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Vibrational spectroscopic and molecular docking study of 2-Benzylsulfanyl-4-[(4-methylphenyl)-sulfanyl]-6-pentylpyrimidine-5-carbonitrile, a potential chemotherapeutic agent

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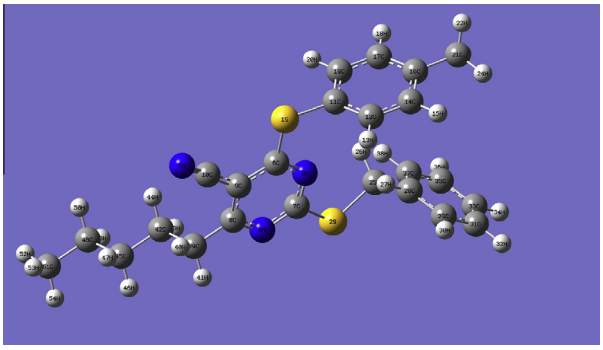
HIGHLIGHTS

- IR, Raman spectra and NBO analysis were reported.
- The wavenumbers are calculated theoretically using Gaussian09 software.
- The wavenumbers are assigned using PED analysis.
- The geometrical parameters are in agreement with XRD data.
- Molecular docking is reported.

GRAPHICAL ABSTRACT



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ABSTRACT

FT-IR and FT-Raman spectra of 2-Benzylsulfanyl-4-[(4-methylphenyl)-sulfanyl]-6-pentylpyrimidine-5-carbonitrile were recorded and analyzed. The structure of the molecule has been optimized and the structural characteristics have been determined by density functional theory. The geometrical parameters (DFT) are in agreement with the XRD results. HOMO and LUMO and other chemical properties are reported. Nonlinear optical properties are reported. A detailed molecular picture of the title compound and its interactions were obtained from NBO analysis. The negative (red and yellow) regions of the MEP are related to electrophilic reactivity and the positive (blue) regions to nucleophilic reactivity, as shown in the MEP plot and the title compound has several possible sites, C≡N, N atom of pyrimidine ring and sulfur atoms for electrophilic attack. From the molecular docking studies it is clear that the title compound binds at the catalytic site of the substrate by weak non-covalent interactions most prominent of which are H-bonding, π–π, alkyl–π, and amide–π interactions.

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Introduction

Pyrimidine derivatives have a long and distinguished history extending from the days of their discovery as important constituents of nucleic acids to their current use as efficient chemotherapeutic agents. The pyrimidine nucleus constitutes the key pharmacophore of several non-nucleoside chemotherapeutic agents. The ability of pyrimidine derivatives to inhibit vital enzymes responsible for DNA biosynthesis is the reason behind their chemotherapeutic efficacy. Several pyrimidine-based derivatives have been developed as anticancer [1–5] and antiviral agents against HIV (Human Immunodeficiency Virus) [6–12], HBV (Hepatitis B Virus) [13,14], HCV (Hepatitis C Virus) [15] and HSV (Herpes Simplex Virus) [16]. In addition, several pyrimidine derivatives have long been identified as potent antibacterial [17–20] and antifungal agents [21,22]. Moreover, several pyrimidine-5-carbonitrile derivatives displayed marked antimicrobial activities [23–28]. In continuation to our interest in the chemotherapeutic properties and molecular structures of pyrimidine-5-carbonitriles [26–31], we present a comprehensive investigation on the molecular structure, electronic properties and vibrational spectra of the title compound (molecular formula $C_{24}H_{25}N_3S_2$). To the best of our knowledge, a detailed description of the spectroscopic behavior of the title compound with the help of vibrational spectral techniques and quantum chemical calculations along with NLO properties has not been given to date. Due to the different potential biological activity of the title compound, molecular docking of the title compound is also reported.

Experimental

The title compound ($C_{24}H_{25}N_3S_2$) was prepared in 89% yield via the reaction of 2-(Benzylsulfanyl)-4-chloro-6-(*n*-pentyl) pyrimidine-5-carbonitrile with 4-thiocresol in pyridine [27]. In the title compound, the *S*-bound benzene rings have orthogonal and splayed orientations with respect to the pyrimidine ring [31]. 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 with an excitation wavelength of 1064 nm, a maximal power 150 mW; measurement on solid sample.

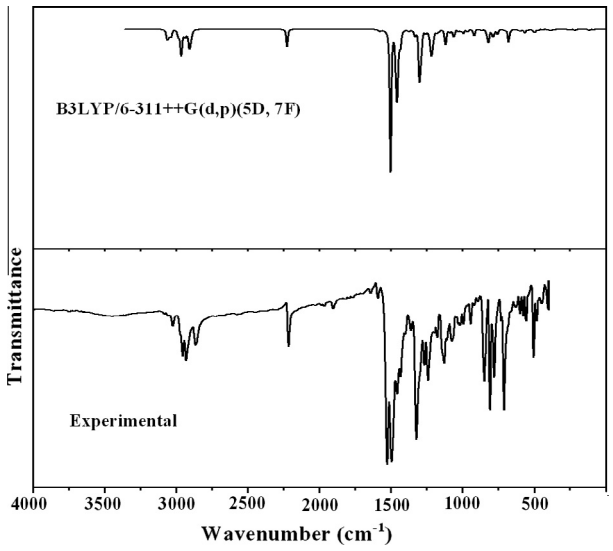

Fig. 1. FT-IR spectrum of 2-Benzylsulfanyl-4-[(4-methylphenyl)-sulfanyl]-6-pentylpyrimidine-5-carbonitrile.

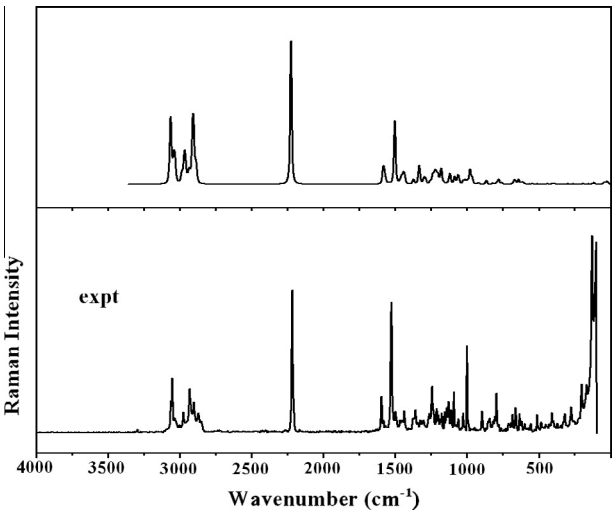

Fig. 2. FT-Raman spectrum of 2-Benzylsulfanyl-4-[(4-methylphenyl)-sulfanyl]-6-pentylpyrimidine-5-carbonitrile.

Computational details

Calculations of the title compound were carried out using Gaussian09 software [32] 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 wavenumbers. Molecular geometries were fully optimized by Berny's optimization algorithm using redundant internal coordinates. Harmonic vibrational wavenumbers were calculated using analytic second derivatives to confirm the convergence to minima on the potential surface. Then frequency calculations were employed to confirm the structure as minimum points in energy. At the optimized structure (Fig. 3) of the examined species, no imaginary wavenumber modes were obtained, proving that a true minimum on the potential 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 [33]. The observed disagreement between theory and experiment could be a consequence of the anharmonicity and of the general tendency of the quantum chemical methods to overestimate the force constants at the exact equilibrium geometry. The optimized geometrical parameters (B3LYP) with XRD data are given in Table S1 (Supporting Material). The assignments of the calculated wavenumbers are aided by the animation option of GaussView program, which gives a visual presentation of the vibrational modes [34]. The potential energy distribution (PED) is calculated with the help of GAR2PED software package [35].

Results and discussion

IR and Raman spectra

The observed IR, Raman bands and theoretical wavenumbers (scaled) and assignments are given in Table 1. In the following discussion, the 1,4-disubstituted phenyl ring, mono-substituted phenyl ring and pyrimidine ring are designated as PhI, PhII and RingIII. Pyrimidines absorb strongly at 1600–1500 cm^{-1} due to the C=C and C=N ring stretching vibrations. Absorptions are also observed at 1640–1620, 1580–1520, 1000–960 and 825–775 cm^{-1} regions [36]. The in-plane and out-of-plane ring deformations are expected in the regions 795 ± 75, 630 ± 10, 380 ± 110 and 770 ± 20, 485 ± 40, 400 ± 15 cm^{-1} respectively [36]. Pyrimidines