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FT-IR, FT-Raman and molecular docking study of ethyl 4-(2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)acetamido)benzoate

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Abstract

FT-IR and FT-Raman spectra of ethyl 4-(2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)acetamido)benzoate were recorded, assigned and compared with theoretical results. Stability of the molecule arising from hyperconjugative interactions, charge delocalization has been analyzed using natural bond orbital analysis. From the optimized geometry of the molecule, molecular electrostatic potential, nonlinear optical properties and frontier molecular orbitals of the title compound were performed at the DFT level. From the molecular electrostatic potential map, it is evident that the maximum negative region is localized over the sulphur atoms and N₃ atom of triazole ring and the maximum positive region is localized on NH group, indicating a possible site for nucleophilic attack. The predicted nonlinear optical properties of the title compound are much greater than that of urea. The molecular docking studies show that the docked ligand, title compound forms a stable complex with pyrrole inhibitor and gives a binding affinity value of -9.5 kcal/mol and this results suggest that the compound might exhibit inhibitory activity against pyrrole inhibitor.

Keywords: DFT; FT-IR; FT-Raman; Quinazoline; Molecular docking.

1. Introduction

Quinazoline derivatives have been reported for their antibacterial, antifungal, anti-HIV [1,2], anthelmintic[3], antitubercular [4], hypotensive [5], anticonvulsant [6], anti-fibrillatory [7], diuretic [8] and antiviral [9,10] activities. Among a wide variety of nitrogen heterocycles that have been explored for developing pharmaceutically important molecules, the quinazolines have played an important role in medicinal chemistry and subsequently emerged as a pharmacophore [11]. In the present study, FT-IR and FT-Raman spectra of the title compound was reported both experimentally and theoretically. From the study of frontier molecular orbital analysis, chemical descriptors are also reported. Due to the different potential biological activity of the title compound, molecular docking study is also reported.

2. Experimental details

A mixture of 2-mercapto-3-phenethylquinazolin-4(3*H*)-one (2 mmol, 564 mg) and ethyl 4-(2-chloroacetamido)benzoate (2.1 mmol, 508 mg) in 15 ml acetone containing anhydrous potassium carbonate (3 mmol, 415 mg) was stirred at room temperature for 12 h. The reaction mixture was filtered, the solvent was removed under reduced pressure and the solid obtained was dried and re-crystallized from ethanol. NMR spectra (^1H and ^{13}C) for the compound were recorded on a 500MHz NMR Spectrometer (Bruker advance, Reinstetten, Germany) using deuteriated DMSO and methanol as the solvent. The chemical shift values (ppm) and coupling constants (J) are given in δ and Hz respectively. Mp: 190-191 $^{\circ}\text{C}$, yield 88%, ^1H NMR (CDCl_3): δ 10.09 (s, 1H), 8.23 (d, 1H, J = 7.50 Hz), 7.88 (d, 2H, J = 8.5 Hz), 7.74 (t, 1H, J = 7.0 Hz), 7.56 (d, 1H, J = 8.0 Hz), 7.44-7.41 (m, 3H), 7.21-7.13 (m, 4H), 7.12 (d, 1H, J = 8.0 Hz), 4.24 (t, 4H, J = 8.0 Hz), 3.94 (s, 2H), 2.99 (t, 2H, J = 8.0 Hz), 1.27 (t, 3H, J = 7.0 Hz). ^{13}C NMR (CDCl_3) δ : 14.3, 34.0, 36.0, 46.8, 60.9, 118.6, 119.3, 121.7, 124.9, 126.9, 127.0, 127.6, 128.8, 129.0, 130.8, 135.2, 137.2, 142.0, 146.4, 157.5, 160.8, 166.0, 166.9. MS: M^+ =487.

The FT-IR spectrum (Fig.1) was recorded using KBr pellets on a DR/Jasco FT-IR 6300 spectrometer. The FT-Raman spectrum (Fig.2) was obtained on a Bruker RFS 100/s, Germany. For excitation of the spectrum the emission of Nd:YAG laser was used, excitation wavelength was 1064 nm, maximal power was 150 mW and measurement was carried out on solid sample.

3. Computational details

Calculations of the title compound were carried out using Gaussian 09 software [12] by utilizing Becke's three parameter hybrid model with the Lee-Yang-Parr correlation functional (B3LYP) method. The 6-311++G(d,p)(5D,7F) basis set was employed to predict the molecular

structure and vibrational wave numbers [13]. At the optimized structure (Fig. 3) of the examined species, no imaginary wave number modes were obtained, proving that a true minimum on the potential energy surface was found. The DFT method tends to overestimate the fundamental modes; therefore scaling factor (0.9613) has to be used for obtaining a considerably better agreement with experimental data [13]. The optimized geometrical parameters (B3LYP) are given in Table S1 (supporting material). The assignments of the calculated wave numbers are aided by the animation option of GAUSSVIEW program [14] and the potential energy distribution (PED) is calculated with the help of GAR2PED software package [15].

4. Results and discussion

4.1 IR and Raman spectra

The calculated scaled wave numbers, observed IR, Raman bands and assignments are given in Table 1. The C=O stretching mode [16-18] is expected in the region $1750\text{--}1650\text{ cm}^{-1}$ and in the present case these modes appears at $1689, 1666\text{ cm}^{-1}$ in the IR spectrum, and at $1672, 1655\text{ cm}^{-1}$ in the Raman spectrum. The DFT calculations give these modes at $1694, 1674, 1664\text{ cm}^{-1}$. The in-plane and out-of-plane C=O bending modes are expected in the regions 625 ± 70 and $540 \pm 80\text{ cm}^{-1}$, respectively [16] and for the title compound, the $\delta\text{C=O}$ in-plane deformation bands are observed at $558, 501\text{ cm}^{-1}$ in the IR spectrum, $619, 551\text{ cm}^{-1}$ in the Raman spectrum and at $616, 554, 500\text{ cm}^{-1}$ theoretically and the bands at $770, 754\text{ cm}^{-1}$ in the IR spectrum, $771, 754, 670\text{ cm}^{-1}$ in the Raman spectrum and at $770, 753, 677\text{ cm}^{-1}$ (DFT) is assigned as $\gamma\text{C=O}$ modes. The C-O-C stretching vibrations are expected in the ranges $1200\text{--}1100\text{ cm}^{-1}$ (asymmetric) and $1050\text{--}950\text{ cm}^{-1}$ (symmetric) [16, 19]. As expected, the asymmetric and symmetric C-O-C vibrations are assigned at 1082 and 997 cm^{-1} theoretically for the title compound, which is in agreement with the literature [18]. Experimentally bands are observed at 996 cm^{-1} in the IR spectrum and at 1083 cm^{-1} in the Raman spectrum.

The N-H stretching vibrations give rise to bands at $3500\text{--}3300\text{ cm}^{-1}$ [20] and according to Roeges the N-H stretching vibration appears strongly and broadly in the region $3390 \pm 60\text{ cm}^{-1}$ [16]. For the title compound N-H stretching mode is assigned at 3436 cm^{-1} theoretically and a strong band is observed in the IR spectrum at 3450 cm^{-1} . Mary et al. [21] reported a band at 3343 cm^{-1} in the IR spectrum, 3340 cm^{-1} in Raman spectrum and 3433 cm^{-1} theoretically as N-H stretching mode. The C-N-H vibration in which N and H atoms move in opposite direction of carbon atom in the amide moiety is reported at 1497 cm^{-1} theoretically, and the C-N-H vibration

in which N and H atoms move in the same direction of carbon atom in the amide group is reported at 1217 cm^{-1} (DFT) [17, 22] and for the title compound the bands at 1488 (IR), 1205, 1486 (Raman) and 1484, 1206 cm^{-1} (DFT) are assigned as N-H in-plane bending modes. The out-of-plane bending of N-H is expected around $650 \pm 50\text{ cm}^{-1}$ [16] and in the present case the band at 682 (Raman) and 684 cm^{-1} (DFT) is assigned as out-of-plane bending of N-H.

Louran et al. [23] reported a value at 1220 cm^{-1} for C-N stretching for poly aniline. In the case of aromatic amines a strong C-N stretching absorption is observed in the region in $1342\text{--}1266\text{ cm}^{-1}$ [17, 18] and Varghese et al. [24] reported C-N stretching mode at 1203 cm^{-1} in the IR spectrum and at 1208 cm^{-1} theoretically. For the title compound, the C-N stretching modes are assigned at 1232, 1146, 1108, 966 cm^{-1} in the IR spectrum, 1232, 1149, 1108, 967 cm^{-1} in the Raman spectrum and in the range $1235\text{--}965\text{ cm}^{-1}$ theoretically. The C=N stretching bands [18] are expected in the range $1450\text{--}1550\text{ cm}^{-1}$ and for the title compound, the bands observed at 1522 cm^{-1} in the IR and 1512 cm^{-1} in Raman spectrum are assigned as C=N stretching modes. DFT calculations give this mode at 1518 cm^{-1} . Haress et al. [25] reported $\nu\text{C=N}$ bands at 1540, 1520 cm^{-1} in the Raman spectrum, at 1535, 1520 cm^{-1} in the IR spectrum and at 1531, 1516 cm^{-1} (DFT) for oxadiazole compound.

For the title compound C-S stretching modes are observed at 632 cm^{-1} in the Raman spectrum and at 797, 635 cm^{-1} theoretically as expected [16].

The stretching vibrations of the CH_2 group (the asymmetric and symmetric stretch) and deformation modes of CH_2 group (scissoring, wagging, twisting and rocking modes) appears in the regions 3000 ± 20 , 2900 ± 25 , 1450 ± 30 , 1330 ± 35 , 1245 ± 45 , $780 \pm 55\text{ cm}^{-1}$ respectively [16,17]. The CH_2 stretching modes are observed at 2940 cm^{-1} in the IR spectrum, 2970 cm^{-1} in the Raman spectrum and in the range $3017\text{--}2929\text{ cm}^{-1}$ theoretically. The deformation modes of CH_2 are assigned at 1447, 1400, 1358, 1342, 1321, 1249, 1131, 996 cm^{-1} in the IR spectrum, 1462, 1359, 1341, 1324, 1250, 1162 cm^{-1} in the Raman spectrum and in the range 1461-1393 (scissoring), 1353-1314 (wagging), 1256-1163 (twisting), 1131-886 (rocking) cm^{-1} theoretically as expected [16].

The CH_3 stretching modes are expected in the region [16] $2900\text{--}3050\text{ cm}^{-1}$. The bands observed at 2986, 2919 cm^{-1} in the IR spectrum, 2985, 2920 cm^{-1} in the Raman spectrum and at 2995, 2984, 2919 cm^{-1} (DFT) are assigned as the stretching modes of the methyl group. Methyl asymmetrical deformations are expected in the region 1460 ± 15 and the symmetrical

deformations at $1350 \pm 20 \text{ cm}^{-1}$ [16]. The DFT calculation gives 1441 , 1429 and 1372 cm^{-1} as asymmetric and symmetric deformation modes for the title compound. The methyl rocking vibration [16] has been observed at $1050 \pm 30 \text{ cm}^{-1}$. The bands observed at 1031 in the IR spectrum and 1131 , 1090 cm^{-1} (DFT) are assigned as rocking modes of the methyl group.

In the following discussion, the mono-, para- and ortho-substituted phenyl rings are designated as PhI, PhII and PhIII, respectively. The quinazoline ring is designated as PhIV. The phenyl CH stretching modes are expected above 3000 cm^{-1} [16, 17] and for the title compound, the CH stretching modes are assigned at $3065, 3054, 3045, 3036, 3033 \text{ cm}^{-1}$ (DFT), 3042 cm^{-1} (IR), $3064, 3053, 3037, 3028 \text{ cm}^{-1}$ (Raman) for PhI, $3092, 3079, 3078, 3049 \text{ cm}^{-1}$ (DFT), 3108 cm^{-1} (IR) for PhII and $3078, 3071, 3061, 3045 \text{ cm}^{-1}$ (DFT), 3078 cm^{-1} (Raman) for PhIII. The phenyl ring stretching modes are assigned at $1578, 1470 \text{ cm}^{-1}$ in the IR spectrum, 1470 cm^{-1} in the Raman spectrum, in the range $1580\text{--}1290 \text{ cm}^{-1}$ (DFT) for PhI, $1553, 1488 \text{ cm}^{-1}$ in the IR spectrum, $1584, 1486, 1438 \text{ cm}^{-1}$ in the Raman spectrum, in the range $1584\text{--}1289 \text{ cm}^{-1}$ (DFT) for PhII and $1584, 1550, 1306 \text{ cm}^{-1}$ in the Raman spectrum, in the range $1583\text{--}1306 \text{ cm}^{-1}$ (DFT) for PhIII as expected [16]. The ring breathing mode of the phenyl ring appears as a weak band near 1000 cm^{-1} in mono-, 1,3-di and tri-substituted benzenes [16, 22]. In the otherwise substituted benzenes, however, this vibration is substituent sensitive and difficult to distinguish from the ring in-plane deformation [16]. In ortho disubstitution the ring breathing mode has three frequency intervals according to whether both substituents are heavy, or one of them is heavy while the other is light, or both of them are light and in the first case the interval is $1100\text{--}1130 \text{ cm}^{-1}$, in the second case $1020\text{--}1070 \text{ cm}^{-1}$, while in the third case it is between 630 and 780 cm^{-1} [22]. For ortho substituted phenyl ring the ring breathing mode is reported at 1041 cm^{-1} [26] and at $1086, 1011 \text{ cm}^{-1}$ (theoretically) [27] and at 1020 cm^{-1} (theoretically) [28]. In the present case, the ring breathing mode is assigned at 1084 cm^{-1} for PhIII (ortho), 1009 cm^{-1} for PhI (mono). The ring breathing mode of the para substituted benzene rings with entirely different substituents has been reported in the range $780\text{--}880 \text{ cm}^{-1}$ [22] and for the title compound, the band observed at 872 cm^{-1} in the IR spectrum is assigned as the ring breathing mode of PhII, which finds support from the computational value at 869 cm^{-1} . Panicker et al. [29] reported the ring breathing mode of para substituted benzene at 873 cm^{-1} (IR) and at 861 cm^{-1} (theoretically). For phenyl rings, the in-plane and out-of-plane CH deformations are expected above and below 1000 cm^{-1} [16]. For the title compound the in-plane CH deformations are assigned at 1174 cm^{-1} (IR), $1176, 1135 \text{ cm}^{-1}$ (Raman), $1311, 1177, 1157, 1136, 1062 \text{ cm}^{-1}$ (DFT), for PhI, 1282 cm^{-1} (IR), 1004 cm^{-1} (Raman), $1282,$

1153, 1100, 1007 (DFT), for PhII and 1205 (Raman), 1265, 1206, 1125, 1084 cm^{-1} (DFT) for PhIII. The bands at 893, 730 (IR), 892, 732 (Raman), 962, 947, 892, 825, 733 (DFT) and 809 (Raman), 960, 947, 839, 811 (DFT) and 967 (Raman), 965, 946, 853, 752 cm^{-1} (DFT) are assigned as the CH out-of-plane deformations for PhI, PhII and PhIII, respectively. Most of the modes are not pure but contains significant contributions from other modes also.

4.2. Natural bonding orbital (NBO) analysis

The natural bond orbitals (NBO) calculations were performed using NBO 3.1 program [30] as implemented in the Gaussian09 package at the DFT/B3LYP level. In NBO analysis large stabilization energy $E(2)$ value shows the intensive interaction between electron-donors and electron-acceptors, and greater the extent of conjugation of the whole system, the possible intensive interaction are given in Table S2 (supporting material).

The various important intra-molecular hyper conjugative interactions are $n_1(\text{S}_1) \rightarrow \pi^*(\text{N}_3-\text{C}_{33})$, $n_2(\text{O}_2) \rightarrow \sigma^*(\text{N}_4-\text{C}_{15})$, $n_1(\text{N}_3) \rightarrow \sigma^*(\text{N}_4-\text{C}_{33})$, $n_1(\text{N}_4) \rightarrow \pi^*(\text{N}_3-\text{C}_{33})$, $n_2(\text{O}_{38}) \rightarrow \sigma^*(\text{C}_{37}-\text{N}_{39})$, $n_2(\text{N}_{39}) \rightarrow \pi^*(\text{C}_{37}-\text{O}_{38})$, $n_2(\text{O}_{52}) \rightarrow \pi^*(\text{C}_{51}-\text{O}_{52})$ with electron densities, 0.37248e, 0.09820e, 0.05944e, 0.37248e, 0.07912e, 0.26307e, 0.26260e and stabilization energies, 24.72, 30.44, 16.08, 56.49, 26.58, 33.96, 48.84 KJ/mol.

The NBO also analysis describes the bonding in terms of the natural hybrid orbital: the orbitals with considerable p-characters are: $n_2(\text{S}_1)$, $n_2(\text{O}_2)$, $n_2(\text{O}_{38})$, $n_2(\text{O}_{53})$, $n_2(\text{O}_{52})$ with higher energy orbitals, -0.25390, -0.24692, -0.26116, -0.32332, -0.25843a.u. and low occupation numbers 1.83076, 1.85315, 1.86036, 1.79430, 1.84664. The orbitals with low p-characters are: $n_1(\text{S}_1)$, $n_1(\text{O}_2)$, $n_1(\text{O}_{38})$, $n_1(\text{O}_{53})$, $n_1(\text{O}_{52})$ with lower energy orbitals, -0.62692, -0.67391, -0.68719, -0.56683, -0.68383a.u. and high occupation numbers, 1.98020, 1.97616, 1.97487, 1.96298, 1.97668.

Thus, a very close to pure p-type lone pair orbital participates in the electron donation to the $n_1(\text{S}_1) \rightarrow \pi^*(\text{N}_3-\text{C}_{33})$, $n_2(\text{O}_2) \rightarrow \sigma^*(\text{N}_4-\text{C}_{15})$, $n_1(\text{N}_3) \rightarrow \sigma^*(\text{N}_4-\text{C}_{33})$, $n_1(\text{N}_4) \rightarrow \pi^*(\text{N}_3-\text{C}_{33})$, $n_2(\text{O}_{38}) \rightarrow \sigma^*(\text{C}_{37}-\text{N}_{39})$, $n_1(\text{N}_{39}) \rightarrow \pi^*(\text{C}_{37}-\text{O}_{38})$ and $n_2(\text{O}_{52}) \rightarrow \pi^*(\text{C}_{51}-\text{O}_{52})$ interactions in the compound. The results are tabulated in Table 2.

4.3. Frontier molecular orbital analysis

The energies of two important molecular orbitals of the title compound, the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) were calculated. Fig.4 shows the HOMO and LUMO of the title compound obtained by DFT method.

The energy gap between HOMO and LUMO is a critical parameter in determining molecular electrical transport properties [31] and for predicting the most reactive position in pi-electron systems and also explains several types of reaction in conjugated system [32]. The conjugated molecules are characterized by a small HOMO-LUMO separation, which is the result of a significant degree of intramolecular charge transfer from end-capping electron-donor groups to the efficient electron-acceptor groups through pi conjugated path leads to the very good for non-linear optical applications [33, 34] and the energy gap between HOMO and LUMO has been used to prove the bioactivity from intramolecular charge transfer [35]. The ionization energy and electron affinity can be expressed through HOMO and LUMO energies as $I = -E_{\text{HOMO}} = 7.324$ eV and $A = -E_{\text{LUMO}} = 5.005$ eV. The calculated energy gap is 2.319 eV and it clearly indicates that charge transfer takes place within the molecule, which increases molecular activity of the molecule. Using the HOMO and LUMO energies, the hardness η and chemical potential μ are given by the following relations, $\eta = (I-A)/2 = 1.160$ eV and $\mu = -(I+A)/2 = -6.165$ eV. Parr et al. [36] proposed the global electrophilicity power of a ligand as $\omega = \mu^2/2\eta = 16.382$ eV. This index measures the stabilization in energy when the system acquires an additional electronic charge from the environment. Electrophilicity encompasses both the ability of an electrophile to acquire additional electronic charge and the resistance of the system to exchange electronic charge with the environment. When two molecules react, which one will act as an electrophile (nucleophile) will depend on which one has a higher (lower) electrophilicity index [37]. The calculated value of the electrophilicity index describes the biological activity of the title compound.

4.4. Nonlinear optical properties

In discussion of nonlinear optical properties, the polarization of the molecule by an external radiation is often approximated as the creation of an induced dipole moment by an external electric field. The dipole moment μ , the mean polarizability α_0 are calculated using Gaussian 09 software and is found to be 1.541 Debye and 5.069×10^{-23} e.s.u respectively. The first order hyperpolarizability of the title compound is calculated and is found to be 9.914×10^{-30} esu. The calculated hyperpolarizability of the title compound is 76.26 times that of the standard NLO material urea (0.13×10^{-30} esu) [38]. The average second hyperpolarizability is $\langle \gamma \rangle = (\gamma_{xxxx} + \gamma_{yyyy} + \gamma_{zzzz} + 2\gamma_{xxyy} + 2\gamma_{xxzz} + 2\gamma_{yyzz})/5$ [39-41]. The theoretical second order hyperpolarizability was calculated using the Gaussian09 software and is equal to -60.424×10^{-37}

e.s.u. We conclude that the title compound and its derivatives are an attractive object for future studies of nonlinear optical properties.

4.5. Molecular Electrostatic Potential (MEP)

MEP of a molecule has always proved to be a good guide in assessing the molecules reactivity towards positively or negatively charged reactants, despite of the fact that the molecular charge distribution remains unperturbed through the external test charge (no polarization occurs) [42, 43]. The MEP provides a visual method to understand the relative polarity of a molecule. Such surfaces depict the size, shape, charge density and site of chemical reactivity of the molecule. In the surface generated, negative electrostatic potential corresponds to an attraction of the proton by the concentrated electron density in the molecules (from lone pairs, pi-bonds, etc.) (coloured in shades of red). Whereas positive electrostatic potential corresponds to repulsion of the proton by the atomic nuclei in regions where low electron density exists and the nuclear charge is incompletely shielded (colored in shades of blue). If the surface is largely white or lighter color shades, the molecule is mostly non-polar. Potential increases in the order of red < orange < yellow < green < blue. The negative (red, orange and yellow) regions of the MEP (Fig.5) are related to electrophilic reactivity. The maximum negative region is localized over the sulphur atoms and N₃ atom of triazole ring and the maximum positive region is localized on NH group, indicating a possible site for nucleophilic attack. These sites give information about the region from which the compound can have intermolecular interactions. This predicted the most reactive site for both electrophilic and nucleophilic attack.

4.6. Molecular docking

Quinazoline are a large class of active chemical compounds possess a wide variety of biological activities such as anti HIV, anticancer [44, 45], antifungal, antibacterial, anti-mutagenic, anticonvulsant etc. [46]. The pyrrole derivatives are anticancer agents [47]. Pyrrole derivatives with potent tubulin polymerization exhibits inhibiting activity as anticancer agents including hedgehog-dependent cancer [48]. High resolution crystal structure of pyrrole inhibitor was downloaded from the protein data bank website (PDB ID: 2B02) and all molecular docking calculations were performed on AutoDock-Vina software [49]. The 3D crystal structure of pyrrole inhibitor was obtained from Protein Data Bank and the protein was prepared for docking by removing the co-crystallized ligands, waters and co-factors. The Auto Dock Tools (ADT) graphical user interface was used to calculate Kollman charges and polar hydrogens and the

ligand was prepared for docking by minimizing its energy at B3LYP/6-311++G(d,p)(5D,7F) level of theory. Partial charges were calculated by Geistenger method and the active site of the enzyme was defined to include residues of the active site within the grid size of 40Å×40Å×40Å. The docking protocol was tested by extracting co-crystallized inhibitor from the protein and then docking the same and the docking protocol predicted the same conformation as was present in the crystal structure with RMSD value well within the reliable range of 2Å [50]. Amongst the docked conformations, one which binded well at the active site was analyzed for detailed interactions in Discover Studio Visualizer 4.0 software. The ligand binds at the active site of the substrate (Figs.6 and 7) by weak non-covalent interactions. Cys164, Lys191, Gln159 and His112 amino acid forms H-bond with C=O, C-O, N-H and quinazoline moiety respectively. Ile160, Leu182, Leu177, Ile237 and Tyr156 form π -alkyl interaction with phenyl ring and CH₃ group. Ile192 and Cys164 amino acid forms π -alkyl interaction with quinazoline moiety. His174 amino acid forms electrostatic interaction (π -cation) with phenyl ring. The docked ligand title compound forms a stable complex with pyrrole inhibitor and gives a binding affinity (ΔG in kcal/mol) value of -9.5 (Table 3). These preliminary results suggest that the compound might exhibit inhibitory activity against pyrrole inhibitor.

4.8. Geometrical parameters

All the carbon-carbon bond lengths in the benzene rings lie in the range 1.3935-1.3997Å for PhI, 1.3857-1.4029Å for PhII and 1.3832-1.4087 for PhIII and bond lengths are somewhere in between the normal values for a single (1.54Å) and a double bond (1.33Å) [51]. In the title compound, the C-S bond lengths are 1.7873 and 1.8305Å while the reported values are in the range 1.7675-1.8641Å [52] and 1.7710-1.8110Å [53]. The bond lengths of C₅-N₃ (1.3832), C₁₅-N₄ (1.4163), C₃₃-N₄ (1.3849Å), C₃₇-N₃₉ (1.3815Å) and C₄₀-N₃₉ (1.4128Å) are shorter than the normal C-N bond length of about 1.48 and this point into the effect of resonance in this part of the molecule [54]. The shortening of the bond length of C₅₁=O₅₂ (1.2107Å) and C₃₇-O₃₈ (1.2178Å) could be assigned a double bond character. The C-O bond lengths of the title compound are C₅₄-O₅₃ = 1.4501 and C₅₁-O₅₃ = 1.3491Å and C₅₁-O₅₃ is greater than the average distance of 1.362Å found among phenols [55] and the increase is due to the noticeable intra molecular hydrogen bonding experienced by the molecule [56]. At C₂₂ position, the bond angles are C₂₃-C₂₂-C₃₁ = 118.6, C₂₃-C₂₂-C₁₉ = 120.6 and C₃₁-C₂₂-C₁₉ = 120.8° and the reduction in the angle C₂₃-C₂₂-C₃₁ is due to presence of adjacent methylene groups. At N₄ position, the bond

angles $C_{15}-N_4-C_{33}$ is increased by 1.0° , $C_{33}-N_4-C_{16}$ is increased by 2.7° and $C_{15}-N_4-C_{16}$ is decreased by 3.8° from 120° and this is due to the interaction between O_2 and the methylene at C_{16} positions. At C_{15} position, the bond angles, $N_4-C_{15}-C_{14}$ is decreased by 5.4° and $C_{14}-C_{15}-O_2$ is increased by 5.1° from 120° and this variation is due to the interactions between O_2 and the adjacent methylene groups. Similarly at C_{33} position, the bond angles $N_3-C_{33}-N_4 = 124.9$ and $N_4-C_{33}-S_1 = 115.3^\circ$ and this asymmetry in angles is due to the interaction between the quinazoline ring and adjacent moieties. At C_{37} position, the bond angles $O_{38}-C_{37}-C_{34} = 122.3$, $C_{34}-C_{37}-N_{39} = 117.9$ and $N_{39}-C_{37}-O_{38} = 119.8^\circ$ and this asymmetry is due to the adjacent methylene and NH groups. At C_{51} position, the bond angles $O_{53}-C_{51}-C_{49} = 112.5$, $O_{53}-C_{51}-O_{52} = 123.3$ and $C_{49}-C_{51}-O_{52} = 124.1^\circ$ and this asymmetry is due to the carbonyl and methoxy oxygen atom and at C_{49} position, the bond angles $C_{45}-C_{49}-C_{46} = 119.0$, $C_{45}-C_{49}-C_{51} = 122.8$ and $C_{46}-C_{49}-C_{51} = 118.2^\circ$ and this asymmetry is due to the interaction between the carbonyl group and H48 atom. At N_{39} and C_{40} the bond angles are respectively, $C_{40}-N_{39}-C_{37} = 132.2$, $C_{40}-N_{39}-H_{50} = 116.0$, $C_{37}-N_{39}-H_{50} = 111.1$ and $C_{41}-C_{40}-C_{42} = 119.2$, $C_{41}-C_{40}-N_{39} = 122.8$, $N_{39}-C_{40}-C_{42} = 118.0^\circ$ and these values in bond angles reveal the hydrogen bonding between H_{50} and the carbonyl group.

The quinazoline moiety is planar with respect to the phenyl ring PhIII, as is evident from the torsion angles $C_{12}-C_{14}-C_{15}-N_4 = 179.1$, $C_{12}-C_{14}-C_5-N_3 = 179.8$, $C_6-C_5-N_3-C_{33} = -179.5$ and $C_6-C_5-C_{14}-C_{15} = -179.9^\circ$ and the CH_2 groups at C_{19} and C_{16} are tilted from the phenyl ring PhI, as is evident from the torsion angles, $C_{25}-C_{23}-C_{22}-C_{19} = 178.4$, $C_{23}-C_{22}-C_{19}-C_{16} = -86.6$, $C_{29}-C_{31}-C_{22}-C_{19} = -178.4$ and $C_{31}-C_{22}-C_{19}-C_{16} = 91.7^\circ$. The acetamido group is tilted from the phenyl ring PhII as is evident from the torsion angles, $C_{45}-C_{41}-C_{40}-N_{39} = 178.9$, $C_{41}-C_{40}-N_{39}-C_{37} = 42.2$, $C_{46}-C_{42}-C_{40}-N_{39} = -178.1$ and $C_{42}-C_{40}-N_{39}-C_{37} = -140.6^\circ$.

5. Conclusion

In the present work, complete vibrational analysis has been made for proper wavenumber assignments of ethyl 4-(2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio) acetamido) benzoate. The vibrational wavenumbers of the fundamental modes of the title compound have been precisely assigned, analyzed and the theoretical results were compared with the experimental values. Molecular electrostatic potential and nonlinear optical properties of the title compound were also performed. HOMO and LUMO gap explains the eventual charge transfer interactions taking place within the molecule. Stability of the molecule arising from hyperconjugative interactions and charge delocalization has been analyzed using natural bond orbital analysis. The

title compound binds at the active site of the substrate by weak non-covalent interactions and Cys164, Lys191, Gln159 and His112 amino acid forms H-bond with C=O, C-O, N-H and quinazoline moiety respectively. Ile160, Leu182, Leu177, Ile237 and Tyr156 form π -alkyl interaction with phenyl ring and CH₃ group. Ile192 and Cys164 amino acid forms π -alkyl interaction with quinazoline moiety. His174 amino acid forms electrostatic interaction (π -cation) with phenyl ring. The docking results suggest that the compound might exhibit inhibitory activity against pyrrole inhibitor.

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Fig.1 FT-IR spectrum of ethyl 4-(2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)acetamido)benzoate

Fig.2 FT-Raman spectrum of ethyl 4-(2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)acetamido)benzoate

Fig.3 Optimized geometry of ethyl 4-(2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)acetamido)benzoate

Fig.4 HOMO-LUMO plots of ethyl 4-(2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)acetamido)benzoate

Fig.5 MEP plot of ethyl 4-(2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)acetamido)benzoate

Fig.6 Schematic for the docked conformation of active site of title compound at pyrrole inhibitor conformation with H-bond(green), alkyl- π (pink) and π -cation (brown)

Fig.7 The ligand and the co-crystallized inhibitor embedded into the catalytic site of pyrrole inhibitor

Table 1. Calculated (scaled) wavenumbers, observed IR, Raman bands and assignments of ethyl 4-(2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)acetamido)benzoate

B3LYP/6-311++G(d,p)(5D,7F)			IR	Raman	Assignments ^a
$\nu(\text{cm}^{-1})$	IR_t	R_A	$\nu(\text{cm}^{-1})$	$\nu(\text{cm}^{-1})$	-
3436	45.00	188.10	3450	-	$\nu\text{NH}(100)$
3092	4.10	103.36	3108	-	$\nu\text{CHII}(99)$
3079	3.53	95.50	-	-	$\nu\text{CHII}(98)$
3078	7.92	252.35	-	3078	$\nu\text{CHIII}(89)$
3078	2.37	31.62	-	-	$\nu\text{CHII}(91)$
3071	8.57	104.06	-	-	$\nu\text{CHIII}(99)$
3065	19.33	367.28	-	3064	$\nu\text{CHI}(93)$
3061	9.26	146.67	-	-	$\nu\text{CHIII}(99)$
3054	24.78	49.76	-	3053	$\nu\text{CHI}(99)$
3049	5.89	73.55	-	-	$\nu\text{CHII}(99)$
3045	3.62	78.97	-	-	$\nu\text{CHIII}(97)$
3045	8.07	85.24	3042	-	$\nu\text{CHI}(99)$
3036	0.92	88.60	-	3037	$\nu\text{CHI}(94)$
3033	6.74	21.09	-	3028	$\nu\text{CHI}(98)$
3017	0.03	38.41	-	-	$\nu\text{CH}_2(100)$
3014	6.37	13.12	-	-	$\nu\text{CH}_2(95)$
2995	37.57	9.78	-	-	$\nu\text{CH}_3(68), \nu\text{CH}_2(32)$
2984	29.05	119.44	2986	2985	$\nu\text{CH}_3(98)$
2972	9.09	36.62	-	-	$\nu\text{CH}_2(97)$
2969	1.01	96.68	-	2970	$\nu\text{CH}_2(67), \nu\text{CH}_3(32)$
2962	8.04	62.25	-	-	$\nu\text{CH}_2(96)$
2959	18.04	117.11	-	-	$\nu\text{CH}_2(99)$
2936	17.77	134.43	2940	-	$\nu\text{CH}_2(97)$
2929	11.76	110.97	-	-	$\nu\text{CH}_2(97)$
2919	16.13	201.81	2919	2920	$\nu\text{CH}_3(100)$
1694	290.72	212.43	1689	-	$\nu\text{C=O}(76)$

1674	511.63	51.06	-	1672	$\nu\text{C}=\text{O}(72)$
1664	432.16	43.86	1666	1655	$\nu\text{C}=\text{O}(73)$
1584	228.92	406.16	-	1584	$\nu\text{PhII}(63), \delta\text{CHII}(10)$
1583	9.69	160.43	-	1584	$\nu\text{PhIII}(63), \delta\text{CHIII}(11)$
1580	7.91	66.83	1578	-	$\nu\text{PhI}(70), \delta\text{CHI}(14)$
1560	1.09	10.36	-	-	$\nu\text{PhI}(78), \delta\text{CHI}(10)$
1553	5.02	0.56	1553	-	$\nu\text{PhII}(76)$
1546	113.54	16.64	-	1550	$\nu\text{PhIII}(49), \nu\text{C}=\text{N}(15)$
1518	468.37	270.48	1522	1512	$\nu\text{C}=\text{N}(44), \nu\text{PhIII}(11)$
1484	59.74	13.25	1488	1486	$\delta\text{NH}(46), \nu\text{PhII}(42)$
1467	18.43	1.86	1470	1470	$\delta\text{CHI}(10), \nu\text{PhI}(64)$
1461	10.10	1.39	-	1462	$\delta\text{CH}_2(74), \delta\text{CH}_3(16)$
1444	21.49	9.88	1447	-	$\delta\text{CH}_2(81)$
1443	120.57	41.33	-	-	$\delta\text{CHIII}(17), \nu\text{CN}(12),$ $\delta\text{CH}_2(12), \nu\text{PhIII}(49)$
1441	4.34	11.09	-	-	$\delta\text{CH}_3(67), \delta\text{CH}_2(24)$
1438	36.92	93.74	-	1438	$\nu\text{PhII}(54), \delta\text{CHII}(11)$
1431	6.61	5.67	-	-	$\delta\text{CHIII}(13), \delta\text{CH}_2(13),$ $\nu\text{PhIII}(59)$
1429	7.43	10.01	-	-	$\delta\text{CH}_3(97)$
1427	33.10	69.66	-	-	$\delta\text{CH}_2(66)$
1426	0.13	11.29	-	-	$\delta\text{CHI}(22), \nu\text{PhI}(52)$
1393	31.97	0.96	1400	-	$\delta\text{CH}_2(88)$
1372	9.96	5.60	-	-	$\delta\text{CH}_3(52), \delta\text{CH}_2(26),$ $\nu\text{CC}(13)$
1372	7.16	5.34	-	-	$\nu\text{PhIII}(38), \delta\text{CH}(15),$ $\delta\text{CHII}(26)$
1353	23.98	40.53	1358	1359	$\delta\text{CH}_2(72)$
1345	9.32	7.27	1342	1341	$\delta\text{CH}_2(51), \delta\text{CH}_3(36)$
1323	55.30	43.72	1321	1324	$\delta\text{CH}_2(59), \nu\text{C}=\text{N}(15)$

1314	396.08	54.43	-	-	$\nu\text{CC}(47)$, $\delta\text{CH}_2(42)$
1311	3.74	10.42	-	-	$\delta\text{CHI}(76)$, $\delta\text{CH}_2(10)$
1306	56.31	132.13	-	1306	$\nu\text{PhIII}(81)$
1290	2.05	3.34	-	-	$\nu\text{PhI}(75)$
1289	6.94	7.87	-	-	$\nu\text{PhII}(73)$
1282	13.46	29.89	1282	-	$\delta\text{CHII}(74)$
1272	4.73	21.91	-	1274	$\delta\text{CH}_2(78)$
1265	31.61	13.84	-	-	$\nu\text{CN}(14)$, $\delta\text{CHIII}(48)$
1256	29.99	54.04	-	-	$\delta\text{CH}_2(47)$, $\nu\text{CN}(20)$, $\delta\text{CHIII}(25)$
1247	0.92	9.70	1249	1250	$\delta\text{CH}_2(88)$
1235	627.73	194.25	1232	1232	$\nu\text{CN}(41)$, $\nu\text{CO}(34)$
1217	6.54	76.82	-	-	$\delta\text{CH}_2(42)$, $\nu\text{CN}(44)$
1209	122.29	80.49	-	-	$\nu\text{CN}(42)$, $\delta\text{CH}_2(19)$, $\nu\text{PhII}(20)$
1206	19.33	0.80	-	1205	$\delta\text{NH}(42)$, $\delta\text{CHIII}(40)$
1177	0.07	50.40	1174	1176	$\nu\text{CC}(38)$, $\nu\text{PhI}(12)$, $\delta\text{CHI}(42)$
1163	78.85	30.61	-	1162	$\delta\text{CH}_2(43)$, $\nu\text{CC}(16)$, $\delta\text{CHII}(10)$
1157	0.07	3.88	-	-	$\delta\text{CHI}(79)$, $\nu\text{PhI}(14)$
1153	144.24	49.49	-	-	$\delta\text{CHII}(53)$, $\nu\text{PhI}(12)$
1149	123.42	10.27	1146	1149	$\delta\text{CHIII}(23)$, $\nu\text{CN}(41)$, $\delta\text{CH}_2(10)$
1136	0.87	4.55	-	1135	$\delta\text{CHI}(56)$, $\nu\text{PhI}(16)$
1131	3.67	0.84	1131	-	$\delta\text{CH}_2(57)$, $\delta\text{CH}_3(42)$
1125	62.31	7.95	-	-	$\delta\text{CHIII}(44)$, $\nu\text{CN}(20)$
1113	28.79	10.29	-	-	$\delta\text{CH}_2(72)$
1110	112.47	17.53	1108	1108	$\nu\text{CN}(44)$, $\delta\text{CH}_2(29)$
1100	59.39	3.17	-	-	$\nu\text{CO}(18)$, $\delta\text{CH}_2(11)$, $\delta\text{CHII}(41)$

1090	16.39	14.24	-	-	$\delta\text{CH}_3(52)$, $\nu\text{CC}(12)$, $\delta\text{CHII}(25)$
1084	1.74	1.87	-	-	$\nu\text{PhIII}(52)$, $\delta\text{CHIII}(40)$
1082	220.21	9.92	-	1083	$\nu\text{CO}(47)$, $\delta\text{CH}_3(10)$, $\nu\text{PhII}(12)$
1062	12.35	1.41	-	-	$\nu\text{PhI}(26)$, $\delta\text{CHI}(55)$
1009	7.56	18.15	-	-	$\nu\text{PhI}(52)$, $\delta\text{PhI}(13)$, $\delta\text{CHI}(12)$
1007	8.57	35.78	-	1004	$\nu\text{PhII}(19)$, $\delta\text{CHII}(53)$
997	50.48	2.64	996	-	$\nu\text{CC}(43)$, $\nu\text{CO}(40)$
996	44.42	1.11	996	-	$\delta\text{CH}_2(44)$, $\delta\text{PhIV}(14)$
990	0.23	1.82	-	-	$\delta\text{PhII}(42)$, $\nu\text{CC}(16)$, $\nu\text{PhII}(15)$
990	4.87	48.02	-	-	$\nu\text{CC}(72)$, $\delta\text{CH}_2(14)$
978	0.03	49.64	-	-	$\delta\text{PhI}(63)$, $\nu\text{PhI}(36)$
965	0.18	0.26	-	967	$\gamma\text{CHIII}(87)$, $\tau\text{PhIII}(11)$
965	9.62	2.72	966	967	$\nu\text{CN}(52)$, $\delta\text{C}=\text{O}(20)$
962	0.46	1.50	-	-	$\gamma\text{CHI}(72)$, $\tau\text{PhI}(13)$
960	0.35	0.13	-	-	$\gamma\text{CHII}(90)$
947	0.05	0.02	-	-	$\gamma\text{CHI}(86)$, $\tau\text{PhI}(10)$
947	0.34	0.32	-	-	$\gamma\text{CHII}(70)$, $\tau\text{PhII}(15)$
946	0.92	0.07	-	-	$\gamma\text{CHIII}(86)$
899	7.58	4.84	-	-	$\nu\text{CC}(42)$, $\nu\text{PhII}(21)$, $\delta\text{PhII}(25)$
892	1.53	4.14	893	892	$\gamma\text{CHI}(76)$, $\tau\text{PhI}(11)$
886	4.37	9.98	-	-	$\delta\text{CH}_2(66)$, $\gamma\text{C}=\text{O}(20)$
869	11.34	5.51	872	-	$\delta\text{PhII}(22)$, $\delta\text{PhIV}(11)$, $\nu\text{PhII}(52)$
854	4.29	4.08	856	857	$\nu\text{CO}(40)$, $\delta\text{CH}_3(21)$, $\nu\text{CC}(31)$
853	0.83	0.02	-	-	$\gamma\text{CHIII}(69)$, $\tau\text{PhIII}(10)$
839	28.18	1.17	-	-	$\gamma\text{CHII}(58)$, $\tau\text{PhII}(10)$,

					$\gamma\text{CC}(16)$
832	9.59	31.89	-	-	$\nu\text{CO}(35)$, $\delta\text{C}=\text{O}(22)$
827	11.31	3.43	829	827	$\nu\text{CS}(11)$, $\delta\text{PhIII}(31)$, $\nu\text{PhIII}(30)$
825	0.20	0.20	-	-	$\gamma\text{CHI}(97)$
811	0.36	2.24	-	809	$\gamma\text{CHII}(92)$
800	5.34	21.08	-	-	$\nu\text{CC}(37)$, $\nu\text{PhI}(14)$, $\delta\text{PhI}(36)$
797	4.37	31.79	-	-	$\nu\text{CS}(40)$, $\delta\text{C}=\text{O}(11)$, $\nu\text{CC}(20)$
783	0.93	13.07	-	785	$\delta\text{CH}_2(45)$, $\delta\text{CH}_3(31)$
781	0.72	26.80	-	-	$\nu\text{CC}(13)$, $\delta\text{CH}_2(21)$, $\tau\text{PhIII}(13)$, $\gamma\text{CHIII}(17)$
770	1.31	0.77	770	771	$\gamma\text{C}=\text{O}(34)$, $\tau\text{PhIV}(22)$, $\tau\text{PhIII}(14)$, $\gamma\text{CHIII}(16)$
753	41.13	3.44	754	754	$\tau\text{PhII}(30)$, $\gamma\text{C}=\text{O}(25)$, $\gamma\text{CC}(19)$
752	41.30	0.75	-	-	$\gamma\text{CHIII}(56)$, $\tau\text{PhIII}(17)$, $\tau\text{PhIV}(12)$
741	8.92	6.49	-	-	$\delta\text{CH}_2(33)$, $\tau\text{PhI}(26)$, $\gamma\text{CHI}(10)$
733	18.02	0.87	730	732	$\tau\text{PhI}(18)$, $\gamma\text{CHI}(50)$, $\delta\text{CH}_2(23)$
693	15.79	3.70	695	691	$\delta\text{PhIII}(48)$, $\gamma\text{CHI}(14)$
687	32.18	1.81	-	-	$\tau\text{PhII}(44)$, $\gamma\text{C}=\text{O}(10)$, $\gamma\text{CC}(10)$, $\gamma\text{CHII}(10)$
684	48.76	1.04	-	682	$\tau\text{PhI}(52)$, $\gamma\text{NH}(40)$
677	14.73	2.18	-	670	$\tau\text{PhIII}(38)$, $\gamma\text{C}=\text{O}(21)$, $\gamma\text{CHIII}(14)$
667	8.96	9.06	-	-	$\tau\text{PhII}(50)$, $\delta\text{C}=\text{O}(13)$
635	60.54	5.17	-	-	$\gamma\text{CH}(17)$, $\gamma\text{CS}(22)$, $\gamma\text{C}=\text{O}(22)$
635	9.10	0.93	-	632	$\nu\text{CS}(41)$, $\tau\text{PhIV}(30)$

625	14.11	6.56	625	-	$\delta\text{PhII}(65)$
616	15.75	5.16	-	619	$\delta\text{PhIII}(25)$, $\delta\text{C}=\text{O}(18)$, $\delta\text{CS}(10)$
611	0.39	3.93	-	609	$\delta\text{PhI}(84)$
586	0.88	2.38	-	588	$\delta\text{PhIII}(50)$, $\nu\text{CS}(18)$
578	3.47	1.90	-	576	$\delta\text{PhI}(39)$, $\delta\text{PhIV}(20)$
554	18.05	6.91	558	551	$\delta\text{CC}(19)$, $\delta\text{C}=\text{O}(12)$, $\delta\text{PhI}(13)$, $\delta\text{PhIV}(17)$
522	7.71	12.43	525	521	$\delta\text{PhIV}(47)$, $\delta\text{PhIII}(20)$
516	7.62	0.74	-	-	$\tau\text{PhIII}(60)$, $\tau\text{PhIV}(13)$
500	12.53	8.60	501	-	$\gamma\text{C}=\text{O}(18)$, $\tau\text{PhII}(10)$, $\gamma\text{CC}(13)$, $\delta\text{CO}(10)$
493	6.74	3.07	-	-	$\tau\text{PhI}(37)$, $\gamma\text{CC}(28)$
491	24.81	11.16	488	491	$\gamma\text{C}=\text{O}(18)$, $\delta\text{CH}_2(22)$, $\delta\text{CO}(25)$
476	19.25	4.10	-	-	$\tau\text{PhII}(36)$, $\gamma\text{CC}(31)$
455	1.86	1.19	-	-	$\delta\text{PhIV}(34)$, $\delta\text{PhI}(31)$
445	25.27	2.61	444	443	$\delta\text{C}=\text{O}(17)$, $\delta\text{CO}(14)$, $\delta\text{CH}_2(11)$, $\delta\text{CC}(17)$
428	2.24	1.73	430	426	$\tau\text{PhIII}(61)$, $\tau\text{PhIV}(15)$
407	1.27	3.43	419	409	$\tau\text{PhII}(81)$
398	0.19	0.17	-	400	$\tau\text{PhI}(81)$
390	3.56	1.64	-	388	$\delta\text{CN}(42)$, $\delta\text{C}=\text{O}(16)$, $\tau\text{PhI}(12)$
371	3.38	5.03	-	369	$\delta\text{CS}(36)$, $\delta\text{PhIV}(24)$
358	8.34	1.46	-	356	$\delta\text{CH}_2(40)$, $\delta\text{C}=\text{O}(11)$, $\delta\text{CO}(10)$
348	3.82	1.14	-	-	$\delta\text{CC}(25)$, $\delta\text{C}=\text{O}(18)$, $\delta\text{CS}(23)$
335	2.69	4.81	-	-	$\gamma\text{CN}(18)$, $\delta\text{CH}_2(18)$, $\tau\text{PhI}(11)$, $\delta\text{CC}(10)$, $\tau\text{PhIII}(10)$

329	1.02	0.29	-	331	$\delta\text{CC}(35)$, $\gamma\text{CN}(15)$, $\tau\text{PhI}(19)$
315	10.05	2.44	-	314	$\gamma\text{CC}(23)$, $\tau\text{PhII}(15)$, $\delta\text{CS}(14)$
280	0.94	1.60	-	-	$\tau\text{PhIII}(34)$, $\tau\text{PhIV}(22)$
280	1.94	1.71	-	281	$\tau\text{PhIII}(25)$, $\delta\text{C}=\text{O}(19)$, $\tau\text{PhIV}(30)$
268	5.46	1.91	-	267	$\delta\text{CO}(22)$, $\delta\text{PhII}(36)$, $\delta\text{CC}(18)$
251	0.18	0.86	-	252	$\tau\text{CH}_3(52)$, $\delta\text{PhII}(10)$
245	2.35	1.01	-	-	$\tau\text{CH}_3(25)$, $\delta\text{CC}(11)$, $\tau\text{PhI}(10)$
235	2.13	1.78	-	236	$\tau\text{PhI}(51)$, $\delta\text{CH}_2(10)$
207	3.86	0.89	-	-	$\delta\text{CC}(22)$, $\delta\text{CS}(18)$, $\tau\text{CH}_2(22)$
173	4.95	4.32	-	168	$\delta\text{CH}_2(36)$, $\delta\text{CS}(18)$
153	0.05	0.77	-	-	$\tau\text{PhIV}(45)$, $\tau\text{PhIII}(18)$
146	0.61	0.68	-	-	$\tau\text{CO}(24)$, $\tau\text{PhII}(14)$, $\tau\text{PhIV}(10)$
131	5.34	1.84	-	-	$\gamma\text{CN}(21)$, $\tau\text{PhIV}(29)$
117	5.15	1.17	-	-	$\delta\text{CO}(25)$, $\tau\text{CC}(27)$, $\tau\text{CS}(10)$
103	1.07	1.78	-	-	$\tau\text{C}=\text{O}(21)$, $\tau\text{CC}(18)$, $\tau\text{PhIV}(30)$
96	1.05	1.53	-	-	$\tau\text{CO}(18)$, $\tau\text{CC}(36)$
84	2.56	1.84	-	-	$\tau\text{PhIV}(23)$, $\tau\text{CS}(11)$, $\tau\text{PhIII}(10)$, $\gamma\text{CC}(12)$
82	0.40	5.88	-	-	$\gamma\text{CC}(27)$, $\delta\text{CH}_2(18)$, $\tau\text{PhIV}(19)$
77	0.76	0.43	-	-	$\tau\text{CH}_2(42)$, $\tau\text{C}=\text{O}(36)$
68	0.12	1.35	-	-	$\tau\text{CH}_2(45)$, $\tau\text{CC}(10)$
61	1.11	2.30	-	-	$\tau\text{CC}(37)$, $\tau\text{CH}_2(33)$
58	1.34	1.72	-	-	$\tau\text{CC}(23)$, $\tau\text{C}=\text{O}(15)$, $\tau\text{PhII}(10)$
46	0.45	1.65	-	-	$\tau\text{CH}_2(23)$, $\tau\text{C}=\text{O}(15)$, $\delta\text{CS}(10)$, $\tau\text{CC}(16)$

34	1.05	1.88	-	-	τ CC(43), τ CS(26)
31	0.91	1.59	-	-	τ CC(17), τ PhIV(15), γ CN(14), δ CH ₂ (18)
23	0.13	2.38	-	-	τ CC(50), τ CH ₂ (17)
18	0.24	3.08	-	-	τ CC(24), τ C=O(19), τ PhII(10)
16	0.44	1.86	-	-	τ CH ₂ (28), τ CC(42), τ C=O(10)
11	0.07	2.71	-	-	τ CS(22), τ CC(31), τ CH ₂ (13)
7	0.05	1.58	-	-	τ C=O(26), τ CS(20), τ CC(22)

^a ν -stretching; δ -in-plane deformation; γ -out-of-plane of deformation; τ -torsion; PhI-mono substituted phenyl ring; PhII-para substituted phenyl ring; PhIII-ortho-substituted phenyl ring; PhIV-Quinazoline ring; Potential energy distribution (%) is given in brackets in the assignment column.

Table 2

NBO results showing the formation of Lewis and non-Lewis orbitals.

Bond(A-B)	ED/e ^a	EDA%	EDB%	NBO	s%	p%
σ S1-C33	1.97424	45.07	54.93	0.6713(sp ^{5.32})S+	15.72	84.28
-	-0.65126	-	-	0.7412(sp ^{2.43})C	29.09	70.91
π O2-C15	1.98343	69.74	30.26	0.8351(sp ^{1.00})O+	0.00	100.0
-	-0.36621	-	-	0.5501(sp ^{1.00})C	0.00	100.0
σ N3-C33	1.98659	58.95	41.05	0.7678(sp ^{1.60})N+	38.39	61.61
-	-0.89897	-	-	0.6407(sp ^{1.68})C	37.35	62.65
π N3-C33	1.87202	61.73	38.27	0.7857(sp ^{1.00})N+	0.00	100.0
-	-0.33421	-	-	0.6186(sp ^{1.00})C	0.00	100.0
σ N4-C15	1.98123	64.46	35.54	0.8028(sp ^{2.02})N+	35.15	64.85
-	-0.79366	-	-	0.5962(sp ^{2.47})C	28.77	71.23
σ N4-C33	1.98729	62.55	37.45	0.7909(sp ^{1.88})N+	34.73	65.27
-	-0.84663	-	-	0.6120(sp ^{1.98})C	33.53	66.47
σ C5-C6	1.97557	51.19	48.81	0.7155(sp ^{1.81})C+	35.55	64.45
-	-0.69070	-	-	0.6986(sp ^{1.93})C	34.14	65.86
σ C5-C14	1.97300	49.32	50.68	0.7023(sp ^{1.82})C+	35.49	64.51
-	-0.69908	-	-	0.7119(sp ^{1.95})C	33.84	66.16
σ C14-C15	1.97504	51.66	48.34	0.7188(sp ^{2.26})C+	30.68	69.32
-	-0.67889	-	-	0.6953(sp ^{1.60})C	38.41	61.59
σ C16-C19	1.97252	50.48	49.52	0.7105(sp ^{2.51})C+	28.51	71.49
-	-0.59715	-	-	0.7037(sp ^{2.94})C	25.37	74.63
σ C37-N39	1.98837	36.94	63.06	0.6078(sp ^{2.21})C+	31.13	68.87
-	-0.84056	-	-	0.7941(sp ^{1.72})N	36.80	63.20
σ C40-C41	1.97495	51.05	48.95	0.7145(sp ^{1.72})C+	36.70	63.30
-	-0.72180	-	-	0.6997(sp ^{1.92})C	34.20	65.80
σ C40-C42	1.97442	51.17	48.83	0.7153(sp ^{1.78})C+	35.94	64.06
-	-0.71638	-	-	0.6988(sp ^{1.92})C	34.26	65.74
σ C49-C51	1.97388	52.42	47.58	0.7240(sp ^{2.29})C+	30.42	69.58
-	-0.67352	-	-	0.6898(sp ^{1.60})C	38.50	61.50
σ C51-O52	1.99654	34.28	65.72	0.5855(sp ^{1.96})C+	33.72	66.28
-	-1.08727	-	-	0.8107(sp ^{1.36})O	42.14	57.86

π C51-O52	1.98257	30.59	69.41	0.5530(sp ^{1.00})C+	0.00	100.0
-	-0.38025	-	-	0.8332(sp ^{1.00})O	0.00	100.0
σ C51-O53	1.99227	30.97	69.03	0.5565(sp ^{2.59})C+	27.76	72.24
-	-0.92213	-	-	0.8309(sp ^{2.02})O	33.12	66.88
σ C54-C57	1.99218	50.16	49.84	0.7082(sp ^{2.38})C+	29.54	70.46
-	-0.62692	-	-	0.7060(sp ^{2.60})C	27.73	72.27
n1S1	1.98020	-	-	sp ^{0.45}	69.06	30.94
-	-0.64252	-	-	-	-	-
n2S1	1.83076	-	-	sp ^{1.00}	0.00	100.0
-	-0.25390	-	-	-	-	-
n1O2	1.97616	-	-	sp ^{0.72}	58.15	41.85
-	-0.67391	-	-	-	-	-
n2O2	1.85315	-	-	sp ^{99.99}	0.01	99.99
-	-0.24692	-	-	-	-	-
n1N3	1.89324	-	-	sp ^{2.65}	27.38	72.62
-	-0.34204	-	-	-	-	-
n1N4	1.59189	-	-	sp ^{99.99}	0.02	99.98
-	-0.26722	-	-	-	-	-
n1O38	1.97487	-	-	sp ^{0.71}	58.28	41.72
-	-0.68719	-	-	-	-	-
n2O38	1.86039	-	-	sp ^{99.99}	0.08	99.92
-	-0.26116	-	-	-	-	-
n1N39	1.68082	-	-	sp ^{99.99}	0.25	99.75
-	-0.27525	-	-	-	-	-
n1O52	1.97668	-	-	sp ^{0.73}	57.81	42.19
-	-0.68383	-	-	-	-	-
n2O52	1.84664	-	-	sp ^{1.00}	0.01	99.99
-	-0.25843	-	-	-	-	-
n1O53	1.96298	-	-	sp ^{1.60}	38.42	61.58
-	-0.56683	-	-	-	-	-
n2O53	1.79430	-	-	sp ^{1.00}	0.00	100.00
-	-0.32332	-	-	-	-	-

Table 3. The binding affinity values of different poses of the titlecompound predicted by AutodockVina.

Mode	Affinity (kcal/mol)	Distance from best mode (Å)	
		RMSD l.b.	RMSD u.b.
-	-		
1	-9.5	0.000	0.000
2	-9.3	3.115	6.298
3	-9.1	1.008	4.879
4	-9.1	2.900	5.453
5	-8.9	2.960	5.292
6	-8.9	2.003	4.873
7	-8.7	3.221	5.223
8	-8.7	3.279	8.100
9	-8.7	1.688	5.973

Fig.1 FT-IR spectrum of
ethyl 4-(2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)acetamido)benzoate

Fig.2 FT-Raman spectrum of
ethyl 4-(2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)acetamido)benzoate

Fig.3 Optimized geometry of ethyl 4-(2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)acetamido)benzoate

Fig.4 HOMO-LUMO plots of ethyl 4-(2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)acetamido)benzoate

Fig.5 MEP plot of ethyl 4-(2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)acetamido)benzoate

Fig.6 Schematic for the docked conformation of active site of title compound at pyrrole inhibitor conformation with H-bond(green), alkyl- π (pink) and π -cation (brown)

Fig.7 The ligand and the co-crystallized inhibitor embedded into the catalytic site of pyrrole inhibitor

Highlights

- * IR, Raman spectra, MEP, NLO and NBO analysis were reported.
- * The wavenumbers are calculated theoretically using Gaussian09 software.
- * Molecular docking the results suggest that the compound might exhibit inhibitory activity against pyrrole inhibitor.