

Structural and Spectroscopic (Ft-Ir, Ft-Raman, Nmr, Uv-Vis) Investigations on 4-Methoxyacetophenone Using Quantum Computational Methods

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Abstract- In the present study, Gaussian computations are carried out using B3LYP method with 6-311++G (d,p) basis sets and the corresponding results are compared with the experimental values. FT-IR, FT-Raman, NMR and UV spectra of 4-Methoxyacetophenone (4MAP) are recorded, the fundamental vibrational frequencies are tabulated and assigned. The change in the chemical environment of the compound is studied. The ¹³C NMR and ¹H NMR chemical shifts are calculated using the gauge-independent atomic orbital (GIAO) method, with the B3LYP functional and the 6-311++G (d,p) basis set and their spectra is compared with the experimental spectra. A study on the electronic and optical properties; absorption wavelengths, excitation energy, dipole moment and frontier molecular orbital energies are also performed using HOMO – LUMO methods. The calculated HOMO and LUMO are displayed with energy gap, which show the occurrence of charge transformation within the molecule. NLO properties related to polarizability, hyper-polarizability are discussed and also performed thermodynamical properties. The Docking of the molecule with different virus/ bacteria is carried out in order to understand the biological activity of the molecule.

Index Terms- DFT, FT-IR, FT-Raman, Docking Thermodynamical analysis, NMR, UV-Vis analysis.

1. INTRODUCTION

Acetophenone is one of the most typical aromatic carbonyl, which shows interesting photochemical properties [1,2]. It is of additional interest that aminoacetophenone derivatives possess some degree of local anesthetic activities [3]. Acetophenone is one of the most aromatic carbonyl compound it shows interesting photochemical properties. It acts as an anticancer agents, an intermediate for pharmaceutical industry, and also a accelerator of photopolymer. 4'-Methoxyacetophenone is found in alcoholic beverages [4]. Acetophenone is a colorless liquid with a sweet pungent taste and odor resembling the odor of oranges. A mild irritant to skin and eyes. Vapors can be narcotic in high concentrations. Used as a flavoring, solvent, and polymerization catalyst. Acetophenone is a methyl ketone that is acetone in which one of the hydrogens of the methyl group has been replaced by a phenyl group. It has a role as a photosensitizing agent, an animal metabolite and a xenobiotic. This colourless, viscous liquid is a precursor to useful resins and fragrances. Acetophenone has been identified in many types of plants and as a volatile component of honey. Acetophenone is used as an intermediate for pharmaceutical, plastic and resin production [5]. It is primarily used as a riot-control agent (tear gas) and in Chemical Mace [6,7] 4'-Methoxyacetophenone is a trace constituent of oil of Piper longum (long pepper). 4'-Methoxyacetophenone is present in cranberry (*Vacciniumoxycoccus*) and other fruits, tomato, anise

(Pimpinellaanisum), grilled and roasted beef and sherry [8]. 4'-Methoxyacetophenone is a solid, pale yellow flavoring agent with a hawthorn like odor. It is soluble in most fixed oils and propylene glycol, and it is insoluble in glycerin and mineral oil. It is obtained by chemical synthesis. This flavoring substance or its adjuvant may be safely used in food in the minimum quantity required to produce its intended flavor. It can be used alone or in combination with other flavoring substances or adjuvant. It is also termed p-methoxyacetophenone. [9]. 4'-Methoxyacetophenone absorbed on silica-alumina catalyst [10]. 4'-Methoxyacetophenone is a flavouring ingredient and adjuvant; useful in vanilla, nut, tobacco and butter flavor. Actophenone and its derivatives, having additionally substituted saturated alkyls, oxygenated alkyl groups, thio groups, additional aromatic groups, unsaturated aliphatic side chains, and other functional groups, are serving as flavor & fragrance ingredient in soaps, detergents, cosmetics, and perfumes as well as in foods, beverages, and tobacco. 4'-Methoxyacetophenone is used as a component of perfumes and as chemical intermediate in the manufacture of pharmaceuticals, resins, flavouring agents. Hence, many works have been reported time to time on Acetophenone and its derivatives [1-7], however the quantum computational analysis supported by spectral studies has not been reported on 4-Methoxyacetophenone so far, hence the present work is undertaken to analyse the NBO, NLO, HOMO – LUMO, NMR, UV and Vibrational characteristics of the molecule using DFT methods and spectral techniques.

2. METHODS

2.1. Experimental details

The compound under investigation 4-Methoxyacetophenone was purchased in the powder form from Sigma-Aldrich chemicals company, USA. The FT-IR spectrum of the compound was recorded using a Bruker IFS 66 V spectrometer in the range of 4000-400 cm^{-1} . The spectral resolution is $\pm 2 \text{ cm}^{-1}$. The sample was prepared using KBr pellet technique. The FT-Raman spectrum of 4-Methoxyacetophenone was recorded at in the region 4000-130 cm^{-1} of wavelength using Nd-YAG laser at 1064 nm. The NMR spectra were recorded in (CdCl_2) chloroform solvent phase in the range of 0-200 ppm for ^{13}C with the scanning interval of 20 ppm and ^1H in the range 0-12 ppm with the scanning interval of 1ppm. The UV-Visible spectrum was recorded in the range of 200-1100 nm, with the scanning interval of 100 nm, using UV-1700 series instrument.

2.2. Quantum chemical calculations

All the quantum chemical computations in the present work are performed using the Gaussian 09 software programs with Gaussview [11,12] on a Pentium IV/3.02GHz personal computer and the wave numbers and geometrical parameters were computed using B3LYP (Becke's three parameter Lee-Yang Parr highbred methods) functional with 6-311++G (d, p) basis set. Density functional theory (DFT) has been proved to be extremely useful in treating electronic structure of molecules. The vibrational frequency and structural parameter of 4-Methoxyacetophenone was done using the same B3LYP functional and 6-311++G (d, p) basis sets for optimized geometry and the purity of the modes are confirmed by the total energy distribution (TED) method, computed using VEDA-4 program[13].

The geometry corresponding to the minimum energy has been obtained using the potential energy surface (PES) scan technique. The electronic transitions were identified using the NBO (Natural bonding orbitals) analysis, HOMO-LUMO (Gaussum3.0) [14] prediction of excitation energies and oscillator strength using time-dependent TD-SCF-B3LYP method. Same thing is also verified using UV-Vis experimental spectrum. The NMR chemical shift was carried out by gauge independent atomic orbitals (GIAO) method in combination with B3LYP and 6-311++G(d, p) methods. In addition, Mullikan charges, dipole moment and thermodynamical properties of the title molecule are also computed using the same functional and basis set.

3. RESULT AND DISCUSSION

3.1. Conformational analysis

The optimized molecular structure of the present molecule was used for conformational analysis, which was performed by potential energy surface scan techniques using a semi empirical method PM6, which is proven to be much efficient and quicker [15] than B3LYP, by varying the dihedral angle in the steps of 10° over one complete rotation. The graphical result, total energy (Hartree) verses scan coordinates of the conformer, is presented in Fig 1. The graph clearly shows that there are four conformers at

minimum energy levels one at 61° the second at the 180° and the third and fourth at 301° , 420° respectively. All the minimum energy level has the same value of energy -0.09557 Hartree. These conformers are structurally identical, serve as the most stable conformer of the compound. The maximum energy is observed for the conformer at 121° , 241° and 361° with energy value -0.09378 Hartree, this is the least stable or most unstable conformer of the compound. One of the most stable conformer is used for all the computational analysis in the present work.

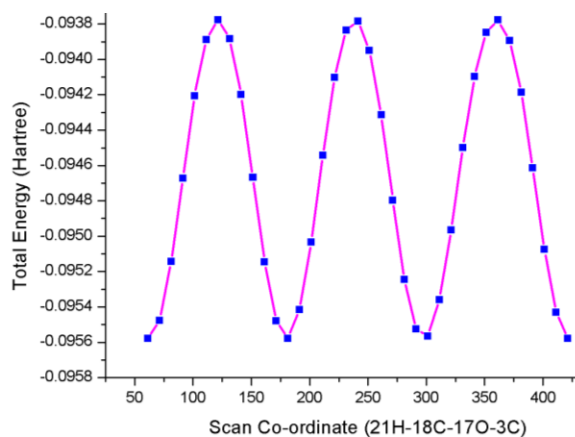


Fig. 1. The potential energy curve of 4-Methoxyacetophenone

3.2. Molecular geometrical analysis

The optimized molecular structure of the title molecule 4-Methoxyacetophenone along with the numbering of atoms is presented in Fig.2. The optimized structural parameters bond length, bond angle, dihedral angle of the compound calculated by B3LYP functional and 6-311++G(d,p) basis sets is presented in Table 1. In the case of C-C single bonds, the bond lengths are expected at 1.45 Å and C=C around 1.35Å [16]. In the title molecule, among CC bonds within the benzene ring, C2-C3, C3-C4, C1-C6 get the value as 1.39 Å, 1.404 Å and 1.407 Å respectively. This value is slightly less than the expected value for single bond and slightly higher than that of double bond, this show there is a kind of electronic redistribution around the ring, known as Conjugation, which makes the bond length almost equal them. The other CC bond lengths C1-C2, C4-C5 and C5-C6 are 1.38, 1.393 and 1.397Å, which show there is unevenness in the distribution of electrons among the bonds within the ring. This unevenness may be due to the methoxy groups attached to the phenyl ring, the highly electronegative O atoms may influence the electronic arrangement within the ring.

The value of O17- C18 bond length value is 1.42 Å, which is in agreement with reference value 1.43 Å [17], but the bond length value of C3-O17 is 1.357 Å. This shows that the electronic distribution around the carbon atom within the benzene ring is completely different from that methyl group. The C11-O13 bond length value is

1.21 Å, which is clearly a double bond, as it agrees with reference value 1.20 Å [18] for double bond.

The comparison of the C-H bond lengths in the molecule gives an interesting result; all the C-H bonds in the benzene ring have values closer to 1.08 Å. This shows the aromaticity (conjugation) in the benzene ring has considerably reduced the C-H bond lengths due to delocalization of the electrons.

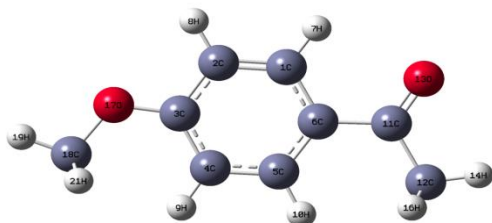


Fig.2 Structure of 4-Methoxyacetophenone

3.3. Mullikan and Natural charge analysis

The atomic charge on the atoms of the molecule has an important influence on the dipole moment, molecular polarization, electronic structure, molecular reactivity and vibrational frequency of different bonds. It is also pertinent to NMR chemical shift and NLO property of molecular system. The charges on the atom of the molecule 4-Methoxyacetophenone was computed by both Mullikan population analysis (MPA) method and Natural atomic charge (NAC) method using B3LYP functional with 6-311++G (d, p) basis set [20], which is presented graphically in Fig. 3 and the values are tabulated Table. 2.

All the carbon atoms in the benzene ring are expected to be equally negative as there used to electronic conjugation within the ring. But, the MPA predicts that C1, C4 and C6 are positive and C6 & C1 are highly positive, with values 1.362655 & 0.583199 respectively. C4 has the least positive value 0.022901. The carbon atom C6 have maximum positive charge in Mullikan atomic charge due to the attachment of phenone group and it is predicted to be negative in Natural Atomic charge. The carbon atom C4 (0.022 & -0.296) shows that it is nearer to neutral in Mullikan Atomic Charge but it is negative in Natural charge. The Carbon atom C3 (-0.418 & 0.348) is negative Mullikan charge and positive in Natural charge. This variation occurs due to the presence of methoxy group at C4. The carbons atoms C2 (-0.609 & -0.238) is found to be negative in both methods and C5 (-1.214 & 0.148) shows maximum negative charge in Mullikan Atomic Charge.

From the methoxy group, the carbon atom C18 (-0.309 & -0.206) atom is found to be negative in both methods. The O17 (-0.151 & -0.533) is also negative in both the cases. In phenone group, the carbon atom C11 (-0.275) is found to be negative in Mullikan Atomic charge and maximum positive C11 (0.554) in Natural charge due to the attachment of electrophilic influence of C=O. Remaining carbon C12 (-0.465 & -0.667) atom in this group shows negative in both the cases.

All the hydrogen atoms are found to be positive in both MPA and NAC methods. But there is considerable variation in their magnitudes around 0.15, the variation is naturally due to the presence of O atoms in the functional groups.

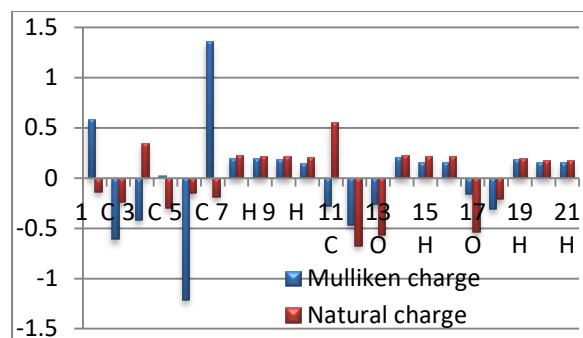


Fig. 3. The graphical plot of MAC and NAC in 4-Methoxyacetophenone

3.4. NMR Assessment

The ^1H and ^{13}C chemical shift calculations of the compound was made by gauge independent atomic orbital (GIAO) theory in combination with B3LYP method using 6-311+G(d,p) basic set in gas and CDCl_3 phases. The calculated ^{13}C and ^1H NMR chemical shifts (ppm) of 4-Methoxyacetophenone are shown in Fig.4 & 5 respectively. The shifts are calculated for gas and CDCl_3 solvent phases and the experimental values are presented in the Table.3. The aromatic carbon atoms are generally having the shifts in the range of 120-130 ppm [21]. The chemical shift value of C3, C11 are found experimentally at 160, 196 ppm respectively. This value is very high when compared to other carbon atoms in the aromatic ring which may be due to the attachment of O atoms with these carbon atoms. The C12 and C18 chemical shift values are 26 and 55 ppm respectively; these are adjacent C atoms, so the charges would have been pulled from them, besides they are also in aliphatic group. Hence the shift is found to be lower than the expected value. Remaining C1, C2, C4, C5 and C6 chemical shift values are within the literature range.

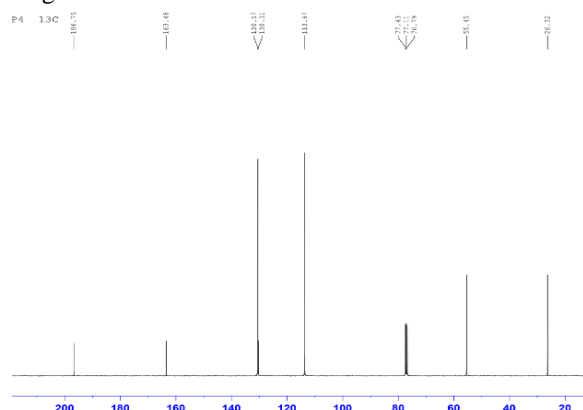


Fig. 4. ^{13}C NMR Experimental spectrum for 4-Methoxyacetophenone

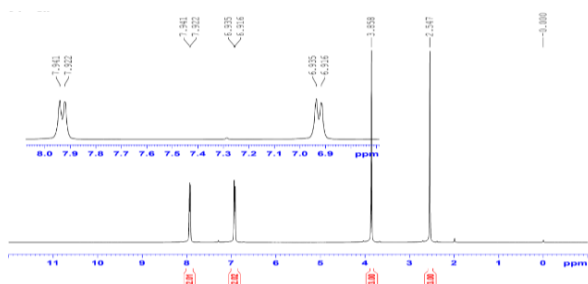


Fig. 5. ^1H NMR Experimental spectrum for 4-Methoxyacetophenone

3.5. Vibrational Analysis

The title molecule contains 21 atoms and hence 57 normal modes of vibrations. All these fundamental modes are identified in recorded FT-IR and FT-Raman spectra along with their intensity, the corresponding theoretical values are also stimulated. The experimental and stimulated spectra are given in Fig. 6 & 7 respectively. The theoretical frequencies were scaled using suitable scaling factors, comparing with the experimental frequencies. The experimental and theoretical frequencies, both scaled and un-scaled, along with the assignments are presented in Table.4.

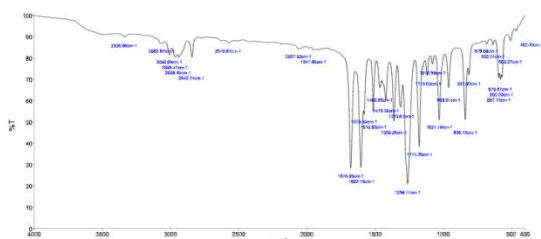


Fig. 6. Experimental Infrared spectra of 4-Methoxyacetophenone

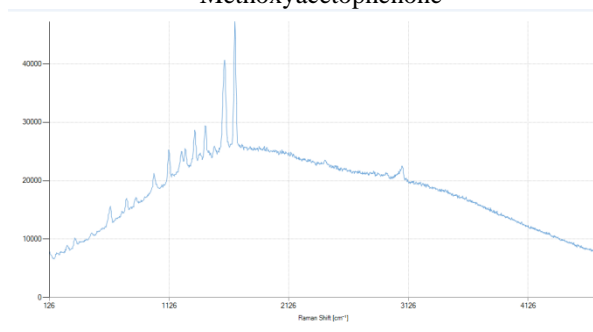


Fig. 7. Experimental Raman spectra of 4-Methoxyacetophenone

C-H vibrations

The C-H stretching vibrations in phenyl ring are normally observed in the region $3100\text{--}3000\text{ cm}^{-1}$ and less than 3000 cm^{-1} for non-aromatic compounds [23]. In the present molecule, C-H bands observed in between the values $3103\text{--}2911\text{ cm}^{-1}$. FT-IR values are found at $3115, 3061, 3036, 2980, 2972, 2930$ and 2910 cm^{-1} and at $3084, 3061, 3003\text{ cm}^{-1}$ in FT-Raman. There are only Four CH bonds in phenyl ring, but six bands have more than 3000 cm^{-1} wave number, which indicates even the CH bonds in aliphatic substitutional groups have acquired the value of aromatic CH, this may naturally be due to the presence of O atoms in aliphatic group.

The C-H plane bending vibrations for both ring and methyl group are expected in the region $1286\text{--}1127\text{ cm}^{-1}$ and very useful for characterization purposes [24]. In this study, these bands are observed at $1284\text{--}1128\text{ cm}^{-1}$ in scaled value. The FT-IR values are found at $1315, 1278, 1278, 1197$ and 1064 cm^{-1} & $1276, 1150, 1100, 1080$ and 1022 cm^{-1} in FT-Raman are agreed with expected value.

C=C and C-C vibrations

These C=C & C-C stretching modes are usually assigned in aromatic compounds between $1600\text{--}1500\text{ cm}^{-1}$ for C=C and $1500\text{--}1400\text{ cm}^{-1}$ for C-C respectively [25, 26]. In the present case, the CC double bonds are observed at 1664 & 1550 cm^{-1} in FT-Raman and FT-IR respectively. The first band value is higher than the expected range, which may be due to the attachment of ketonic group. Those corresponding scaled theoretical values are 1588 and 1551 cm^{-1} .

The C-C single bond is observed at 1483 cm^{-1} in FT-IR and $1463, 1439, 1428, 1425, 1420\text{ cm}^{-1}$ in FT-Raman. All these above values are in very much within the expected range. The corresponding theoretical values are $1487, 1453, 1443, 1430, 1426$ and 1422 cm^{-1} respectively. This observation is much significant in the spectrum of present molecule as the values are highly characteristic of the aromatic ring itself. All the modes are confirmed by their PED values. The PED values are also supporting the intensities of vibrations. The bands assigned to CCC in plane bending and out of plane bending vibrations are observed between $990\text{--}710$ & $339\text{--}250\text{ cm}^{-1}$ respectively. The CCC out of plane bending vibrations has appeared in combination with CH out of plane bending vibrations.

C=O and C-O Vibrations

The C=O stretching mode is expected in the region $1740\text{--}1660\text{ cm}^{-1}$ [27]. In this present work, the C=O asymmetric stretching is assigned at 1751 cm^{-1} in FT-IR. The deformation mode of C=O is expected in the regions, 625 ± 70 and 540 ± 80 [28]. In this molecule the deformation mode of C=O is present at 686 and 684 cm^{-1} in FT-IR and Raman respectively. These deformation modes are found mixed with CC bending modes.

The C-O bond stretching modes of vibrations are usually observed in the region $1150\text{--}1000\text{ cm}^{-1}$ [29]. In this molecule, the C-O stretching vibrations are found at 1197 cm^{-1} in FT-IR and 1158 cm^{-1} in FT-Raman, whose theoretical values are found at 1161 and 1155 cm^{-1} respectively. The band was found within the allowed region. The bending vibration found at 578 and 488 cm^{-1} in FT-IR and FT-Raman. Its observed scale factor value is 567 and 489 respectively. There is small shift in frequencies towards higher side which may be due to the influence of phenyl ring from where the these bonds may derive charges due to the presence of oxygen atom.

3.6. NBO Analysis

The Natural bonding orbital (NBO) analyses is an important method of studying the various possible donors and acceptors in the molecule, with their occupancy, hybridization values and the stabilization energy for each transition in each position. The inter and intra molecular interaction can also be studied using NBO analysis [30]. This overall stabilization energy $E(2)$ for all the donor –

acceptor transitions from the second-order perturbation theory is reported in table. 5. The NBO occupied orbital is Lewis-type (bond or lone pair) and unoccupied orbital is non-Lewis type (anti-bond or Rydberg). NBO analysis was performed on the 4-methoxyacetophenone molecule at the B3LYP/6-311+G(d,p) level. The fock matrix was elucidating in the donor-acceptor interactions in the NBO analysis [31].

$$E(2) = \Delta E_{ij} = q_i \frac{F(i,j)^2}{E_i - E_j}$$

Where q_i is the donor orbital occupancy, ε_i and ε_j are Fock matrix diagonal elements and $F(i,j)$ is the off diagonal element [32].

The high stabilization energy of the transitions gives a measure of the probabilities of the transitions; which indicate the highly probable transitions in this molecule are C3-C4 to C1-C2 ($\pi - \pi^*$, 34.9 Kcal/mol), O17 to C3-C4 ($n - \pi^*$, 31.8 Kcal/mol), C3-C4 to C5-C6 ($\pi - \pi^*$, 23.8 Kcal/mol), C1-C2 to C3-C4 ($\pi - \pi^*$, 23.4Kcal/mol), C5-C6 to C1-C2 ($\pi - \pi^*$, 20.5Kcal/mol), O13 to C11-C12 ($n - \sigma^*$, 19.9 Kcal/mol), C5-C6 to C11-O13 ($\pi - \pi^*$, 19.5 Kcal/mol), O13 to C6-C11 ($n - \sigma^*$, 18.44Kcal/mol), C5-C6 to C3-C4 ($\pi - \pi^*$, 16.4Kcal/mol), C1-C2 to C5-C6 ($\pi - \pi^*$, 16.23 Kcal/mol) and O17 to C3-C4 ($n - \sigma^*$, 13.92Kcal/mol). The list indicates that all the $\pi - \pi^*$ transitions are taking place within the benzene ring, while the first $n - \pi^*$ transition takes place in aceto group and the second $n - \pi^*$ which seems relatively less probable in methoxy group. $n - \sigma^*$ also takes place in aceto group. But, the experimental UV-Vis spectrum shows only three peaks; two in $\pi - \pi^*$ region and one in $n - \pi^*$ region, which means all other transitions are not favored by the selection rules. The HOMO-LUMO analysis can predict exactly which transitions appear in experimental and theoretical spectra, as discussed below.

3.7. UV-Visible study

The UV-Visible of 4-Methoxyacetophenone are computed at B3LYP/6-311++G (d,p) level along with TD-SCF functional. The computations are performed for both gas and solvent (Ethanol) phases. The calculated and experimental excitation energies, oscillator strength (f) and absorption wavelength (λ) and HOMO-LUMO contributions are presented in the Table 6.

In this case of electronic transitions, the energy gap in gas phase are found to be 3.834, 4.688, 4.797, 4.317, 4.395, 4.544, 4.755, 4.772, 4.936 and 5.052eV, their respective absorption wavelength are 323.3,264.4, 258.4, 231.6, 227.4, 220.0, 210.2, 209.5, 202.5 and 197.9 nm. The respective oscillator strength, which theoretically predict the intensity of the bands are 0.0001,0.3692, 0.0019, 0.000, 0.0059, 0.1338, 0.004, 0.0203, 0.000, 0.0024 respectively, which indicate only the second transition will appear in the spectrum as its oscillator strength is considerably large. In solvent (Ethanol) phase where the experimental spectrum is recorded, the respective energy gaps are 3.986, 4.514, 4.747, 4.444, 4.538, 4.610, 4.941, 5.042, 5.088, 5.166 eV, the wavelengths are 311.0, 274.6, 261.1, 225.1, 220.3, 216.8, 202.3, 198.2, 196.5, 193.5.nm respectively. The oscillator strengths for these values 0.0001, 0.4672, 0.0019, 0.1616, 0.000, 0.0058, 0.0063, 0.0003, 0.0777, 0.3173 respectively. According to these

oscillator strength values, the three peaks in the experimental spectrum are 205, 216, and 271 nm respectively. Though the first two $\pi - \pi^*$ transitions are not expected theoretically, they have been recorded experimentally. Based on the NBO analysis, the first two peaks in the experimental spectrum are due to the electronic transitions; C1-C2 to C3-C4 ($\pi - \pi^*$, 23.4Kcal/mol), and O13 to C11-C12 ($n - \sigma^*$, 19.9 Kcal/mol) respectively. The strong peak at 271 nm is due to the O17 to C3-C4 ($n - \pi^*$, 31.8 Kcal/mol), whose HOMO - LUMO contribution is the highest, 97%. It is the reason why only this peak appears in the theoretical spectrum.

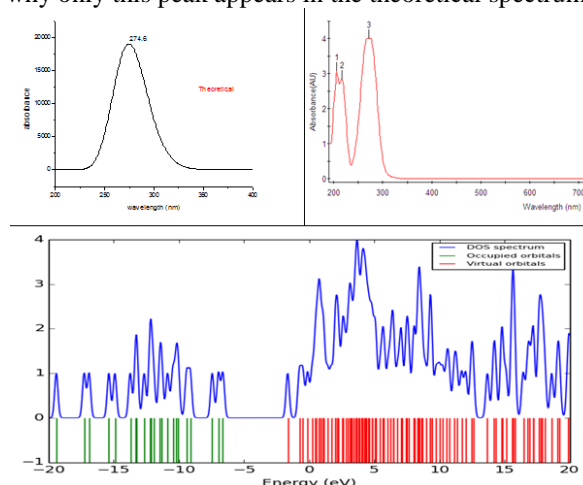


Fig. 8. Experimental and Theoretical and UV-Vis Spectra of using 4-Methoxyacetophenone

3.8. HOMO-LUMO Analysis

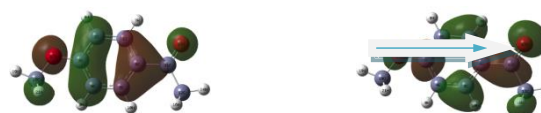


Fig. 9. Frontier molecular orbitals of 4-Methoxyacetophenone

Electrophilicity index is a measure of the energy lowering due to the maximum electron flow between the donor (HOMO) and the acceptor (LUMO). The Table 7 shows that the electrophilicity index of the title molecule using B3LYP method was -0.13462 eV. The dipole moment in a molecule is another electronic property which determines the strength of the interaction. When a molecule has a large dipole moment inter molecular interaction are very strong. The calculated dipole moment value of the component is 4.9769 Debye in gas phase. The chemical hardness is a good indicator of the chemical stability. The chemical hardness of the title molecule found to be around -0.00895 eV. The chemical softness was around -11.1769 eV.

3.9. MEP (molecular electrostatic potential) Analysis

The MEP is used to analysis the reactive sites of molecules in three dimensions by DFT computation. A MEP surface is an electron density mapping in terms of electrostatic potential energy. The MEP surface also determines the molecular size, shapes, charge densities and reactive sites.

Different values of electrostatic potential at the surfaces are represented by different colours [33]. Red represents region of most negative electrostatic potential, blue represents region of most positive electrostatic potential and green represents region close to zero electrostatic potential. In most MEP diagrams Fig. 10., electrophilic site is indicated as red and nucleophilic site is represented in blue.

The electrostatic potential increase in the order red<orange<yellow<green<blue [34]. The colour code of the maps found to vary in the range of -5.636×10^{-2} (deepest red) to 5.636×10^{-2} (deepest blue). In this present molecule C11=O13 is red and yellow regions of the MEP surfaces are related to electrophilic reactivity. The methoxy group (O-CH₃) lies in the blue region. The benzene ring of the present molecule lies in the region of greenish blue it clearly shows that potential is close to zero. The atoms C12, H14, H16 are also in the greenish blue region.

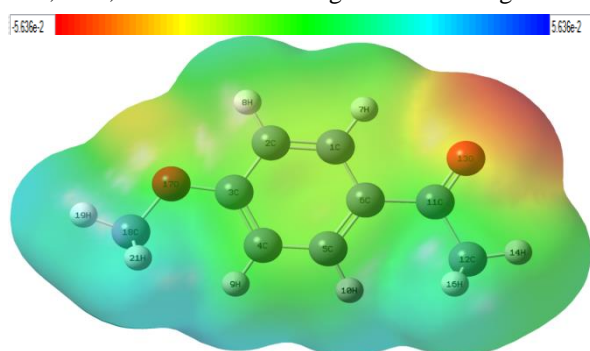


Fig. 10 MEP of 4-Methoxyacetophenone

3.10. Thermodynamic properties

From vibrational analysis of the present molecule, the thermodynamic functions such as standard heat capacities (C_m^0), standard entropies (S_m^0) and standard enthalpy changes (H_m^0) were obtained from theoretical harmonic frequencies at B3LYP/6-311++G (d,p) level, and the values are presented in Table 8. Based on table, as the temperature increases from 100 K to 300K, the thermodynamic functions also increase linearly at one atmospheric pressure. This increase may be due to the fact that vibrational intensities are increasing with increase temperature, along with the increase in rotational and translational energy in accordance with equipartition theorem [35,36]. The correlation graphs are shown in Fig.11.

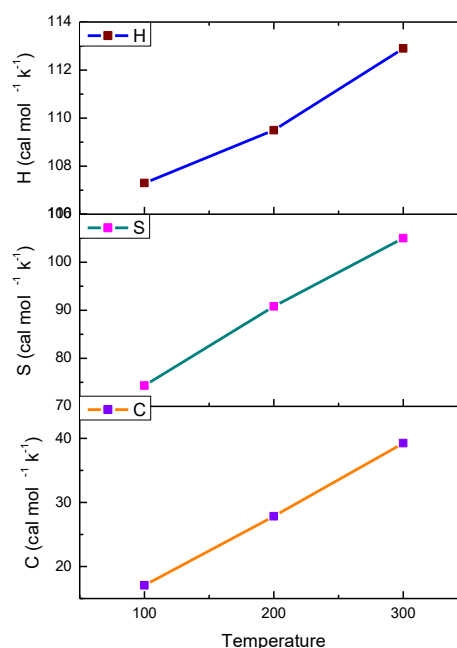


Fig. 11. Thermodynamic analysis of 4-methoxy Acetophenone

3.11. Docking Analysis

Molecular docking is an innovative technique for predicting and clearly understanding the molecular mechanisms of the molecule under study as ligands. This technique determines the probable ligand- protein interactions and the binding affinity values of the molecules at the binding sites. To investigate the binding affinity of the present molecule with many target proteins, the Auto Dock program 4.0 [37] was used. The structure of protein-ligand binding is determined using Activity Spectra (PASS) [38] and other online tools for various activities. The optimized geometry of the present molecule is used as ligand.

In present studies, the docking with high resolution is found with (5VCX) as receptor. The analysis shows that the docking take place at two sites CYS 190 and ASP 251, using Hydrogen bonds at C₁₁=O₁₃(phenone group) and O₁₇(Methoxy group) of title ligand molecule, with bond length of 2.0, 2.3 Å respectively. This details of the ligand-protein interaction is shown in Table.9.and the graphical representation is shown in Fig.12. The present docking study indicates the possibility that the title molecule may be used as anti cancer agent.

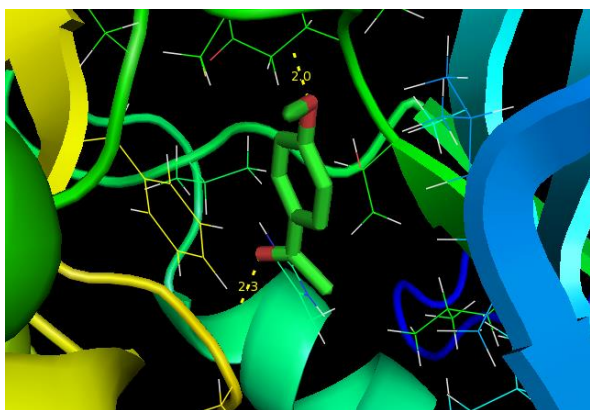


Fig. 12. Docking analysis of 4-Methoxyacetophenone

4. CONCLUSION

The molecule 4-Methoxyacetophenone is subjected to conformational analysis for finding the most stable configuration. The structural analysis of the compound indicates that there is considerable change in the structural parameters due to the presence of O atoms in both aceto and methoxy groups, these structural changes have caused respective vibrational changes which are identified and discussed. There is also a considerable variation in the atomic charges, which lead to variation in NMR chemical shift values. The NBO analysis predicted all the most probable sites in the molecule for electronic transitions, which are confirmed by the experimental UV-Vis spectrum recorded. The main transitions are found to be due to the same substitutional groups, methoxy and ketone groups. The docking study reveals that this molecule can be used as anti-cancer.

5. TABLES:

Table 1.

Optimized Geometrical parameter for 4-Methoxyacetophenone Computed at B3LYP/6-311++G(d,p).

Bond Length (Å)		XR D	Bond Angle (°)		XRD
C1-C2	1.38	1.37	C2-C1-C6	121	121
C1-C6	1.40	1.41	C2-C1-H7	120.5	120.5
C1-H7	1.08	1.08	C6-C1-H7	119.0	119.0
C2-C3	1.40	1.41	C1-C2-C3	119.3	119.3
C2-H8	1.03	1.09	C1-C2-H8	121.9	121.9
C3-C4	1.39	1.39	C3-C2-H8	118.8	118.8
C3-O17	1.35	1.35	C2-C3-C4	120.5	120.5
C4-C5	1.39	1.40	C2-C3-O17	115.3	115.3
C4-H9	1.08	1.08	C4-C3-O17	124.1	124.1

C5-C6	1.39	1.42	C3-C4-C5	115.3	119.3
C5-H10	1.08	1.08	C3-C4-H9	122.1	122.1
C6-C11	1.49	1.46	C5-C4-H9	117.3	117.3
C11-C12	1.51	1.51	C4-C5-C6	120.6	120.6
C11-O13	1.21	1.24	C4-C5-H10	117.5	117.5
C12-H14	1.07	1.09	C6-C5-H10	120.5	120.5
C12-H15	1.09	1.09	C1-C6-C5	117.6	117.6
C12-H16	1.09	1.09	C1-C6-C11	119.8	119.8
O17-C18	1.42	1.35	C5-C6-C11	122.6	122.6
C18-H19	1.08	1.09	C6-C11-C12	120.2	120.2
C18-H20	1.09	1.09	C6-C11-O13	121.0	121.0
C18-H21	1.09	1.09	C12-C11-O13	118.8	118.8

Taken from ref. [19]

Table 2.

Charges of 4-Methoxyacetophenone with B3LYP/6-311++G(d,p) basis set.

Atoms	B3LYP/6-311++G(d,p)	
	Mullikan Charge	Natural Charge
1 C	0.58319	-0.1336
2 C	-0.60929	-0.23825
3 C	-0.41809	0.34814
4 C	0.022901	-0.29677
5 C	-1.21423	-0.1484
6 C	1.362685	-0.18275
7 H	0.202525	0.23101
8 H	0.194486	0.22067
9 H	0.182218	0.21246
10 H	0.143902	0.20645
11 C	-0.27543	0.55464
12 C	-0.46566	-0.66787
13 O	-0.25818	-0.56694
14 H	0.207455	0.22837
15 H	0.153484	0.2175
16 H	0.153354	0.21746
17 O	-0.15116	-0.53339
18 C	-0.30908	-0.20621

19 H	0.180659	0.19453
20 H	0.157094	0.17147
21 H	0.157168	0.17149

Table. 3.
Calculated ¹H and ¹³C NMR Chemical shifts (ppm) of
4-Methoxyacetophenone

Atom	Gas	CdCl ₂	Exp.
1C	135.59	134.42	130.57
2C	122.82	122.39	113.67
3C	170.06	170.95	163.48
4C	109.50	111.24	130.31
5C	135.82	134.42	130.31
6C	134.58	134.42	130.57
11C	198.50	202.1	196.75
12C	26.32	27.26	26.32
18C	55.20	55.74	55.45
7H	8.40	8.32	7.941
8H	7.14	7.17	6.935
9H	6.61	6.88	6.88
10H	7.86	8.08	7.922
14H	1.93	1.87	1.90
15H	2.55	2.75	2.40
16H	2.55	2.75	2.40
19H	4.05	4.14	4.00
20H	3.63	3.77	3.85
21H	3.63	3.77	3.60

Table.4.
Vibrational Assignment

Experimental frequency cm ⁻¹		Assignment	
FT-IR	FT-Raman	Scaled	Band
3115		3103	vCH
	3084	3096	vCH
		3082	vCH
3061	3061	3079	vCH
3036		3038	vCH
	3003	3035	vCH
2980		2987	vCH
2972		2970	vCH
2930		2931	vCH
2910		2911	vCH
1751		1678	vCO
	1664	1588	vCC
1550		1551	vCC
1483		1487	vCC

	1463	1453	vCC
	1439	1443	vCC
	1428	1430	vCC
	1425	1426	vCC
	1420	1422	vCC
	1402	1401	β CH
1348		1338	β CH
1315		1307	β CH
1278	1276	1284	β CH
1250		1244	β CH
1235		1234	β CH
1197		1161	vCO
	1150	1155	vCO
	1100	1128	β CH
	1080	1097	β CH
1064		1054	β CH
	1022	1017	β CH
	1002	1007	β CO
990		988	β CC
970		964	β CC
936		923	β CC
	918	915	β CC
833		827	β CC
	795	794	β CC
	750	788	β CC
710		715	β CC
686	684	660	γ CH
630		623	γ CH
592		577	γ CH
578		567	β CO
	488	489	β CO
	461	469	γ CH
452		443	γ CH
399		406	γ CH
	332	314	γ CH
	292	285	γ CH
250		258	γ CH
	218	211	γ CH
	150	161	τ CCH
	138	136	τ CCH
	126	121	τ CCC
		68	τ CCC
		55	τ CCC

v-stretching; β-in-plane bending; γ-out of plane bending; and τ-torsion.

Table 5.

Second order perturbation theory of Fock matrix in NBO basis of 4-Methoxyacetophenone

Donor	Type	Occupancy	Acceptor	Type	Occupancy	E(2)
C3-C4	□	1.97	C1-C2	□	□□	34.9
O17	n	1.89	C3-C4	□	□□	31.8
C3-C4	□	1.64	C5-C6	□	□□	23.8
C1-C2	□	1.70	C3-C4	□	□□	23.4
C5-C6	□	1.66	C1-C2	□	□□	20.5
O13	n	1.89	C11-C12	□	□□	19.9
C5-C6	□	1.66	C11-O13	□	□□	19.5
O13	n	1.97	C6-C11	□	□□	18.4

Table 6Theoretical electronic absorption spectra of 4-Methoxyacetophenone (absorption wavelength λ (nm), excitation energies E (eV) and oscillator strengths (f) using TD-DFT/B3LYP/6-311++G(d,p) method.

λ (nm)	E(eV)		(f)	Major contribution
	T	E		
323		3.834	0.0001	H-1->LUMO (97%)
264		4.688	0.3692	HOMO->LUMO (95%)
258		4.797	0.0019	H-2->LUMO (57%)
231		4.317	0.0000	H-1->L+1 (100%)
227		4.395	0.0059	HOMO->L+2 (99%)
220		4.544	0.1338	H-2->LUMO (41%)
210		4.755	0.0041	HOMO->L+3 (99%)
209		4.772	0.0203	H-1->L+2 (80%)
202		4.936	0.0000	HOMO->L+4 (94%)
197		5.052	0.0024	H-2->L+2 (94%)

Ethanol				
311		3.986	0.0001	H-1->LUMO (97%)
274	271	4.514	0.4672	HOMO->LUMO (97%)
261		4.747	0.0019	H-2->LUMO (64%)
225		4.444	0.1616	H-2->LUMO (34%)
220		4.538	0.0000	H-1->L+1 (100%)
216		4.610	0.0058	HOMO->L+2(97%)
202		4.941	0.0065	HOMO->L+3 (96%)
198		5.042	0.0003	HOMO->L+4(96%)
196		5.088	0.0777	H-1->L+2 (78%)
193		5.166	0.3173	H-2->L+1 (70%)

Table 7.

Homo-Lumo of 4-Methoxyacetophenone.

Parameters	ethanol
E_{HOMO} (eV)	0.24468
E_{LUMO} (eV)	0.06574
$\Delta E_{HOMO-LUMO\ gap}$ (eV)	0.17894
Electronegativity (χ) (eV)	-0.15521
Global hardness (η)(eV)	-0.08947
Global softness (S)(eV)	-11.1769
Electrophilicity index (ω)(eV)	-0.13462
Dipole Moment (μ) (debye)	4.9769

Table 8:

Thermodynamic properties at different temperatures of 4-Methoxyacetophenone

T (K)	C_m° (cal mol ⁻¹ K ⁻¹)	S_m° (cal mol ⁻¹ K ⁻¹)	ΔH_m° (cal mol ⁻¹ K ⁻¹)
100	17.05	74.33	107.3
200	27.85	90.83	109.5
300	39.27	105.0	112.9

 C_m° - Heat capacity; S_m° -Entropy; ΔH_m° -Enthalpy**Table 9.**

Molecular docking analysis of 4-Methoxyacetophenone

Protein (PDB ID)	No. of hydrogen bonds	Bonded Residues	Bond Distance Å
5VCX	2	CYS 190	2.0
		ASP 251	2.3

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