Potential Energy Surface (PES) scan of gas-phase L-proline

Anouar El Guerdaoui*, Yassine El Kahoui, Malika Bourjila, Rachida Tijar, Abderrahman El Gridani

Laboratory of Physical Chemistry, Department of Chemistry, Faculty of Science,
Ibn Zohr University, Agadir, Morocco

*E-mail address: anouarelguerdaoui@gmail.com

ABSTRACT

We performed here a systematic ab initio calculations on neutral gas-phase L-proline. A total of 8 local minima were located by geometry optimization of the trial structures using density functional theory (DFT) with B3LYP three parameter hybrid potential coupled with the 6-31G)d(basis set. The absolute minimum obtained will be subject to a rigid potential energy surface (PES) scan by rotating its carboxylic group using the same method with more accurate basis set B3LYP/6-311++G(d,p), to get a deeper idea about its conformational stability. The main aim of the present work was the study of the rigidity of the L-proline structure and the puckering of its pyrrolidine ring.

Keywords: ab initio calculations; L-proline; density functional theory; potential energy surface

1. INTRODUCTION

Amino acide present a great challenge for computational methods in quantum chemistry for different reasons. First, they often contain different types of atoms with different electronic properties, such as H, C, N, O, S. In fact, the different electronegativities lead to a broad charge transfer inter-and intra-molecular. Second, the biomolecules have a wide variety of types of connections from ionic and covalent bonds and hydrogen bonds to Van Der Waals interactions. Finally, the potential energy surfaces (PES) of these molecular systems are very complex, which may have many local minima very close in energy, often separated by low energy barrier. These minima may be located in very flat PES where wide change of the geometry of the molecule can occur with low energy change regions [1-4].

Proline features the amino group as part of a five-membered ring, differing thus from other amino acids in that its chain is bonded to the backbone nitrogene atom and to the alpha carbon atom (noted C_1 See **Figure 1**). This cyclic structure influences greatly protein architecture. It is unique among amino acids because it features only one hydrogen bound to the amino nitrogen. The pyrrolidine of Pro residue may adopt two distinct down and up puckered conformations [5] that are almost equally favorable [6-11], it prevents rotations

about the alpha carbon atom and the nitrogen bond. This reduces greatly the number of conformations available to proline [12].

The structural features of pro and its derivatives have been studied by experimental techniques (X-ray crystallography [13-15], NMR [16], and IR [17,18] spectroscopy) and theretical molecular mechanics [15,19], perturbed configuration interaction with localized orbitals (PCILO) [20] and ab initio [19,21-24] calculations.

To further the understanding of the conformational landscape of gaseous L-proline, this work provides a thorough theoretical search using reliable computational techniques at high levels of ab initio electronic-structure theory, usingThe DFT/B3LYP)Becke3-Lee-Yang-Parr functional [25,26]   method in the search of Pro conformers as it was known to provide accurate molecular structures and the associated vibrational frequencies and infrared intensities [27-29], with various basis sets, e.g., 6-31G(d) and 6-311++G(d,p).

2. AB INITIO CALCULATIONS: METHODOLOGY

A series of 22 trial structures were generated for neutral proline by allowing for all combinations of internal single-bond rotamers, as shown in **Figure 1**. These possible geometries were submitted to full geometry optimisation using density functional theory (DFT), with 6-31G(d) basis. Excluding major conformers with steric clashes and conformers that converged to the same minimum, a total of 8 possible structures for the neutral L-proline molecule are obtained. All calculations were performed with the GAUSSIAN 09 program package [30].
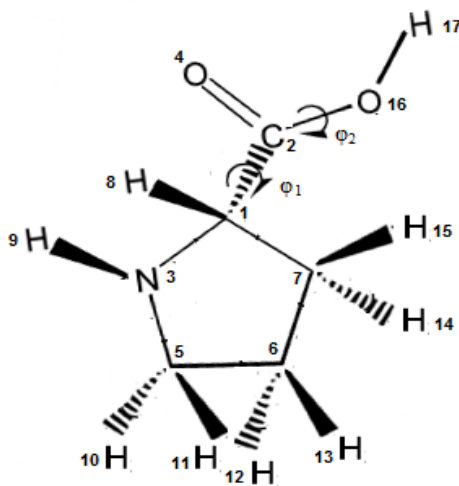
φ_1 : 30°, 60°,90°, 120°,
150°,180°,210°
240°, 270°, 300°, 330°
φ_2 : 0°,180°

Figure 1. Schematic illustration of the rotational degrees of freedom and Labeling of the atoms of L-proline.

The 2D potential energy surface (PES) of the neutral L-proline (absolute minimum, see **Figure 2**) was calculated along the dihedral angle of the carboxylic group φ_2 and the torsion φ_1 about the bond (C_1-C_2) connecting it to the the pyrrolidine ring (see **Figure 1**).
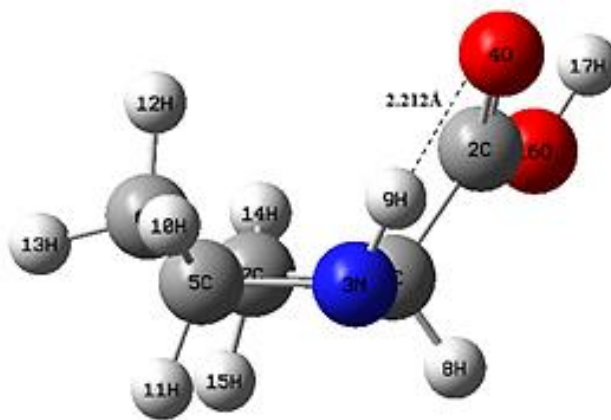

Figure 2. The lowest lying conformer of neutral L-proline located at B3LYP/6-31G(d) level of theory.
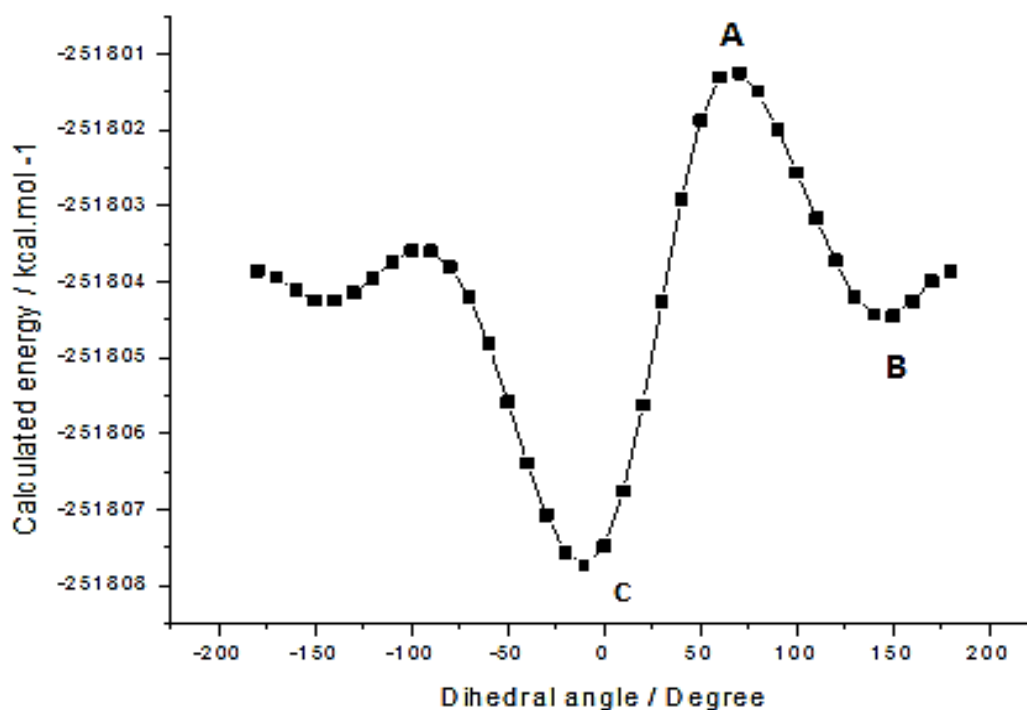
3. RESULTS AND DISCUSSION

Figure 3. The potential energy surface of L-proline at the B3LYP/6-311++G (d,p) level for $\varphi_2 = 0°$.

A rigid potential energy surface scan was performed on the optimized geometry of L-proline (absolute minimum see **Figure 2**) found previously, with more accurate basis set 6-311++G(d,p) [31,32], in order to ascertain the structural accuracy and stability using the same method (DFT/B3LYP) by rotating the carboxylic group [φ_1 : dihedral angle of atom O_4 and N_3 with respect to the bond C_1– C_2, **Figure 1**] between -180° and +180° with the increment of 10°. Dihedral φ_2 [φ_2 : angle of atom O_4 and H_{17} with respect to the bond C_2–O_{16}, **Figure 1**] has fixed to 0° and 180° respectively. The energy curves for pyrrolidine rotation of L-proline are given in **Figure 3** and **Figure 4** respectively.
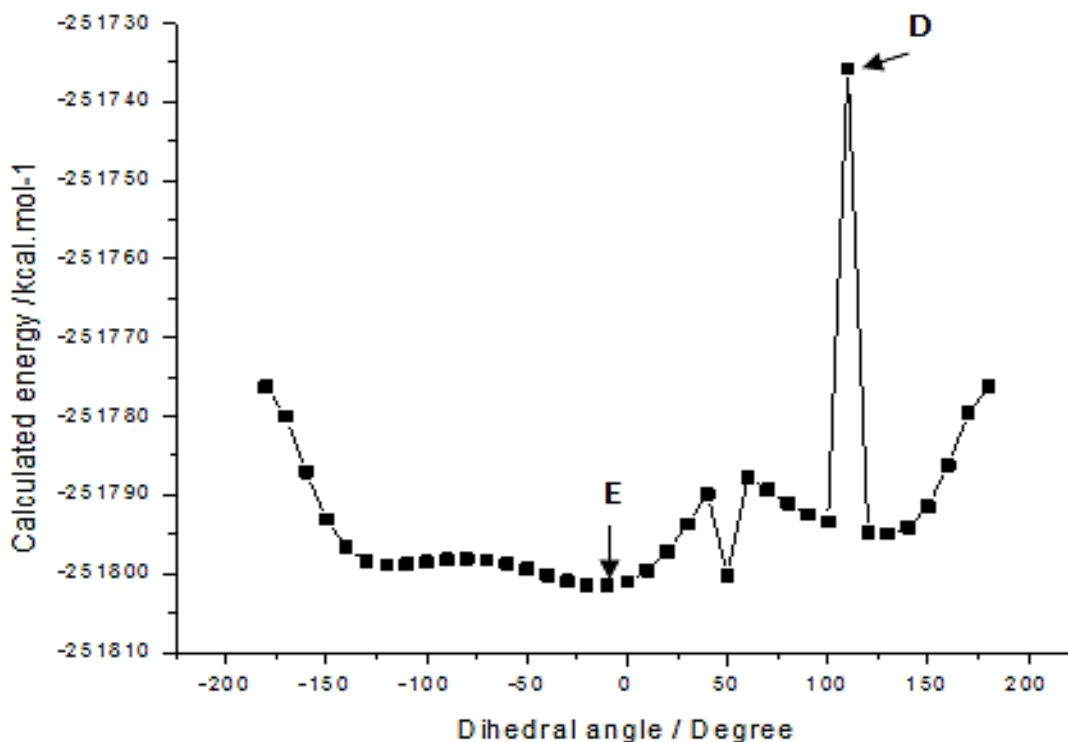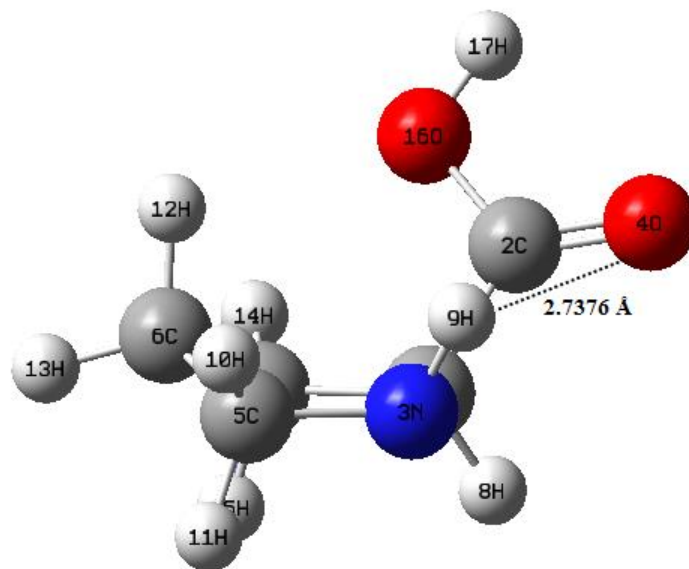

Figure 4. The potential energy surface of L-proline at the B3LYP/6-311++G (d,p) level for φ_2 = 180°

The potential energy curve for carboxylic group rotation of L- proline for φ_2 = 0° (i.e cis arrangement of –COOH group) is given in **Figure 3**. The maximal position in the curve is presented by the highest energy conformer **A** (E_A= -251801,3 kcal·mol^{-1}) with dihedral angle φ_1= 70°.

Two low energy wells are also identified in the curve **Figure 3** and they are presented by conformations **B** with dihedral angle φ_1 = 160° and **C** with dihedral angle φ_1 = - 10°, respectively (E_B = -251804,3 Kcal·mol^{-1} and E_C = -251806,8 kcal·mol^{-1}).

Conformer **A** of higher energy, adopts an endo puckering structure of the pyrrolidine ring and up orientation of the imino group N_3-H_9, with a weeker hydrogen bond between the oxygen of the carbonyl group C_2=O_4 and the hyrogen of the imino group N_3-H_9 (using a distance of 2.80 Å as a cutoff for near-atom interactions).

The two low energy conformers **B** and **C** adopt an endo puckering structure and up orientation of the imino group N_3-H_9. They differ only by the dihedral angle $\varphi2$ and have very similar intramolecular interactions. their separation can be attributed to the interaction between the hydrogen of the imino group N-H and the oxygen of the hydroxyl group which is lower than that of the carbonyl oxygen atom. Energy Barriers of rotation for the –COOH group ($\varphi_2 = 0°$, i.e cis arrangement) are 3 and 6.5 kcal.mol^{-1} for **B** and **C** respectively indicate that the rotation of the –COOH group is relatively much restricted. Structure of highest and lowest energy conformers are given in **Figure 5.**
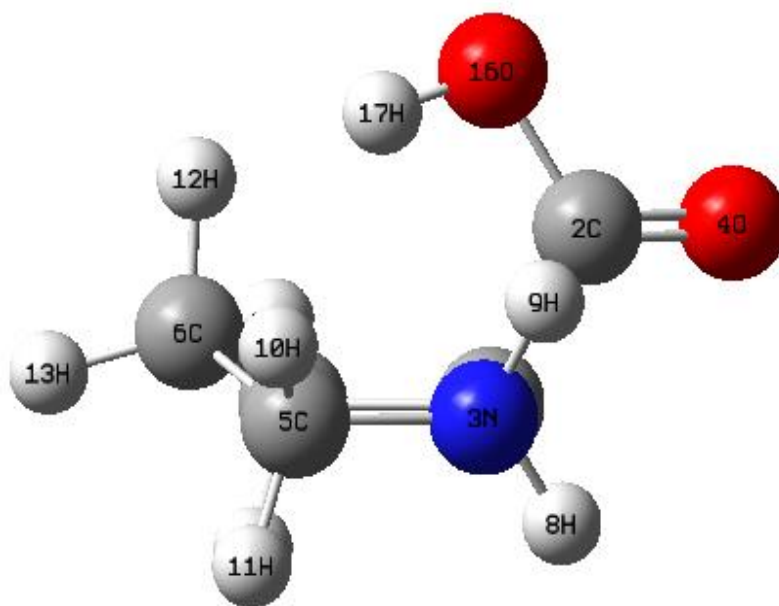

(A)
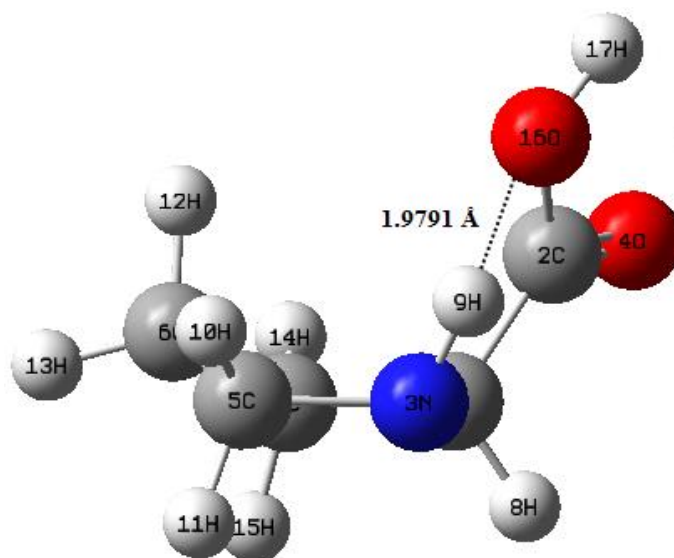
(B)
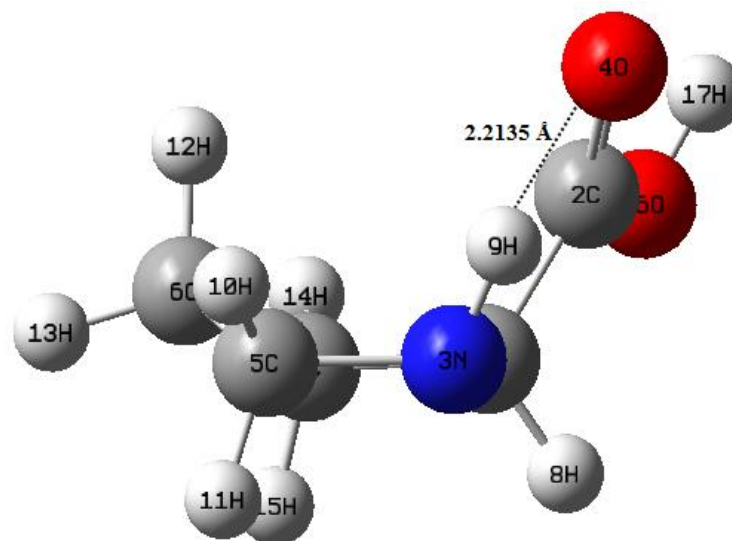
(C)

Figure 5. Highest and lowests energy conformations of L-proline for $\varphi_2 = 0°$ (i.e cis arrangement of -COOH group). All the conformations related to **Figure 3**.

The potential energy curve for carboxylic group rotation of L- proline for $\varphi_2 = 180°$ (i.e trans arrangement of –COOH group) is given in **Figure 4**. The highest energy conformer of the energy curve is named **D** where E_D = -251735,9 kcal·mol^{-1} with dihedral angle $\varphi_1 = 110°$ and the lowest energy conformer in the same curve is named **E** where E_E = -251801,5 kcal·mol^{-1} with dihedral angle $\varphi_1 = -10°$.
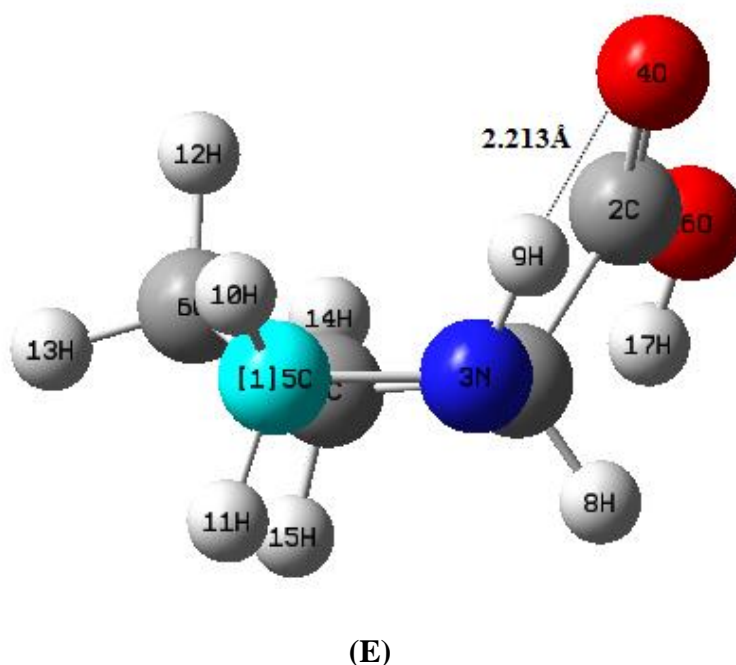

(D)

(E)

Figure 6. highest and lowest energy conformations of L-proline for $\varphi_2 = 180°$ (i.e trans arrangement of $-$ COOH group). The two conformations related to **Figure 4.**

Structures of conformers **D** and **E** are given in **Figure 6.** Both **D** and **E** have an endo puckering structure of the pyrrolidine ring and up orientation of the imino group N_3-H_9. The high stability of the lowest conformer **E** can be explained by the presence of the hydrogen bond between the hydrogen of the imino group and the oxygen carbonyl NH_9----$_4O$=C (2.21 Å). The low stability of the conformer **D** is obvious, considering the lack of any hydrogen bonding. Barrier of rotation for the –COOH group ($\varphi_2 = 180°$, i.e trans arrangement) is of 65.6 kcal·mol^{-1} for conformer **E**. This value of energy barrier of rotation is very significant because it can provide information on the conformational preference of the neutral L-proline, a large value indicates that the rotation of the –COOH group is very much restricted. These results describe the anti-COOH structure be more fit, which is in good agreement with the theoretical results already established [33].

4. CONCLUSIONS

The potential energy surface (PES) scan of the neutral gas-phase L-proline was performed using DFT-B3LYP/6-311++G(d,p) level of theory for both cis and trans arrangement of the carboxylic group –COOH. The pyrrolidine ring in proline was calculated to be almost planar at the RHF level with the STO-3G and 6-31G basis sets [34]. while, more elaborate electronic-structure results, especially those employing polarization functions in the basis set [35], show that the ring is considerably puckered in all conformers. In All highests and lowests energy conformers in the etablished energy curves the character of the N atom is pyramidal, and all these conformers adopt an endo puckering structure of the pyrrolidine ring.

The potential energy scan of L-proline by rotating the tans arrangement –COOH group shows energy barrier of rotation of 65.6 kcal·mol^{-1}, what it means that the rotation of the trans

arrangement –COOH group is very much restricted and therefore a rigid global structure, also this big value of barrier energy suggests rigidityin inprotein's structures by the effect of the interactions that the carboxylic group in the trans form can do with other atoms and therefore this imposes very precise spatial positioning of these proteins.

References

[1] L. C. Snoek, E. G. Robertson, R. T. Kroemer, J. P. Simons, *Chem. Phys. Lett*. 321 (2000) 49.

[2] Z. Huang, W. Yu, Z. J. Lin, *THEOCHEM* . 758 (2006) 195.

[3] (a) K. T. Lee, J. Sung, W. J. Lee, S. K. Kim, Y. D. Park, *Chem. Phys. Lett.* 368 (2003) 262;
(b) Y. Lee, J. Jung, B. Kim, P. Butz, L. C. Snoek, R. T.Kroemer, J. P. Simons, *J. Phys. Chem A*. 108 (2004) 69.

[4] S. K. Burley, G. A. Petsko, *J.Am. Chem. Soc*. 108 (1986) 7995.

[5] F. A. Momany, R. F. McGuire, A.W. Burgess, H. A. Scheraga, *J. Phys. Chem.* 79 (1975) 2361.

[6] D. F. DeTar, N. P. Luthra, *J. Am. Chem. Soc.* 99 (1977) 1232.

[7] V. Madison, *Biopolymers*. 6 (1977) 2671

[8] G. Némethy, K. D. Gibson, K. A. Palmer, C. N. Yoon, G. Paterlini, A. Zagari, S. Rumsey, H. A. Scheraga, *J. Phys. Chem.* 96 (1992) 6472.

[9] Y. K. Kang, *J. Phys. Chem*. 100 (1996) 11589.

[10] Y. K. Kang, J. S. Jhon, S. J. Han, *J. Peptide. Res.* 53 (1999) 30.

[11] Y. K. Kang and H.S. Park, *J. Mol. Struct*. 593 (2002) 55.

[12] A. M. Sapse, *Molecular orbital calculations for Amino Acids and Peptide*, Birkhäuser, Boston, 2000, p. 63-72.

[13] R. L. Kayushina, B. K. Vainstein, *Sov. Phys. Crystallogr*. 10 (1966)698.

[14] R. Balasubramanian, A. V. Lakshminarayanan, M. N. Sabesan, G. Tegoni, K. Venkatesan, G. N. Ramachandran, *Int. J. Pept. Protein Res*. 3(1971) 25.

[15] D. F. DeTar, N. P. Luthra, *J. Am. Chem. Soc.* 99 (1977) 1232

[16] C. A. G. Haasnoot, F. A. A. M. De Leeuw, H. P. M. De Leeuw, C. Altona, *Biopolymers.* 20 (1981) 1211.

[17] I. D. Reva, S. G. Stepanian, A. M. Plokhotnichenko, E. D. Radchenko, G. G. Sheina, Yu. P. Blagoi, *J. Mol. Struct.* 318 (1994) 1.

[18] A. W. Herlinger, T. V. Long II, *J. Am. Chem. Soc.* 92 (1970)6481.

[19] M. Ramek, A. M. Kelterer, S. Nikolic*, Int. J. Quantum. Chem.* 65 (1997) 1033.

[20] D. Cabrol, H. Brock, D. Vasilescu, *Int. J. Quantum. Chem*. 6 (1979)365.

[21] A. M. Sapse, L. Mallah-Levy, S. B. Daniels, B. W. Erickson, *J. Am. Chem. Soc*. 109 (1987) 3526.

[22] A. G. Csaszar, A. Perczel, Progr. *Biophys. Mol. Biol*. 71 (1999) 243.

[23] P. Tarakeshwar, S. Manogaran, *J. Mol. Struct*. 365 (1996) 167.

[24] S. G. Stepanian, I. D. Reva, E. D. Radchenko, L. Adamowicz, *J. Phys. Chem*. *A*. 105 (2001) 10664.

[25] A. D. Becke, *Phys. Rev. B*. 38 (1988) 3098.

[26] C. Lee, W. Yang, R. G. Parr. *Phys. Rev. B.* 37 (1988) 785.

[27] S. G. Stepanian, I. D. Reva, E. D. Radchenko, L. Adamowicz, *J. Phys. Chem. A*. 102 (1998) 1041.

[28] S.G. Stepanian, I.D. Reva, E.D. Radchenko, L. Adamowicz, *J. Phys. Chem.* A 102 (1998) 4623.

[29] S. G. Stepanian, I. D. Reva, E. D. Radchenko, L. Adamowicz. *J. Phys.Chem. A* 103 (1999) 4404.

[30] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fu- kuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, "Gaussian 09," Revision A.1, Gaussian, Inc., Wallingford, 2009.

[31] P. C. Hariharan, *J. A, Theor. Chim. Acta.* 28 (1973) 213.

[32] T. Clark, J. Chandrasekhar, G. W. Spitznagel, P.Von Rague Schleyer, *J. Comput. Chem*. 4 (1983) 294.

[33] T. Marino, N. Russo, E. Tocci, M. Toscano*, International Journal of Quantum Chemistry* 84 (2001) 2.

[34] A.M. Sapse, L. Mallah-Levy, S. B. Daniels, B. W. Erickson, *J. Am. Chem. Soc*. 109 (1987) 3526.

[35] M. J. Frisch, J. A. Pople, J. E. Del Bene, *J. Phys. Chem.* 89 (1985) 3664.