

NBO AND TOPOLOGY (MESP, ELF, LOL) ANALYSIS OF 2-HYDROXYPROPANAMIDE

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Abstract: In the present work, the optimized molecular geometry of 2-Hydroxypropanamide calculated by DFT/B3LYP method with 6-31 G(d,p) basis set has been computationally investigated for its fundamental reactive properties by a combination of density functional theory (DFT) calculations. Natural bond orbital analysis (NBO) has been performed on title compound using B3LYP/6-31 G(d,p) levels in order to elucidate intermolecular hydrogen bonding, intermolecular charge transfer (ICT) and delocalization of electron density. Total and partial density of states (TDOS and PDOS) plots were presented. Besides frontier molecular orbitals (FMO), MESP, electron localization function (ELF) and localized orbital locator (LOL) analysis were performed. Energy gap (ΔE), electronegativity (χ), chemical potential (μ), global hardness (η), softness (S) electrophilicity (ω) and thermodynamic properties of the title compound were also calculated.

Keywords: 2-Hydroxypropanamide; DFT; NBO;MESP;ELF,LOL,

I INTRODUCTION

2-Hydroxypropanamide is an amide derived from lactic acid. It can be prepared by the catalytic hydration of lactonitrile. [1-2]. It is a monocarboxylic acid that is lactic acid in which the carboxylic acid group has been converted to corresponding carboxamide and it is a monocarboxylic acid amide and a secondary alcohol. It is derived from a rac-lactic acid [3]. Hyperosmotic agents (2 M urea or 2 M DL-lactamide), perfused into the internal carotid artery of Rhesus monkeys, produced a marked decrease in intraocular pressure and an increase in aqueous humor protein. Fenestrae of the ciliary capillaries were broken immediately following the perfusion and the nonpigmented epithelium was separated from the pigmented epithelium. The pigmented epithelium especially of the pars plana then became degenerative [4].

II COMPUTATIONAL DETAILS

All theoretical calculations were carried out with Gaussian 09 program package [5] using B3LYP [6-7] methods in conjunction with 6-31G(d,p) basis

set. The molecular structure, MEP surfaces were visualized with Gauss View 5 program [8]. Natural Bond Orbital (NBO) calculations were performed using NBO 3.1 program [9] as implemented in the Gaussian 09 package at DFT/B3LYP levels. The second order Fock-matrix was carried out to evaluate the donor (i) and acceptor (j) interaction in the NBO basis [10]. For each donor (i) and acceptor (j), the stabilization energy $E^{(2)}$ is associated as:

$$E^{(2)} = E_{ij} = q_i \frac{F(i,j)^2}{(\epsilon_i - \epsilon_j)}$$

The larger the $E^{(2)}$ value, the more intensive is the interaction between electron donor and electron acceptor which means more donating tendency from electron donors to acceptors and a greater extent of conjugation of the whole system.

III RESULTS AND DISCUSSIONS

3.1 Molecular Geometry

The molecule has 13 atoms. A molecule consisting of N atoms has a total of 3N degrees of freedom, corresponding to the Cartesian coordinates of

each atom in the molecule. In a nonlinear molecule, 3 of these degrees belong to the rotational, 3 of these degrees belong to the translational motions of the molecule and so the remaining corresponds to its vibrational motions. The net number of the vibrational modes is $3N-6$. Therefore, for the title molecule, three Cartesian displacements of 13 atoms provide 33 normal vibration modes. The molecular structure of the molecule is shown in Fig.1.

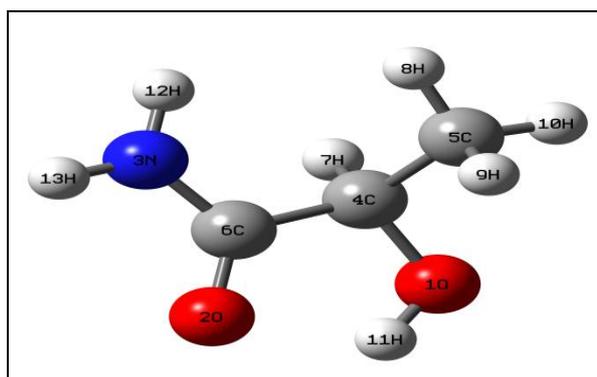


Figure 1 Molecular structure of the title compound

3.2 Natural Bonding Orbital analysis

Natural bonding orbital (NBO analysis) calculations were done with the help of NBO 3.1 program implemented in Gaussian 09 W Suite at DFT/B3LYP/6 -31 G(d, p) level of theory and the second order interactions obtained by NBO analysis are listed in Table 1.

The important intermolecular hyper conjugative interactions are: O2-C6 from N3 of LP(N3) \rightarrow σ^* (O2-C6), C4-C6 from O2 of LP(O2) \rightarrow σ^* (C4-C6), C4-C6 from O1, of LP(O1) \rightarrow σ^* (C4-C6), O2-C6 from N3-H12 of σ (N3-H12) \rightarrow σ^* (O2-C6), O1-C4 from C5-H8 of σ (O1-C4) \rightarrow σ^* (C5-H8), C4-C6 from N3-H13 of σ (N3-H13) \rightarrow σ^* (C4-C6), N3-C6 from O1-C4 of σ (O1-C4) \rightarrow σ^* (N3-C6), N3-H12 from O2-C6 of σ (O2-C6) \rightarrow σ^* (N3-H12), with electron densities 0.01413, 0.02114, 0.07767, 0.05843 and 0.02478e and stabilization energies 4.72, 3.94, 3.92, 2.22 and 1.57 kJ/mol. respectively [11].

Table 1: Second-order perturbation theory of Fock matrix in NBO basis corresponding to the intramolecular bonds of the title compound

Donor (i)	Type	ED/e	Acceptor (j)	Type	ED/e	E(2) ^a (Kcal/mol)	E(j)- E(i) ^b (a.u)	F(i,j) ^c (a.u)
O1-C4	σ	1.99129	N3-C6	σ^*	0.05843	2.22	1.24	0.047
O1-C4	σ	1.99129	C5-H8	σ^*	0.00700	1.34	1.22	0.036
O1-H11	σ	1.98986	C4-C6	σ^*	0.07767	1.02	1.04	0.030
O2-C6	σ	1.99440	N3-H12	σ^*	0.00977	1.57	1.48	0.043
O2-C6	σ	1.99440	C4-C5	σ^*	0.02478	1.52	0.72	0.030
N3-C6	σ	1.99501	N3-H12	σ^*	0.00977	0.59	1.31	0.025
N3-C6	σ	1.99501	N3-H13	σ^*	0.01064	0.71	1.32	0.027
N3-H12	σ	1.99003	O2-C6	σ^*	0.01413	4.72	1.20	0.067
N3-H13	σ	1.99002	C4-C6	σ^*	0.07767	3.92	1.03	0.058
C4-C5	σ	1.97789	C5-H10	σ^*	0.00625	0.66	1.07	0.024
C4-C6	σ	1.98073	N3-C6	σ^*	0.05843	0.56	1.10	0.022
C4-C6	σ	1.98073	N3-H13	σ^*	0.01064	3.01	1.10	0.052
C4-H7	σ	1.96939	O2-C6	σ^*	0.01413	1.73	1.02	0.038
C4-H7	σ	1.96939	C5-H9	σ^*	0.00751	2.65	0.96	0.045
C5-H8	σ	1.98591	O1-C4	σ^*	0.02114	3.94	0.77	0.049

C5-H9	σ	1.98996	C4-H7	σ^*	0.02971	2.46	0.94	0.043
C5-H10	σ	1.98577	C4-C6	σ^*	0.07767	3.32	0.85	0.048
LP O1	σ	1.97790	C4-C6	σ^*	0.07767	3.40	0.90	0.050
LP O1	π	1.95866	C4-C5	σ^*	0.02478	5.94	0.63	0.055
LP O1	π	1.95866	C4-H7	σ^*	0.02971	5.69	0.70	0.057
LP O1	π	1.95866	C5-H8	σ^*	0.00700	0.83	0.70	0.022
LP O2	σ	1.97552	O1-H11	σ^*	0.03205	1.39	1.12	0.035
LP O2	σ	1.97552	N3-C6	σ^*	0.05843	1.14	1.14	0.032
LP O2	σ	1.97552	C4-C6	σ^*	0.07767	2.67	1.04	0.048
LP O2	π	1.86198	O1-H11	σ^*	0.03205	5.97	0.69	0.059
LP O2	π	1.86198	N3-C6	σ^*	0.05843	21.79	0.71	0.114
LP O2	π	1.86198	C4-C6	σ^*	0.07767	16.47	0.61	0.091
LP N3	σ	1.73438	O2-C6	σ^*	0.01413	70.56	0.26	0.121

a $E^{(2)}$ means energy of hyper conjugative interaction (stabilization energy).

b Energy difference between donor and acceptor i and j NBO orbitals.

c $F(i,j)$ is the Fock matrix element between i and j NBO orbitals.

3.3 Topology analyses

The DFT method is useful in determining some important physical properties of the molecule like thermodynamic properties such as thermal energy, molar heat capacity and entropy, dipole moment and chemical reactivity. For the title compound, these parameters are calculated at B3LYP/6-31 G(d,p) level and collected in Table.2

The thermodynamic data can be used to study the physical behaviour and intermolecular interactions. The total dipole moment of the compound is equal to 6.7670 Debye.

The frontier molecular orbitals energy levels of the title molecule show that 24 of 68 molecular orbitals are occupied. Fig.2 shows that HOMO is mainly localized on nitrogen, oxygen, hydroxyl group and on the methyl group of the molecule. LUMO are mainly localized on NH_2 group, Oxygen attached to C6, and also on the carbon attached to methyl group. Energy barriers between HOMO and LUMO orbitals are equal to 7.03252eV [12].

The HOMO and LUMO energy gap can be used to explain the molecular chemical stability and chemical reactivity of the molecules. Global reactivity descriptors are presented in Table 2. The chemical reactivity descriptors of compounds such as electro negativity (χ), chemical potential (μ), hardness (η), softness (S) and electrophilicity index (ω) are evaluated using the following equations [13-17]:

$$\chi = \frac{I+A}{2}$$

$$\mu = -\frac{I+A}{2}$$

$$\eta = \frac{I-A}{2}$$

$$S = \frac{1}{2\eta}$$

$$\omega = \mu^2/2\eta$$

Table.2 Calculated molecular parameters of the title compound

Parameters	B3LYP/6-31 G(d,p)
SCF energy (a.u.)	-323.64382
Field Independent Dipole moment (Debye)	
μ_x	-0.9798
μ_y	3.7247
μ_z	-2.6175
μ_{total}	4.6567
Zero point vibrational energy (kcal/mol)	67.92300
Total thermal energy (kcal/mol)	72.135
Molar heat capacity at const.volume C_v (cal mol ⁻¹ K ⁻¹)	24.072
Total entropy, S (cal mol ⁻¹ K ⁻¹)	80.445
Vibrational Energy (Kcal/Mol)	70.358
Frontier Molecular Orbital Energies (eV)	
E_{HOMO} (eV)	7.06326
E_{LUMO} (eV)	0.03074
$E_{HOMO} - LUMO$ gap (eV)	7.03252
Global Reactivity Descriptors (eV)	
Chemical hardness (η)	3.51626
Softness (S)	0.14219
Chemical potential (μ)	-3.547
Electronegativity (χ)	3.547
Electrophilicity index (ω)	1.78900

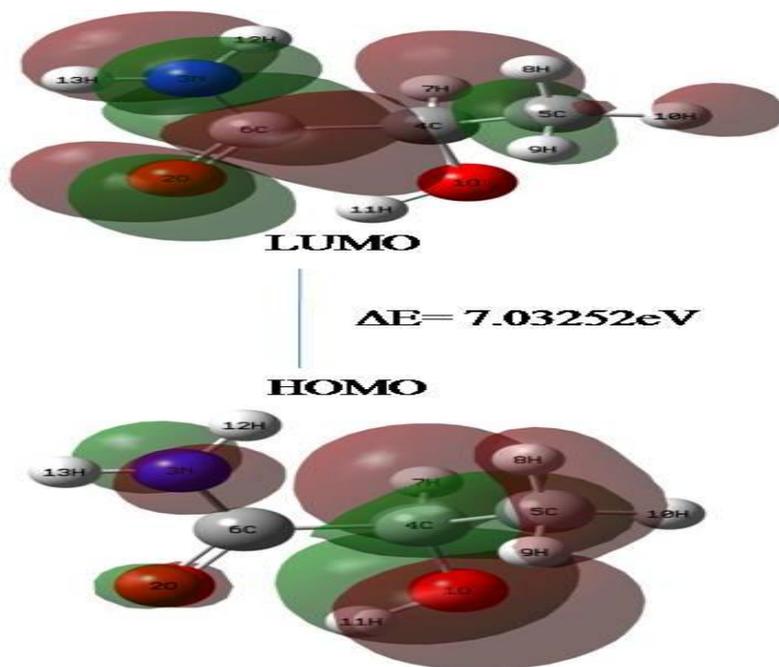


Figure 3. The Frontier Molecular Orbitals of the title compound.

The analysis such as TDOS and PDOS plots, ELF and LOL were performed using Multiwfn 3.7. [18] which is a multifunctional wave function analysis program. The main use of DOS plots is to provide a pictorial representation of molecular orbital compositions and their contributions to chemical bonding [19]. The

calculated total density of electronic states (TDOS) have been displayed in Fig.3. The partial density of states (PDOS) mainly presents the composition of the fragment orbitals contributing to the molecular orbitals which is seen in Fig.4.

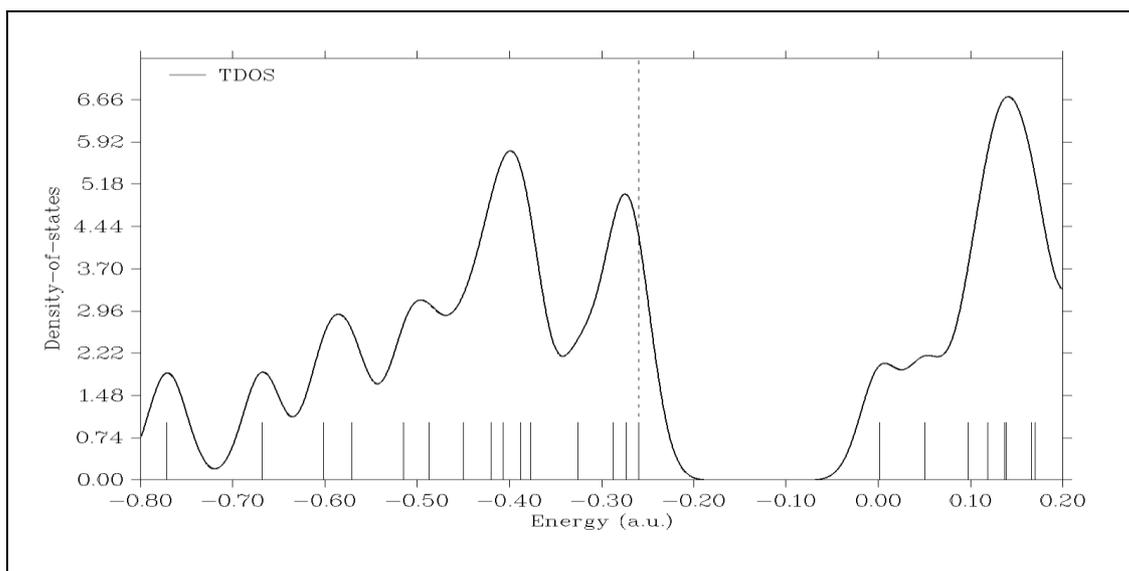


Figure 4. Calculated total density of states (TDOS) of the title compound

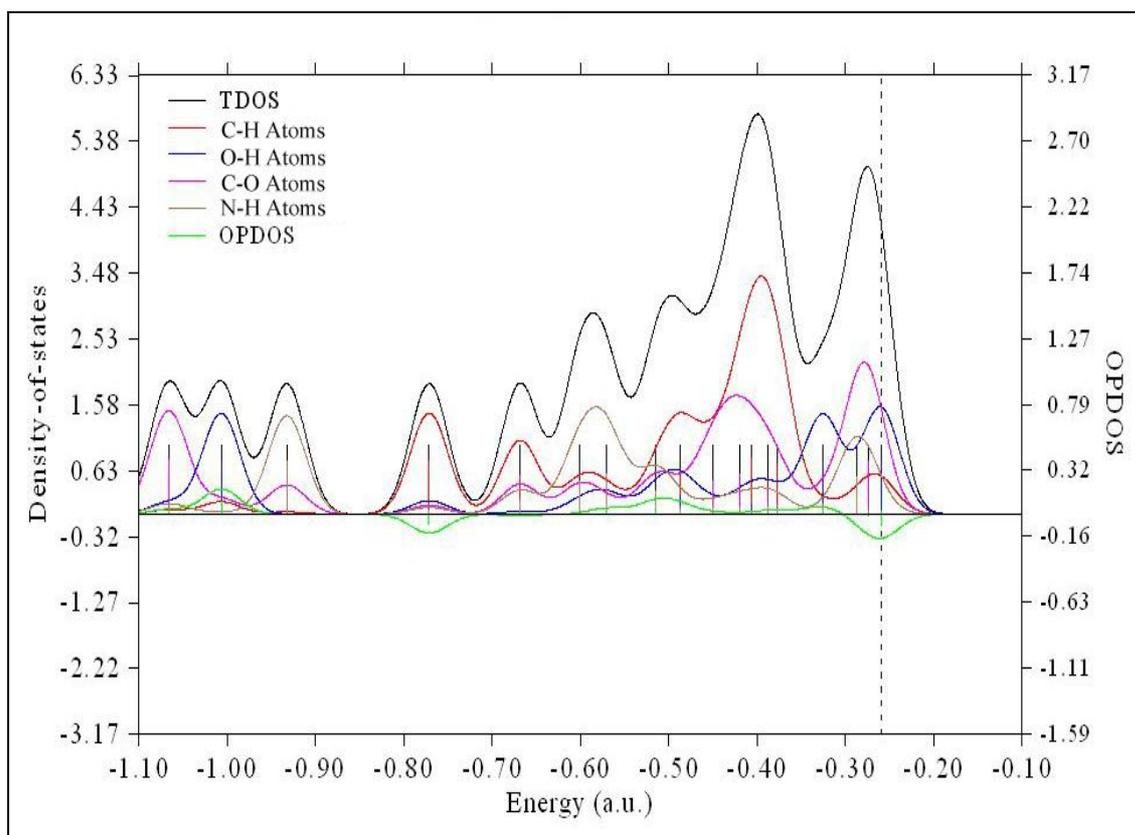


Figure 5 .Calculated partial density of states (PDOS) of the title compound

The topological analyses of the Electron Localization function (ELF) and Localized orbital locator (LOL) are tools used for performing covalent bonding analysis, as they reveal regions of molecular space where the probability of finding an electron pair is high [20-21] and ELF and LOL figures of the title molecule were presented in Fig.6(a) and Fig.6 (b) and the relief map with projection of Electron localization function is shown in Fig.6 respectively. It can be seen that the covalent regions have high LOL value (red region), the electron depletion regions between valence shell and inner shell are shown by the blue circles around nuclei. The core regions are characterized by circular localization domains with high (≈ 1) values of electron localization (red) whilst the chemical bonds C-N and C-O are described by irregular localization domains (orange) with smaller values of electron localization (0.8-0.9). Thus both bonds have a

covalent character and exhibit high electron localization, typical for shared electron (covalent) bonding. From ELF map, the regions around C4, C6, N3, were found to have lesser value where electrons are expected to be delocalized whereas the regions around hydrogen atoms have comparatively larger values indicating bonding and non-bonding localized electron. So, a large ELF or LOL value [22-23] in a region indicates high localization of electrons due to the presence of covalent bond, a lone pair of electrons or a nuclear shell in that region. Also it is clear from LOL figure, that red colour intrude into interstitial space between boundary atoms. The low stabilization energy as observed from NBO results between carbon nitrogen bonds is reflected as comparatively low values in LOL figure as it is seen as distortion observed between N3-C6 atoms.

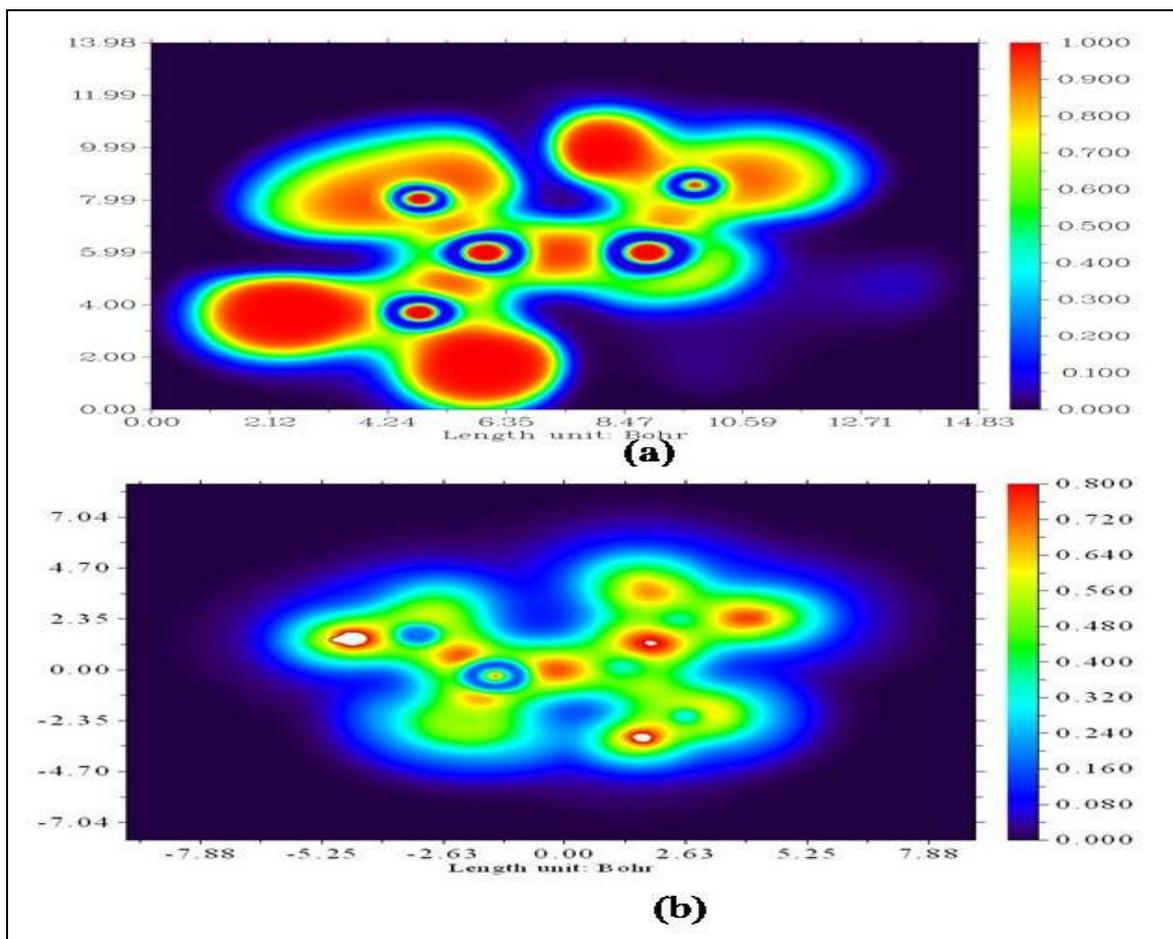


Figure 6 . (a) ELF colour filled map (b) LOL colour filled map of the title compound

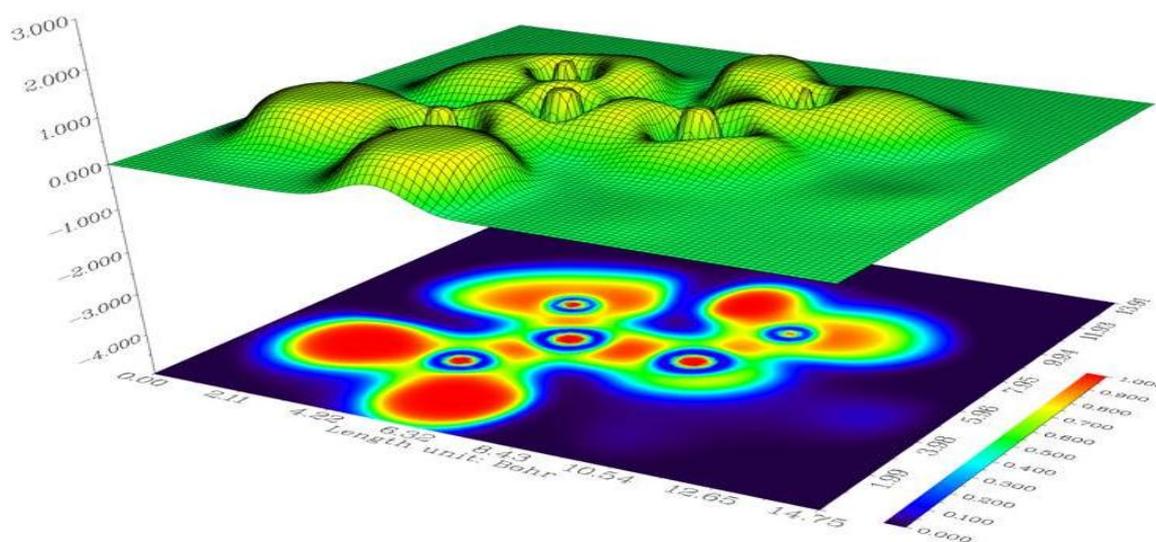


Figure 7. Relief map with projection of Electron localization function of the title compound.

3.4 Molecular electrostatic potential (MESP) analysis

A useful tool in the analysis of chemical activity of molecules and their physiochemical properties is molecular electrostatic potential surface (MESP) analysis. From molecular electrostatic potential analysis, it is possible to obtain knowledge about interaction between molecules and biological particles, such as protein and enzymes [24]. The different colours on MEP surface represent different values of the electrostatic potential. The potential increases from the least to the most negative according to the following order: blue<green<yellow<red [25-26].

To investigate reactive sites for electrophilic and nucleophilic attack, the regions of the MEP for the title compound was composed at DFT calculation using the optimized geometry at the B3LYP/6-31 G(d,p). It is clear from Fig.8 , red and yellow colors indicate negative regions in MEP corresponding to electrophilic reactivity, while bluish green colors indicate for positive regions corresponding to nucleophilic reactivity. So, the compound has one major possible site for electrophilic attack.

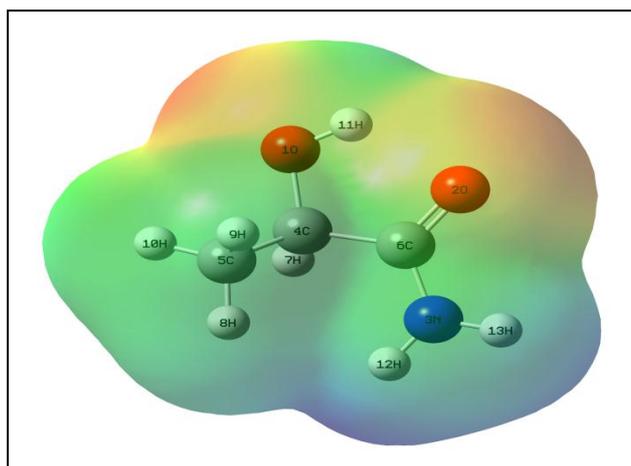


Figure 8. Molecular Electrostatic Potential of the title compound

In the investigated compound, the main areas of negative electrostatic potential are localized on oxygen atoms. According to the calculated results, the region of MEP indicates that the negative molecular electrostatic potential on oxygen atoms indicating the

major possible site for electrophilic attack and positive potential sites are around carbon and hydrogen atoms. The determination of MESP regions is best suitable for identifying sites for inter and intra molecular interactions.

IV CONCLUSION

Density functional calculations have been successfully performed for the title molecule 2-Hydroxypropanamide. The stability of the molecule arising from hyper-conjugative interaction and charge delocalization has been analyzed using NBO analysis. The important intermolecular hyper conjugative interactions are: O2-C6 from N3 of LP(N3) \rightarrow σ^* (O2-C6), C4-C6 from O2 of LP (O2) \rightarrow σ^* (C4-C6), C4-C6 from O1, of LP (O1) \rightarrow σ^* (C4-C6). The HOMO and LUMO energy values were calculated from which the band energy gap of the title molecule was determined to be 7.03252eV and TDOS and PDOS graph were plotted.. The electron distribution and the reactive sites on the surface of the title compound were analyzed using MESP, ELF and LOL analysis.

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