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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 N_3 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.

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 (^{1}H and ^{13}C) for the compound were recorded on a 500 MHz NMR Spectrometer (Bruker advance, Reinstetten, Germany) using deuterated 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 °C, yield 88%, ^{1}H 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,

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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 1750–1650 cm^{-1} and in the present case these modes appears at 1689, 1666 cm^{-1} in the IR spectrum, and at 1672, 1655 cm^{-1} in the Raman spectrum. The DFT calculations give these modes at 1694, 1674, 1664 cm^{-1}. The in-plane and out-of-plane C=O bending modes are expected in the regions 625 ± 70 and 540 ± 80 cm^{-1}, respectively [16] and for the title compound, the δC=O in-plane deformation bands are observed at 558, 501 cm^{-1} in the IR spectrum, 619, 551 cm^{-1} in the Raman spectrum and at 616, 554, 500 cm^{-1} theoretically and the bands at 770, 754 cm^{-1} in the IR spectrum, 771, 754, 670 cm^{-1} in

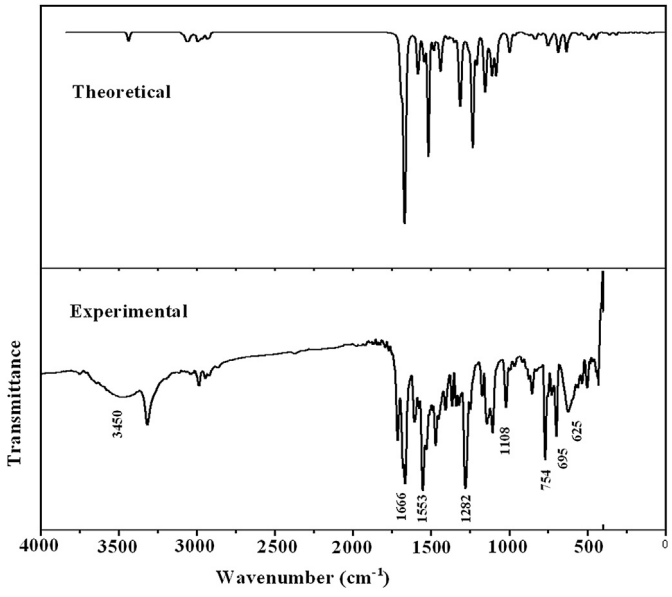

Fig. 1. FT-IR spectrum of ethyl 4-(2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)acetamido)benzoate.

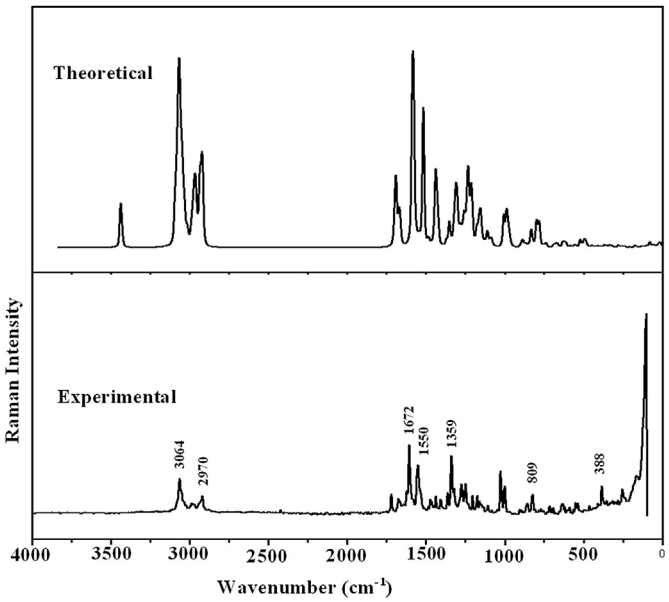

Fig. 2. FT-Raman spectrum of ethyl 4-(2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)acetamido)benzoate.

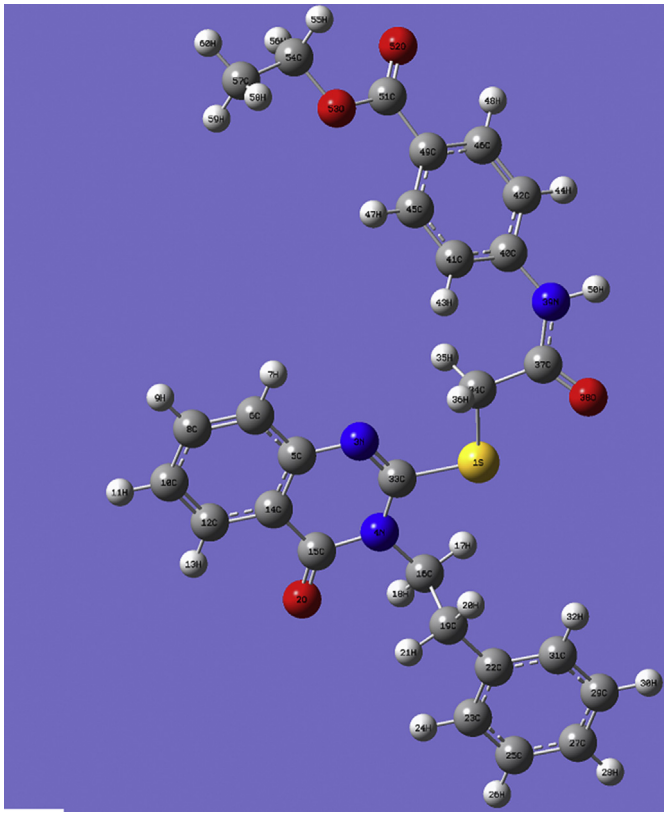

Fig. 3. Optimized geometry of ethyl 4-(2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)acetamido)benzoate.