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Vibrational spectra, HOMO, LUMO, NBO, MEP analysis and molecular docking study of 2,2-diphenyl-4-(piperidin-1-yl)butanamide

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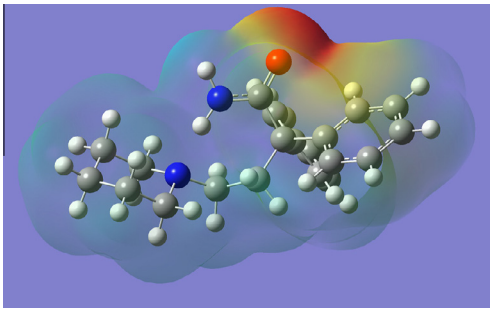
HIGHLIGHTS

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

GRAPHICAL ABSTRACT



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ABSTRACT

The Fourier-Transform Infrared and Fourier-Transform Raman spectra of 2,2-diphenyl-4-(piperidin-1-yl) butanamide were recorded in the region 4000–400 cm^{-1} and 4000–0 cm^{-1}. The vibrational wavenumbers are computed using HF and DFT methods. The complete vibrational assignments were performed on the basis of potential energy distribution using GAR2PED program. The geometrical parameters of the title compound are in agreement with the XRD data. From the MEP study, the negative electrostatic potential regions are mainly localized of carbonyl group and are possible sites for electrophilic attack and the positive regions are localized all the rings, indicating possible sites for nucleophilic attack. Stability of the molecule arising from hyper-conjugative interaction and charge delocalization has been analyzed using natural bond orbital analysis. The calculated HOMO and LUMO energies also confirm that charge transfer occurs within the molecule. PASS analysis of the title compound predicts among other activities, antidyskinetic activity. Molecular docking results draw us to the conclusion that the compound might exhibit inhibitory activity against adenosine A2A and may act as antidyskinetic agent.

Introduction

2,2-Diphenyl-4-(piperidin-1-yl)butanamide is an intermediate used in the synthesis of biologically and pharmaceutically active compounds like loperamide, darifenacin, fenpiverine, etc. The synthesis and antimycobacterial activity of some new related 2,2-di-phenylacetamide derivatives has been reported by Guzel et al. [1]. Piperidine is one of the most recognizable structural entities among heterocyclic molecules [2] and many piperidine natural products with substitution on nitrogen and carbons are frequently encountered among lysine derived alkaloids, like homoproline [3],

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pseudoconhydrine [4], sedamine [5], dihydropinidine [6], solemopsine [7], deoxoprosopinine [8]. Some piperidines are found to possess high biological activities like cyto-toxic and anticancer properties [9]. The piperidine ring is a feature of oral anesthetics and narcotic analgesics [10,11] and the derivatives are used clinically to prevent post operative vomiting, to speed up gastric emptying before anesthesia, to facilitate radiological investigation and to correct variety of disturbances of gastrointestinal functions [12]. The crystal structures of N,N-diphenylacetamide [13], 4,4′-dime thylbiphenyl-2,2′-dicarboxylic acid [14], 4′-methylbiphenyl-2-car boxylic acid [15] and 4′-(2-butyl-4-chloro-5-formylimidazol-1-yl methyl) biphenyl-2-carbonitrile [16], 2-hydroxy-N-(3-oxo-1-thi a-4-azaspiro[4,5]dec-4-yl)2,2-diphenylacetamide [17] and 2-chlor o-N-[4-chloro-2(2-chlorobenzoyl)phenyl]acetamide [18] have been reported. The crystal structure of the title compound is reported by Siddegowda et al. [19]. In the present work, FT-IR and FT-Raman spectra of the title compound were reported both experimentally and theoretically. The energies, degrees of hybridization, population of the lone pairs of oxygen, nitrogen atoms, energies of their interaction with the anti-bonding of the rings and the electron density distributions and $E(2)$ energies have been calculated by NBO analysis using DFT method to give clear evidence of stabilization originating from the hyper-conjugation of various intra-molecular interactions. There has been growing interest in using organic materials for nonlinear optical devices because of the large second order electric susceptibilities and since the second order electric susceptibility is related to first hyperpolarizability, the search for organic chromophores with large first hyperpolarizability is fully justified. Due to the different potential biological activities of the title compound, molecular docking of the title compound is also reported.

Experimental details

The title compound was obtained as a gift sample from R.L. Fine Chem. Bangalore, India. 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 RFS100/s FT-Raman spectrometer (Nd:YAG laser, 1064 nm excitation).

Computational details

Calculations of the title compound are carried out with Gaussian09 [20] using the HF/6-31G (6D, 7F), B3LYP/6-31G (6D, 7F) and B3LYP/SDD basis sets to predict the molecular structure and vibrational wavenumbers. The DFT hybrid B3LYP functional and SDD methods tend to overestimate the fundamental modes; therefore scaling factor of 0.9613 has to be used for obtaining a considerably better agreement with experimental data [21] and for HF method, a scaling factor of 0.8929 is used [21]. The Stuttagard/Dresden effective core potential basis set [22] was chosen particularly because of its advantage of doing faster calculations with relatively better accuracy and structures [23]. Then frequency calculations were employed to confirm the structure as minimum points in energy. Parameters corresponding to optimized geometry of the title compound (Fig. 3) with XRD data are given in Table 1. The absence of imaginary wavenumbers on the calculated vibrational spectrum confirms that the structure deduced corresponds to minimum energy. The assignments of the calculated wavenumbers are aided by the animation of option Gaussview program, which gives a visual presentation of the vibrational modes [24]. The potential energy distribution is calculated with the help of GAR2PED software [25].

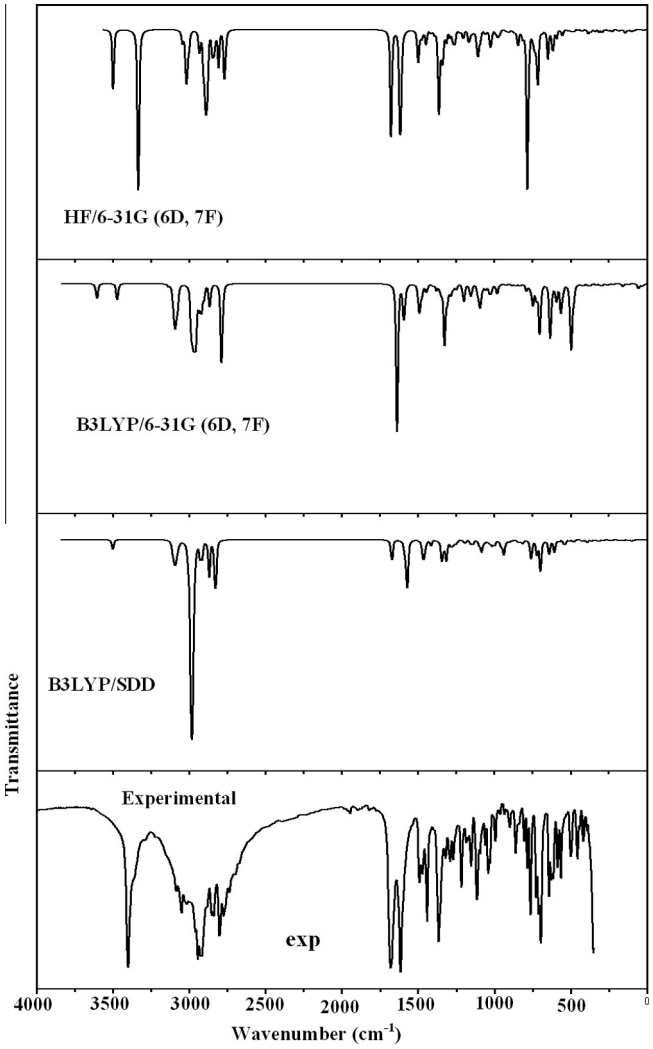

Fig. 1. FT-IR spectrum of 2,2-diphenyl-4-(piperidin-1-yl)butanamide.

Results and discussion

IR and Raman spectra

The calculated (scaled) wavenumbers, observed IR, Raman bands and assignments are given in Table 2. In the following discussion, the mono substituted phenyl rings at C_{40}, $C2_9$ and the piperidine ring are designated as PhI, PhII and RingIII, respectively and the experimentally observed frequencies are compared with B3LYP/SDD values.

The NH_2 asymmetric stretching vibrations [26] give rise to a strong band in the region $3390 \pm 60\ cm^{-1}$ and the symmetric NH_2 stretching in the region $3210 \pm 60\ cm^{-1}$ with a somewhat weaker intensity. The DFT calculations give these modes at 3501 and $2957\ cm^{-1}$ as asymmetric and symmetric NH_2 stretching modes. The bands observed at 3403, $2961\ cm^{-1}$ in the IR spectrum and 3490, $2960\ cm^{-1}$ in the Raman spectrum are assigned as NH_2 stretching mode for the title compound. The symmetric stretching of NH_2 is downshifted due to strong hydrogen bonding as reported in literature [27,28]. The NH_2 deformation band [26] δNH_2 is expected in the region $1610 \pm 30\ cm^{-1}$. For the title compound, δNH_2 band is observed at $1675\ cm^{-1}$ in the IR spectrum, $1679\ cm^{-1}$ in the Raman spectrum and at $1672\ cm^{-1}$ theoretically. The in-plane NH_2 rock absorbs in the region [rgoes] $1250 \pm 45\ cm^{-1}$. The band at $1195\ cm^{-1}$ (DFT) is assigned to