Molecular Structure, Vibrational Spectral Investigations (FT-IR and FT-Raman), NLO, NBO, HOMO-LUMO, MEP Analysis of (E)-2-(3-pentyl-2,6-diphenylpiperidin-4-ylidene)-N-phenylhydrazinecarbothioamide Based on DFT and Molecular Docking Studies

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Abstract: The molecular spectroscopic investigations of (E)-2-(3-pentyl-2,6-diphenylpiperidin-4-ylidene)-N-phenylhydrazine carbothioamide (3-PDPPPHC) are studied. The FT-IR and FT-Raman experimental spectra of the molecule have been recorded in the range of 4000–400 cm⁻¹ and 4000–50 cm⁻¹ respectively. The molecular structure, fundamental vibrational frequencies, and intensities of the vibrational bands were interpreted to aid structure optimizations based on the density functional theory (DFT) method with B3LYP/6-311++G(d,p) level of basis set. The complete vibrational assignments of wavenumbers were made based on total energy distribution (TED). The calculations’ results were applied to the title compound’s simulated spectra, which show good agreement with observed spectra. The dipole moment, polarizability, and first hyperpolarizability values were also computed. The stability of the molecule analyzing from hyper-conjugative interaction and charge delocalization of the title compounds were studied by NBO analysis. Frontier molecular orbitals (FMOs), molecular electrostatic potential (MEP), and thermodynamic properties were performed. Mulliken charges of the title molecule were also calculated and interpreted. The thermodynamic properties such as heat capacity, entropy, and enthalpy of the title compound were calculated at different gas-phase temperatures. To establish information about the interactions between protein and this novel compound theoretically, docking studies were carried out in detail.

Keywords: FT-IR; FT-Raman; NLO; NBO; FMO; molecular docking.

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1. Introduction

Nitrogen-containing heterocyclic compounds, especially piperidones, gain considerable importance owing to their varied biological properties. Thiosemicarbazones show very interesting and important biological activity in pharmaceutical and industrial aspects as antibacterial [1], antifungal [2], antimalarial [3,4] antioxidant activity [5,6] anticancer [7-9]
and anticonvulsant [10] antimycobacterial activity [11], antiproliferative activity [12,13], Toxicity [14], cytotoxicity [15] and several biological activity of thiosemicarbazones [16-21]. However, little is known about piperidine-4-ones substituted with a thiosemicarbazone moiety possessing potential pharmacological activities such as antiviral and antiprotozoal activities [22-25]. A few semicarbazones, just as their sulfur analogs and their derivatives, have proved their efficiency and efficacy in combating various diseases [26]. Theoretical investigations of thiosemicarbazones were reported by DFT method [27-29]. NLO materials play a vital role in various fields such as fiber optics communications and optical signal processing. In the last two decades, intensive research has shown that organic crystals also exhibit non-linear optical efficiencies of greater magnitude than inorganic materials. Semicarbazones and thiosemicarbazone of substituted heterocyclic organic compounds, ketones, and acetophenones were accounted for to be potential organic NLO [30–32] materials. The FT-IR and FT-Raman spectra joined with quantum chemical computations have been recently used as an effective tool in the vibrational analysis of drug molecules [33], biological compounds [34] and natural products [35], since FT-Raman spectra and processed outcomes can help unambiguous distinguishing proof of the vibrational modes as well as the bonding and structural features of organic molecular systems. Both the IR and Raman spectroscopic investigations have been used to obtain the structural information on molecules. The present study aimed to investigate the molecular structural properties, vibrational and energetic data of 3-PDPPPHC, in the gas phase, due to its pharmaceutical importance. The ground and the excited state properties of the title molecule are B3LYP/6-311++G(d,p) hybrid functional is used for density functional theory (DFT) calculation. As vibrational and electronic spectroscopic studies provide very useful information about the structure and conformation of the molecules if utilized in collaboration with quantum chemical calculations, to obtain a complete description of molecular dynamics, vibrational wavenumber calculation, and the normal mode analysis has been administered at the DFT theory. The investigation of geometry, dipole moment, polarizability, first static hyperpolarizability, along with the molecular electrostatic potential surface will lead to a better understanding of the structural and spectral characteristics of the compound chosen for the study.

2. Materials and Methods

2.1. Experimental details.

2.1.1. Synthesis procedure.

(E)-2-(3-pentyl-2,6-diphenylpiperidin-4-ylidene)-N-phenylhydrazinecarbothioamide was synthesized by subsequent the procedure described in the literature [36]. The spectral data are reliable with the reported values [36].

2.1.2. FT-IR and FT-Raman spectra details.

The FT-IR spectrum of the synthesized 3-PDPPPHC was measured in the range 4000–400 cm⁻¹ in AVATAR-330 FT-IR spectrometer (Thermo Nicolet) using KBr (pellet form) in the Department of Chemistry, Annamalai University, Chidambaram, Tamilnadu. FT-Raman spectrum was observed using laser source Nd:YAG 1064 nm as excitation wavelength in the region 4000-50 cm⁻¹ on Bruker IFS 66v spectrophotometer equipped with an FRA 106 FT-
Raman module accessory and at a spectral resolution of 4 cm⁻¹. The FT-Raman spectrum was recorded at SAIF Laboratory, IIT Madras.

2.2. Computational details.

2.2.1. DFT Calculation.

The DFT method performed the entire quantum chemical calculations using the Gaussian 09W program package [37]. The optimized structural bond parameters and fundamental vibrational frequencies were calculated. The vibrational frequency assignments were made with a high degree of accuracy. The TED analysis was made using the VEDA4 program [38]. The NBO calculations were performed using NBO 3.1 program [39] as implemented in the Gaussian 09W [37] package. The DOS spectrum was drawn with the help of the Gauss sum 3.0 program [40]. In the present work, the DFT approach with 6-311++G(d,p) as a basis for computation of molecular structure, vibrational frequencies, and energies of optimized structures was utilized. The Bond parameters, NLO, NBO, HOMO-LUMO, Mulliken atomic charges, MEP, and thermodynamic parameters were calculated using the B3LYP/6-311++G(d,p) basis set.

2.2.2. Molecular docking.

Metallo-β-lactamases (MBLs) one of the most significant and boundless components of protection from β-lactam antimicrobials, against which no clinically helpful inhibitors are as of now accessible. We report thus a structure-based high-throughput docking (HTD) crusade on clinically-applicable procured MBLs.

The study's objective is to demonstrate that piperidone derivatives bind to beta-lactamase enzymes and evaluate whether these molecules can be used as a potential drug. The structural information and the data for the target were collected from the “Protein Data Bank” (PDB). The PDB ID: 1EVE [41] was used as the template for our studies. They were predicting the most likely conformation of how a ligand will bind to a macromolecule and some relevant residues of the protein considered flexible during the docking simulation. Basic potential parameters fit protein-ligand binding, and data scoring functions are comparable with new hydrogen bonding term and new charge schemes.

Docking calculations were carried out on the Beta-lactamase enzyme protein model [42]. Essential hydrogen atoms, Kollman united atom type charges, and solvation parameters were added with AutoDock tools' aid [43].

3. Results and Discussion

3.1. Geometrical parameters.

The optimized molecular structure of 3-PDPPPHC with atom numbering scheme is shown in Fig. 1. The optimized structural parameters, such as bond lengths, bond angles, and dihedral angles, were determined at the DFT/B3LYP/6-311++G(d,p) basis set. The values are listed in Table 1. In this study, the C-C, C-N, C=S, N-H, and C-H bond distances are calculated and compared with structurally related molecules [44]. The calculated C-C bond distances in the heterocyclic ring are in the range of 1.573 – 1.518 Å, compared with the reported DFT value (1.585 – 1.508 Å) [44]. In addition, the DFT value of C-C bond lengths in phenyl also rings agreement with literature values [44]. The C=S bond length is calculated at 1.662 Å and
is also related to reported data 1.681 Å. The C-N bond lengths in the range 1.470 – 1.380 Å by the B3LYP method, respectively, are in agreement with the reported values 1.471 – 1.288 Å [44]. The optimized N-H bond lengths fall in the range 1.017 – 1.013 Å by B3LYP method with 6-311++G(d,p) basis set and comparing these values with literature value 1.000 – 0.993 Å, respectively. Also, the bond angles of C2-C1-N9 (107.96°) and C4-C5-N9 (108.32°), which are calculated at DFT/B3LYP/6-311++G(d,p) basis set and are form to decrease from 120°. This is due to the phenyl group's substitution in connection with C1 and C5 carbon atoms in the piperidone ring. The piperidone ring essentially adopts chair conformation with all substituents equatorial as evident from the torsional angles N9–C1–C2–C3 = -58.88 and N9–C5–C4–C3 = 55.76 by B3LYP, respectively. In the optimized molecular structure, the thiosemicarbazone analog is nearly planar with the dihedral angle N26–N27–C32–N28 (176.62°) adopts an E-configuration concerning the C3-N26 bond. The calculated values are comparable with reported values [44].

![Figure 1. The optimized molecular structure of 3-PDPPPHC.](https://doi.org/10.33263/BRIAC114.1183311855)

| Bond Lengths (Å) | DFT | Bond Angles (°) | DFT | Dihedral Angles (°) | DFT |
|------------------|-----|----------------|-----|---------------------|-----|
| C1-C2            | 1.573 | C2-C1-N9       | 107.96 | N9-C1-C2-C3         | -58.8837 |
| C1-N9            | 1.470 | C2-C1-H35      | 106.62 | N9-C1-C2-H6         | 51.5304 |
| C2-C3            | 1.530 | C2-C1-C36      | 113.40 | N9-C1-C2-C11        | 166.6641 |
| C2-C11           | 1.540 | N9-C1-H35      | 112.05 | H35-C1-C2-C3        | 61.6846 |
| C3-C4            | 1.511 | N9-C1-C36      | 109.02 | H35-C1-C2-H6        | 172.0987 |
| C3-N26           | 1.286 | H35-C1-C36     | 107.84 | H35-C1-C2-C11       | -72.7675 |
| C4-C5            | 1.551 | C1-C2-C3       | 105.63 | C36-C1-C2-C3        | -179.791 |
| C4-H7            | 1.097 | C1-C2-H6       | 104.44 | C36-C1-C2-H6        | -69.3772 |
| C4-H8            | 1.091 | C1-C2-C11      | 114.25 | C36-C1-C2-C11       | 45.7565  |
| C5-N9            | 1.468 | C3-C2-H6       | 104.96 | C2-C1-N9-C5         | 61.2724  |
| C5-H34           | 1.105 | C3-C2-C11      | 120.28 | C2-C1-N9-H10        | -174.666 |
| C5-C46           | 1.518 | H6-C2-C11      | 105.82 | H35-C1-N9-C5        | -55.8321 |
| N9-H10           | 1.017 | C2-C3-C4       | 111.64 | H35-C1-N9-H10       | 68.2296  |
| C11-H12          | 1.095 | C2-C3-N26      | 133.27 | C36-C1-N9-C5        | -175.125 |
| C11-H13          | 1.100 | C4-C3-N26      | 114.36 | C36-C1-N9-H10       | -51.0632 |
| C11-C14          | 1.539 | C3-C4-C5       | 108.36 | C2-C1-C36-C37       | 72.8434  |
| C14-H15          | 1.098 | C3-C4-H7       | 111.30 | C2-C1-C36-C38       | -107.06  |
| C14-C16          | 1.538 | C3-C4-H8       | 109.66 | N9-C1-C36-C37       | -47.4609 |
| C14-C33          | 1.098 | C5-C4-H7       | 108.45 | N9-C1-C36-C38       | 132.6359 |
| C16-H17          | 1.098 | C5-C4-H8       | 109.90 | H35-C1-C36-C37      | -169.34  |
| C16-H18          | 1.099 | H7-C4-H8       | 109.15 | H35-C1-C36-C38      | 10.7569  |
| C16-C19          | 1.536 | C4-C5-N9       | 108.32 | C1-C2-C3-C4         | 62.4067  |
| C19-H20          | 1.099 | C4-C5-H34      | 106.17 | C1-C2-C3-N26        | -107.045 |
| C19-H21          | 1.100 | C4-C5-C46      | 111.85 | H6-C2-C3-C4         | -47.6392 |
3.2. Vibrational assignments.

The 3-PDPPPHC molecule has 68 atoms and belongs to C\textsubscript{1} point group symmetry; hence 198 normal modes of vibrations are possible and are distributed as $\Gamma_{\text{vib}} = 133\text{A}^\prime + 65\text{A}^\prime\prime$. All the vibrations are active in both IR and Raman absorption. With the exclusion of the anharmonicity factor and the basis set used, certain theoretical frequencies are not matched with experimental values. Hence, in this study, a linear scaling procedure is used to scale down the harmonic frequencies; we have followed the uniform scaling factor 0.9608 for DFT method [45]. After scaling the calculated frequencies, the observed values' deviation is less than 10 cm\textsuperscript{-1} with few exceptions. The scaled frequencies, observed frequencies (FT-IR, FT-Raman) with their intensities, force constants, reduced masses, and proposed vibrational assignments along with TED values are summarized in Table 2. The simulated, observed FT-IR and FT-Raman spectra are shown in Figs. 2 & 3, respectively.

3.2.1. N-H vibrations.

In general, the $v_{\text{N-H}}$ modes are expected to occur in the region 3200-3400 cm\textsuperscript{-1} [46]. In agreement with these observations, the harmonic bands at 3435, 3421 & 3383 cm\textsuperscript{-1} (mode nos: 1, 2 & 3) is designated as $v_{\text{N-H}}$ mode, while the experimental FT-IR bands at 3433, 3374 & 3308 cm\textsuperscript{-1} and 3434, 3375 & 3310 cm\textsuperscript{-1} in FT-Raman spectrum and is a pure mode (TED: 92, 92 & 99%), respectively. The harmonic wavenumber for $\beta_{\text{NNH}}$ & $\theta_{\text{NNC}}$ lies at 1516/421 cm\textsuperscript{-1}, respectively having considerable TED value (25 & 56%) and its corresponding mode nos: 48 & 161. On comparing the present investigation with the above literature, the lowering/increasing of wavenumbers may be due to the delocalization of electrons in the piperidone ring.

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3.2.2. Aromatic C-H vibrations.

Aromatic compounds commonly exhibit multiple bands in the region of 3000-3100 cm\(^{-1}\) due to CH stretching vibrations. In 3-PDPPPHC the C-H bands were observed at 3083 cm\(^{-1}\) in FT-Raman and 3084 cm\(^{-1}\) in FT-IR spectra, while the calculated frequencies are in the range of 3084 cm\(^{-1}\) (mode no: 5). In addition, C-H vibrations are observed in the region of 3057, 3030, 2949, 2930 & 2860 cm\(^{-1}\) in FT-Raman spectrum and 3058, 3028, 2948, 2925 & 2855 cm\(^{-1}\) in FT-IR spectrum and the corresponding harmonic values lies at 3057, 3042, 2950, 2934 & 2882 cm\(^{-1}\), respectively (mode nos: 14, 18, 23, 25 & 32). These assignments are well supported by their TED value.

In general, the C-H in-plane bending vibrations normally occur as a number of strong and weak bands in the region 1000-1400 cm\(^{-1}\). Similarly, the C-H out-of-plane bending vibrations are expected in the region of 809-950 cm\(^{-1}\) [47]. In 3-PDPPPHC the C-H in-plane bending vibrations are assigned at 1444, 1382 & 1325 cm\(^{-1}\) in FT-IR spectrum and 1445, 1385 & 1328 cm\(^{-1}\) in FT-Raman spectrum and their related harmonic frequencies are: 1446, 1385 & 1328 cm\(^{-1}\) (mode nos: 51, 57, 63). The C-H out-of-plane bending vibration of 3-PDPPPHC molecule was observed at 828, 807 cm\(^{-1}\) in the FT-IR spectrum. In contrast, the Raman bands are observed at 829, 806 cm\(^{-1}\), respectively. The calculated frequencies are 832 & 806 cm\(^{-1}\) (mode nos: 128, 130) also find support from TED values for the same mode.

3.2.3. C=C vibrations.

In General, the C=C and C-C stretching vibrations are usually occur in the region 1450-1625 cm\(^{-1}\) [48]. Hence in the present investigation, the FT-IR band identified at 1444 cm\(^{-1}\) and FT-Raman band at 1445 cm\(^{-1}\) is assigned to C-C stretching vibration of 3-PDPPPHC in mode no: 51 TED 25%. The \( \beta_{\text{CCH}} \) vibrations are assigned at 1068 cm\(^{-1}\) in FT-IR and 1030 cm\(^{-1}\) in FT-Raman spectrum. Its corresponding harmonic values lie at 1036 cm\(^{-1}\) with TED 45% (mode no: 98). Similarly, \( \Gamma_{\text{HCCH}} \) mode ascribed to wavenumbers at 980 cm\(^{-1}\) (mode no: 116). These assignments have considerable TED values and compare with experimental values (FT-IR/941 and FT-Raman/940 cm\(^{-1}\)), respectively. These results conclude that the positive/negative deviation of wavenumbers may be due to the piperidone ring’s resonance.

3.2.4. C=N, C-N, and N-N vibrations.

In general, the identification of C=N and C-N vibrations was very difficult, as the mixing of several bands become possible in this region. Silverstain and Webster [49] assigned the C-N stretching absorption in the region 1689–1417 cm\(^{-1}\) for aromatic amines. In 3-PDPPPHC, the C=N stretching band is found at 1594 cm\(^{-1}\) in FT-IR and 1595 cm\(^{-1}\) in Raman band. The computed wavenumbers 1646 cm\(^{-1}\) (mode no: 35) are assigned with TED value of 78%. From Table 2, C-N stretching vibration is observed at 1535 cm\(^{-1}\) and 1537 cm\(^{-1}\) in FT-IR & FT-Raman bands, respectively. The DFT calculation gave bands at 1576 cm\(^{-1}\) (mode no: 41). The in-plane (\( \beta_{\text{HNC}} \): FT-IR/1382 & FT-Raman/1385 cm\(^{-1}\)) and out-of-plane bending \( \Gamma_{\text{CCNH}} \) appeared at 1300 (FT-IR) and 1299 cm\(^{-1}\)(FT-Raman), this vibration shows in good agreement with the theoretical frequency of 1359 & 1320 cm\(^{-1}\) (mode nos: 59 & 65) by B3LYP/6-311++G(d,p) method. The theoretically computed N-N stretching has been calculated at 1115 cm\(^{-1}\), which mode no. 93 (TED: 25%) is in agreement with FT-IR value 1109 cm\(^{-1}\) and FT-Raman 1112 cm\(^{-1}\), respectively.
3.2.5. C=S vibrations.

In this study, the mode no: 139 are ascribed to ν\textsubscript{C=S} vibrations at 698 cm\textsuperscript{-1} in FT-IR band and ν\textsubscript{CS}/699 cm\textsuperscript{-1} in FT-Raman band and its corresponding harmonic wavenumbers at 672 cm\textsuperscript{-1} to support from TED value (>23%), respectively following the literature [50]. The harmonic frequencies 650 and 573 cm\textsuperscript{-1} (mode nos: 144, 152) are designated as β\textsubscript{CS} (FT-IR: 645 & FT-Raman: 648 cm\textsuperscript{-1}) and Γ\textsubscript{CS} modes (FT-IR: 570 & FT-Raman: 572 cm\textsuperscript{-1}), respectively. These assignments are found support from TED values >20%. It should be discussed here that the present assignment ν\textsubscript{C=S} vibrations have deviated from the literature, which may be due to unhybridized orbital of sulfur-containing two electrons form part of the delocalized electron cloud by lateral overlapping with an unhybridized orbital of carbon atoms. Electron pair in one of the hybrid orbital remains shared.

3.2.6. CH\textsubscript{3} and CH\textsubscript{2} group vibrations.

Generally, the C-H stretching in alkanes occurs at lower frequencies than those of the aromatic ring (3150–3050 cm\textsuperscript{-1}). The CH\textsubscript{3} stretching is expected at 2980–2870 cm\textsuperscript{-1} [51], and usually, the bands are weak. In the present study, the 3-PDPPPHC possesses methyl (CH\textsubscript{3}) and methylene (CH\textsubscript{2}) groups. Methyl group symmetric stretching appeared at 3028 cm\textsuperscript{-1} in FT-IR band and at 3030 cm\textsuperscript{-1} in FT-Raman spectrum agree with the theoretical values of 3042 cm\textsuperscript{-1} (mode no: 18 by B3LYP/6-311++G(d,p) method and it has considerable TED (63%) value.

The experimental vibration bands at 1444 cm\textsuperscript{-1} (FT-IR) and 1445 cm\textsuperscript{-1} (FT-Raman) are assigned to CH\textsubscript{2} vibrations. The DFT value lies in the range 1446 cm\textsuperscript{-1} (mode no: 51) by the B3LYP method, respectively. The out-of-plane bending mode, such as wagging and twisting modes of CH\textsubscript{2} group, were observed at 1300, 1269 cm\textsuperscript{-1} (FT-IR) and 1299, 1268 cm\textsuperscript{-1} (FT-Raman). The DFT calculation gave the bands at 1374 and 1322 cm\textsuperscript{-1} (mode nos: 65 & 74). The twisting and torsion modes of methyl vibrations are identified below 500 cm\textsuperscript{-1} and are supported by the harmonic value with TED distribution.

3.3. Non-linear optical property.

The NLO activity provides the key functions for frequency shifting, optical modulation, optical switching, and optical logic for the developing technologies in areas such as communication, signal processing, and optical inter-connections [52]. NLO describes the behavior of media. The dielectric polarizability ‘\textit{P}’ responds nonlinearly to the electric field \textit{E} of the light. In this study, the polarizability and hyperpolarizability values are calculated by DFT/6-311++G(d,p) basis set. The polarizability (α\textsubscript{0}=0.32671x10\textsuperscript{-30}esu) and first-order hyperpolarizability (β\textsubscript{0}=9.52518x10\textsuperscript{-30}esu) are calculated and listed in Table 3. The first order hyperpolarizability β\textsubscript{0} value is twenty-six times greater than that of urea. Hence, the title molecule possesses good NLO activity.

3.4. Natural bond orbital analysis.

NBO analysis is an essential tool for studying intra- and inter-molecular bonding interactions and a convenient basis for investigating charge transfer or conjugative interaction in molecular systems. Some orbitals are electron donors. Some are acceptors; the energy difference between bonding and anti-bonding orbitals makes the molecule susceptible to interactions [53]. The interactions result in a loss of occupancy from the localized NBO of the
idealized Lewis structure into an empty non-Lewis orbital. For each donor (i) and acceptor (j), the stabilization energy $E^{(2)}$ associated with the delocalization $i, j$ is estimated as

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

Where $q_i$ is the donor orbital occupancy, $\epsilon_i$ and $\epsilon_j$ are diagonal elements. $F(i, j)$ is the off-diagonal NBO Fock matrix element. The larger the energy difference $E^{(2)}$ value, the more intensive the interaction is, i.e., more is donating tendency of an electron from one orbital. More is the accepting tendency of another orbital, which makes the interaction between them stronger. The analysis of the various donors and acceptors indicate that there are only two types of donors $\sigma$ & $\pi$, and two types of acceptors $\sigma^*$ & $\pi^*$, respectively. Comparable with $\sigma$-$\sigma^*$, $\pi$-$\pi^*$ transfer more energies in the present system.

The $E^{(2)}$ energy values and types of the transition are shown in Table 4. The hyperconjugative interactions $\pi$(C37-C39)$\rightarrow$$\pi^*$(C36-C38), $\pi$(C41-C43)$\rightarrow$$\pi^*$(C51-C53) and $\pi$(C47-C49)$\rightarrow$$\pi^*$(C46-C48) transfer more stabilization energy: 86.94, 87.11 and 87.03 KJ/mol to the molecular system. In 3-PDPPPHC, the lone pair of sulfur and nitrogen atoms play a great role, i.e., the S31, N28, and N27 atoms transfer maximum energy 55.48, 224.26, and 238.28 KJ/mol to (N27-C32, (CS31-C32) & (S31-C32) bonds, respectively. Also, the $\pi^*$-$\pi^*$ bond also transfers more energies to its anti-bonding orbitals. The maximum hyperconjugative $E^{(2)}$ energy is exhibited during the intermolecular interaction, which leads the molecule towards medicinal and biological applications [53].

3.5. HOMO-LUMO analysis.

The HOMO and the LUMO are named as frontier molecular orbitals (FMOs). The FMOs play an important role in the optical and electric properties and quantum chemistry. The HOMO-LUMO orbitals of 3-PDPPPHC molecule are calculated in the gas phase using the DFT method with B3LYP/6-311++G(d,p) Fig. 4. The green and red colors represent the positive phase and negative phase, respectively. It is clear from the figure that the HOMO is located over thiosemicarbazone moiety, and LUMO is located over the entire molecule except for CH$_2$ and CH$_3$ groups. The calculated energy values of HOMO, LUMO and HUMO-1, LUMO+1 are -5.249 eV, -0.951 eV and -5.527 eV, -0.368 eV, respectively. The energy gap value between the HOMO and LUMO is 4.298 eV, and HOMO-1 and LUMO+1 is 5.159 eV, respectively. The energy values of HOMO ($\pi$-donor) and LUMO ($\pi$-acceptor) and their energy gap reflect the molecule's chemical activity. The physicochemical properties such as Ionization potential (IP), Electron affinity (EA), electronegativity ($\chi$), hardness ($\eta$) and Electrophilicity index ($\omega$) are deduced from ionization potential and electron affinity values [53] using the following equations:

$$\text{Electronegativity (}\chi) = \frac{IP+EA}{2}$$

$$\text{Chemical hardness (}\eta) = \frac{IP-EA}{2}$$

$$\text{Electrophilicity index (}\omega) = \frac{\chi^2}{2\eta}$$

The energy values of highest occupied molecular orbital (HOMO)-Lowest unoccupied molecular orbital (LUMO), energy gap, electron affinity, electrophilicity index, chemical potential, and hardness of the title molecule are listed in Table 5.
3.6. Density of states.

The density of states (DOS) spectrum for 3-PDPPPHC was obtained using Gauss Sum 3.0 program [40] and is shown in Fig. 5. The spectrum is used to explain the contribution of electrons to the conduction and valence band. The spectrum gives an idea about how many states are available at certain energy states. The lines at the starting end of the plot's energy axis, from -20 eV to -5 eV, are called filled orbital, and from -5 eV to 0 eV, they are called a virtual orbital. The virtual orbital is not occupied and is also called an acceptor orbital. In contrast, the filled orbital is called the donor orbital.

![Figure 2. The theoretical and experimental FT-IR spectra of 3-PDPPPHC.](image1)

![Figure 3. The theoretical and experimental FT-Raman spectra of 3-PDPPPHC.](image2)

A high-intensity DOS at specific energy levels means that there are many states available for occupation. A DOS of zero intensity means that the system can occupy no states. The variation in the peak height is due to electrons’ movement between the C=C and C-C in the ring of the molecule. The peak at certain energies decreases from the value due to electrons’ movement between the C=C and C-C in the ring of the molecule.

3.7. Molecular electrostatic potential analysis.

In this study, a 3D MEP, ESP, and TD plot of 3-PDPPPHC molecule are shown in Fig. 6. In MEP map, the maximum positive/negative regions are preferred sites for nucleophilic/electrophilic attack. They are represented by Blue/Red color, respectively. The
importance of MEP lies in the fact that it simultaneously displays molecular size, shape, and positive, negative, and neutral electrostatic potential regions in terms of color grading (Fig. 6) and is very useful in research of molecular structure with its physiochemical property relationship [54]. The Potential increases in the order: red < orange < yellow < green < blue. In this study, the electrostatic potential plot is based on the ED distribution within the molecule at different points. The lone pair atoms (sulfur & nitrogen) and hydrogen atoms in thiosemicarbazone are covered respectively by Red and blue regions. At the same time, the rest of the molecule is neutral. The positive and negative potential of the 3-PDPPPHC molecule ranges from \(-6.681\times10^{-2}\) a.u to \(6.681\times10^{-2}\) a.u. These two ends of the molecule, which are positively and negatively charged, are prone to the electrophilic and nucleophilic attack of the title molecule.

Figure 4. Frontier molecular orbitals of 3-PDPPPHC.

Figure 5. Density of states (DOS) diagrams for 3-PDPPPHC.
Table 2. The vibrational assignments of 3-PDPPPHC.

| Mode No | Observed Frequencies (cm⁻¹) | Calculated Frequencies (cm⁻¹) | IR Intensity | Raman Intensity | Vibrational Assignments |
|---------|-----------------------------|-------------------------------|--------------|-----------------|-------------------------|
|         | FT-IR FT-Raman              | Un Scaled Scaled*             | Abs.          | ReP.            | Abs. ReP.               | TED≥10%[^a] |
| 1       | 3433 3434                   | 3575 3435                     | 49.82         | 19.71           | 358.58                  | 100.00      | VN2H2O(92) |
| 2       | 3374 3375                   | 3561 3421                     | 54.09         | 21.40           | 219.94                  | 61.34       | VN2H2O(92) |
| 3       | 3308 3310                   | 3521 3383                     | 0.42          | 0.17            | 107.60                  | 30.01       | VN3H2O(99) |
| 4       |                             | 3256 3128                     | 0.99          | 0.39            | 43.74                   | 12.20       | VC3H5(98)  |
| 5       | 3084 3083                   | 3210 3084                     | 13.15         | 5.20            | 327.00                  | 91.19       | VC3H5(98)+(5)+VC3H5(16) |
| 6       | 3210 3084                   | 3084 3084                     | 6.69          | 2.65            | 156.45                  | 43.63       | VC3H5(17)+VC3H5(21)+VC3H5(16) |
| 7       | 3209 3083                   | 3294 11.77                     | 329.42       | 91.87           | VC3H5(24)+VC3H5(16)+VC3H5(58) |
| 8       | 3203 3077                   | 13.65 5.40                     | 166.32       | 46.38           | VC3H5(25)+VC3H5(22)+VC3H5(25)+VC3H5(10) |
| 9       | 3203 3077                   | 45.85 18.14                    | 99.49        | 27.74           | VC3H5(25)+VC3H5(22)+VC3H5(10) |
| 10      | 3194 3069                   | 24.85 9.83                     | 105.08       | 29.30           | VC3H5(51)+VC3H5(40)    |
| 11      | 3192 3067                   | 22.11 8.75                     | 96.55        | 26.93           | VC3H5(10)+VC3H5(27)+VC3H5(40)+VC3H5(14) |
| 12      | 3191 3066                   | 21.72 8.59                     | 105.04       | 29.29           | VC3H5(13)+VC3H5(26)+VC3H5(36)+VC3H5(19) |
| 13      | 3185 3060                   | 0.02 0.01                      | 91.52        | 25.52           | VC3H5(14)+VC3H5(42)+VC3H5(38) |
| 14      | 3058 3057                   | 0.16 0.06                      | 91.16        | 25.42           | VC3H5(20)+VC3H5(49)+VC3H5(25) |
| 15      | 3180 3055                   | 0.62 0.25                      | 103.08       | 28.75           | VC3H5(62)+VC3H5(23)    |
| 16      | 3173 3049                   | 5.87 2.32                      | 20.79        | 5.80            | VC3H5(14)+VC3H5(42)+VC3H5(38) |
| 17      | 3172 3048                   | 6.84 2.71                      | 23.95        | 6.68            | VC3H5(73)+VC3H5(19)    |
| 18      | 3028 3030                   | 16.18 6.40                     | 65.88        | 18.37           | VC3H5(63)+VC3H5(26)+VC3H5(36)+VC3H5(19) |
| 19      | 3144 3021                   | 6.25 2.47                      | 44.47        | 12.40           | VC3H5(88)+VC3H5(12)    |
| 20      | 3115 2993                   | 35.20 13.93                    | 60.81        | 16.96           | VC3H5(88)+VC3H5(10)    |
| 21      | 3113 2991                   | 40.19 15.90                    | 51.90        | 14.47           | VC3H5(59)+VC3H5(28)    |
| 22      | 3087 2966                   | 55.71 22.05                    | 31.51        | 8.79            | VC3H5(63)+VC3H5(19)+VC3H5(11) |
| 23      | 2948 2949                   | 3070 2950                     | 31.11        | 12.31           | 40.89                   | 11.40       | VC3H5(14)+VC3H5(13)+VC3H5(36)+VC3H5(24) |
| 24      | 3065 2945                   | 23.56 9.32                     | 72.15        | 20.12           | VC3H5(18)+VC3H5(22)+VC3H5(35)+VC3H5(19) |
| 25      | 2925 2930                   | 36.20 14.33                    | 95.62        | 26.67           | VC3H5(12)+VC3H5(86)   |
| 26      | 3042 2923                   | 33.58 13.29                    | 132.97       | 37.08           | VC3H5(34)+VC3H5(29)+VC3H5(35) |
| 27      | 3036 2917                   | 4.59 1.82                      | 98.45        | 27.46           | VC3H5(51)+VC3H5(20)   |
| 28      | 3035 2916                   | 31.01 12.27                    | 46.07        | 12.85           | VC3H5(10)+VC3H5(34)+VC3H5(32) |
| 29      | 3026 2907                   | 11.10 4.39                     | 28.99        | 9.08            | VC3H5(10)+VC3H5(11)   |
| 30      | 3024 2905                   | 48.80 19.31                    | 26.78        | 7.47            | VC3H5(29)+VC3H5(53)   |
| 31      | 3010 2892                   | 22.39 8.86                     | 142.31       | 39.69           | VC3H5(17)+VC3H5(66)+VC3H5(14) |
| 32      | 2855 2860                   | 37.04 14.66                    | 71.82        | 20.03           | VC3H5(10)+VC3H5(30)+VC3H5(55) |
| 33      | 2940 2825                   | 36.57 14.47                    | 38.49        | 10.74           | VC3H5(98)               |
| 34      | 2923 2808                   | 33.45 13.24                    | 26.61        | 7.42            | VC3H5(98)               |
| 35      | 1594 1595                   | 1713 1646                     | 2.57 1.02     | 1282.17        | 357.57                  | VN3C6H6(78) |
| 36      | 1662 1597                   | 4.86 1.92                      | 108.43       | 30.24           | VC6C5(31)+VC6C5(14)+βC6C5C6(14) |
| 37      | 1660 1595                   | 5.35 2.12                      | 91.31        | 25.47           | βC6C5C5C6(13)+VC6C5C6(37)+VC6C5C6(10) |
| 38      | 1660 1595                   | 50.28 19.90                    | 343.94       | 95.92           | VC6C5C6(19)+VC6C5C6(16)+VC6C5C6(12)+βC6C5C6C6(12) |
| R | 1180 | 1180 | 1229 | 1181 | 221.27 | 87.56 | 18.18 | 5.07 | VΝr(25) |
|---|---|---|---|---|---|---|---|---|---|
| 83 | 1175 | 252.70 | 100.00 | 86.21 | 24.04 | VCAr(18) |
| 84 | 1221 | 1173 | 126.58 | 50.09 | 54.18 | 15.11 | VCAr(21) |
| 85 | 1162 | 2.63 | 1.04 | 14.14 | 3.94 | βΗα≤CαCσ(20)+βΗα≤CσCτ(21)+Ηα≤CαCσ(15)+Ηα≤CσCτ(18) |
| 86 | 1160 | 5.61 | 2.22 | 10.96 | 3.06 | τCτCτCρHα(13) |
| 87 | 1157 | 7.78 | 3.08 | 5.69 | 1.59 | βΗα≤CαCσ(11)+Ηα≤CσCτ(11) |
| 88 | 1155 | 3.27 | 1.29 | 4.76 | 1.33 | βΗα≤CαCσ(12)+βΗα≤CσCτ(12)+Ηα≤CαCσ(12)+Ηα≤CσCτ(10) |
| 89 | 1140 | 0.83 | 0.33 | 8.95 | 2.50 | βΗα≤CσCτ(22)+βΗα≤CσCτ(18)+Ηα≤CσCτ(35) |
| 90 | 1140 | 0.04 | 0.02 | 6.93 | 1.93 | βΗα≤CσCτ(19)+βΗα≤CσCτ(15)+Ηα≤CσCτ(33) |
| 91 | 1140 | 1.89 | 0.75 | 5.61 | 1.57 | VCAr(10)+βΗα≤CαCσ(19)+βΗα≤CσCτ(14)+Ηα≤CσCτ(32) |
| 92 | 1135 | 20.27 | 8.02 | 6.19 | 1.73 | βΗα≤Cσ(13) |
| 93 | 1115 | 1.62 | 0.64 | 27.05 | 7.54 | VΝr(25) |
| 94 | 1100 | 14.56 | 5.76 | 31.48 | 8.78 | VΝr(25) |
| 95 | 1090 | 22.19 | 8.78 | 27.38 | 7.64 | VΝr(25)+VCAr(10) |
| 96 | 1075 | 19.58 | 7.75 | 9.09 | 2.53 | VΝr(25)+VCAr(10)+VCAr(12) |
| 97 | 1071 | 8.97 | 3.55 | 1.73 | 0.48 | βΗα≤CσCτ(12) |
| 98 | 1070 | 0.32 | 0.21 | 1.77 | 0.49 | βΗα≤CσCτ(35) |
| 99 | 1062 | 3.82 | 1.51 | 6.89 | 1.92 | βΗα≤CσCτ(30) |
| 100 | 1052 | 3.89 | 1.54 | 7.26 | 2.02 | VCAr(14) |
| 101 | 1051 | 62.39 | 24.69 | 16.96 | 4.73 | VCAr(13)+VCAr(20)+VCAr(11) |
| 102 | 1036 | 0.80 | 0.32 | 7.14 | 1.99 | VCAr(10)+VCAr(33)+VCAr(25) |
| 103 | 1016 | 8.30 | 3.29 | 16.61 | 4.63 | VCAr(25)+VCAr(23) |
| 104 | 1015 | 2.86 | 1.13 | 35.69 | 9.95 | VCAr(10)+VCAr(11)+VCAr(12) |
| 105 | 1014 | 8.53 | 3.37 | 8.07 | 2.25 | VCAr(17)+VCAr(12) |
| 106 | 998 | 1.21 | 0.48 | 8.32 | 2.32 | VCAr(43)+VCAr(13) |
| 107 | 978 | 1.09 | 0.43 | 5.18 | 1.44 | VCAr(11) |
| 108 | 977 | 1.81 | 0.72 | 60.53 | 16.88 | βCτCτCτ(15) |
| 109 | 976 | 1.04 | 0.41 | 14.78 | 4.12 | βCτCτCτ(16)+βCτCτCτ(16) |
| 110 | 974 | 0.20 | 0.08 | 73.54 | 20.51 | βCτCτCτ(17)+βCτCτCτ(20)+βCτCτCτ(35) |
| 111 | 970 | 5.18 | 2.05 | 8.94 | 2.49 | βCτCτCτ(22) |
| 112 | 964 | 0.32 | 0.13 | 1.50 | 0.42 | τΗα≤CτCτHα(22)+τΗα≤CτCτHα(12)+τCτCτCτHα(14) |
| 113 | 963 | 0.26 | 0.10 | 0.46 | 0.13 | τΗα≤CτCτHα(16)+τCτCτCτHα(12)+τHα≤CτCτHα(23) |
| 114 | 958 | 2.69 | 1.07 | 4.61 | 1.28 | τCτCτCτHα(10) |
| 115 | 951 | 0.59 | 0.23 | 1.92 | 0.54 | τCτCτCτHα(10)+τHα≤CτCτHα(13)+Ηα≤CτCτHα(51) |
| 116 | 941 | 0.18 | 0.07 | 0.38 | 0.11 | τHα≤CτCτHα(11)+τHα≤CτCτHα(26)+τHα≤CτCτHα(40) |
| 117 | 940 | 0.35 | 0.22 | 0.22 | 0.06 | τHα≤CτCτHα(30)+τHα≤CτCτHα(40)+τHα≤CτCτHα(10) |
| 118 | 923 | 0.31 | 0.12 | 1.12 | 0.31 | τHα≤CτCτHα(56)+τHα≤CτCτHα(29) |
| 119 | 921 | 0.17 | 0.07 | 6.47 | 1.82 | VCAr(16)+VCAr(15) |
| 120 | 900 | 4.91 | 1.94 | 6.45 | 1.80 | τHα≤CτCτCτHα(18)+τCτCτCτHα(16)+τCτCτCτHα(23) |
| 121 | 899 | 3.03 | 1.20 | 10.25 | 2.86 | τCτCτCτHα(16)+τCτCτCτHα(16)+τCτCτCτHα(21) |
| 122 | 888 | 1.03 | 0.41 | 13.75 | 10.42 | VGC(28) |
| 123 | 879 | 2.06 | 0.81 | 6.12 | 1.15 | VGC(18) |
| 124 | 870 | 3.45 | 1.37 | 1.88 | 0.52 | τCτCτCτHα(29)+τHα≤CτCτCτHα(14)+τHα≤CτCτHα(10) |

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| 125 | 890 | 855 | 2.00 | 0.79 | 2.62 | 0.73 | VC10,C10(10)+VC10,C10H10(14) |
| 126 | 879 | 845 | 35.75 | 14.15 | 7.33 | 2.05 | VNaC10(10)+VC10,C10H(16) |
| 127 | 868 | 834 | 0.91 | 0.36 | 8.21 | 2.29 | GC10,C10NaH1(21)+GC10,C10NaH2(22)+H1Na,C10C10(23) |
| 128 | 828 | 829 | 0.18 | 0.07 | 1.98 | 0.55 | GC10,C10NaH1(24)+GC10,C10NaH2(25)+H1Na,C10C10(23) |
| 129 | 855 | 821 | 0.33 | 0.13 | 3.11 | 0.87 | GC10,C10H1(16) |
| 130 | 807 | 806 | 0.15 | 0.06 | 4.46 | 1.24 | GC10,C10H2(23) |
| 131 | 835 | 802 | 0.55 | 0.22 | 4.60 | 1.28 | GC10,C10H4(37)+H1H1C10C10C10(49) |
| 132 | 811 | 779 | 1.11 | 0.44 | 2.95 | 0.82 | VC15(15) |
| 133 | 753 | 755 | 56.23 | 22.25 | 4.72 | 1.32 | GC10,C10H(46) |
| 134 | 700 | 749 | 12.36 | 4.89 | 13.29 | 3.71 | GC10,C10H(10) |
| 135 | 779 | 748 | 4.01 | 1.59 | 2.16 | 0.60 | GC10,C10H(15) |
| 136 | 776 | 746 | 65.62 | 25.97 | 5.83 | 1.63 | GC10,C10H1(12) |
| 137 | 773 | 743 | 21.88 | 8.66 | 4.29 | 1.20 | VS15C10(10)+H1H1C10C10C10(19)+H1Na,C10C10C10(17) |
| 138 | 751 | 722 | 11.66 | 4.61 | 1.18 | 0.33 | GC10,C10H1(27)+H1C10C10C10H(32) |
| 139 | 698 | 699 | 747 | 718 | 36.27 | 14.35 | 18.70 | 5.22 | VS15C10(23) |
| 140 | 722 | 694 | 38.07 | 15.07 | 2.14 | 0.60 | τC10,C10C10(22) |
| 141 | 718 | 690 | 17.69 | 7.00 | 1.81 | 0.50 | τC10C10C10C10(15)+τC10C10C10C10(47)+τC10C10C10(20) |
| 142 | 715 | 687 | 10.43 | 4.13 | 3.85 | 1.07 | τC10C10C10C10(41)+τC10C10C10C10(10)+τC10C10C10C10(11) |
| 143 | 669 | 670 | 10.10 | 4.00 | 0.87 | 0.24 | τH1C10C10C10C10C10(10)+τH1C10C10C10C10C10(10)+τC10C10C10C10(45) |
| 144 | 645 | 648 | 22.84 | 9.04 | 14.00 | 3.90 | βC10C10C10(24) |
| 145 | 661 | 635 | 1.34 | 0.53 | 8.96 | 2.50 | βC10C10C10(40) |
| 146 | 635 | 610 | 0.38 | 0.15 | 5.67 | 1.58 | βC10C10C10(18)+βC10C10C10(44)+βC10C10C10(13) |
| 147 | 634 | 609 | 0.02 | 0.01 | 3.69 | 1.03 | βC10C10C10C10(20)+βC10C10C10(37) |
| 148 | 599 | 600 | 2.63 | 1.04 | 5.41 | 1.51 | βC10C10C10C10(22)+βC10C10C10C10(33)+βC10C10C10C10(25) |
| 149 | 620 | 596 | 7.12 | 2.82 | 6.14 | 1.71 | βC10C10C10C10(14) |
| 150 | 614 | 590 | 2.16 | 0.86 | 4.58 | 1.28 | βC10C10C10C10C10(16) |
| 151 | 601 | 577 | 2.74 | 1.09 | 1.97 | 0.55 | βC10C10C10C10C10(36) |
| 152 | 570 | 572 | 3.28 | 1.30 | 3.95 | 1.10 | βC10C10C10C10C10(22) |
| 153 | 583 | 560 | 9.60 | 3.80 | 1.59 | 0.44 | βC10C10C10C10C10(16) |
| 154 | 529 | 528 | 10.98 | 4.34 | 2.72 | 0.76 | βC10C10C10(14) |
| 155 | 540 | 519 | 8.50 | 3.36 | 1.25 | 0.35 | βC10C10C10(10) |
| 156 | 501 | 500 | 18.61 | 7.37 | 3.14 | 0.87 | τH2Na2C10C10(21)+τH2Na2C10C10C10(11)+τS1Na2Na2C10(37) |
| 157 | 512 | 492 | 8.15 | 3.22 | 4.03 | 1.12 | τH2Na2C10C10C10(18) |
| 158 | 468 | 470 | 9.73 | 31.59 | 32.99 | 9.20 | τH2Na2C10C10C10(56) |
| 159 | 481 | 462 | 2.24 | 0.89 | 0.97 | 0.27 | βC10C10C10C10(11)+τH1C10C10C10(10) |
| 160 | 438 | 421 | 1.47 | 0.58 | 1.89 | 0.53 | βC10C10C10C10(29) |
| 161 | 421 | 404 | 42.59 | 16.85 | 32.14 | 8.96 | τH2Na2Na2C10(51) |
| 162 | 419 | 403 | 2.75 | 1.09 | 1.57 | 0.44 | τC10C10C10C10C10C10(42) |
| 163 | 418 | 402 | 0.43 | 0.17 | 0.27 | 0.07 | τC10C10C10C10C10C10(42) |
| 164 | 417 | 401 | 0.32 | 0.13 | 1.95 | 0.54 | τC10C10C10C10C10C10(42) |
| 165 | 378 | 378 | 1.37 | 0.54 | 3.26 | 0.91 | βC10C10C10C10(22) |
| 166 | 393 | 378 | 1.37 | 0.54 | 11.20 | 3.12 | τC10C10C10C10+τC10C10C10C10C10C10(18) |
| 167 | 361 | 347 | 22.77 | 9.01 | 3.92 | 1.09 | τH1Na2Na2C10(15)+τC10C10C10C10C10C10(23) |
|   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|
| 168 | 324 | 339 | 326 | 1.18 | 0.47 | 1.29 | 0.36 | βC=C65N=N(23)+βC=N32N(10) |
| 169 | 323 | 310 | 7.49 | 2.96 | 3.33 | 0.93 | βC=C45C(14) |
| 170 | 310 | 298 | 3.32 | 1.32 | 3.53 | 0.98 | βC=C45C(11)+τC=N45C=C(14) |
| 171 | 293 | 282 | 2.20 | 0.87 | 2.20 | 0.61 | βC=C65C(14)+βC=C65C(12) |
| 172 | 281 | 270 | 3.75 | 1.49 | 1.38 | 0.38 | βC=C52C(11) |
| 173 | 263 | 253 | 1.29 | 0.51 | 2.29 | 0.64 | βC=C52C(23)+βC=C52C(14) |
| 174 | 249 | 239 | 0.27 | 0.11 | 0.30 | 0.08 | τC=N32C=C(52) |
| 175 | 232 | 243 | 2.17 | 0.46 | 4.44 | 1.24 | τC=N45C=C(16) |
| 176 | 239 | 230 | 1.88 | 0.74 | 1.23 | 0.34 | τC=N52C=C(25) |
| 177 | 229 | 220 | 0.42 | 0.17 | 3.93 | 1.10 | βC=C52C=C(20) |
| 178 | 207 | 217 | 0.42 | 0.17 | 1.62 | 0.45 | βH32C=52C(11) |
| 179 | 203 | 195 | 0.70 | 0.28 | 7.00 | 1.95 | βN32C=N(12) |
| 180 | 183 | 176 | 0.59 | 0.23 | 1.77 | 0.49 | βC=N32C(14)+βC=N45S(11) |
| 181 | 155 | 161 | 5.17 | 3.23 | 5.69 | 1.59 | βC=N32S(10)+βC=N45C(15) |
| 182 | 142 | 136 | 1.82 | 0.72 | 2.33 | 0.65 | τC=N52C=N(18)+τC=N52C(12) |
| 183 | 121 | 116 | 2.33 | 0.92 | 0.37 | 0.10 | τN32C=N(14) |
| 184 | 116 | 111 | 0.29 | 0.11 | 1.53 | 0.43 | βC=N45C(11)+τN32C=52N(11) |
| 185 | 95 | 91 | 0.21 | 0.08 | 0.90 | 0.25 | τC=N52C=N(38)+τC=N45C=C(31) |
| 186 | 86 | 83 | 0.08 | 0.03 | 2.52 | 0.70 | τC=N52C=N(16)+τC=N45C=C(31) |
| 187 | 79 | 76 | 0.26 | 0.10 | 1.01 | 0.28 | τH32C=C(17) |
| 188 | 71 | 73 | 0.10 | 0.04 | 2.02 | 0.56 | τC=C36C=C(15)+τC=C46C(10) |
| 189 | 51 | 49 | 0.10 | 0.04 | 9.10 | 2.54 | βC=N32C(11)+τC=N32C=N(18) |
| 190 | 49 | 47 | 0.10 | 0.04 | 6.54 | 1.82 | τC=N45C=N(42)+τC=N45C=N(11)+τC=N45C(11) |
| 191 | 43 | 41 | 0.03 | 0.01 | 1.76 | 0.49 | βC=C65N(15)+τC=N45C=N(19)+τC=N45C(10) |
| 192 | 36 | 35 | 0.52 | 0.21 | 0.61 | 0.17 | βC=N45C(11)+τC=N45C(11)+τC=N45C=52N(10) |
| 193 | 32 | 31 | 0.77 | 0.30 | 4.66 | 1.30 | τC=N45N(52)+τC=N52C=52N(16)+τC=N52C(12) |
| 194 | 28 | 27 | 0.40 | 0.16 | 9.35 | 2.61 | τC=52C=N(25)+τC=52C(16) |
| 195 | 25 | 24 | 0.36 | 0.14 | 2.05 | 0.57 | βC=N45C(10)+τC=N52C=N(16)+τC=N52C(16) |
| 196 | 19 | 18 | 0.44 | 0.18 | 1.74 | 0.48 | τC=C52C=N(22) |
| 197 | 18 | 17 | 2.10 | 0.83 | 4.53 | 1.26 | τC=N52C(13)+τC=N45N(13)+τC=N45C(10) |
| 198 | 14 | 13 | 0.0318 | 0.0126 | 2.0202 | 0.5634 | τC=N52C(13)+τC=N52C(15)+τC=C46C(20) |

v: Stretching, β: in-plane-bending, Γ: out-of-plane bending, τ: Torsion, vw: very week, w: week, m: medium, s: strong, vs: very strong,
a Scaling factor: 0.9608,
b Relative IR absorption intensities normalized with highest peak absorption equal to 100,
c Relative Raman intensities calculated and normalized to 100,
d Total energy distribution calculated at B3LYP/6-311++G(d,p) level.
Table 3. The NLO measurements of 3-PDPPPHC.

| Parameter | Hyperpolarizability | Polarizability |
|-----------|---------------------|----------------|
| $\beta_{xxx}$ | 27.0596 | $\alpha_{xx}$ | -195.3236 |
| $\beta_{yy}$ | 60.4279 | $\alpha_{yy}$ | -210.9731 |
| $\beta_{zz}$ | -2.5280 | $\alpha_{zz}$ | -206.3976 |
| $\beta_{xy}$ | -7.16706 | $\alpha_{xy}$ | 12.9496 |
| $\beta_{xz}$ | 20.4510 | $\alpha_{xz}$ | 3.6875 |
| $\beta_{yz}$ | -6.5713 | $\alpha_{yz}$ | -7.3381 |
| $\beta_{xz}$ | 3.7648 | $\alpha_{xz}$ | 0.32671 X10^{-30} esu |
| $\beta_{yz}$ | 17.0146 | $\alpha_{yz}$ | 9.52518 X10^{-30} esu |

Table 4. The NBO analysis of 3-PDPPPHC.

| Type | Donor NBO (i) | ED/e | Acceptor NBO (j) | ED/e | $E^{(2)}$ KJ/mol | $E(j)-E(i)$ a.u. | $F(i, j)$ a.u. |
|------|--------------|------|-----------------|------|-----------------|-----------------|----------------|
| $\pi-\pi^*$ | BD (2) C37 - C39 | 1.66588 | BD*(2) C36 - C38 | 0.35003 | 86.94 | 0.28 | 0.069 |
| $\pi-\pi^*$ | BD (2) C41 - C43 | 1.66448 | BD*(2) C36 - C38 | 0.35003 | 83.97 | 0.28 | 0.067 |
| $\pi-\pi^*$ | BD (2) C47 - C49 | 1.66656 | BD*(2) C46 - C48 | 0.34829 | 84.39 | 0.28 | 0.067 |
| $\pi-\pi^*$ | BD (2) C51 - C53 | 1.66295 | BD*(2) C46 - C48 | 0.34829 | 84.39 | 0.28 | 0.067 |
| $\pi-\pi^*$ | BD (2) C58 - C59 | 1.59541 | BD*(2) C51 - C53 | 0.33318 | 87.11 | 0.28 | 0.068 |
| $n-\sigma^*$ | LP (1) N26 | 1.91379 | BD*(1) C3 - C3 | 0.05081 | 63.14 | 0.29 | 0.096 |
| $n-\sigma^*$ | LP (1) N27 | 1.67942 | BD*(2) C3 - C3 | 0.17095 | 112.93 | 0.31 | 0.084 |
| $n-\sigma^*$ | LP (1) N28 | 1.68391 | BD*(1) C31 - C32 | 0.0695 | 224.26 | 0.29 | 0.07 |
| $n-\sigma^*$ | LP (2) S31 | 1.86707 | BD*(1) N27 - C32 | 0.0695 | 55.48 | 0.59 | 0.08 |
| $\pi^*\pi^*$ | BD*(2) C58 - C59 | 0.40213 | BD*(2) C61 - C65 | 0.34741 | 1285.12 | 0.01 | 0.081 |

Table 5. The Physico-Chemical properties of 3-PDPPPHC.

| Parameters | Values |
|------------|--------|
| HOMO       | -5.249 eV |
| LUMO       | -0.951 eV |
| Energy gap | 4.298 eV |
| HOMO-1     | -5.527 eV |
| LUMO+1     | -0.368 eV |
| Ionization potential (IP) | 5.249 eV |
| Electron affinity (EA) | 0.951 eV |
| Electrophilicity Index (\(\omega\)) | 1.118 |
| Chemical Potential (\(\mu\)) | 3.101 |
| Electro negativity (\(\chi\)) | -3.101 |
| Hardness (\(\eta\)) | -4.298 |

Figure 6. Electrostatic potential (ESP), total density (TD) and the molecular electrostatic potential (MEP) map in gas phase of 3-PDPPPHC.

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3.8. Mulliken atomic charges.

Mulliken atomic charge calculation has an important role in applying quantum chemical calculation to the molecular system since atomic charges affect the dipole moment, molecular polarizability, electronic structure, and many more molecular systems properties. In the present study, the Mulliken charges were calculated by DFT/B3LYP/6-311++G(d,p) basis set. The calculated Mulliken charge values are listed in Table 6 and are plotted in Fig. 7. The C22/C32 atoms have the highest negative/positive charges, respectively, among the other atoms in the 3-PDPPPHC molecule due to the resonance. The Nitrogen and sulfur atoms have negative charges and all hydrogen atoms having net positive charges in the present system.

![Figure 7. The Mulliken atomic charges of 3-PDPPPHC.](image)

Table 6. The Mulliken atomic charges of 3-PDPPPHC.

| Atom | Charges  | Atom | Charges  | Atom | Charges  |
|------|----------|------|----------|------|----------|
| 1C   | 0.02905  | 24H  | 0.10917  | 47C  | -0.1103  |
| 2C   | -0.0741  | 25H  | 0.10188  | 48C  | -0.1221  |
| 3C   | 0.23892  | 26N  | -0.2598  | 49C  | -0.0891  |
| 4C   | -0.1852  | 27N  | -0.403   | 50H  | 0.08993  |
| 5C   | 0.02328  | 28N  | -0.6404  | 51C  | -0.0878  |
| 6H   | 0.10552  | 29H  | 0.26156  | 52H  | 0.0935   |
| 7H   | 0.09778  | 30H  | 0.26132  | 53C  | -0.0834  |
| 8H   | 0.13144  | 31S  | -0.2371  | 54H  | 0.07883  |
| 9N   | -0.5359  | 32C  | 0.36851  | 55H  | 0.09093  |
| 10H  | 0.2498   | 33H  | 0.09341  | 56H  | 0.08292  |
| 11C  | -0.2148  | 34H  | 0.09128  | 57H  | 0.09221  |
| 12H  | 0.12148  | 35H  | 0.07892  | 58C  | 0.32464  |
| 13H  | 0.08562  | 36C  | 0.08201  | 59C  | -0.1392  |
| 14C  | -0.1921  | 37C  | -0.109   | 60C  | -0.0665  |
| 15H  | 0.109    | 38C  | -0.1287  | 61C  | -0.09    |
| 16C  | -0.1669  | 39C  | -0.0888  | 62H  | 0.07336  |
| 17H  | 0.08814  | 40H  | 0.09359  | 63C  | -0.1038  |
| 18H  | 0.09697  | 41C  | -0.0866  | 64H  | 0.12507  |
| 19C  | -0.1976  | 42H  | 0.08828  | 65C  | -0.0832  |
| 20H  | 0.09682  | 43C  | -0.0836  | 66H  | 0.08265  |
| 21H  | 0.09424  | 44H  | 0.08443  | 67H  | 0.0974   |
| 22C  | -0.3193  | 45H  | 0.09818  | 68H  | 0.0875   |
| 23H  | 0.1123   | 46C  | 0.08639  |      |          |

3.9. Thermodynamic properties.

Based on the vibrational analysis carried out at the B3LYP/6-311++G(d,p) level, the standard statistical thermodynamic functions such as heat capacity (Cp), entropy (S), and enthalpy changes (ΔH) are calculated for the present molecule. The values are listed in Table 7. It can be observed that these thermodynamic functions are increasing with temperature. The obvious reason for this almost linear increase is the increase in the molecule's internal energy.
in accordance with the kinetic theory of gases [55]. The correlation equations between thermodynamic functions and temperatures were fitted by quadratic formula. The corresponding fitting factors (R²) for these thermodynamic properties are found to be 0.99878, 0.99998, and 0.99952, respectively. The corresponding correlation graphs are shown in Fig. 8.

\[
\begin{align*}
C_{p,m}^0 &= -0.77064 + 0.49207 T - 1.90845 \times 10^{-4} T^2 \quad (R^2 = 0.99878) \\
S_{m}^0 &= 78.34872 + 0.48239 T - 8.82755 \times 10^{-5} T^2 \quad (R^2 = 0.99998) \\
H_{m}^0 &= -4.65157 + 0.04631 T + 1.42948 \times 10^{-4} T^2 \quad (R^2 = 0.99952)
\end{align*}
\]

**Figure 8.** The thermodynamic properties at different temperatures of 3-PDPPPHC.

**Table 7.** The Thermodynamic properties at different temperatures of 3-PDPPPHC.

| T       | S(J/mol.K) | Cp(J/mol.K) | ddH(kJ/mol) |
|---------|------------|-------------|-------------|
| 100     | 367.21     | 122.43      | 9.87        |
| 200     | 451.17     | 189.58      | 26.22       |
| 300     | 533.29     | 256.41      | 51.47       |
| 400     | 612.32     | 324.51      | 89.12       |
| 500     | 685.21     | 381.24      | 121.18      |
| 600     | 755.02     | 424.81      | 160.37      |
| 700     | 821.71     | 461.23      | 196.68      |
| 800     | 882.51     | 490.24      | 249.68      |
| 900     | 939.72     | 514.31      | 295.45      |
| 1000    | 992.91     | 534.19      | 345.72      |

**3.10. Molecular docking studies.**

The dock, glide energy, and hydrogen bonding interactions of the title compound and co-crystallized ligand are given in Table 8. A view of the X-ray crystal structure of the title compound in the Beta-lactamase Receptor active site showing the key hydrogen contacts between inhibitor and enzyme is depicted in Fig. 9. The co-crystallized ligand in the Beta-lactamase Receptor active site showing the key hydrogen contacts between inhibitor and enzyme is depicted in Fig. 10. The surface diagram showing the title compound docked at Beta-lactamase Receptor's active site is depicted in Fig. 11.

X-ray crystal structures confirmed the expected binding mode. Considering binding orientation and electronic properties enabled optimization to Piperidone as a more potent second-generation lead.

The title compound is shown to be an effective inhibitor. The amide group in the GLY286 interacts with the carbonyl group's oxygen atom at a distance of 2.8 & 3.0 Å. The co-crystallized ligand also docked well, and it shows better interactions with residues GLY and
THR, respectively. The results show that the title compound has better binding energy, and the co-crystallized ligand has comparable interactions.

Figure 9. The title compound in the Beta-lactamase Receptor active site showing the key hydrogen contacts between Piperidone inhibitor and enzyme.

Figure 10. The co-crystallized ligand (dexamethasone) in the Beta-lactamase Receptor active site showing the key hydrogen contacts between inhibitor and enzyme.

Figure 11. Surface diagram showing the Piperidone docked at the active site of beta-lactamase Receptor.

Table 8. Hydrogen bond interactions of Piperidone with amino acids at the active site of Beta-lactamase Receptor.

| Compound | Docking Score | Hydrogen Bonding Interactions |
|----------|--------------|-------------------------------|
|          |              | Donor | Acceptor | Distance (Å) |
| Piperidone | -6.1         | N-H   | O(GLY-286) | 2.8          |
|           |              | N-H   | O*        | 3.0          |
|           |              |       | O-H[THR263] | 3.2          |
|           |              |       | O*        | 2.9          |
| Co-Crystal | -5.4         | N-H[THR316] | O*        | 3.0          |
|           |              |       | O-H[GLY263] | 3.5          |

* Ligand
Table 9. Prediction of ADME/Tox.

| ID                        | Value          |
|---------------------------|----------------|
| BBB                       | 7.65083        |
| Buffer_solubility_mg_L    | 1.63674        |
| Caco2                     | 36.2157        |
| CYP_3A4_substrate         | Substrate      |
| HIA                       | 95.447711      |
| MDCK                      | 18.6595        |
| Plasma_Protein_BINDING    | 87.031791      |
| Water_solubility_mg_L     | 0.000931924    |
| Skin_Permeability         | -1.79587       |
| SKlogD_value              | 5.71791        |
| SKlogP_value              | 7.06189        |
| SKlogS_buffer             | -5.45874       |
| SKlogS_pure               | -8.70334       |

BBB-blood-brain barrier penetration
HIA-Human intestinal absorption

3.11. ADME analysis.

In drug discovery, physicochemical properties were seen to find the vital properties affecting the biological functions (ADME). In this analysis, some important physicochemical properties were given in Table 9. The concept of absorption, distribution, metabolism, and excretion (ADME) shows small molecules' toxicity levels [56]. Drug discovery in silico method has been used to predict pharmacokinetic properties for instant ADMET accurately.

4. Conclusions

The FT-IR and FT-Raman spectra of 3-PDPPPHC have been recorded and analyzed for the first time. The detailed interpretations of the vibrational spectra have been carried out. The optimized geometrical parameters were calculated and compared with a structurally related molecule, which shows the chair conformation. The calculated and experimental results of all the fundamental vibrational modes of 3-PDPPPHC are examined with TED contribution. Besides, the first hyperpolarizability value of the molecule is high, i.e., twenty-six times greater than that of urea; hence, the molecule's NLO activity will also be proportionately high. The NBO result reflects more hyperconjugative interaction energy during π-electron transfer within π-π* interaction, and it leads that the molecule becomes more active. The lowering of the HOMO-LUMO energy gap value has a substantial influence on the ICT and bioactivity of the molecule. The Mulliken atomic charges were calculated and analyzed. The MEP surface predicts the nucleophilic and electrophilic reaction sites of the molecule. The thermodynamic properties such as heat capacity, entropy, and enthalpy at different temperatures were also calculated. Molecular docking results show that the title compound having better binding energy, and the co-crystallized ligand has comparable interactions.

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Conflicts of Interest

The authors declare no conflict of interest.

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