Journal of Molecular Structure 1153 (2018) 212–229

Contents lists available at ScienceDirect

Journal of Molecular Structure

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

Synthesis, characterization and computational study of the newly synthetized sulfonamide molecule

P. Krishna Murthy [a], V. Suneetha [b], Stevan Armaković [c], Sanja J. Armaković [d], P.A. Suchetan [e], L. Giri [f], R. Sreenivasa Rao [b, *]

[a] Department of Chemistry, Bapatla Engineering College (Autonomous), AcharayaNagarjuna University Post Graduate Research Centre, Bapatla-522 102, A.P., India
[b] Department of Chemistry, Bapatla College of Arts and Sciences, Baptla-522 101, A.P., India
[c] University of Novi Sad, Faculty of Sciences, Department of Physics, Trg D. Obradovića 4, 21000 Novi Sad, Serbia
[d] University of Novi Sad, Faculty of Sciences, Department of Chemistry, Biochemistry and Environmental Protection, Trg D. Obradovića 3, 21000 Novi Sad, Serbia
[e] Department of Studies and Research in Chemistry, University College of Science, Tumkur University, Tumkur-572 103, Karnataka, India
[f] Solid State & Supramolecular Structural Chemistry Laboratory, School of Basic Sciences, Indian Institute of Technology Bhubaneswar, Bhubaneswar 751 008, India

ARTICLE INFO

Article history:
Received 14 July 2017
Received in revised form
27 September 2017
Accepted 7 October 2017
Available online 8 October 2017

Keywords:
Sulfonamide
SCXRD
Hirshfeld surface analysis
DFT calculations
Vibrational analysis

ABSTRACT

A new compound *N*-(2,5-dimethyl-4-nitrophenyl)-4-methylbenzenesulfonamide (NDMPMBS) has been derived from 2,5-dimethyl-4-nitroaniline and 4-methylbenzene-1-sulfonyl chloride. Structure was characterized by SCXRD studies and spectroscopic tools. Compound crystallized in the monoclinic crystal system with $P2_1/c$ space group $a = 10.0549$, $b = 18.967$, $c = 8.3087$, $\beta = 103.18$ and $Z = 4$. Type and nature of intermolecular interaction in crystal state investigated by 3D-Hirshfeld surface and 2D-finger print plots revealed that title compound stabilized by several interactions. The structural and electronic properties of title compound have been calculated at DFT/B3LYP/6-311G++(d,p) level of theory. Computationally obtained spectral data was compared with experimental results, showing excellent mutual agreement. Assignment of each vibrational wave number was done on the basis of potential energy distribution (PED). Investigation of local reactivity descriptors encompassed visualization of molecular electrostatic potential (MEP) and average local ionization energy (ALIE) surfaces, visualization of Fukui functions, natural bond order (NBO) analysis, bond dissociation energies for hydrogen abstraction (H-BDE) and radial distribution functions (RDF) after molecular dynamics (MD) simulations. MD simulations were also used in order to investigate interaction of NDMPMBS molecule with 1WKR and 3ETT proteins protein.

1. Introduction

SO_2—NH group is a key constituent of sulfonamide pharmaceuticals, which are promising chemotherapeutic agents used for treatment of various diseases [1]. Sulfa-drugs possess a wide verity of medicinal chemistry applications such as antiprotozoal [2], antibacterial [3], antifungal [4], insecticidal [5], anti-inflammatory [6], carbonic anhydrase inhibitor [7] and rheumatoid arthritis [8]. Recent literature reports indicate that sulphonamides are also applied in the cases of Alzheimer's [9], cancer [10,11] and HIV [12] diseases as well. Besides pharmaceutical applications, sulphonamides are also used as reagents in analytical chemistry for concentration, separation, selective qualitative and quantitative determination of the 3d transition metal cations [13–15]. Sulfonamide compounds have been studied extensively and numerous experimental and computational reports. Xing et al. reported the crystal structure of 4-methyl-*N*-(4-nitrophenyl)benzenesulfonamide [16]. Sarojini et al. reported synthesis, structural, spectroscopic and computational studies of 4-methyl-*N*-(3-nitrophenyl) benzene sulfonamide combining experimental and theoretical approaches [17]. Rajamani et al. investigated electronic absorption, vibrational spectra, nonlinear optical properties, NBO analysis and thermodynamic properties of *N*-(4-nitro-2-phenoxyphenyl) methanesulfonamide molecule within the Hartree-Fock and

* Corresponding author.
E-mail address: rsrchemhod@gmail.com (R.S. Rao).

https://doi.org/10.1016/j.molstruc.2017.10.028
0022-2860/

density functional approaches [18]. Govindarasu et al. carried out detailed experimental and computational DFT study of *N*-phenylbenzenesulfonamide [19].

In this paper we report synthesis, detailed spectroscopic and computational characterization of *N*-(2,5-dimethyl-4-nitrophenyl)-4-methylbenzenesulfonamide (NDMPMBS) molecule. In order to uniquely characterize the title compound we have measured FT-IR, Raman and NMR spectra. Spectral data were also computed within DFT approach in order to validate the used level of theory. Computational investigation within DFT approach has proven to be effective tool for investigation of physical and chemical properties of various organic molecules [20–24] and in this study we used it to study both global and local quantum-molecular descriptors of the title compound. Taking into account that organic pharmaceutical molecules such as NDMPMBS represent great threat for water resources [25–30], we have also investigated sensitivity of NDMPMBS towards autoxidation and hydrolysis, in order to gain an insight into its possible degradation properties.

2. Material and methods

2.1. General remarks

FT-IR spectrum (Fig. 1) was recorded in solid state using KBr disc in the range of 4000–600 cm^{-1} on ATR module ALPHA-T Bruker FT-IR spectrophotometer. FT-Raman spectrum (Fig. 2) was measured for solid sample on Bruker RFS 100/s, Germany using Nd:YAG laser source, excitation wave length 1064 nm with spectral resolution 2 cm^{-1} in the region of 0–4000 cm^{-1}.^{1}H and ^{13}C NMR chemical shift values were reported in ppm using TMS as internal standard on Bruker 400 MHz spectrometer.

2.2. Synthesis of N-(2,5-dimethyl-4-nitrophenyl)-4-methylbenzenesulfonamide

To a stirred solution of 2,5-dimethyl-4-nitroaniline (0.5 g, 3.01 mmol) in pyridine (5 mL), 4-methylbenzene-1-sulfonyl chloride (0.86 g, 4.51 mmol) was added. The reaction mixture was stirred for 16 h at room temperature. After completion of reaction by TLC, the reaction mixture was diluted with D.M.water and acidified with dilute HCl solution. Solid was filter, washed with D.M.water, MTBE and followed by 1:1 ethyl acetate: hexane. Dried under vacuum to afford (0.67 g, 69%) of *N*-(2,5-dimethyl-4-nitrophenyl)-4-methylbenzene-1-sulfonamide as pale yellow solid (Scheme-1 supporting information). Suitable single crystals were grown by slow evaporation solution growth technique at ambient temperature using chloroform: methanol (1:3) solvent.

2.3. X-ray data collection and refinement details

A suitable prism like crystal was selected and mounted on a Bruker APEX-II CCD diffractometer using graphite monochromated MoKa (λ = 0.71073 Å) radiation and detector (CCD). The crystal was kept at 273 (2) K during data collection. The structure was solved using Olex2 software with the olex2. solve [31] structure solution program using Charge Flipping and the structure was refined with the ShelXL [32] refinement package using Least Squares minimization. All the non-hydrogen atoms were revealed in the first difference Fourier map itself and were refined anisotropically. All the hydrogen atoms were positioned geometrically. All H atoms were positioned geometrically, with C–H = 0.96 Å for methyl H, C–H = 0.93 Å for aromatic H, and refined using a riding model with $U_{iso}(H) = 1.5U_{eq}(C)$ for methyl H and $U_{iso}(H) = 1.2U_{eq}(C)$ for aromatic H. The nitrogen bound H atom was located in a difference map and was refined isotropically with the bond length restraint N–H = 0.86 (2) Å. All the geometrical calculations were carried out using the program *PLATON* [33] within the WinGX suite [34]. The molecular and packing diagrams were generated using the software *MERCURY* [35]. The crystallographic data and refinement parameters are summarized in Table 1.

2.4. Computational details

Firstly, molecular structure of the title compound was extracted from the single crystal X-ray structure to be used as a starting geometry for geometry optimization. The molecular geometry optimization in gas phase together with vibrational analysis, frontier orbital analysis (HOMO-LUMO), MEP, surface analysis and Mullikan atomic charges calculation were performed at DFT level of theory with B3LYP [36] hybrid exchange-correlation functional and 6-311G++(d,p) (5D, 7 F) basis set, using Gaussian 09 software package [37]. The assignment and PED analysis of wave number were done by GaussView 5.0 program [38] and VEDA4 program [39]. For better agreement of calculated wavenumber number with

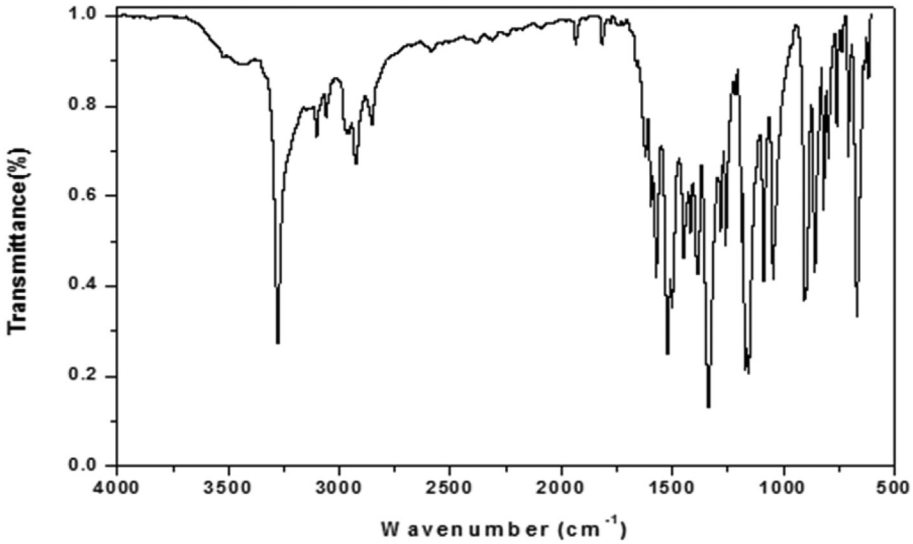

Fig. 1. FT-IR spectrum of *N*-(2,5-dimethyl-4-nitrophenyl)-4-methylbenzenesulfonamide.