

Theoretical approach to the crystal structure of 2-Amino-1-(4-methoxy-phenyl)-5-oxo-4,5-dihydro-1H-pyrrole-3-carboxylic acid ethyl ester

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DOI: 10.6088/ijaser.030400012

Abstract: Gaussian-09 software programme is used to carry out the Ab initio and DFT calculations performed at RHF and B3LYP methods using the same basis set 6-31G** for the molecular structure of 2-Amino-1-(4-methoxy-phenyl)-5-oxo-4,5-dihydro-1H-pyrrole-3-carboxylic acid ethyl ester. The title molecule crystallized in to monoclinic crystal system having crystallographic parameters $a = 4.088$, $b = 27.696$, $c = 11.763$ Å and $\beta = 93.76(0)^\circ$ with space group $P2_1/n$. Using Gaussian 09 programme, for the title molecule bond lengths, bond angles, torsional angles, molecular energies, total energy and atomic charge distributions have been calculated. The computed geometrical parameters are compared with the experimental results and found to be in good agreement with them.

Keywords: DFT calculations, Molecular structure, Crystal system, space group.

1. Introduction

Pyrrole, five-membered unsaturated ring structure composed of four carbon atoms and one nitrogen atom, is one of the significant classes of organic heterocyclic compounds widely used in drug discovery (Toja et al., 1987) which also possesses a range of biological activity such as anticancer, aldose reductase inhibition, anti-inflammatory and analgesic activities. One of the series of substituted pyrrole derivatives, the title compound, 2-Amino-1-(4-methoxy-phenyl)-5-oxo-4,5-dihydro-1H-pyrrole-3-carboxylic acid ethyl ester, C₁₄H₁₆N₂O₄, is being synthesized, investigated and reported by us, as a part of our interest in studying the heterocyclic compounds (Patel et al., 2012; Patel et al., 2012; Patel et al., 2013) and also in systematic theoretical approach to similar heterocyclic compounds (Patel et al., 2012; Patel et al., 2013). Using ab-initio and DFT calculations employing different molecular geometries for the title compound bond lengths, bond angles and torsional angles, the total energy and atomic charge distributions of a molecule are determined. Both the ab-initio and the density functional theory (DFT) methods have become an increasingly useful tool for theoretical studies. The molecular energies like HOMO (Highest occupied molecular orbital) and LUMO (Lowest Unoccupied Molecular Orbital) and dipole moment are also calculated. Since both of these methods express the small molecules more reliably and therefore a thorough theoretical approach to quantum calculations is used in this paper, which takes advantage of both the high interpretive power of the theoretical studies and the exactness and consistency of the experimental method.

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Received on May 28, 2014; Accepted on July 07, 2014; Published on August 30, 2014

2. Experimental

For the title compound, the synthesis and crystal structure of have been earlier reported by us (Patel et al, 2013). The SEM photograph of one the crystals is depicted in Figure: 1. In Figure: 2, 50% probability displacement ellipsoids with numbering scheme, the ORTEP diagram of the title molecule is shown.

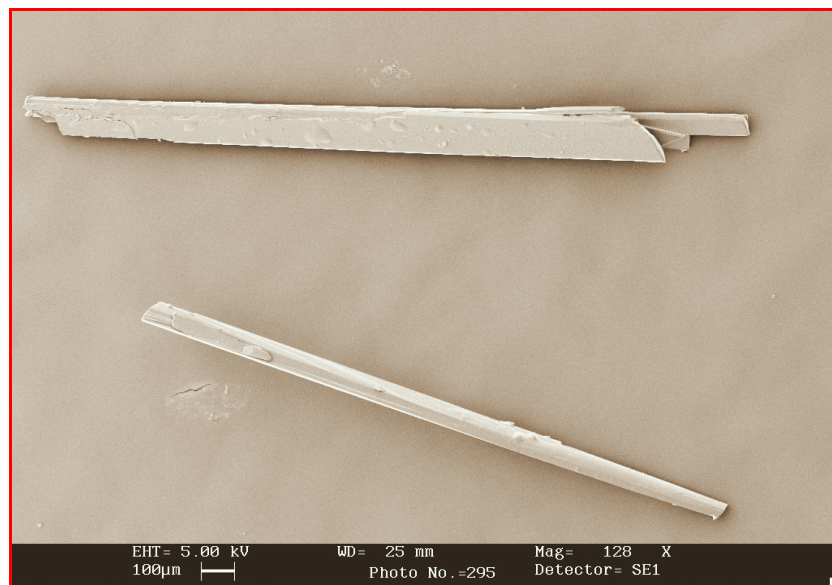


Figure 1: The SEM photograph of the title crystal

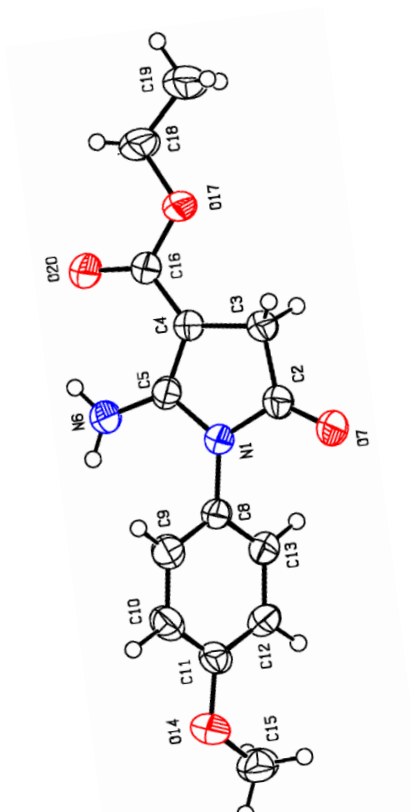


Figure 2: The title molecule in ORTEP diagram with the numbering scheme and 50% probability displacement ellipsoids

3. Computational methods

The Gaussian-09 program package is a powerful tool to carry out the theoretical calculations for compounds. For the title compound, considering the default convergences criteria in ab-initio and density functional theory (DFT) methods at the RHF/ 6-31G** and B3LYP/ 6-31G** levels, the theoretical calculations were performed (Frisch et al, 2009) at Department of Physics, Sardar Patel University, Vallabh Vidyanagar.

4. Results and discussion

4.1 Molecular geometry

For the title compound, using Gaussian-09 programme, the ab initio and DFT (Density Functional Theory) calculations at the RHF/ 6-31G** and B3LYP/ 6-31G** levels of the theory were performed to know selected optimized geometric parameters bond lengths, bond angles and torsional angles which are listed in Table: 1, Table: 2 and Table: 3 respectively. The calculated geometrical parameters were compared with those of the experimental values. The comparison of the bond lengths in Table: 1 shows the biggest difference between experimental and theoretical values occurs in C18-C19 bond with the difference -0.0343 Å for B3LYP method and in same bond, with the different values being -0.0308 Å for RHF method. The comparison of the bond angles in Table: 2 shows the biggest difference takes place in the bond angle of O7-C2-N1, with difference value of -4.7332° and in the bond angle of C11-O14-C15, with difference value of -3.3981° for B3LYP and RHF methods respectively and the most predicted values are matching with the experimental values. Due to the crystal packing in the molecules the differences between the calculated and observed geometry could be seen. However, the inspection of collective intramolecular interactions N-H...O and intermolecular interactions N-H...O, C-H...O and off-centric π - π interactions provide confirmation of collective effect of all these interactions on crystal packing in the unit cell in a molecular structure.

Table: 1 Comparison of experimental values of bond lengths with RHF and B3LYP methods

Sr. No.	Atoms	Bond lengths (Å) calculation by		
		Exp.	B3LYP/ 6-31G**	RHF/ 6-31G**
1.	N1-C2	1.385(3)	1.4155	1.3948
2.	N1-C5	1.402(3)	1.4009	1.3858
3.	C3-C2	1.499(3)	1.5269	1.5172
4.	C3-C4	1.495(3)	1.5026	1.5036
5.	C4-C16	1.410(3)	1.4332	1.4332
6.	C5-C4	1.362(3)	1.3768	1.3626
7.	N6-C5	1.330(3)	1.3503	1.3330
8.	O7-C2	1.212(2)	1.2117	1.1876
9.	C8-N1	1.433(3)	1.4260	1.4247
10.	C8-C9	1.380(3)	1.4039	1.3916

11.	C8-C13	1.376(3)	1.3959	1.3797
12.	C9-C10	1.374(3)	1.3881	1.3759
13.	C10-C11	1.384(4)	1.4029	1.3942
14.	C11-C12	1.376(3)	1.4005	1.3869
15.	C12-C13	1.381(3)	1.4029	1.3880
16.	O14-C11	1.368(3)	1.3623	1.3437
17.	O14-C15	1.422(3)	1.4205	1.4015
18.	O17-C16	1.352(3)	1.3604	1.3295
19.	O17-C18	1.438(3)	1.4412	1.4208
20.	C18-C19	1.483(4)	1.5173	1.5138
21.	O20-C16	1.218(3)	1.2363	1.2087

Table: 2 Comparison of experimental values of bond angles with B3LYP and RHF methods

Sr. No.	Atoms	Bond angles (°) calculation by		
		Exp.	B3LYP/ 6-31G**	RHF/ 6-31G**
1.	C5-N1-C2	109.49(18)	109.9666	110.3888
2.	C8-N1-C2	123.69(17)	124.1283	123.9909
3.	C8-N1-C5	126.51(17)	125.9009	125.6164
4.	N1-C2-C3	107.74(18)	106.788	107.1991
5.	O7-C2-C3	127.5(2)	128.6807	128.4845
6.	O7-C2-N1	124.7(2)	129.4332	124.3161
7.	C4-C3-C2	103.69(18)	103.5253	102.7103
8.	C3-C4-C16	128.9(2)	129.4332	128.7172
9.	C5-C4-C3	107.98(18)	108.624	108.7397
10.	C5-C4-C16	123.2(2)	121.8301	122.5345
11.	N1-C5-C4	111.09(18)	111.0599	110.958
12.	N1-C5-N6	120.0(2)	121.5237	120.1472
13.	N6-C5-C4	128.9(2)	127.4067	128.8898
14.	N1-C8-C13	119.2(2)	120.0728	120.3625
15.	C9-C8-C13	119.5(2)	119.4021	119.3165
16.	C8-C9-C10	120.0(3)	120.2395	120.3889
17.	C9-C10-C11	120.5(2)	120.2996	120.1556
18.	C10-C11-C12	119.6(2)	119.5719	119.702
19.	O14-C11-C10	115.8(2)	115.6687	115.7296
20.	O14-C11-C12	124.6(2)	124.7592	124.5683
21.	C11-C12-C13	119.7(2)	119.9094	119.5983
22.	C8-C13-C12	120.7(2)	120.5563	120.8339
23.	C11-O14-C15	116.6(2)	118.3706	119.9981
24.	O17-C16-C4	112.68(19)	112.7317	112.9478
25.	O20-C16-C4	125.5(2)	125.1329	124.9254
26.	O20-C16-O17	121.8(2)	122.1347	122.1266

27.	C16-O17-C18	116.40(18)	115.8952	117.5545
28.	O17-C18-C19	109.3(2)	107.4078	107.392

Table: 3 Comparison of experimental values of torsional angles with RHF and B3LYP methods

Sr. No.	Atoms	Torsional angles (°) by		
		Exp.	B3LYP/ 6-31G**	RHF/ 6-31G**
1.	C5-N1-C2-C3	0.3(3)	1.8581	0.5542
2.	C5-N1-C2-O7	-179.5(3)	-178.1385	-179.2623
3.	C8-N1-C2-C3	174.2(2)	2.5731	-178.7678
4.	C8-N1-C2-O7	-5.7(4)	2.5731	1.4156
5.	C2-N1-C5-C4	-0.7(3)	-1.1238	-0.2234
6.	C2-N1-C5-N6	178.4(2)	179.9226	-179.4775
7.	C8-N1-C5-C4	-174.4(2)	178.149	179.0851
8.	C8-N1-C5-N6	4.7(4)	-0.8046	-0.169
9.	C4-C3-C2-N1	0.1(3)	-1.836	-0.6371
10.	C4-C3-C2-O7	180.0(3)	178.1604	179.1693
11.	C2-C3-C4-C5	-0.6(3)	1.2121	0.5174
12.	C2-C3-C4-C16	178.9(3)	-174.9162	-178.4238
13.	C3-C4-C16-O17	2.2(4)	-2.3451	-0.7384
14.	C3-C4-C16-O20	-177.6(3)	177.3379	179.109
15.	C5-C4-C16-O17	-178.5(2)	-178.026	-179.549
16.	C5-C4-C16-O20	1.8(5)	1.657	0.2984
17.	N1-C5-C4-C3	0.8(3)	0.736	-0.2138
18.	N1-C5-C4-C16	-178.7(2)	176.3448	178.8063
19.	N6-C5-C4-C3	-178.2(3)	178.741	178.9576
20.	N6-C5-C4-C16	2.4(5)	-4.7782	-2.0224
21.	C9-C8-N1-C2	124.3(3)	126.8711	102.8396
22.	C9-C8-N1-C5	-62.8(4)	-52.3032	-76.3787
23.	C13-C8-N1-C2	-54.4(3)	-51.567	-76.6133
24.	C13-C8-N1-C5	118.4(3)	129.2586	104.1684
25.	N1-C8-C9-C10	-179.7(3)	-179.9576	179.8816
26.	C13-C8-C9-C10	-0.9(4)	-1.509	-0.6598
27.	N1-C8-C13-C12	178.3(2)	178.859	179.5385
28.	C9-C8-C13-C12	-0.5(4)	0.4036	0.0802
29.	C8-C9-C10-C11	1.6(4)	1.472	0.8065
30.	C9-C10-C11-C12	-0.9(4)	-0.3229	-0.3711
31.	C9-C10-C11-O14	179.4(3)	179.5371	179.7484
32.	C10-C11-C12-C13	-0.5(4)	-0.779	-0.2032
33.	O14-C11-C12-C13	179.2(3)	179.3746	179.666
34.	C11-C12-C13-C8	1.2(4)	0.736	0.3479
35.	C15-O14-C11-C10	176.8(3)	-178.9294	-178.0819

36.	C15-O14-C11-C12	-2.8(4)	0.9224	2.0442
37.	C18-O17-C16-O20	0.8(4)	-0.0293	0.0805
38.	C18-O17-C16-C4	-179.0(3)	179.6645	179.9328
39.	C16-O17-C18-C19	-176.7(3)	179.1419	179.8793

The relation between the calculated and experimental results is also studied by comparing their respective values of bond lengths and bond angles. The linear function formulae of $y = 1.102x - 0.142$ ($R^2 = 0.968$) for RHF/6-31G*** and $y = 1.022x - 0.017$ ($R^2 = 0.973$) for B3LYP/6-31G*** for bond lengths and $y = 1.004x - 0.392$ ($R^2 = 0.982$) for RHF/6-31G*** and $y = 1.030x - 3.418$ ($R^2 = 0.972$) for B3LYP/6-31G** for bond angles as shown in Figure 3.

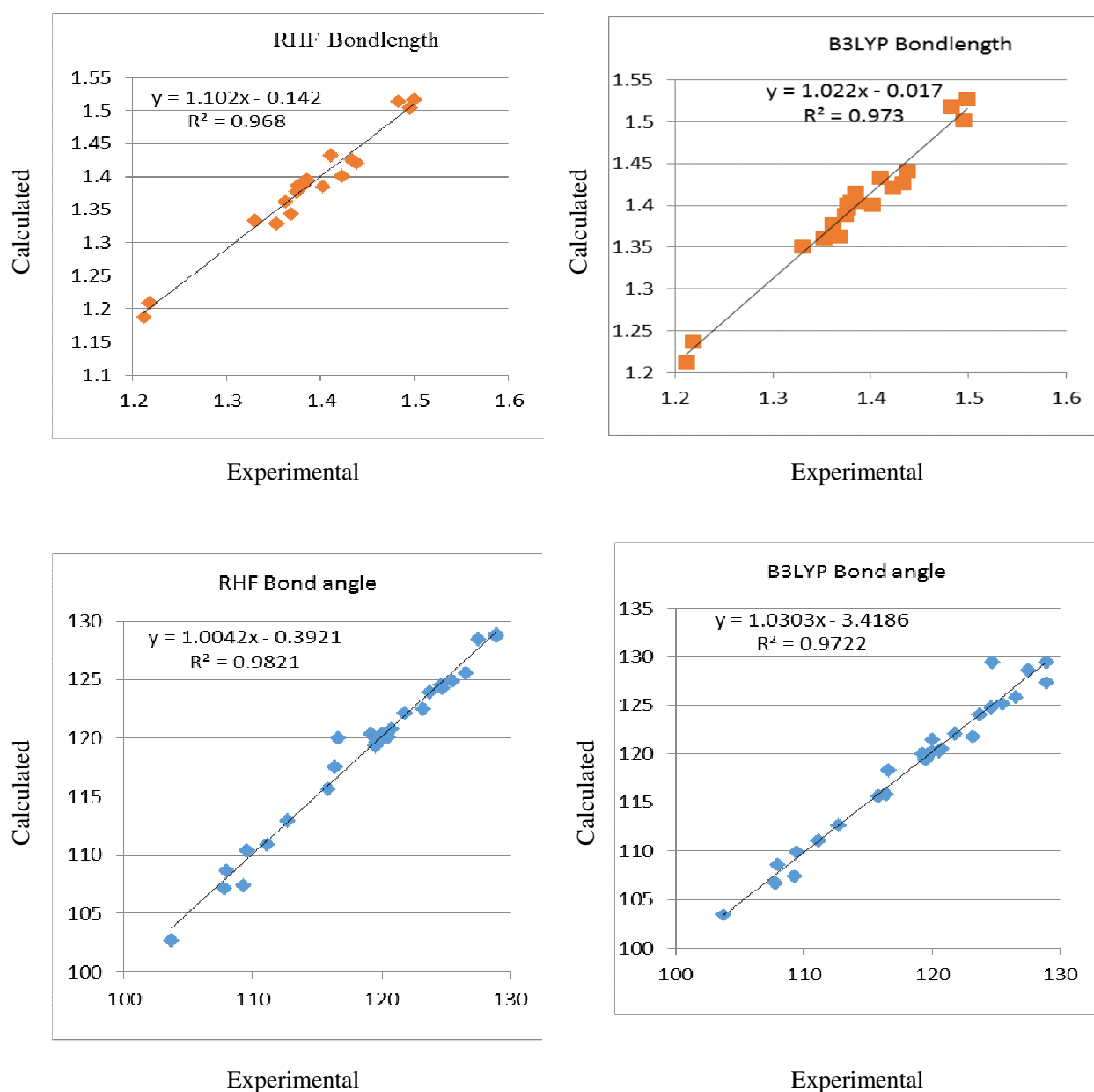


Figure 3: Computational correlations of bond lengths and bond angles for RHF and B3LYP methods

4.2 HOMO and LUMO energy calculation

As it is well known that the electron absorption is described by the transition from the ground state to the first or higher excited states. This transition corresponds to one electron excitation from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO). Using Gaussian 09 programme employing the B3LYP/ 6-31G** and RHF/ 6-31G** methods, the HOMO-LUMO energy gap calculated for the title compound is -0.18274 and -0.42347 respectively. This energy gap gives an idea about the chemical activity of the molecule. Table: 4 shows the HOMO and LUMO energy calculations, Total energy (a.u.) and Dipole moment (D) of the title compound and their respective comparison between two methods.

Table: 4 Calculation and comparison of HOMO and LUMO energy, Total energy (a.u.) and Dipole moment (D) for the title compound using two methods

Methods	HOMO	LUMO	ΔE	Total energy (a.u.)	Dipole moment (D)
RHF/6-31G**	-0.29911	0.12436	-0.42347	-947.62879	3.7272
B3LYP/6-31G**	-0.19835	-0.01561	-0.18274	-953.29167	3.1768

4.3 Mulliken charge analysis

Gaussian 09 programme has also been used to calculate and to analyze the Mulliken charge population for the title molecule using RHF/ 6-31G** and B3LYP/ 6-31G** methods and listed in Table: 5. Figure: 4 and Figure: 5 show the corresponding charts of Mulliken charge distribution using RHF/ 6-31G** and B3LYP/ 6-31G** methods respectively. It is examined for extreme values of charges for N1, N2, C8, C10, C11, C13, O1, O2 and O3 atoms. It is revealed from that the negative charge on nitrogen atom N2 has the value (-0.857661 and -1.015841), the negative charge on carbon atom C13 has the value (-0.625488 and -0.630104), the negative charge on carbon atom C8 has the value (-0.541284 and -0.551246), the negative charge on nitrogen N1 has the value (-0.515057 and -0.678393), the negative charge on oxygen atom O3 has the value (-0.432908 and -0.555355), the negative charge on oxygen atom O2 has the value (-0.337097 and -0.452502), the negative charge on oxygen atom O1 has the value (-0.324234 and -0.441994), and the highest positive charge on carbon atom C10 has the value (0.666085 and 0.871355) for B3LYP and RHF methods respectively. Among all non-hydrogen atoms, the nitrogen atoms N2, N1 and carbon atom C13 have more negative charges and carbon atoms C10 and C11 have more positive charges. Nitrogen atoms N1 and N2, having negative charges are connected with the carbon atom C10 having the highest opposite positive charge. As far as hydrogen atoms are concerned, a net positive charge is observed for all the hydrogen atoms in particular; the significantly large net positive charges have been observed on hydrogen atoms H90 and H91. The atoms N1, N2, O1, O2, O3, H90 and H91 having significant amount of charges on them predict the existence of hydrogen bonding interactions in the crystalline phase. The crystallographic investigations have also been confirmed these kind of intermolecular interactions in the molecule.

Table: 5 Calculation and comparison of Mulliken charge for the title Compound using B3LYP/ 6-31G** and RHF/ 6-31G** level

Sr no.	Atom	Mulliken charge by	
		B3LYP	RHF
1.	C8	0.220926	0.193386
2.	O7	-0.487613	-0.571394
3.	O14	-0.516895	-0.659334
4.	O20	-0.574303	-0.676994
5.	C9	-0.105764	-0.109864
6.	H9	0.113675	0.178880
7.	N1	-0.626417	-0.875481
8.	O17	-0.501365	-0.656610
9.	C10	-0.127913	-0.193469
10.	H10	0.103696	0.176419
11.	C11	0.361666	0.424178
12.	N6	-0.670040	-0.804242
13.	H61	0.309330	0.366788
14.	H62	0.273709	0.322053
15.	C12	-0.149009	-0.228831
16.	H12	0.095246	0.164851
17.	C13	-0.074252	-0.093887
18.	H13	0.113530	0.177597
19.	C5	0.570455	0.796974
20.	C3	-0.304531	-0.260988
21.	H31	0.150109	0.167242
22.	H32	0.149060	0.166414
23.	C4	-0.081489	-0.368481
24.	C2	0.578829	0.773016
25.	C15	-0.082738	-0.034253
26.	H151	0.118060	0.120974
27.	H152	0.113996	0.115702
28.	H153	0.129113	0.145804
29.	C16	0.599581	0.863603
30.	C18	0.068423	0.107170
31.	H181	0.114564	0.128192
32.	H182	0.112432	0.127378
33.	C19	-0.338632	-0.351995
34.	H191	0.107057	0.115148
35.	H192	0.118341	0.126774
36.	H193	0.119163	0.127277

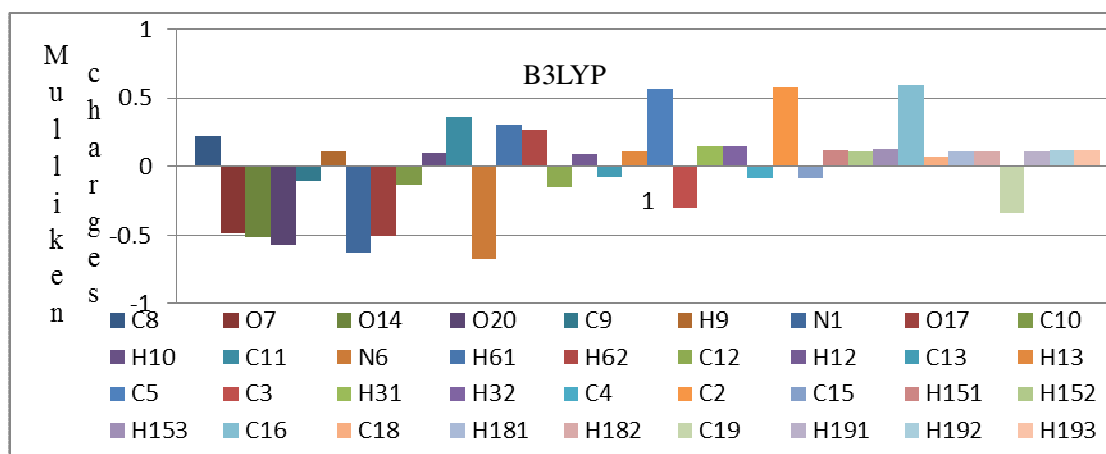


Figure 4: The chart for the title compound showing Mulliken charge distribution by B3LYP/ 6-31G** level

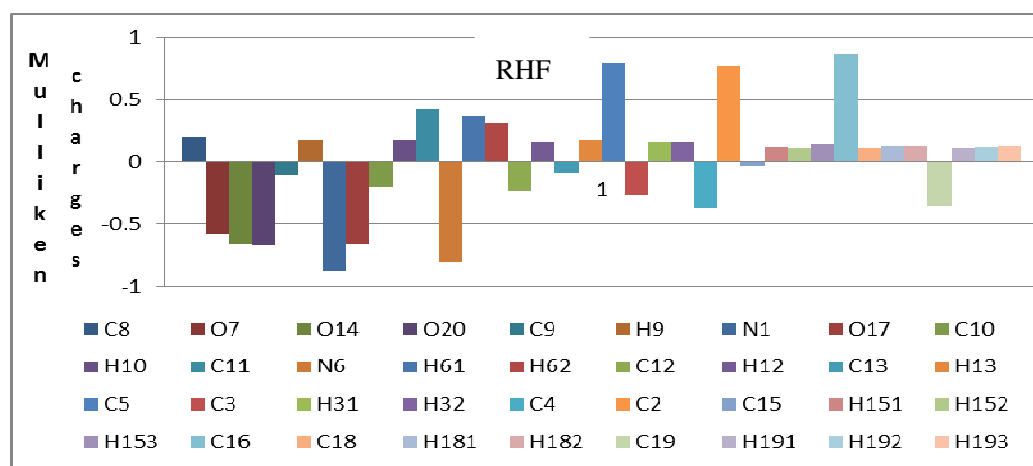


Figure 5: The chart for the title compound showing Mulliken charge distribution by RHF/ 6-31G** level

5. Conclusions

The optimized geometries and HOMO-LUMO analysis of 2-Amino-1(4-Bromo-phenyl)-5-oxo-4,5-dihydro-1-H-pyrrole-3-carboxylic acid ethyl ester were performed and analyzed at RHF and DFT methods like B3LYP level of theories utilizing 6-31G** (d) and 6-31G** basis sets using Gaussian 09 programme. The present investigations show an enhanced conformity between the experimental and computed data obtained by the DFT method of B3LYP level with a 6-31G** basis set. From the analysis of Mulliken charge population observed in the molecule, it has been concluded that there are more chances of chemical bonding among those atoms in the molecule which are having more opposite charges.

Acknowledgement

The computer facility provided to authors to carry out the research by Department of Physics, Sardar Patel University, Vallabh Vidyanagar is gratefully acknowledged. One of the authors, BDP is also gratified to

Natubhai V Patel College of Pure and Applied Sciences, Vallabh Vidyanagar for giving the required permission to accomplish the research work and also to UGC for funding towards the minor research project (No. 47-2163/11 (WRO)).

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