Journal of Molecular Structure 1113 (2016) 133–145

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: http://www.elsevier.com/locate/molstruc

DFT and experimental (FT-IR and FT-Raman) investigation of vibrational spectroscopy and molecular docking studies of 2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)-N-(3,4,5-trimethoxyphenyl) acetamide

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ARTICLE INFO

Article history:
Received 22 August 2015
Received in revised form
9 February 2016
Accepted 9 February 2016
Available online 11 February 2016

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

ABSTRACT

A comprehensive structural and vibrational study of 2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)-N-(3,4,5-trimethoxyphenyl) acetamide is reported. FT-IR and FT-Raman wavenumbers were compared with the theoretical values obtained from DFT calculations. Theoretical values agree well with the experimental values. Molecular electrostatic potential, frontier molecular orbital analysis and nonlinear optical properties were investigated using theoretical calculations. Natural bond orbital analysis shows that charge in electron density in σ^* and π^* antibonding orbitals and E(2) energies confirms the occurrence of intermolecular charge transfer within the molecule. Nonlinear optical property has also observed by predicting the first and second order hyperpolarizability parameters. As can be seen from the molecular electrostatic potential map of the title molecule, negative region is mainly localized over the carbonyl groups and the mono substituted phenyl ring and the maximum positive region is localized on the NH and hydrogen atoms. Molecular docking results show that the docked ligand title compound forms a stable complex with BRCA2 complex and gives a binding affinity value of −7.6 kcal/mol and results suggest that the compound might exhibit inhibitory activity against BRCA2 complex.

1. Introduction

Quinazolines are widely used for the extraction and analytical determination of metal ions and nitraquinazone, a quinazoline derivative has been found to possess potent phosphodiesterase inhibitory activity [1] which is potentially useful in the treatment of asthma [2]. Phenyl acetamide derivatives are important and biologically active compounds and have been reported as possible metabolites of antimicrobial active benzoxazoles [3]. These derivatives show various types of biological properties such as antihelmenthic, antihistaminic, antifungal and antibacterial [3]. Quinazoline derivatives have been reported for their anti-bacterial, anti-fungal, anti-HIV [4,5], anthelmintic [6], anti-tubercular [7], hypotensive [8], anti-convulsant [9], anti-fibrillatory [10], diuretic [11] and antiviral [12–14] 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 phamacophore [15]. In the present study, FT-IR and FT-Raman spectra, NBO, MEP and NLO properties of the title compound were reported. Due to the different potential biological activities of the title compound molecular docking of the title compound is also reported.

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http://dx.doi.org/10.1016/j.molstruc.2016.02.038

2. Experimental details

A mixture of 2-mercapto-3-phenethylquinazolin-4(3*H*)-one (2 mmol, 564 mg) and 2-chloro-*N*-(3,4,5-trimethoxyphenyl)acetamide (2.1 mmol, 544 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 recrystallized from ethanol. Mp: 218–219 °C, yield 94%, ^{1}H NMR (DMSO-d$_6$): δ 10.39 (s, 1H), 8.52 (d, 1H, $J = 3.0$ Hz), 8.07 (d, 1H, $J = 7.5$ Hz), 7.80–7.73 (m, 2H), 7.52 (d, 1H, $J = 8.0$ Hz), 7.44 (t, 1H, $J = 7.5$ Hz), 7.34 (d, 1H, $J = 7.5$ Hz), 7.27 (t, 1H, $J = 5.0, 6.0$ Hz), 7.01 (s, 2H), 4.45 (t, 2H, $J = 7.5, 8.0$ Hz), 4.21 (s, 2H), 3.73 (s, 6H), 3.66 (s, 3H), 3.20 (t, 2H, $J = 7.5, 8.0$ Hz). ^{13}C NMR (DMSO-d$_6$) δ: 35.2, 36.9, 43.9, 55.6, 60.0, 79.1, 96.9, 118.7, 121.9, 123.2, 125.7, 126.4, 133.5, 134.6, 135.1, 136.7, 146.6, 149.1, 152.7, 156.0, 157.5, 160.4, 165.5. MS: $M^+ = 505$. 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 (Fig. 3).

3. Computational details

Calculations of the title compound were carried out using Gaussian 09 software [16] 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 [17,18]. 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 [19] and the optimized geometrical parameters are given in Table 1. The assignments of the calculated wave numbers are aided by the animation option of GAUSSVIEW program [20] and the potential energy distribution (PED) is calculated with the help of GAR2PED software package [21].

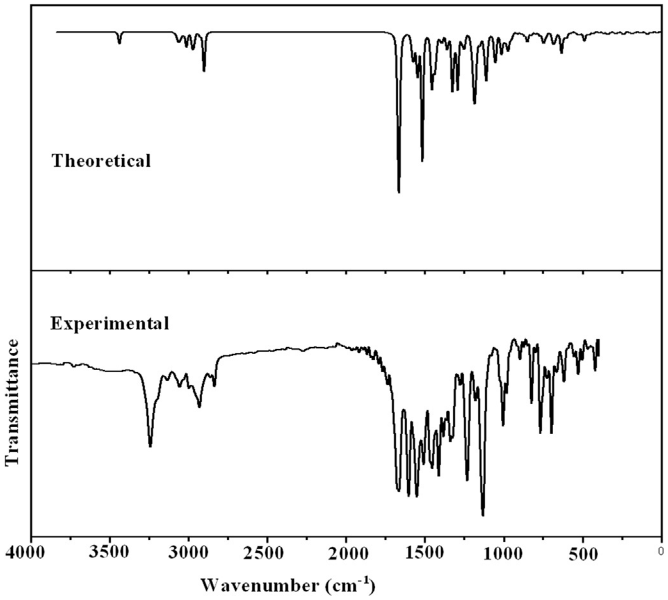

Fig. 1. FT-IR spectrum of 2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)-N-(3,4,5-trimethoxyphenyl) acetamide.

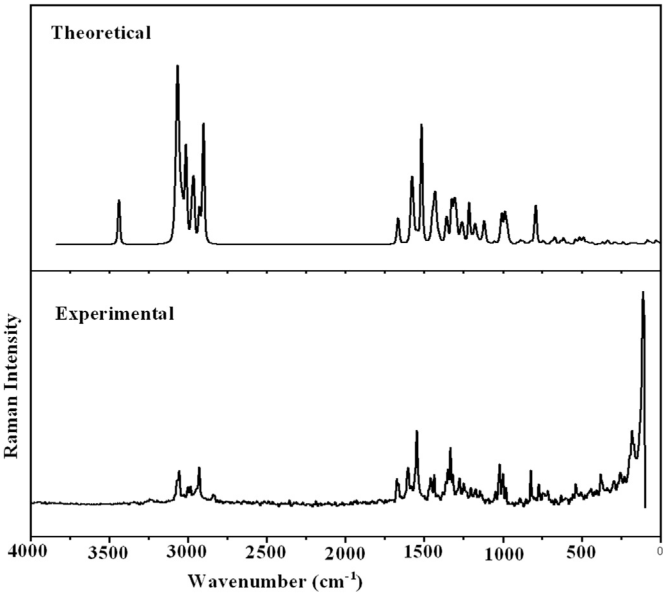

Fig. 2. FT-Raman spectrum of 2-(4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-ylthio)-N-(3,4,5-trimethoxyphenyl) acetamide.

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 2. The C=O stretching mode [22–24] is expected in the region 1750–1650 cm^{-1} and in the present case these modes appears at 1670 cm^{-1} in the IR spectrum, and at 1675, 1664 cm^{-1} in the Raman spectrum. The DFT calculations give these modes at 1670 and 1663 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 [22]. For the title compound, the C=O deformation bands are observed at 700, 618 cm^{-1} in the IR spectrum, 618 cm^{-1} in the Raman spectrum and at 693, 636, 618, 611 cm^{-1} theoretically. The C–O–C stretching vibrations are expected in the range 1200–850 cm^{-1} [22,25]. The skeletal C–O deformation can be found in the region 320 ± 50 cm^{-1} [22]. As expected, the asymmetric and symmetric C–O–C vibrations are assigned at 1198, 1009, 978, 948, 911, 848 cm^{-1} theoretically for the title compound, which is in agreement with the literature [24]. Experimentally bands are observed at 915 cm^{-1} in the IR spectrum and at 1201, 980, 915 cm^{-1} in the Raman spectrum.

The N–H stretching vibrations give rise to bands at 3500–3300 cm^{-1} [26]. According to Roeges the N–H stretching vibration appears strongly and broadly in the region 3390 ± 60 cm^{-1} [22]. For the title compound N–H stretching mode is assigned at 3439 cm^{-1} theoretically and a strong band is observed in the IR spectrum at 3243 cm^{-1} and at 3235 cm^{-1} in the Raman spectrum. Mary et al. [27] 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. For the title compound the band at 1409 cm^{-1} (DFT) is assigned as N–H in-plane bending mode and experimentally at 1411 cm^{-1} in both the spectra. The out-of-plane bending of NH is expected around 650 ± 50 cm^{-1} [22]. In the present case the band at 665 (IR), 667 (Raman) and 669 cm^{-1} (DFT) is assigned as out-of-plane bending of N–H.

Louran et al. [28] reported a value at 1220 cm^{-1} for υC-N for poly aniline. In the case of aromatic amines a strong C–N stretching absorption is observed in the region in 1342–1266 cm^{-1} [23,24].