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Spectroscopic analysis (FT-IR, FT-Raman and NMR) and molecular docking study of ethyl 2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)-acetate

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ABSTRACT

The vibrational wavenumbers, molecular structure, MEP, NLO, NBO and HOMO, LUMO analysis of Ethyl 2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)-acetate (EPDA) were reported. The change in electron density in the antibonding orbitals and stabilization energies have been calculated by NBO analysis to give clear evidence of stabilization in the hyperconjugation of hydrogen bonded interaction. The difference in HOMO and LUMO energy support the charge transfer interaction within the molecule. NMR studies and Fukui functions are also reported. From molecular electrostatic potential plot it is evident that the negative charge covers the carbonyl groups, phenyl rings and the positive region is over the CH_2 groups with the acetate group. Molecular docking studies shows that the title compound forms a stable complex with pyrrole inhibitor and gives a binding affinity value of −8.3 kcal/mol and the results suggest that the compound might exhibit inhibitory activity against pyrrole inhibitor.

1. Introduction

Cancer is continuing to be a major health problem in developed as well as undeveloped countries and the great cancer incidence worldwide increases the search for new, safer and efficient anticancer agents, aiming the prevention or cure of cancer [1–3]. Quinazolines are frequently used in medicine because of their wide spectrum of biological activities [4–7]. Quinazoline derivatives have been reported for their antibacterial, antifungal, anti-HIV, anthelmintic, anti-tubercular, hypo-tensive, anti-convulsant, anti-fibrillatory, diuretic and antiviral activities [8–18]. 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 phamacophore [19]. The present investigation was undertaken to study the vibrational spectra of the title molecule completely and to identify the various modes with greater wave number accuracy. The DFT calculation has been performed to support the wave number assignments, geometrical parameters, hyperpolarizability calculation; NBO and HOMO-LUMO band gap have also been studied. Molecular docking of the title compound is also reported due to the different potential biological activity of the title compound.

2. Experimental details

A mixture of 2-mercapto-3-phenethylquinazolin-4(3*H*)-one (10 mmol, 2.82 g), ethyl bromoacetate (11 mmol, 1.84 g), and anhydrous potassium carbonate (12 mmol, 1.66 g) in 50 ml dry acetone was stirred at room temperature for 6 h. The reaction mixture was filtered, the solvent was removed under reduced pressure, and the solid obtained was dried and recrystallized from

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ethanol. Melting Point: 132–134 °C, yield 95%. MS: ($M^+ = 368$, 63, 100%).

Nuclear magnetic resonance (^1H and ^{13}C NMR) spectra were recorded on Bruker 500 MHz spectrometer using chloroform ($CDCl_3$) as solvent; the chemical shifts are expressed in δ ppm using tetramethylsilane (TMS) as internal standard. 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 [20] 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 (Fig. 3) and vibrational wave numbers [21,22] and a scaling factor (0.9613) has to be used for obtaining a considerably better agreement with experimental data [23]. 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 [24] and the potential energy distribution (PED) is calculated with the help of GAR2PED software package [25].

4. Results and discussion

4.1. Geometrical parameters

In the following discussion, the mono-, ortho-substituted phenyl rings and quinazoline rings are designated as PhI, PhII and PhIII, respectively. In the title compound, the C–S bond lengths are 1.7883 Å and 1.8261 Å while the reported values are in the range 1.7675–1.8641 Å [26] and 1.7710–1.8110 Å [27]. The bond lengths of C_5-N_3 (1.3835 Å), $C_{15}-N_4$ (1.4167 Å) and $C_{33}-N_4$ (1.3842 Å) are shorter than the normal C–N bond length of about 1.48 Å and this point into the effect of resonance in this part of the molecule [28]. The shortening of the bond length of $C_{15}-O_2$ (1.2200 Å) and $C_{37}-O_{38}$ (1.2019 Å) could be assigned a double bond character. The C–O bond lengths of the title compound are $C_{37}-O_{39} = 1.3521$ Å and $C_{40}-O_{39} = 1.4474$ Å and $C_{40}-O_{39}$ is greater than the average distance of 1.362 Å found among phenols [29] and the increase is due to the noticeable intra molecular hydrogen bonding experienced by the molecule [30]. All the carbon–carbon bond lengths in the benzene rings lie in the range 1.3936–1.3996 Å for PhI and 1.3833–1.4086 Å for PhII and the bond lengths are somewhere in between the normal values for a single (1.54 Å) and a double bond (1.33 Å) [31]. At C_{22} position, the bond angles are $C_{31}-C_{22}-C_{23} = 118.6°$, $C_{31}-C_{22}-C_{19} = 120.8°$ and $C_{23}-C_{22}-C_{19} = 120.6°$ and the reduction in the angle $C_{31}-C_{22}-C_{23}$ is due to presence of adjacent methylene groups. At N_4 position, the bond angles $C_{33}-N_4-C_{15}$ is increased by 1.0°, $C_{33}-N_4-C_{16}$ is increased by 2.8° 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 interaction 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 $N_4-C_{33}-S_1 = 115.4°$ and this asymmetry in angles is due to the interaction between the quinazoline ring and adjacent moieties. At C_{37} position, the bond angles $O_{39}-C_{37}-C_{34} = 116.7°$, $O_{39}-C_{37}-O_{38} = 119.5°$ and $C_{34}-C_{37}-O_{38} = 123.7°$ and this asymmetry is due to the adjacent methylene and methoxy groups. The quinazoline moiety is planar with respect to the phenyl ring PhII, as is evident from the torsion angles $C_6-C_5-N_3-C_{33} = -179.8°$, $C_6-C_5-C_{14}-C_{15} = -179.7°$, $C_{12}-C_{14}-C_{15}-N_4 = 179.3°$ and $C_{12}-C_{14}-C_5-N_3 = 179.9°$ 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, $C_{29}-C_{31}-C_{22}-C_{19} = -178.3°$, $C_{31}-C_{22}-C_{19}-C_{16} = 91.1°$, $C_{25}-C_{23}-C_{22}-C_{19} = 178.4°$ and $C_{23}-C_{22}-C_{19}-C_{16} = -87.2°$.

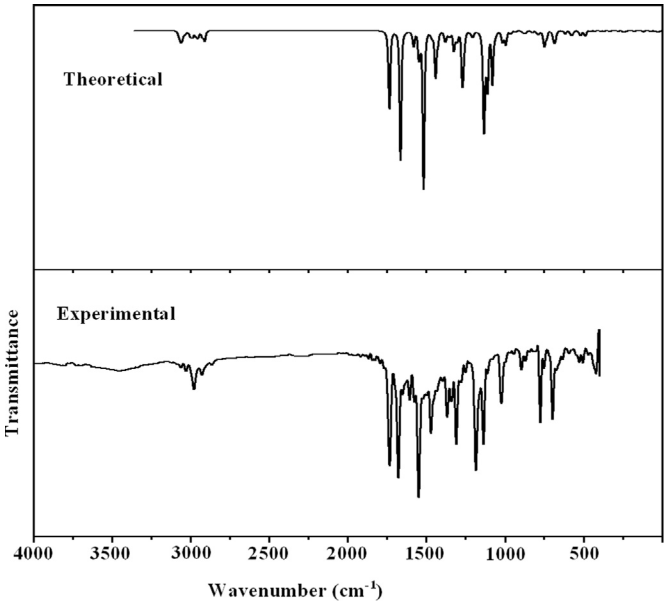

Fig. 1. FT-IR spectrum of EPDA.

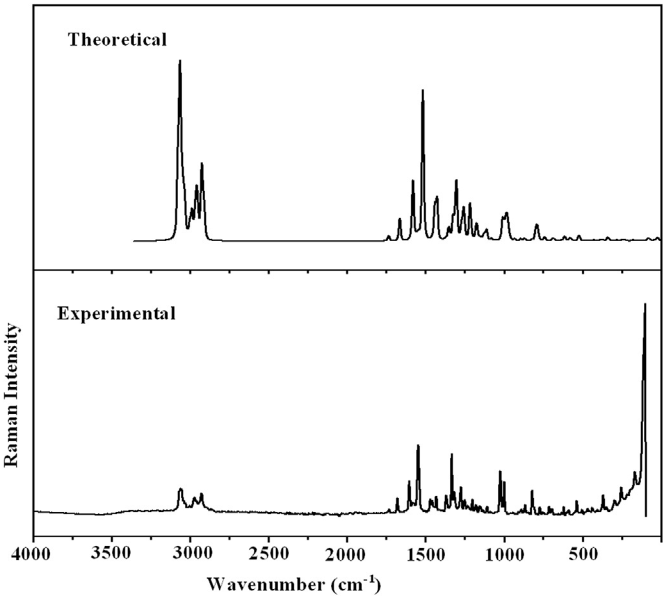

Fig. 2. FT-Raman spectrum of EPDA.

4.2. IR and Raman spectra

The calculated (scaled) wave numbers, observed IR, Raman bands and assignments are given in Table 1.