Journal of Molecular Structure 1130 (2017) 208–222

Contents lists available at ScienceDirect

Journal of Molecular Structure

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

Vibrational spectroscopic investigations, molecular dynamic simulations and molecular docking studies of *N*′-diphenylmethylidene-5-methyl-1*H*-pyrazole-3-carbohydrazide

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ARTICLE INFO

Article history:
Received 3 June 2016
Received in revised form
6 October 2016
Accepted 7 October 2016
Available online 11 October 2016

Keywords:
DFT
Pyrazine
Molecular dynamics
FT-IR
FT-Raman
Docking

ABSTRACT

FT-IR and FT-Raman spectra of *N*′-diphenylmethylidene-5-methyl-1*H*-pyrazole-3-carbohydrazide were recorded and analyzed. Due to the industrial and biological importance of pyrazole derivatives, we have carried out an extensive quantum chemical study on *N*′-diphenylmethylidene-5-methyl-1*H*-pyrazole-3-carbohydrazide. The theoretical ground state geometry and electronic structure of the title molecule were optimized by DFT/B3LYP/6-311G++(d,p) method and compared with those of the crystal data. The wave numbers obtained are assigned by potential energy distribution. The ring breathing modes of the benzene rings are assigned theoretically at 1009 cm^{-1} for the mono substituted phenyl rings. The first order hyperpolarizability is comparable with that of similar derivatives and 16 times that of the standard NLO material urea. Conformational analysis was conducted in order to locate all possible conformations of the title compound, followed by investigation of local reactivity properties by MEP and ALIE surfaces. Natural bond orbital analysis has been carried out to analyse the stability of the molecule arising from hyper-conjugative interactions and charge delocalization. Further, reactive properties via autoxidation and hydrolysis mechanisms have been assessed through calculations of bond dissociation energies and radial distribution functions. Docking results confirmed that the compound was a potential inhibitor of CDK2s and were in agreement with the previous reported studies.

1. Introduction

Hydrazides, carbohydrazides and similar compounds are well known as useful building blocks for the synthesis of variety of heterocyclic rings. The carbohydrazide derivatives represent an important pharmacophoric group in several classes of therapeutically useful substances [1-4] and a very large number of heterocyclic carbohydrazides and their derivatives were reported to exhibit significant biological activities [3,5]. Compounds including pyrazole nucleus are known to possess analgesic, anti-inflammatory, hypotensive, anti-diabetic and antibacterial activities [6]. Pyrazole derivatives have large applications in the agrochemical and the pharmaceutical industry as herbicides and insecticides [7,8]. COX-2 inhibition activity of one of the pyrazole derivatives were reported by Meena et al. [9]. The synthesis of pyrazole derivatives with sugar moieties has received considerable attention due to their broad spectrum of biological activities [10,11]. DFT studies of certain bipyrazole derivatives as potential corrosion inhibitors have been previously reported by Wang et al. [12]. Pyrazine derivatives containing hydrazide moiety has wide application in the treatment of tuberculosis and also exhibits fungicidal activity [13]. A series of similar pyrazine hydrazone complexes had been

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http://dx.doi.org/10.1016/j.molstruc.2016.10.032
0022-2860/

reported previously [14]. Spectroscopic studies of different pyrazole and carbohydrazides were reported by several authors [15-17].

However, no studies have been done on the ground state electronic properties, vibrational characteristics and chemical reactivity of the title molecule *N*′-diphenylmethylidene-5-methyl-1*H*-pyrazole-3-carbohydrazide. Therefore, in this work, we explore the uses of DFT to investigate the ground-state optimized structure, vibrational characteristics, conformational analysis, Molecular Dynamic (MD) simulations, HOMO-LUMO energy gap, natural bond orbital (NBO) analysis, NLO properties, chemical reactivity and biological activity of the title molecule. The molecular electrostatic potential and average local ionization energy maps (MEP and ALIE, respectively) of the compound are useful for understanding the connection between the biological activity and molecular structure. To investigate the oxidation properties of the title compound, bond dissociation energies (BDE) have been calculated. Radial distribution functions (RDF) based on Molecular Dynamic (MD) simulations have been calculated in order to understand interactions with water, while biological activity of the title molecule, was tested by molecular docking study.

2. Experimental details

The title compound was synthesized according to the reported protocol in literature [18]. The FT-IR (Fig. 1) and FT-Raman (Fig. 2) spectra were recorded using KBr pellets on a DR/Jasco FT-IR 6300 spectrometer and on a Bruker RFS 100/s, Germany. For excitation of the Raman spectrum the emission of Nd:YAG laser was used, excitation wavelength 1064 nm, maximal power 150 mW, measurement on solid sample. The spectral resolution after apodization was 2 cm^{-1}.

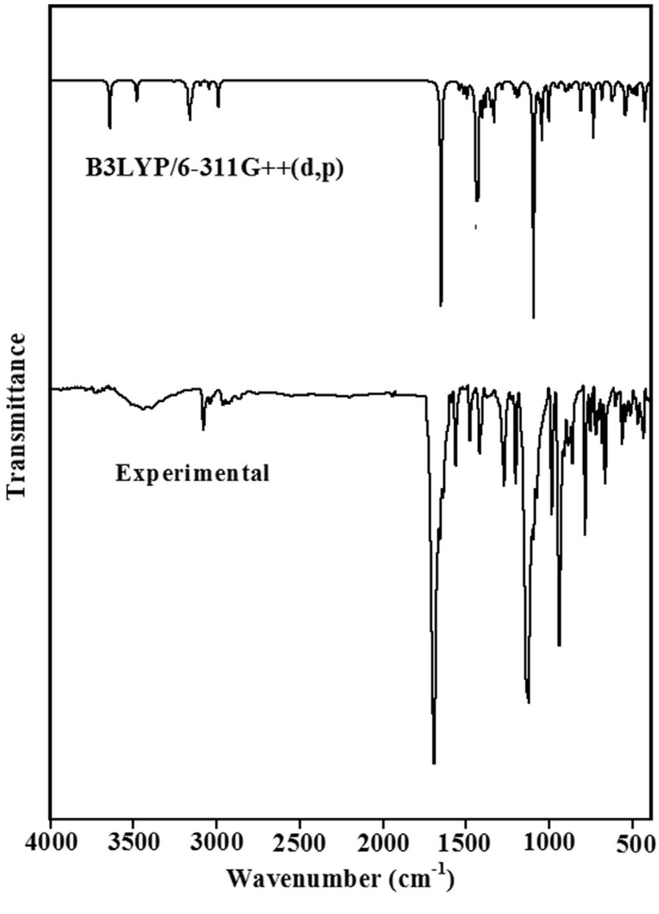

Fig. 1. FT-IR spectrum of *N*′-diphenylmethylidene-5-methyl-1*H*-pyrazole-3-carbohydrazide.

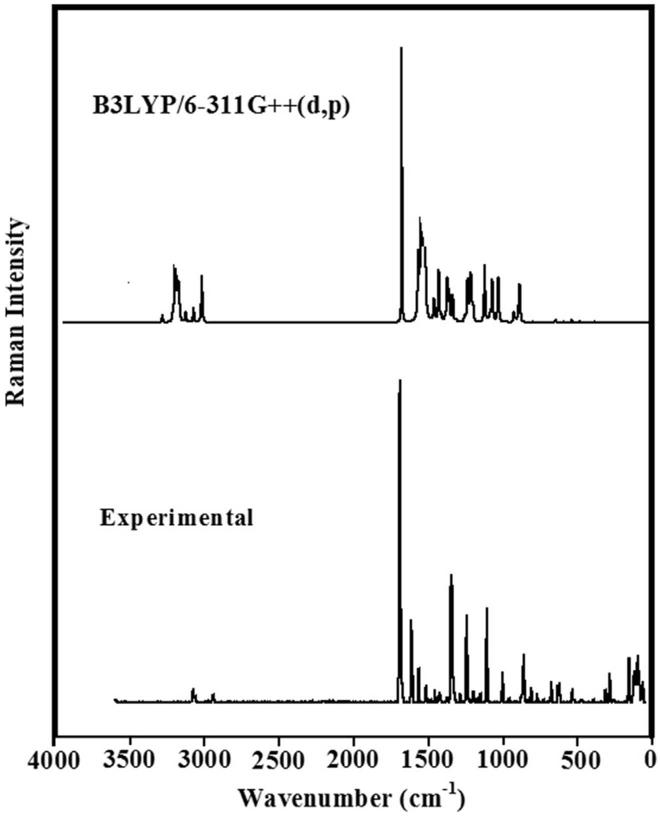

Fig. 2. FT-Raman spectrum of *N*′-diphenylmethylidene-5-methyl-1*H*-pyrazole-3-carbohydrazide.

3. Computational details

DFT computations were performed using Jaguar 9.0 program, as implemented in Schrödinger Material Suite 2015-3 [19,20]. In order to investigate possible molecular structures of *N*′-diphenylmethylidene-5-methyl-1*H*-pyrazole-3-carbohydrazide, we have employed the conformational search module of MacroModel 11.0, also implemented in Schrödinger Material Suite 2015-3. Conformational geometries further were geometrically optimized using the B3LYP exchange-correlation functional with 6-311++G(d,p) basis set, while their true ground states were confirmed through vibrational analysis which yielded only positive frequencies. To predict the molecular structure and vibrational wave numbers of the most stable confirmer, frequency calculations of the title compound were carried out with the Gaussian09 program [21] using B3LYP/6-311++G(d,p) basis set, while scaling factor of 0.9613 is used for obtaining a considerably better agreement with the experimental data [22]. The DFT calculations were reported to provide excellent vibrational wave numbers of organic compounds if the calculated wave numbers are scaled to compensate for the basis set deficiencies and for the anharmonicity [23]. Parameters corresponding to the optimized geometry of the title compound with XRD data are given in Table 1. The assignments of the calculated wave numbers are done by the animation option of the GAUSSVIEW program [24] and GAR2PED software package [25].

Molecular dynamics simulations were performed using the Desmond program [26-29] as implemented in Schrödinger