.23687	0.24217
A (eV)	$A= - E_{LUMO}$	0.03836	0.03716
X (eV)	X= 1+A/2	0.51918	0.51858
n (eV)	n = 1-A/2	0.48082	0.48142
S (eV)	S = 1/2n	1.03989	1.03859
μ_{total}		0.68230	1.73720
μ_x		-0.09750	0.79250
μ_y		0.63660	1.37380
μ_z		-0.22530	-0.70900

3.3. UV–Vis spectral studies

The electronic absorption is primarily defined by one electron excitation from HOMO to LUMO, which is equivalent to the transition from ground to the first excited state. Typically, the categorization of electronic transitions is based on the orbitals involved or certain sections of the molecule concerned [29, 30]. The most frequent electronic transfer occurred in organic molecules from π (donor) – π* (acceptor). The source of the absorption in organic compounds causes the vibration of the electrons from the ground state to excited state [31, 32]. According to the Franck Condon principle, the maximum absorption peak was equivalent to the vertical excitation. Figure 4 reveals the UV spectrum measurement in ethanol. It was found that the first electron transition of Phe occurred at 276 nm with oscillator strength 0.0332 corresponding to H-1/L, the second transition occurred at 238 nm with 0.0046 oscillator strength, and the third on at 235 nm with 0.05 oscillator strength, corresponding to H-2/L. Figure 4b shows three electronic transitions of Tyrosine, which located at 274, 242, and 233 nm with oscillator strength 0.02, 0.0032, and 0.0079, respectively. The results approve that Tyr is a more stable compound because it has a less excitation energy compared by phenylalanine.

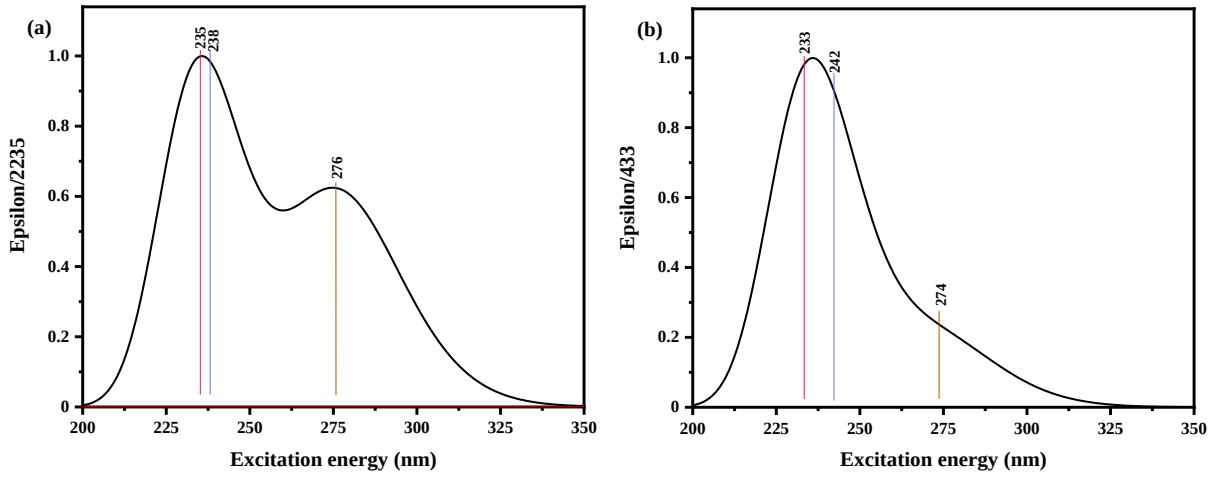


Figure 4. UV spectrum on the TD-DFT//B3LYP/6-311++G(d,p) level in ethanol a) Phenylalanine b) Tyrosine

3.4. Molecular electrostatic potential

Electrostatic potential map (EPM) shows the 3D charge distributions of molecules, which is known as electrostatic potential energy map, therefore the load differences can be found in the various areas of the molecule. If the distributions of charges are known, the essence of the interaction between the molecules can be elucidated. Besides, the analysis and anticipation of a molecule's reactive behavior can be effectively carried out using the EMP. The space surrounding the nuclei and electrons in a molecule is considered as the generate charge distributions[33, 34]. Various colors denote different electrostatic potential values, where red indicates the most negative value and blue represents the most positive value. In accordance with the color spectrum, colors allocate the intermediate potentials, such that: red < orange < yellow < green < blue. The red areas on the map represents the maximum electrons abundance; while the blue areas exposes the lowest electron concentration [35, 36]. For the compound, the MEP map's color code ranged from -0.06074 a.u. (Extreme red) to 0.06074 a.u. (Extreme blue) are the strongest attraction and the strongest repulsion, respectively.

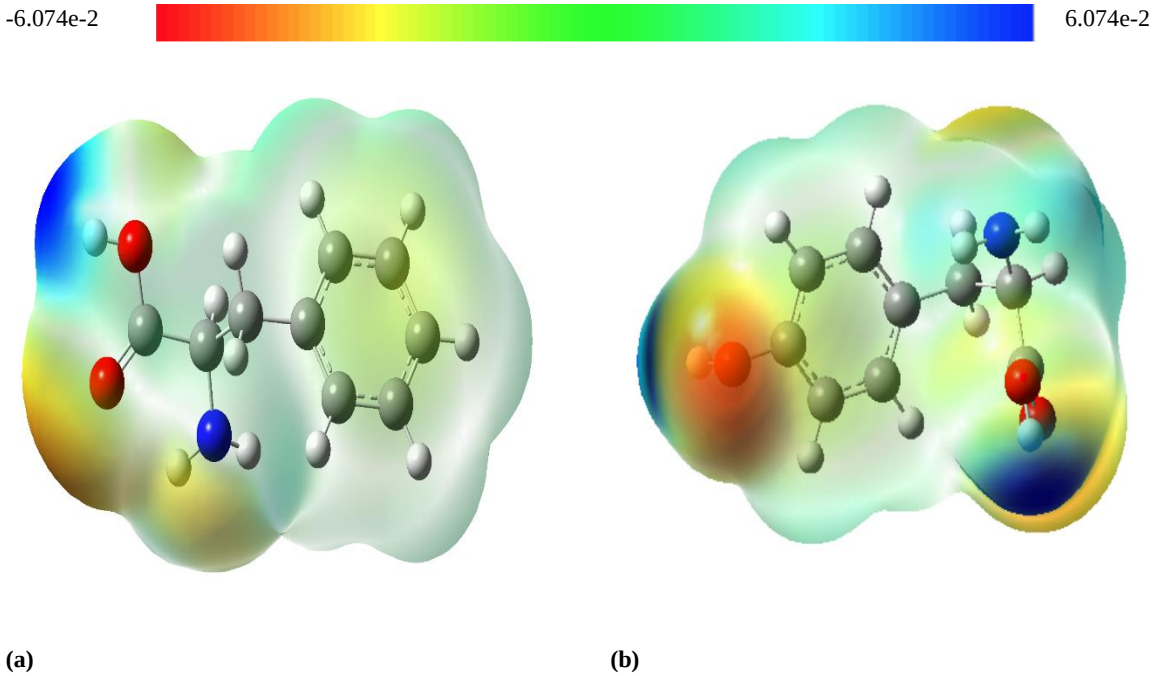


Figure 5. Molecular electrostatic potential calculated at B3LYP/6-31++G(d,p) level. a) Phenylalanine b) Tyrosine.

Figure 5 shows the mapping of the potentially electrostatic surface for the Phe and Tyr compounds. Red and blue signify the greatest repulsion and greatest attraction, respectively. The result shows that the light red color (negative) has appeared on the (C=O) groups and the blue color (positive) was appeared on the hydrogen of the (OH) group in Phe molecule, while the deep red color in Tyr molecule has appeared on the hydroxyl group of the phenyl and the blue color appeared on the hydrogen of the (OH) groups. Also, the overall results confirm that the Tyr molecule are more attractive with electrophiles than phenylalanine, which is due to the OH group in the Tyr molecule.

3.5. Atomic Charge Distributions

The distributions of charges over the atoms suggest the creation of donor and acceptor pairs that require the transfer of charges within the molecule. Table 3 displays the Mulliken atomic charges of our compounds for carbon and oxygen atoms, calculated at the level of B3LYP/6-311++G(d,p) with the molecule in the gas phase.

Table 3. Atomic charges distribution (*e*) of the Phenylalanine and Tyrosine title compound in gas phase.

phenylalanine		Tyrosine	
Atom	Charge	Atom	Charge
N1	-0.43012	C1	-0.05399
C2	-113.456	C2	-105.566
C3	0.23728	C3	-0.18587
C4	-0.70471	C4	-0.25410
C5	103.836	C5	108.035
C6	-0.44246	C6	-0.15452
C7	-0.47620	H7	0.33801
C8	-0.40982	H8	0.33893
C9	-0.27919	H9	0.33047
C10	-0.25798	H10	0.32079
H11	0.35185	C11	-0.89210
H12	0.33987	C12	-0.51829
H13	0.33599	C13	-0.22598
H14	0.28690	N14	-0.47708
H15	0.26519	O15	-0.28066
H16	0.28381	O16	-0.21678
H17	0.29835	H17	0.37870
H18	0.32553	H18	0.37350
H19	0.24924	H19	0.31678
O20	-0.28971	H20	0.31174
O21	-0.32614	H21	0.31293
H22	0.34637	H22	0.38406
H23	0.39217	O23	-0.55498
		H24	0.38374

Mulliken method imposes that the negative atomic charges of the oxygen in the hydroxyl groups of the phenyl in Tyr molecule, which is not in the Phe this is the big difference between to molecule. The oxygen of the carboxylic acid in Phe was a greater negative charge compared with the carboxyl group in tyrosine.

Mulliken charge distribution is very popular to determine dipole moments, atomic charge effects, molecular polarization, electronic structures, and other properties of a molecule [37, 38].

4. Conclusion

Structural analysis and electronic investigation for both Phe and Tyr have been carried out using DFT/B3LYP methods with basis set 6-311++G(d,p). Bond length, bond angle, and dihedral angle were calculated by B3LYP on the basis set 6-311++G(d,p) to find the geometrical structures for both compounds. The reactivity and structure properties of the molecules were determined throughout the energy bandgaps between HOMO and LUMO, which were calculated by B3LYP/6-311++G(d,p). The band gap between HOMO and LUMO for Phe was equal to 0.19851 eV, which has a good argument with its reactivity compared to tyrosine with energy band gap of 0.20501 eV. For the phenylalanine, the maximum excitation energy was obtained by TD/DFT, which show that the molecule is more reactive than tyrosine. Molecular electrostatic potential maps and charge distribution showed that the OH of the carboxylic groups has positive potential sites around in both Phe and tyrosine. Also, a deep negative potential site was found around the OH of the phenyl groups in Tyr molecule which was not observed in the phenylalanine.

Conflict of interest

The authors declare that they have no conflict of interest.

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