



STRUCTURAL ANALYSIS AND ORBITAL INTERACTIONS OF PROLINE

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ABSTRACT

In this work, proline (*Pro*) was studied theoretically at the Density Functional Theory (DFT) methods with B3LYP/6-311++G(d,p) level and four conformers with minimum energy were found. The calculations were done for these conformers. Electronic energies, Gibbs energies, the Highest Occupied Molecular Orbital (HOMO) and Lowest Unoccupied Molecular Orbital (LUMO) energy values were calculated. The Natural Bond Orbital (NBO) interactions were analyzed, and plotted. Electron density surfaces of the selected NBOs for *Pro* conformers showing the dominant orbital interactions, calculated at the Becke3LYP/6-311++G(d,p) level, were drawn. For *Pro* conformers, orbital energies for NBO pairs were calculated by Fock matrix equation.

Keywords: Amino Acid, Proline, NBO

1. INTRODUCTION

Amino acids are organic molecules of great biological importance. Although there are more than seven hundred amino acids in nature, only 20-22 of them are basic amino acids encoded by DNA and forming proteins. The difference in the number, variety and sequence of amino acids results in the different types of proteins in each living being [1-3]. Therefore, it is very important to know their structures. Among these proline (*Pro*; IUPAC: Pyrrolidine-2-carboxylic acid; $C_5H_9NO_2$) is a proteinogenic (protein creating) amino acid that is used in the biosynthesis of proteins.

In present study, the approximate geometry of the *Pro* in three dimensions was drawn in the GaussView 5.0 molecular imaging program [4] to get stable state and the space arrangement of the atoms in the molecule. Natural Bond Orbital (NBO) calculations of the *Pro* were made and analyzed.

2. THEORITICAL DETAILS

The calculation of energies and optimization for the *Pro* conformers were performed using the Density Functional Theory (DFT) integrated in the Gaussian 09 [5] program. The calculations were done using the 6-311++G(d,p) basis set. The three-parameter hybrid density functional, which includes Becke's gradient exchange correction [6] and the Lee, Yang and Parr [7], is called Becke3LYP. Stabilization energies and orbital analysis of the *Pro* were clarified using the NBO theory. The method was used considering Weinhold and co-workers, by NBO 3.1 [8] as integrated in Gaussian 09.

3. RESULTS AND DISCUSSION

Pro molecule was optimized using DFT with Becke3LYP/6-311++G(d,p) basis set and the geometries of this molecule with minimum energy. This molecule has four conformers (Figure 1). According to the calculations, Pro1 is more stable than the other three conformers. The calculated energies of all the *Pro* conformers are tabulated in Table 1.

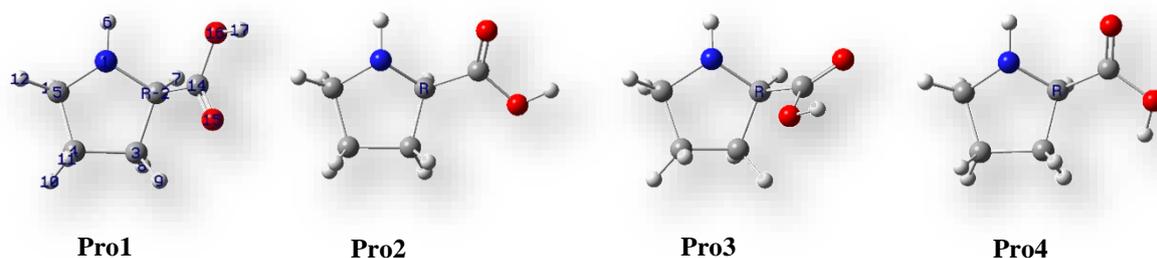


Figure 1. The molecular structure of *Pro* and its conformers, calculated by Becke3LYP/6-311++G(d,p) level

Table 1. Calculated electronic energies (with and without zero point vibrational energy), Gibbs energies, and their relative energies, dipole moments, obtained from Becke3LYP/6-311++G(d,p) calculations.

Energies	Pro1	Pro2	Pro3	Pro4
E(R3BLYP) (hartree)	-401.27910	-401.27825	-401.27780	-401.26963
E(ZPV) (hartree)	-401.13511	-401.13439	-401.13376	-401.12603
Gibbs (hartree)	-401.16864	-401.16762	-401.16708	-401.15911
μ (debye)	2.2928	2.2465	2.4518	5.0133
ΔE (kJ mol ⁻¹)	0	2.228	3.423	24.874
ΔE (ZPV) (kJ mol ⁻¹)	0	1.882	3.537	23.847
ΔG (kJ mol ⁻¹)	0	2.681	4.098	25.016

Conformers of the *Pro* molecule were found depending on the arrangements of the carboxylic group. In this arrangements, three low energy conformations (Pro1, Pro2 and Pro3) were formed when the dihedral angle of the carboxylic group N–C–C=O was 0 degrees. The formation of the high-energy conformer (Pro4) was determined by the scanning of O=C–O–H dihedral angle. Calculated ground state potential energy surface of the *Pro* were plotted in Figures 2 and 3.

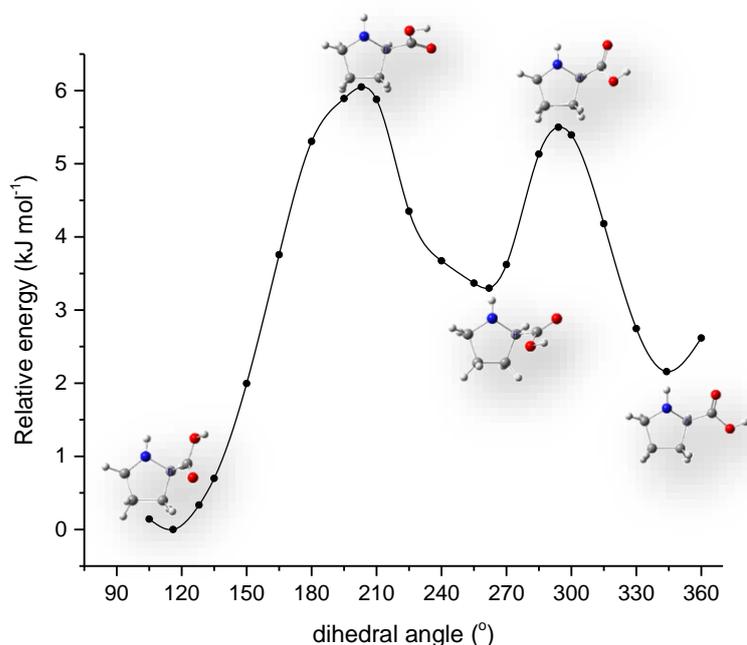


Figure 2. Potential energy profile resulting from the rotation of the N–C–C=O dihedral angle in 15 degree steps.

According to the calculations, the Pro1 conformer is more stable than the Pro3 conformer by *ca.* 3.42 kJ mol⁻¹, the Pro1 → Pro3 barrier amounts to *ca.* 5.89 kJ mol⁻¹, and a the Pro2 → Pro3 barrier amounts

to *ca.* 3.34 kJ mol⁻¹. The Pro2 conformer is more stable than the Pro3 form by *ca.* 1.20 kJ mol⁻¹, and the Pro2 → Pro3 barrier amounts to *ca.* 2.97 kJ mol⁻¹.

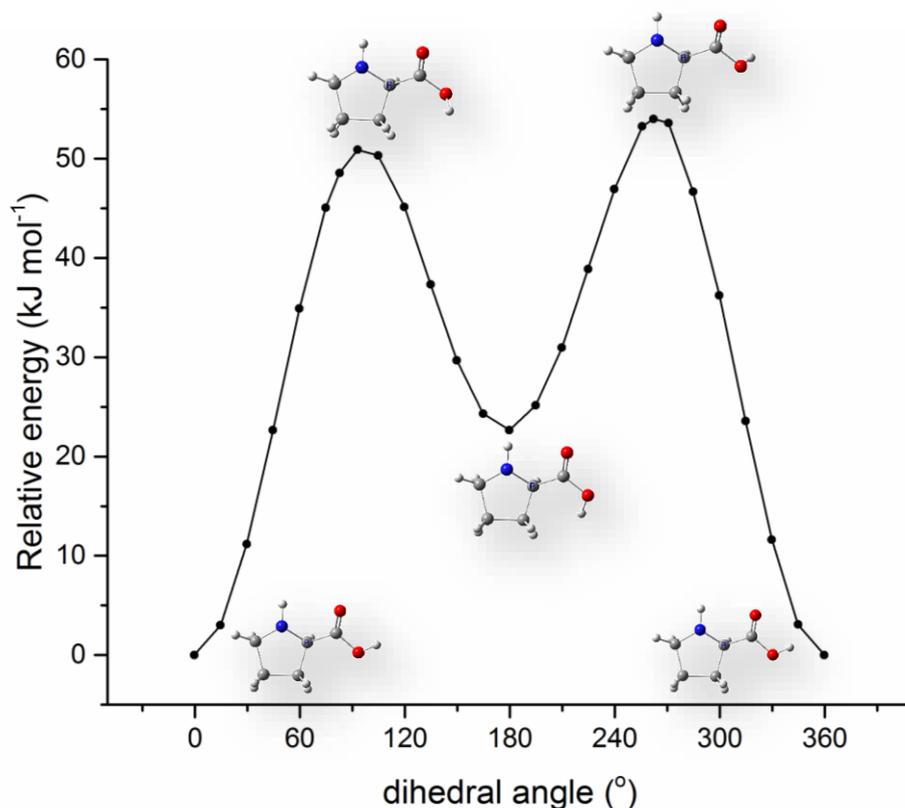


Figure 3. Potential energy profile resulting from the rotation of the O=C-O-H dihedral angle in 15 degree steps.

The Pro2 conformer is more stable than the Pro4 conformer by *ca.* 22.70 kJ mol⁻¹, and the Pro2 → Pro4 barrier amounts to *ca.* 50.30 kJ mol⁻¹, and reversible barrier amounts to *ca.* 53.24 kJ mol⁻¹.

The energies given in the Table 2 were calculated using the Fock matrix equation. $E(2)$ stabilization energies, between filled (donor; lone pairs) and empty (acceptor; non Lewis and Rydberg orbitals) NBOs, were estimated by the second-order perturbation approach [9],

$$E(2) = \Delta E_{ij} = q_i \frac{F_{ij}^2}{\varepsilon_j - \varepsilon_i} \quad (1)$$

where q_i is the donor orbital occupancy, ε_i and ε_j are the diagonal elements and F_{ij} is NBO the off-diagonal NBO Fock matrix element.

According to the NBO results, the strongest polarization exhibited from oxygen atom (O16) to C14–O15 bond. And they were hybridized pure p character. the second strong polarization was from oxygen atom (O15) to C14–O16 bond and hybridized as a sp^2 character. NBO interactions for all conformers are given in Table 2.

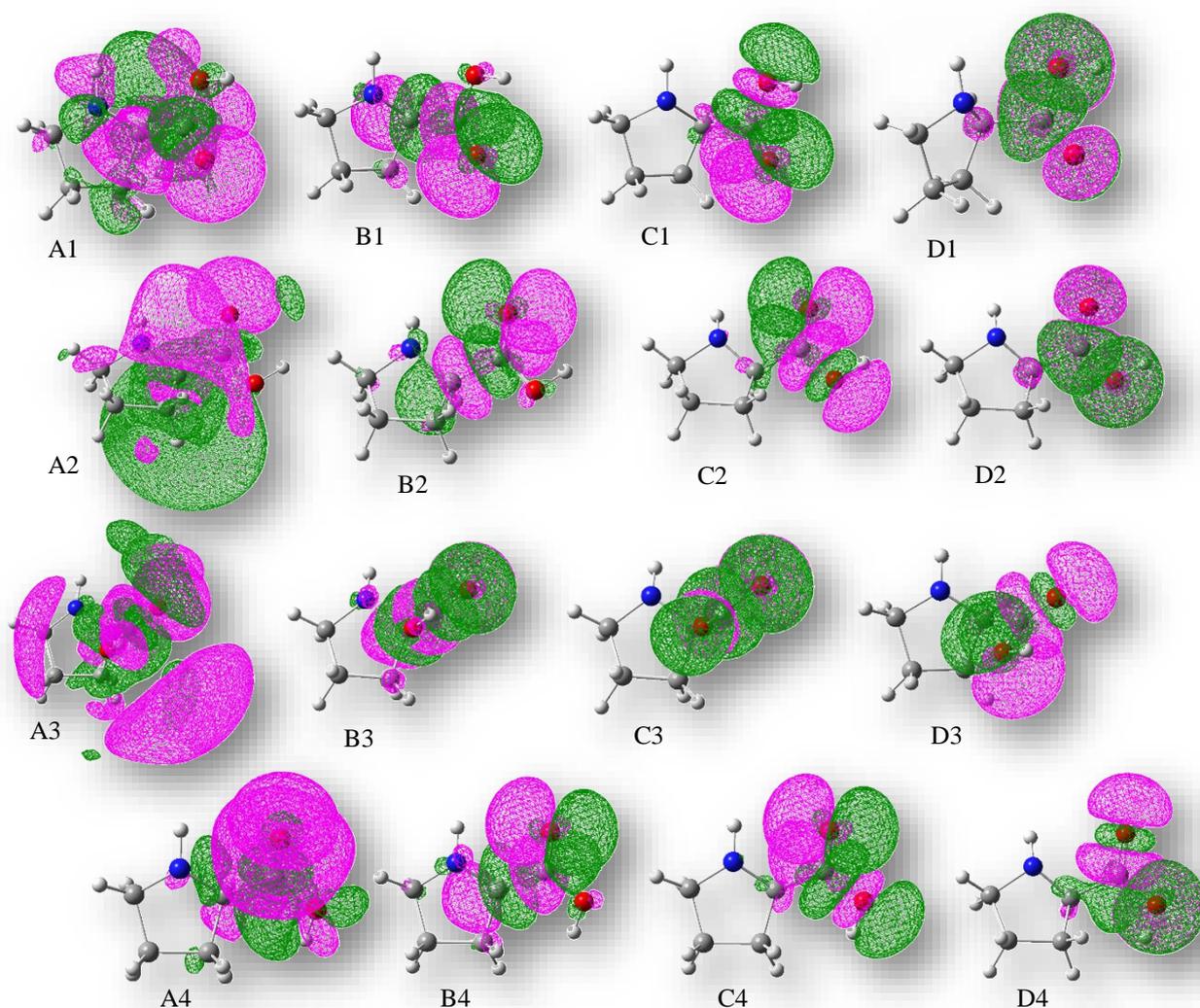


Figure 4. Electron density surfaces for the selected NBOs of all *Pro* conformers calculated at the Becke3LYP/6 311++G(d,p) level effective orbital interactions (given in Table 2). green and pink and indicate the states of positive and negative wave functions, respectively.

As seen in Table 2, the most important NBO interactions of Pro1 and Pro2 conformers are of the same type, at the same time their relative significance is similar with each other's. For Pro1 and Pro2, interactions of types C and D show delocalization as a π -system of the molecule (Figure 4, D1 and D2) and reflected over the C=O bond between lone pair orbital of O16. C1 and C2 pairs interacted as a σ -type (Figure 4, C1 and C2). This conclusion agreed with the study of acrylic acid [10]. On the other hand, for Pro3 and Pro4, the most orbital interaction types are σ -type (Figure 4, C3, D3, C4 and D4).

For all conformers, NBO analyzes associated with orbital pairs A and B were not considered, as there were less significant orbital interactions.

Table 2. Donor and acceptor pairs, orbital energies for NBO pairs as calculated by the Fock matrix equation (Eq.1) in the NBO basis for *Pro*^a.

Conformer	Pair	Donor NBO (<i>i</i>)	Acceptor NBO (<i>j</i>)	<i>E</i> (2) kJ mol ⁻¹	$\epsilon_i - \epsilon_j$ au	<i>F</i> _{<i>ij</i>} au
Pro1	A1	LP1(O15)	Ry1*(C14)	73.69	1.67	0.153
	B1	LP2(O15)	σ^* (C2–C14)	75.53	0.64	0.098
	C1	LP2(O15)	σ^* (C14–O16)	140.70	0.61	0.130
	D1	LP2(O16)	π^* (C14=O15)	179.36	0.35	0.111
Pro2	A2	LP1(O15)	Ry1*(C14)	71.85	1.71	0.153
	B2	LP2(O15)	σ^* (C2–C14)	78.46	0.65	0.098
	C2	LP2(O15)	σ^* (C14–O16)	141.49	0.61	0.130
	D2	LP2(O16)	π^* (C14=O15)	178.28	0.35	0.110
Pro3	A3	LP1(O15)	Ry1*(C14)	68.26	1.71	0.149
	B3	LP2(O15)	σ^* (C2–C14)	71.44	0.64	0.095
	C3	LP2(O15)	σ^* (C14–O16)	140.36	0.61	0.130
	D3	LP2(O16)	σ^* (C14=O15)	181.62	0.35	0.111
Pro4	A4	LP1(O15)	Ry1*(C14)	75.07	1.70	0.156
	B4	LP2(O15)	σ^* (C2–C14)	77.96	0.63	0.099
	C4	LP2(O15)	σ^* (C14–O16)	141.83	0.60	0.129
	D4	LP2(O16)	σ^* (C14=O15)	166.99	0.36	0.108

^aSee atom numbering in Figure 1. LP: lone pair orbital, Ry: Rydberg orbital.

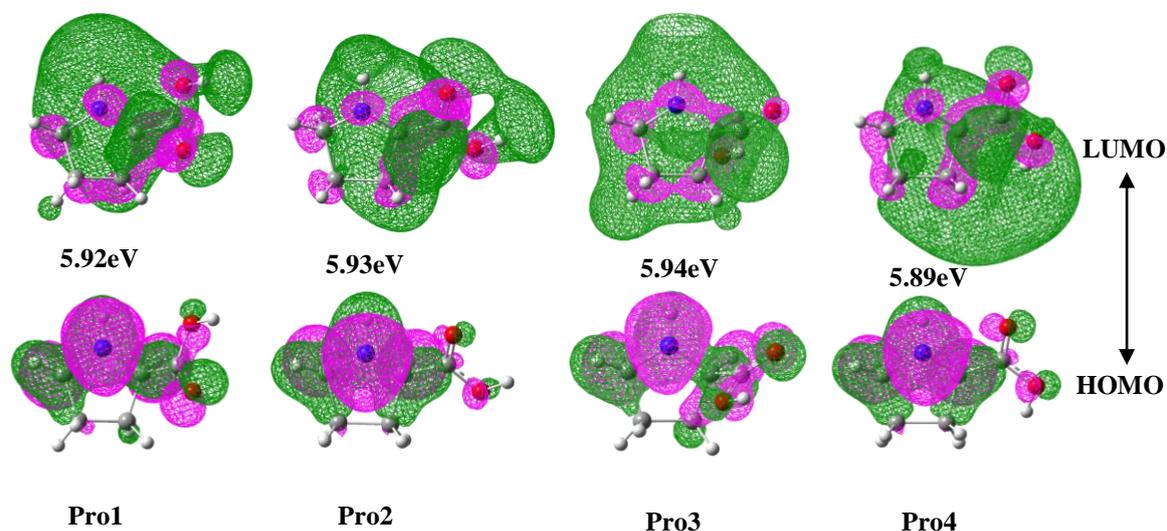


Figure 5. The difference of HOMO-LUMO energies for all the conformers of *Pro* calculated at the Becke3LYP/6-311++G(d,p) level.

Energy gaps between the Highest Occupied Molecular Orbital (HOMO) and Lowest Unoccupied Molecular Orbital (LUMO) for *Pro* conformers (the calculated with the DFT/6-311++G(d,p)) and their orbital schemes are shown in Figure 5. These values are 5.92, 5.93, 5.94 and 5.89 eV in gas phase for Pro1, Pro2, Pro3 and Pro4, respectively.

4. CONCLUSIONS

The conformers of *Pro* were calculated in the ground electronic state using B3LYP/6-311++G(d,p) level. Pro1 was more stable than the other conformers *ca.* 2.23, 3.42 and 24.87 kJ mol⁻¹, respectively. The stabilization energies of the *Pro* molecule were determined using the NBO method. It was used potential energy profiles to plotted the barrier energies. Most important orbital interactions of conformers were analyzed and discussed. HOMO-LUMO energies were also determined and their orbitals were plotted.

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