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Quantum Chemical computation and Vibrational spectral Investigation of 1-Acetyl-2-(4-benzyloxy-3-methoxyphenyl)cyclopropane for Drug Design Applications

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Abstract

In this study, quantum chemical and vibrational spectroscopic investigations were carried out on 1-Acetyl-2-(4-benzyloxy-3-methoxyphenyl)cyclopropane to explore its potential relevance in drug design applications. The molecular geometry was optimized using Density Functional Theory (DFT) at the B3LYP/6-311++G(d,p) level, and key electronic properties such as HOMO-LUMO energies, global reactivity descriptors, and molecular electrostatic potential (MEP) maps were analyzed to evaluate the compound's chemical stability and reactive sites. Vibrational spectra were simulated and compared with experimentally obtained FT-IR and FT-Raman spectra, showing good correlation and confirming the structural integrity of the molecule. The Potential Energy Distribution (PED) analysis provided detailed vibrational mode assignments. These results collectively suggest that the compound exhibits favorable physicochemical and structural characteristics, supporting its relevance as a potential candidate in pharmaceutical and medicinal chemistry.

1. INTRODUCTION

Aromatic compounds such as Benzene derivative compounds are commonly used for chronic inflammation treatment products in pharmaceutical products. Benzene is frequently used as an industrial solvent, especially for degreasing metal [1].

Phenyl group is also referred to as aryl phenols, are compounds composed of a phenolic group connected directly to another aromatic ring [2].Possesses pharmacological properties and used as antioxidant, analgesics, choleretic, etc

[3].Phenyl groups are present in many natural as well as synthetic organic compounds [4].Phenyl groups (similar to all other aromatic compounds) have relatively higher stability than aliphatic (non-aromatic) groups. This enhanced stability is due to the special properties of molecular orbitals in aromatic form [5].

In recent times cyclopropane and its derivatives have gained importance for their biological and pharmaceutical applications [6]. Cyclopropane derivatives are interesting molecules for theoretical studies due to their relatively small size and similarity to biological species. Also this three membered ring compound exhibits notable antimicrobial activities [7]. Cyclopropane ring systems are omnipresent in nature and are present in a large number of natural products, insecticides, and pharmaceutical drug candidates. Cyclopropanes are handy intermediates in the synthesis of complex molecules because of their ready reactivity. Cyclopropane analogues are proved to show varied biological applications such as anti-HIV, anticancer, antibacterial, antifungal, antiviral, antitumor, COX-II inhibitor properties. [8].

Therefore, the present investigation was undertaken to study the vibrational spectra of 1-acetyl -2-(4-benzyloxy-3-methoxy phenyl) cyclopropane. The effects of title compound have been investigated using B3LYP calculations with 6-31G(d) basis set. The spectroscopic studies along with HOMO, LUMO analysis have been used to elucidate information regarding charge transfer within the molecule [9]. Along with that the NBO analysis, Mulliken atomic charge, topology analysis of Electon Localization Function (ELF), Localized Orbital Locator (LOL) and Reduced Density Gradient (RDG) has been found.

2. COMPUTATIONAL DETAILS:

The molecular geometry of the 1-acetyl-2-(4-benzyloxy-3-methoxy phenyl) cyclopropane (ABMPC) is calculated by Density Functional Theory (DFT) and calculating the electronic structures of molecule by basic sets B3LYP 6- 31G(d, p) was augmented by a 'd' polarization function for heavy atoms and 'p' polarisation for hydrogen atoms. All the quantum chemical computations in the present work are performed using the Gaussian 09 software programs [10]. From the optimized geometry of the molecule 1-acetyl-2-(4-benzyloxy-3-methoxy phenyl) cyclopropane the geometric structural parameters like bond length and bond angle and dihedral angles were calculated using the Gaussian 09W [11]. The donor-acceptor interactions in the natural bond orbitals (NBO) were calculated to second- order Fock matrix, using NBO version 3.1 which is implemented in the Gaussian 09W package[12].The paper further explains the charge distribution analysis and electronic property with HOMO-LUMO energy gap. Mullikan charges dipole moment of the title molecule are also computed using B3LYP method with same basis set 6-31G(d) [13]. The vibrational studies, topology analysis of ELF, LOL and RDG scattering were calculated for the title compound.

3. RESULT AND DISCUSSION:

3.1 OPTIMIZED GEOMETRY:

The structural parameters bond length, bond angle and dihedral angles were obtained for the most stable conformer of the compound using B3LPYfunctional and 6-31G(d) basic set and the values are presented inTable.1[14].The Optimized structure of the ABMPC is shown in figure 1.

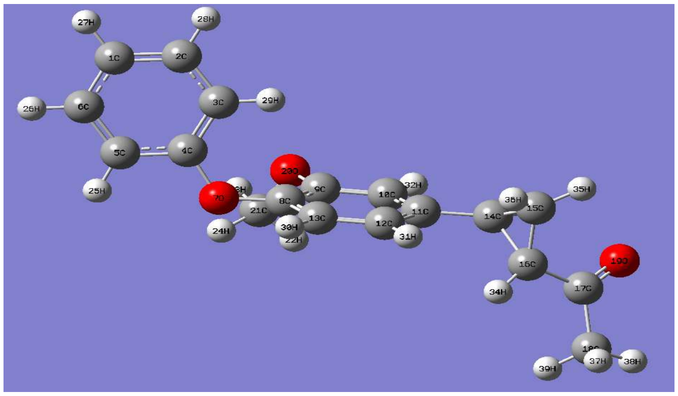

Figure 1: Optimized molecular structure of 1-Acetyl-2-(4-benzoloxy-3-methoxyphenyl) cyclopropane

The molecule consisting different functions substitutes to the benzene ring causes some changes in structural and electronic properties. From the computed values, the C–C aromatic distances within the ring are found to be equal around 1.4Å (C1–C2 = C2–C3 = C4–C5 = C5–C6) which indicates the indistinctness between the single and double bond due to the π conjugation of electrons [15].

Among the C–O bond, the bond length of C9–O20 (1.36A^0) is shorter due to presenting single and double bond between the carbon and oxygen atoms elucidating the more electrons are participated in the double bond [16]**.** In 1997, Zhou and Liu studied the vibrational spectra of trimethyl cyclopropane, a similar compound to the title compound, and found that the bond length of the carbon atoms present in the cyclopropane ring was of the order 1.452 Å, but here in the title compound we observe the bond length of carbon atoms in the cyclopropane ring to be 1.49 Å, 1.514 Å and 1.49 Å. This increase in the value of the bond length may be attributed to the heavy substitution of hydrogen atoms around the cyclopropane ring [17].

The CC bond lengths of phenyl rings are remain undisturbed. This means the electronic conjugation within the rings is identical and uninfluenced by the methoxy. Inside the ring CC single bonds which are expected around 1.45Å, the C8-C9 (1.4012) and C12-C13 (1.4013) values are almost near the expected value. This may be due to the presences of oxygen atom, which might have increased the positive charges among the carbon atoms, resulting in repulsion between them [18].

In the case of CH bond lengths, it is observed that all the CH bond lengths in both phenyl rings show the same value of 1.08 Å [19]. This shows that these bond lengths are also not affected by the influence of substitutional groups.

The CH bonds in the methoxy and acetyl groups are found to be 1.09 Å, which indicate that there is no difference in electronic distribution in these groups [20].

In the benzene ring, endocyclic C–C–C bond angles are found to be around 120^0.0, among these, a small reduction in three angles (C2–C3–C4= 119^0.1, C3–C4–C5 =1170 .1 and C4-C5-C6=119^0.5) and small increases in two angles (C1–C2–C3 = 120^0.8 and C3–C4–C5 = 120^0.6) are observed due to the substitution in the ring which is not sharing the electrons [21].

However, the variation of the bond angle depends on the factors such as lone pair of electrons in the central atom, size of ligand atoms, electro negativity and hybridization of the central atom. For example, the bond angle decreases when the size of the central atom increases and the bond angle increases when the size of ligand atom increases [22].

The bond angle decreases due to the presence of lone pairs which causes more repulsion on the bond pairs tend to come closer. It is evident that the bond angle C3–C4–O7 (123^0 .7) is less than the bond angle C4–C5–C6 (119^0.5) that shows the oxygen being more electronegative than carbon atom [23].

In this title molecule, all the CCC bond angles C1-C2-C3, C2-C3-C4, C3-C4-C5 and C4-C5-C6 are in the range of 120^0.The bond angle of the carbon atom in the benzene ring is around 120 due to sp2 hybridization [24]. The acetyl group bond angles are (C17-C18-H37), (C17-C18-H38), (C17-C18-H39) are in the range 110^0 because of the positive hydrogen atom.

Table 1: Optimized geometric parameters of 1-Acetyl-2-(4-benzoloxy-3-methoxyphenyl) cyclopropane molecule on B3LYP/6–31G(d) basis set

Bond Length	**Value**	**Bond Angle**	**Value**	**Dihedral Angle**	**Value**
C1-C2	1.3922	C6-C1-H27	120.3535	C6-C1-C2-H28	179.8131
C1-C27	1.0835	C1-C2-C3	120.8951	H27-C1-C6-C5	-179.9727
C2-C3	1.3954	C1-C2-H28	120.0565	C1-C2-C3-C4	0.0065
C2-C28	1.0843	C2-C3-C4	119.1032	C1-C2-C3-H29	179.6646
C3-C4	1.3933	C2-C3-H29	120.4515	C2-C3-C4-C5	-0.0459
C3-H29	1.0821	C3-C4-C5	120.6246	C2-C3-C4-O7	179.8176

C4-C5	1.3959	C3-C4-O7	123.7788	C3-C4-C5-C6	0.0907
C4-O7	1.3838	C4-C5-C6	119.5707	C3-C4-C5-H25	-179.7204
C5-C6	1.3905	C4-C5-H25	118.9966	C3-C4-O7-C8	4.6922
C5-H25	1.0835	C5-C6-H26	119.3749	C4-C5-C6-H26	-179.9524
C6-H28	1.0843	C4-O7-C8	119.7485	C4-O7-C8-C9	-90.3756
O7-C8	1.3854	O7-C8-C9	120.5104	O7-C8-C9-C10	-178.1073
C8-C9	1.4012	C8-C9-C10	119.0499	C9-C8-C13-H30	-179.3692
C9-C10	1.395	C10-C9-O20	118.6042	C8-C9-C10-C11	0.5178
C9-O20	1.3697	C9-C10-C11	121.7481	O20-C9-C10-C11	176.9229
C10-C11	1.3987	C11-C10-H32	120.5951	C10-C9-O20-C21	115.6169
C10-H32	1.0843	C10-C11-C12	118.2012	C9-C10-C11-C12	0.4807
C11-C12	1.4013	C12-C11-C14	122.9827	H32-C10-C11-C12	-179.93
C11-C14	1.4896	C11-C12-C13	120.6078	C10-C11-C12-C13	-0.604
C12-C13	1.3906	C13-C12-H31	118.8204	C14-C11-C12-C13	179.9118
C12-H31	1.084	O8-C13-H30	118.4914	C12-C11-C14-C15	-26.243
C13-H30	1.0838	C11-C14-C15	123.4339	C12-C11-C14-H33	-174.6203
C14-C15	1.4941	C11-C14-H33	114.693	H31-C12-C13-C8	179.5035
C14-H33	1.0844	C14-C15-H35	116.8629	C11-C14-C15-H35	-145.053
C15-C16	1.5142	C14-C15-H36	118.6132	C11-C14-C15-H36	1.2848
C15-H35	1.0832	C14-C16-H34	115.622	C11-C14-C16-H34	-5.6384
C15-H36	1.0832	C15-C16-C17	118.6531	C14-C16-C17-C18	-140.5718
C16-C17	1.493	C16-C17-C18	116.4347	C14-C16-C17-O19	38.984
C16-H34	1.084	C16-C17-O19	121.5897	C15-C16-C17-C18	152.2473
C17-C18	1.5142	C17-C18-H37	110.0458	C16-C17-C18-H37	-60.3697
C17-O19	1.2164	C17-C18-H38	110.0931	C16-C17-C18-H38	178.584
C18-H37	1.0951	C17-C18-H39	110.0953	C16-C17-C18-H39	57.2927
C18-H38	1.0891	O9-O20-C21	116.3624	C9-O20-C21-H22	-61.445
C18-H39	1.0949	O20-C21-H22	110.2542	C9-O20-C21-H23	-179.7872
O20-C21	1.4354	O20-C21-H23	105.8854	C9-O20-C21-H24	60.8488
C21-C22	1.0953	O20-C21-H24	111.3777		
C21-C23	1.0891				
C21-C24	1.0915				

3.2 NBO ANALYSIS:

NBO analysis is an efficient method that can be used to study intra and inter molecular bonding, interaction among bonds and also provides a convenient means to investigate charge transfer or conjugative interactions in a molecular system [25]. It can be used to estimate the transfer of electron density from the bonding orbitals to the anti-bonding orbitals, and study about how these interactions contribute to the stability of the molecule [26]. Natural Bond Analysis (NBO) analysis contributes a convenient basis for inspecting the high electron density in the orbital bonding of the molecular system [27]. NBO analysis has proved to be an effective tool for chemical interpretation of hyper conjugative interaction and electron density transfer (EDT) from a filled lone pair to an unfilled anti-bonding orbital in the hydrogen bonding system [28]. The lowering of orbital energy is due to the interaction between the doubly occupied orbital and the unoccupied ones is a very convenient guide to interpret the molecular structure [104]. Delocalization of electron density between occupied Lewis-type (bond or lone pair) NBO orbitals and formally unoccupied (antibond or Rydberg) non-Lewis NBO orbitals corresponds to a stabilizing donor-acceptor interaction [29].The Energy E(2) associated with each donor (i) to an acceptor (j) delocalization is determined from the second-order perturbation method is estimated as:

E(2) = ΔEij = qi [F(i,j)2/(Ei –Ej)]

where qi is the population of donor orbital tenancy, are Ei and Ej are orbital energies (diagonal elements) of donor and acceptor orbitals and F(i,j) is the off-diagonal NBO Fock matrix elements [30] respectively.

Table 2: Second order perturbation theory analysis of Fock matrix in NBO basis

Donor	ED	Acceptor	ED	Energy E(2) kcal/mol	Energy difference E(j)-E(i) a.u.	Polarized energy F(i,j) a.u.
π C1-C2	1.6831	π* C3-C4 π* C5-C6	0.3825 0.3309	17.94 22.22	0.28 0.29	0.064 0.071
σ C2-C3	1.9741	σ * C4-O7	0.0350	5.27	1.06	0.067
π C3-C4	1.6620	π* C1-C2 π* C5-C6	0.3381 0.3330	22.09 17.68	0.30 0.30	0.072 0.065
π C5-C6	1.7008	π* C1-C2 π* C3-C4	0.3381 0.3825	17.73 22.37	0.29 0.28	0.065 0.073
π C8-C9	1.6499	π* C10-C11 π* C12-C13	0.3625 0.3457	18.52 21.57	0.31 0.30	0.068 0.072
π C10-C11	1.6574	π* C8-C9 π* C12-C13	0.4050 0.3457	23.50 19.69	0.28 0.28	0.073 0.067
π C12-C13	1.6908	π* C8-C9 π* C10-C11	0.4050 0.3625	19.87 21.30	0.28 0.29	0.068 0.072
σ C14-C15	1.9438	σ * C15-C16	0.0317	5.31	0.89	0.062
σ C14-C16	1.8986	σ * C14-C15 σ * C15-C16	0.0311 0.0317	5.23 6.58	0.89 0.87	0.062 0.069
σ C15-C16	1.9252	σ * C14-C15 σ * C14-C16	0.0311 0.0458	5.78 7.04	0.90 0.87	0.065 0.070
LP(1) O7	1.9322	σ * C3-C4	0.0280	6.68	1.11	0.078
LP(2) O7	1.8580	π* C8-C9 π* C3-C4	0.4050 0.3825	7.77 26.64	0.55 0.36	0.064 0.093
LP(2) O19	1.8791	σ * C16-C17 σ * C17-C18	0.0715 0.0567	21.11 21.70	0.69 0.66	0.109 0.108
LP(1) O20	1.9418	σ * C8-C9	0.0485	5.77	1.04	0.059
LP(2) O20	1.9175	π* C8-C9 σ *C9-C10 σ *C21-H22	0.4050 0.0271 0.0191	6.48 5.76 5.84	0.40 0.96 0.78	0.050 0.057 0.061

The intra-molecular hyper-conjugative interactions are formed by the orbital overlap between π(C–C) and π*(C–C) bond orbitals, which results in intra-molecular charge transfer (ICT) causing stabilization of the system. The hyper-conjugative interactions of π(C1– C2)→π*(C3–C4), π(C1–C2)→π*(C5–C6), π(C3–C4)→π*(C1–C2), π(C3–C4)→π*(C5–C6), π(C5–C6)→π*(C1–C2) and π(C5–C6)→π*(C3–C4)are found to be 17.94, 22.22, 22.09, 17.68, 17.73, and 22.37 kcal/mol, respectively[106].Likewise, for LP (2) O7— π* (C3-C4) orbital the stabilization energy is quite higher comparative to all the other occurrences range the energy is 26.64 KJ/mol[31].

The intra molecular interaction are formed by the orbital overlap between bonding C–C and C–H anti-bond orbital which results intra molecular charge transfer (ICT) causing stabilization of the system [32]. The electron lone pair orbital interactions on Oxygen atoms play a significant role in the stabilization of the compound. The interaction of atoms in title compound contain lone pair of electrons localized on (LP2) O19 with the adjacent atoms σ* (C16-C17) and σ* (C17-C18) with reasonably high stabilization values such as 21.11 and 21.70 kJ/mol respectively [33]. Contributions from other interactions such as σ→σ*, π→π*, LP(1)→ σ*, LP(2)→ σ* and LP(2)→π* in stabilizing the molecular structure were also observed. These interactions also play a very significant role in formation of many hydrogen bonds leading to stable crystal structure of all the compounds [34].

In Cyclopropane BD(C14-C15)→$BD*(C15 – C16)$, BD(C14-C16)→ $BD*(C14 − C315)$, $BD(C14 – C16) \rightarrow BD*(C14 – C16)$, $BD(C15 – C16) \rightarrow BD*(C14 – C15)$ $BD(C15 – C16) \rightarrow BD*(C14 – C16)$ have stabilization energies of 5.31 kcal/mol, 5.23kcal/mol, 6.58 kcal/mol, 5.78 kcal/mol and 7.04 kcal/mol respectively. Hence, they give stronger stabilization to the molecule [35].

3.3 MULLIKEN POPULATION ANALYSIS:

The Mulliken population analysis of the title molecule is calculated using B3LYP level of theory with 6-31G(d) basic set. The calculation of atomic charges plays an important role in the application of quantum mechanical calculations to molecular systems [36].Mulliken Population Method can be used for interpreting and predicting the reactive behavior of a wide variety of chemical systems in both electrophilic and nucleophilic reactions [37].

Table 3: Mulliken atomic charges of 1-Acetyl-2-(4- benzoloxy-3-methoxyphenyl) cyclopropane performed by density functional calculations

Atom	Mulliken Atomic Charge	Natural Charge
C	-0.335668	-0.23188
C	-0.047765	-0.17695
C	-0.016669	-0.27212
C	-0.258708	0.32018
C	-0.195692	-0.24234
C	-0.098102	-0.18269
O	-0.068545	-0.53994
C	-0.135411	0.25127
C	-0.369960	0.28881
C	-0.045613	-0.21671
C	0.931424	-0.02772
C	-0.558319	-0.21054
C	-0.017247	-0.20767
C	-0.156954	-0.20399
C	-0.768761	-0.35209
C	0.133103	-0.31185
C	0.034166	0.57423
C	-0.539596	-0.66074
O	-0.281885	-0.57126
O	-0.091580	-0.56729

C	-0.268279	-0.19021
H	0.126690	0.16034
H	0.162672	0.18389
H	0.175134	0.17232
H	0.154737	0.21305
H	0.168127	0.20217
H	0.139502	0.20330
H	0.187179	0.20191
H	0.148120	0.21824
H	0.182213	0.21607
H	0.147287	0.20092
H	0.183034	0.21439
H	0.279519	0.22991
H	0.232729	0.21658
H	0.206737	0.22738
H	0.171721	0.20976
H	0.156425	0.21890
H	0.178045	0.22270
H	0.156192	0.21965

The calculated mulliken charge is given in table 3 and the Mulliken plot shown in Figure 2. According to Mulliken method, the obtained atomic charge shows that the C11 atoms has bigger positive atomic charges, than the other carbon, oxygen and hydrogen atoms because it is attached to a alkayl group. The carbon atoms in both benzene rings are expected to be equally negative [38], as they share the electrons within the ring equally due to conjugation. The oxygen atom O7, O19 and O20 exhibit negative charge because oxygen atoms are donar atom and they are highly electronegative. All the hydrogen atom in title compound exhibits a positive charge, which is an acceptor atom.

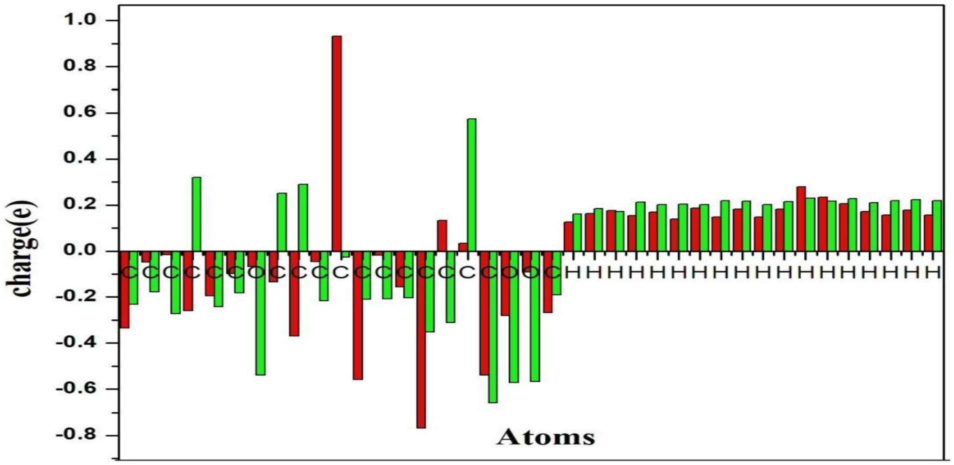

Figure 2: Mulliken atomic charge distribution for 1-Acetyl-2-(4-benzoloxy-3-methoxyphenyl) cyclopropane.

3.4 FRONTIER MOLECULAR ORBITAL ANALYSIS:

Frontier molecular orbitals determine the way the molecule interacts with other species [31] by using the density functional theory (DFT). The reactivity of any molecule can be predicted efficiently through the frontier molecular orbitals (FMOs) analysis [39]. Frontier Molecular Orbitals (FMO) lie at the outermost boundaries for the electrons in a system. The highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) are known as FMO, which play a vital role in chemical reactions [40]. The Highest Occupied Molecular Orbital (HOMO) signifies the ability to donate an electron (nucleophile) and the energy of HOMO is directly connected to the ionisation potential (I). The Lowest Unoccupied Molecular Orbital LUMO value implies the tendency to gain an electron (electrophile) and LUMO energy associated directly with electron affinity (A) [41]. The HOMO-LUMO plot is given in figure 3.

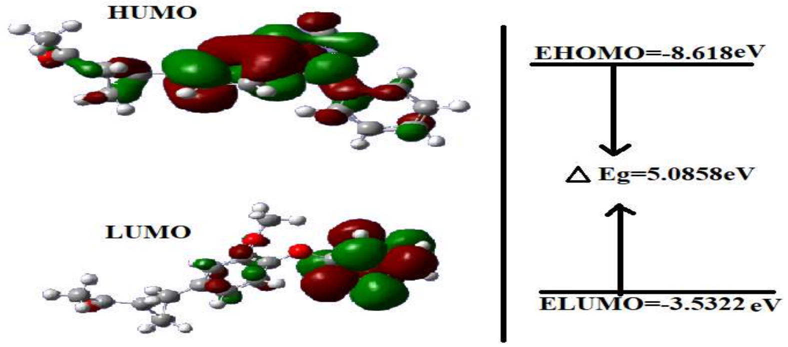

Figure 3: Frontier molecular orbital of 1-Acetyl-2-(4-benzoloxy-3-methoxyphenyl) cyclopropane

The simplest way to calculate the excitation energy is by taking the difference between HOMO and LUMO of a neutral system. The HOMO–LUMO energy gap for 1 acetyl-2(4 benzyloxy-3 methoxy phenyl cyclopropane) (5.07eV) has been calculated using DFT level. The eigen values of LUMO and HOMO and their energy gap reflect the biological activity of the molecule. The HOMO and LUMO show that a donor-to-acceptor charge transfer interaction occurs in the title compound proving its bioactivity. In addition, the decrease in the HOMO and LUMO energy gap explains the eventual charge transfer interaction taking place within the molecule which is responsible for the bioactivity of the molecule [42]. The important quantities such as global hardness (η), softness (s), chemical potential (μ) and global electrophilicity index (ω) were deduced from ionization potential and electron affinity values [43]. Using the parameters the stability and reactivity associated with a molecular system can also be characterized [120]. The chemical stability of the molecule is arising from the global hardness and softness of the molecule which represents a good indication of the chemical stability of the compound. The energy gap value is utilized to find whether the molecule is soft or hard [44].

Table 4: HOMO – LUMO energy gap and other physical relationship for1-Acetyl-2-(4-benzoloxy-3-methoxyphenyl) cyclopropane

Molecular Properties	**Mathematical Description**	**Energy(eV)**
E_{HOMO}	Energy of HOMO	-8.6118
E_{LUMO}	Energy of LUMO	3.5322
Energy Gap	$\Delta E_g = E_{HOMO} - E_{LUMO}$	5.0795
Ionization Potential (IP)	$IP = -E_{HOMO}$	8.6118
Electron Affinity (EA)	$EA = -E_{LUMO}$	-3.5325
Electronegativity (χ)	$\chi = -1/2(E_{LUMO} + E_{HOMO})$	2.5397
Chemical potential (μ)	$\mu = 1/2(E_{LUMO} + E_{HOMO})$	-2.5397
Global Hardness(η)	$\eta = 1/2(E_{LUMO} - E_{HOMO})$	6.0720
Softness (S)	$S = 1/2\eta$	0.0823
Electrophilicity index (ω)	$\omega = \mu^2/2\eta$	0.5311

3.5 VIBRATIONAL ANALYSIS:

The title molecule under investigation has 39 numbers of atoms and therefore 111 normal modes of fundamental vibrations [45]. Most of them are found active either in FTIR experimental and theoretical values as compared. The calculated wave numbers are found slightly higher than the observed values for the majority the normal modes. Two factors may be responsible for the discrepancies between the experimental and computed wave numbers; the first is caused by the unpredictable electronic distribution among the different bonds in the molecule and the second reason is the anharmonic nature of the vibrations which cannot be accounted completely by theory [46]. Scaling strategies were used to bring computed wave numbers to coincide with observed values. In this study, the scaling factors used is 0.967 as advised by the earlier work [47]. All the computed and experimental wave numbers values are presented in Table. The theoretical and experimental FTIR are shown in Figure 4.

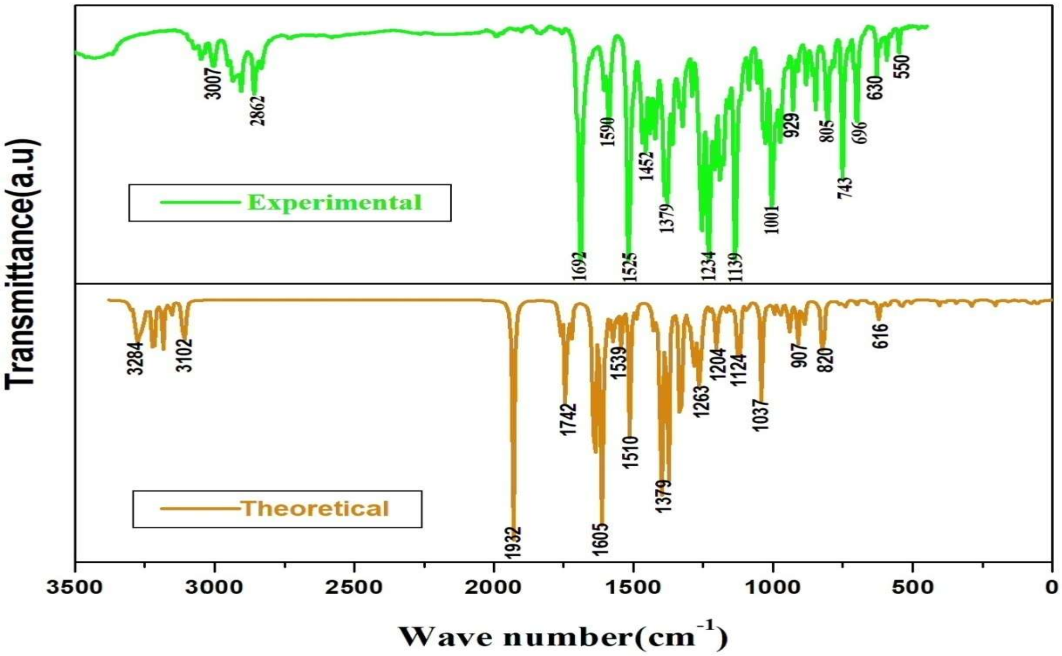

Figure 4: Combined FT-IR Spectrum of 1-Acetyl-2-(4-benzoloxy-3-methoxyphenyl) cyclopropane molecule

3.5.1 C-C Vibration:

The C-C stretching vibrations in the benzene derivatives appear in the range of 1650-1590 cm-1 [48,49]. In our compound, the C-C stretching vibration is observed in IR at 1590cm^{-1}.The phenyl ring exhibit C-C stretching vibrations in the range 1650-1100 cm-1 [50- 51]. The peaks are assigned at 1590, 1525, 1452,1379,1234,1139 cm^{-1} in IR due to the C-C stretching vibrations, the corresponding theoretical values have been computed in the span 1639-1120 cm^{-1}.

Table 5: Comparison of the experimental (FT-IR) wavenumbers (cm−1) and theoretical wavenumbers (cm−1) of 1-Acetyl-2-(4-benzoloxy-3-methoxyphenyl) cyclopropane molecule calculated by B3LYP/6–31G(d) level of theory

Wave Number		IR	Vibrations
Calculated	Scaled		
3415	3302	-	γ_{asy}- CH_2
3408	3295	-	γ C_3H_{29}
3393	3281	-	γ C_5H_{25}
3390	3278	-	γ $C_{13}H_{30}$
3384	3272	-	γ C_1H_{27}

3380	3268	-	$\gamma\ C_{18}H_{32}$
3369	3257	-	$\gamma\ C_{12}H_{31}$
3368	3256	-	$\gamma\ C_6H_{26}$
3360	3249	-	$\gamma\ C_{14}H_{33}$
3358	3247	-	$\gamma\ C_2H_{28}$
3350	3239	-	$\gamma\ C_{16}H_{34}$
3330	3220	-	$\gamma_{asy}-CH_3$
3325	3215	-	$\gamma_{sym}-CH_2$
3324	3214	-	$\gamma\ C_{18}H_{38}$
3292	3183	-	$\gamma_{asy}-CH_3$
3262	3154	-	$\gamma_{asy}-CH_2$
3215	3108	-	$\gamma_{sym}-CH_3$
3206	3100	3007	$\gamma_{sym}-CH_3$
1995	1929	-	$\gamma\ C_{17}O_{19}$
1822	1761	-	γ CC
1803	1743	-	γ CC
1793	1733	-	γ CC
1779	1720	1692	γ CC
1695	1639	-	γ CC
1668	1612	-	γ CC
1659	1604	-	γ CC
1655	1600	1590	$\beta_{in}-CH_3$
1644	1589	-	$\beta_{out}-CH_2$
1629	1575	-	$\beta_{in}-CH_3$
1625	1571	-	$\beta_{out}-CH_2$
1619	1565	-	γ CC
1609	1555	-	$\beta_{in}-CH_3$
1595	1542	-	$\beta_{in}-CH_3$
1564	1512	1525	$\beta_{in}-CH_2$
1540	1489	1452	$\beta_{out}-CH_3$
1482	1433	-	$\beta_{out}-CH_3$
1473	1424	-	$\beta_{out}-CH_2$
1447	1399	-	γ CC
1421	1374	1379	β CC
1376	1330	-	γ CC
1344	1299	-	γ CC
1340	1295	-	$\beta_{out}-CH_3$
1328	1284	-	γ CC
1323	1279	-	$\beta_{out}-CH_3$
1311	1267	-	$\beta_{in}-CH_3$
1304	1260	-	$\beta_{out}-CH_2$
1292	1249	-	$\beta_{out}-CH_2$

1291	1248	1234	γ CC
1265	1223	-	$\beta_{out} - CH_2$
1245	1203	-	γ CC
1223	1182	-	$\beta_{out} - CH_3$
1217	1176	-	γ CC
1213	1172	-	$\beta_{out} - CH_2$
1204	1164	-	$\beta_{out} - CH_2$
1184	1144	1139	γ CC
1169	1130	-	$\beta_{out} - CH_2$
1159	1120	-	β CC
1130	1092	-	$\beta_{out} - CH_2$
1127	1089	-	β CC
1113	1076	-	$\beta_{out} - CH$
1093	1056	-	$\beta_{out} - CH$
1088	1052	-	$\beta_{in} - CC$
1082	1046	-	$\beta_{out} - CH$
1075	1039	-	$\beta_{out} - CH_3$
1048	1013	1001	$\beta_{out} - CH$
1029	990	-	γ CC
1011	977	-	$\beta_{out} - CH$
1003	969	-	$\beta_{in} - CH$
974	941	-	$\beta_{out} - CH$
961	929	929	$\beta_{out} - CH$
941	909	-	γ CC
935	904	-	$\beta_{out} - CH$
918	887	-	β CC
869	840	-	γ CC
851	822	-	$\beta_{in} - CH_2$
848	820	805	β CH
806	779	-	γ CH
784	758	743	$\beta_{in} - CH_2$
766	740	-	$\beta_{out} - CH$
723	699	696	$\beta_{out} - CC$
679	656	-	γ CC
670	647	-	β CC
659	637	630	$\beta_{out} - CH_3$
644	622	-	$\beta_{out} - CH_3$
626	605	-	β CC
608	587	550	$\beta_{out} - CH_3$
565	546	-	$\beta_{in} - CH$
554	535	-	γ CC
521	503	-	γ CH
461	445	-	$\beta_{in} - CH$

448	433	-	$\beta_{out} - CH_2$
419	405	-	$\beta_{in} - CH_3$
398	384	-	$\beta_{out} - CH_3$
354	342	-	$\beta_{out} - CO$
319	308	-	$\beta_{in} - CH$
302	292	-	$\beta_{out} - CH_3$
296	286	-	$\beta_{out} - CH_3$
230	222	-	$\beta_{in} - CH_2$
214	206	-	$\beta_{in} - CH_2$ $\beta_{in} - CH_3$
196	189	-	$\beta_{in} - CH$
165	159	-	$\beta_{in} - CH_3$
155	149	-	$\beta_{in} - CH_3$ $\beta_{out} - CH$
149	144	-	$\beta_{in} - CH_3$
124	119	-	$\beta_{in} - CH_3$ $\beta_{in} - CH_2$
88	85	-	$\beta_{in} - CH_3$
78	75	-	$\beta_{in} - CH_3$
55	53	-	$\beta_{in} - CH_3$
36	34	-	$\beta_{in} - CH_3$ $\beta_{in} - CH$
34	32	-	$\beta_{in} - CH$ $\beta_{in} - CH_3$
24	23	-	$\beta_{in} - CH_3$
15	14	-	$\beta_{in} - CH$

3.5.2 C-H Vibration:

The hetero aromatic organic compounds commonly exhibit multiple week bands in the region 3100– 3000cm−1 due to C–H stretching vibrations [52-53]. In our compound, the C-H stretching vibration is observed in IR at 3007cm^{-1}.The C-H in plane bending vibrations were appeared in the range of 1000-1300cm^{-1} and are very useful for characterization purposes [54-55]. The observed series of strong bands in IR at 1234 and weak band in IR at 1139, 1001 cm^{-1} is assigned to the C-H in plane bending vibration. The C-H out of plane bending vibrations occur in the region 1000-750 cm-1 [56]. The C-H out of plane bending is observed in IR at 929 and 805cm^{-1}. The theoretically computed wavenumbers of CH vibrations calculated by B3LYP/6-31G(d) methods show excellent agreement with the recorded spectrum as well as literature data. [57].

3.5.3 CH_2 vibrations:

In the title molecule, the asymmetric and symmetric stretching vibrations are exhibited by CH_2 group [58]. In CH_2 all the modes of vibrations are expected to be depolarized.[59]. The asymmetric vibrations occur at higher wavenumber compared with the symmetric vibration. The asymmetric vibrations are generally observed above 3000 cm^{-1} while the symmetric stretching will appear between 3000 -2900 cm^{-1}[60]. In the current study, the theoretical wavenumbers are computed at 3302 and 3154 cm^{-1} for γ_{asym} and 3215 cm^{-1} for γ_{sym} and the experimental values are not found. The corresponding theoretical and experimental peak values are shifted away from the general range.

3.5.4 CH_3Vibrations:

CH_3 groups are generally referred to as electron donating substituents in the aromatic ring systems. The methyl hydrogen atoms in the molecule are simultaneously subjected to hyperconjugation and back donation, which cause the decrease of stretching wavenumbers and IR intensities [61].

The assignments of methyl group vibration make a significant contribution to the titled compound. The asymmetric C-H vibration for methyl group usually occurs in the region between 2975 cm-1 and 2920 cm-1. The theoretically computed values by B3LYP/6-31G(d)method for C-H vibrations are not found within the range.In the title compound the methyl in-plane bending modes occur in the range 1479-1411 cm-1. The FTIR experimental values occur at 1452 cm^{-1}. The C-H out-of plane bending vibrations occur at 805 cm^{-1} .The assignments are in agreement with the literature values [62].

3.5.5 O-C Vibration

The O-C vibration are expected in the range from 1000-1300cm-1 [63].The O-C vibration of this compound was observed at 1234 cm^{-1} in FT-IR.The theoretical wavenumber of scaled frequency falls from1299-1013 respectively.

3.6 TOPOLOGY ANALYSIS OFELF AND LOL:

The topology analysis of Electron Localization Function (electrons are greatly localized) ELF and Localized Orbital Locator LOL, were performed using Multiwfn program [64]**.** 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 [65-66]. The ELF indicates where pairs of electrons exist in the system, including lone pairs and bonding pairs. It is a dimensionless quantity, in the range of 0–1, with the purpose of providing a visual description of the chemical bond for almost all compounds[67]. Color shade maps of the ELF and LOL for the title molecule are presented in Figure. The value of ELF, ranges from0.0to1.0, where relatively large values in the interval 0.5 and 1.0 indicate regions containing bonding and nonbonding localized electrons, whereas smaller values (<0.5)describe regions where electron are expected to be delocalized [68]. The Shaded surface maps with projection effect of electron localization function (ELF) and localized orbital locator(LOL) of 1-Acetyl-2-(4-benzoloxy-3-methoxyphenyl) cyclopropane is shown in figure 5.

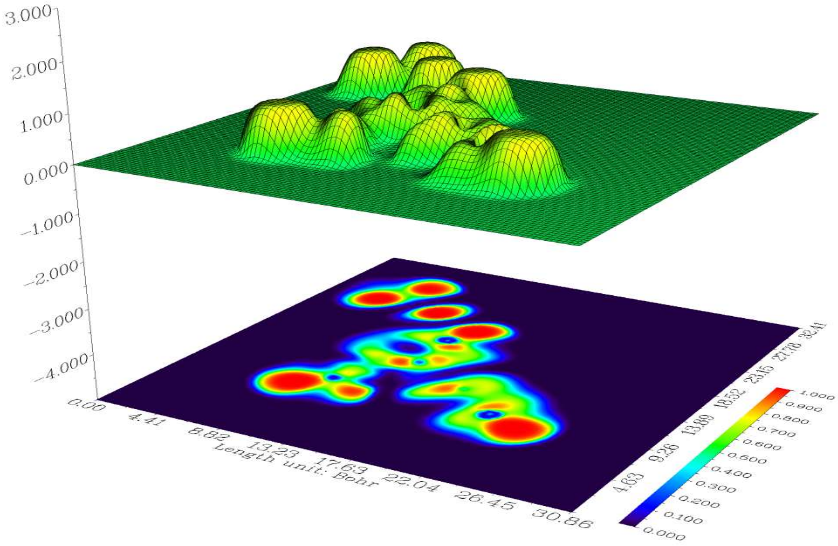

Figure 5: Shaded surface maps with projection effect of electron localization function (ELF) of 1-Acetyl-2-(4-benzoloxy-3-methoxyphenyl) cyclopropane

The LOL, attains large values (>0.5) in regions where the electron density is dominated by electron localization [69].The high ELF regions are seen around hydrogen atoms indicating the presence of highly localized bonding and non- bonding electrons [70]. The blue regions around few carbon atoms show the delocalized electron cloud around it. The central region of a carbon and oxygen atom is white, indicating that electron density exceeds the upper limit of color scale (0.80). The covalent regions are seen between hydrogen atoms, indicated by red color with high LOL value, the electron depletion regions between valence shell and inner shell are shown by the blue circles around the carbon and oxygen nuclei [71].

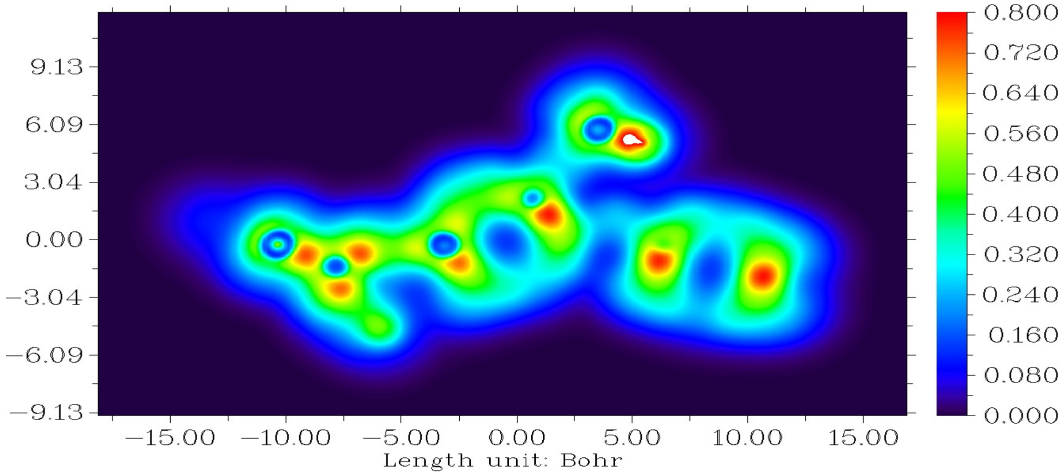

Figure 6: Shaded surface maps with projection effect of localized orbital locator(LOL) of 1-Acetyl-2-(4-benzoloxy-3-methoxyphenyl) cyclopropane

3.7 RDG SCATTERING:

RDG approach is a topological tool which reveals noncovalent interactions such as van der Waals, hydrogen bonds and steric effect using Multiwfn and plotted by visual molecular dynamics (VMD) program [72-73]. The region of these interactions and their graphical visualization is provided using the RDG analysis based on the electron density and its derivatives [74]. RDG scatter graph is generated between RDG versus sign (λ2)ρ, where sign(λ2)ρ is the second Eigen value of the electron density which provides useful information regarding the strength and nature of the interactions[75]. The value and sign of sign (λ2)ρ are used to explain the nature of interactions,sign (λ2)ρ > 0 for repulsive interaction, sign (λ2)ρ < 0 for attractive interaction and sign (λ2)ρ nearly zero for vander Waals weak interaction [76]. The Graphical representation of the reduced density gradient versus the electron density and the different types of interactions of 1-Acetyl-2-(4-benzoloxy -3-methoxyphenyl) cyclopropane is shown in figure 7.

From RDG iso-surface plot red colour scatter near the carboxylic group shows steric effect which is also evident from the scatter plot between the positive region 0.05–0.01 a.u [77]. Green colour scatter denotes the presence of van der Waals force non-covalent H…H inter scatter from 0.01-0.02. Blue colour scatter is not seen from the RDG plot between the negative region −0.02 to −0.05 a. u, which specifies that there is no involvement of strong interaction of H-bond. Iso-surface density plots illustrating the non-bonded interactions from the RDG graph the red scatter appear in high range between 0.05 to - 0.01 a. u [78]. The RDG scatter graph shows the strong repulsion steric effect and van der Waals force interaction occurs in the 1-acetyl-2(4 benzyloxy-3 methoxy phenyl cyclopropane) compound.

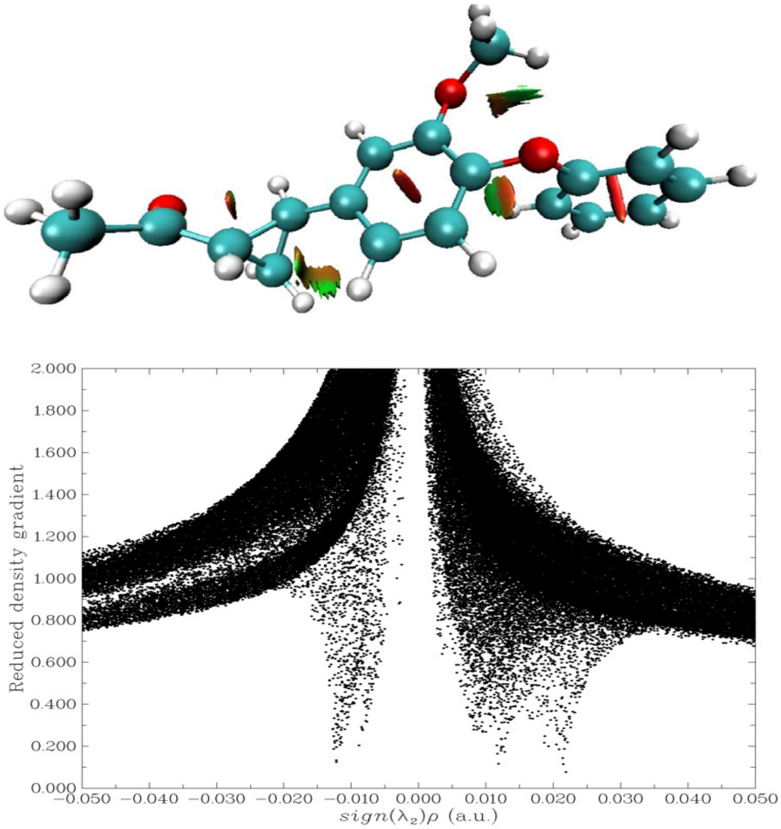

Figure 7: Graphical representation of the reduced density gradient versus the electron density and the different types of interactions of 1-Acetyl-2-(4-benzoloxy -3-methoxyphenyl) cyclopropane

4. CONCLUSION

Geometric optimization, FT-IR spectra have been computed by DFT using B3LYP/6- 31G(d) level of theory and basis set. The result shows that there is a good agreement between the experimental and theoretical data indicating the validity of the DFT level of theory and basis applied to 1-acetyl-2(4 benzyloxy-3 methoxy phenyl cyclopropane) molecule for prediction of both structural and spectroscopic data of the title compound. The vibrational assignments of the molecules have been calculated and analyzed. The total energy distribution of an individual was calculated by using the VEDA program privileges. The hyperconjucative interaction and the possible interaction were identified using NBO analysis. The HOMO and LUMO energies of 1-acetyl-2(4 benzyloxy-3 methoxy phenyl cyclopropane) molecules were calculated. The energy gap indicates that the chemical stability of the molecule, which is the measure of anti-oxidant and anti-cancer activity of the molecule. The Presence of electron density was identified using localized orbital locater.

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