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Synthesis, characterization, antibacterial activity and quantum chemical studies of N’-Acetyl propane sulfonic acid hydrazide

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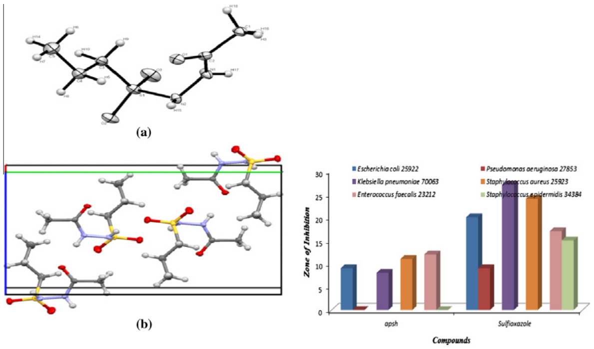
HIGHLIGHTS

- Synthesis of N’-Acetyl propane sulfonic acid hydrazide (*Apsh*).
- Characterization of *Apsh*.
- ^{1}H and ^{13}C shielding tensors for crystal structure with GIAO/DFT/B3LYP/6-311++G(d,p) methods.
- The vibrational band assignments for crystal structure with B3LYP/6-311++G(d,p)/(SQMFF).
- Antimicrobial activities of *Apsh*.

GRAPHICAL ABSTRACT

N’-Acetyl propane sulfonic acid hydrazide has been synthesized for the first time and investigated its antibacterial activity. Also ^{1}H and ^{13}C shielding tensors for crystal structure were calculated with GIAO/DFT/B3LYP/6-311++G(d,p) methods in $CDCl_3$.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ABSTRACT

A new N’-Acetyl propane sulfonic acid hydrazide, $C_3H_7—SO_2—NH—NH—COCH_3$ (Apsh, an sulfon amide compound) has been synthesized for the first time. The structure of *Apsh* was investigated using elemental analysis, spectral (IR, $^{1}H/^{13}C$ NMR) measurements. In addition, molecular structure of the Apsh was determined by single crystal X-ray diffraction technique and found that the compound crystallizes in monoclinic, space group P 21/c. ^{1}H and ^{13}C shielding tensors for crystal structure were calculated with GIAO/DFT/B3LYP/6-311++G(d,p) methods in $CDCl_3$. The structure of Apsh is optimized using Density Functional Theory (DFT) method. The vibrational band assignments were performed at B3LYP/6-311++G(d,p) theory level combined with scaled quantum mechanics force field (SQMFF) methodology. The theoretical IR frequencies are found to be in good agreement with the experimental IR frequencies. Nonlinear optical (NLO) behaviour of Apsh is also examined by the theoretically predicted values of dipole moment (μ), polarizability (α_0) and first hyperpolarizability (β_{tot}). The antibacterial activities of synthesized compound were studied against Gram positive bacteria: *Staphylococcus aureus* ATCC

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25923, *Enterococcus faecalis* ATCC 23212, *Staphylococcus epidermidis* ATCC 34384, Gram negative bacteria: *Eschericha coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Klebsiella pneumoniae* ATCC 70063 by using microdilution method (as MICs) and disc diffusion method.

Introduction

The importance of sulfonamide was realized [1] when sulfonylamide, a key analogue of sulfonamide, was reported [2] to be the first antibacterial drug. Sulfonamides were the first effective chemotherapeutic agents employed systematically for the prevention and the cure of bacterial infections in humans and other animal systems [3,4]. Later on, many thousands of molecules containing the sulfanilamide structure have been created since its discovery, yielding improved formulations with greater effectiveness and less toxicity. Sulfa drugs are still widely used for conditions such as acne and urinary tract infections, and are receiving renewed interest for the treatment of infections caused by bacteria resistant to other antibiotics. Also, a number of other activities, some of which have been recently observed, include endothelin antagonism, anti-inflammatory activity, tubular transport inhibition, insulin release, carbonic anhydrase and saluretic action, among others [5].

In our previous studies, aliphatic/aromatic bis sulfonamides were synthesized and tested for antimicrobial activity [6–9]. Also, we have reported conformational analysis and vibrational spectroscopic investigation of the methanesulfonic acid hydrazide [10] methanesulfonic acid 1-methylhydrazide [11] some methane/ethane sulfonylhydrazone derivatives [12–15]. In this work, N’-Acetyl propane sulfonic acid hydrazide *(Apsh)* was synthesized and characterized by using elemental analyses, FT-IR, NMR, spectrometric methods. *Apsh* has also been characterized by single crystal X-ray diffraction. ^{1}H and ^{13}C shielding tensors for crystal structure were calculated with GIAO/DFT/B3LYP/6-311++G(d,p) methods in $CDCl_3$. The vibrational band assignments were performed at B3LYP/6-311++G(d,p) theory level combined with scaled quantum mechanics force field (SQMFF) methodology. The antibacterial activities of synthesized compounds were studied against Gram positive bacteria: *Staphylococcus aureus* ATCC 25923, *Enterococcus faecalis* ATCC 23212, *Staphylococcus epidermidis* ATCC 34384, Gram negative bacteria: *Eschericha coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Klebsiella pneumoniae* ATCC 70063 by using microdilution method (as MICs) and disc diffusion method.

Experimental

Physical measurements

The crystal structure of N’-Acetyl propane sulfonic acid hydrazide (Apsh) was determined by using a on a Bruker D8 Venture. The solvents used were purified and distilled according to routine procedures. Propane sulfonyl chloride and hydrazine hydrate were commercial products (purum). ^{1}H and ^{13}C-NMR spectra of dimethylsulfoxide-d_6 (DMSO-d_6) solutions of the compounds were registered on a Bruker WM-400 spectrometer (400 MHz) using tetra methyl silane as internal standard. The infrared spectra of the compounds as KBr-disks were recorded in the range of 4000–400 cm^{-1} with a Mattson 1000 FT spectrometer. Melting points of compound was determined with a Gallenkamp melting point apparatus. The microdilusion broth and disc diffusion method were used to determine the antibacterial activity of compounds against Gram positive bacteria: *S. aureus* ATCC 25923, *E. faecalis* ATCC 23212, *S. epidermidis* ATCC 34384, Gram negative bacteria: *E coli* ATCC 25922, *P. aeruginosa*ATCC 27853, *K. pneumoniae* ATCC 70063.

Synthesis of N’-Acetyl propane sulfonic acid hydrazide

The nucleophilic substitution reaction of the hydrazine hydrate with propane sulfonyl chloride was carried out as follows:

An ethanol solution of propane sulfonyl chlorides ($C_3H_7SO_2Cl$) was added dropwise to the ethanol solution of hydrazine hydrate (0.12: 0.62 equiv), maintaining the temperature between 10–12 °C. Then, the reaction mixture was stirred for 1 h at room temperature. After the completion of the reaction, the solvent was removed under vacuum and the viscose residue was taken to ether phase using a continuous extraction method. Then the ether was removed with rotary evaporator. The resulting product was boiled with ethyl acetate and then allowed to stand in the freezer. Bright transparent crystals were obtained after a few weeks. Calc. for $C_5H_{12}N_2O_3S$: C, 33.32; H, 6.71; N, 15.54; O, 26.63; S, 17.79% Found: C, 32.87; H, 6.48; N, 14.98; O, 25.93; S, 17.20%. Yield: 70%, M.p.114–116 °C.

Crystallography

Crystallographic data of the compound were recorded on a Bruker D8 Venture X-ray diffractometer equipped with PHOTON 100 CMOS detector using graphite monochromatized MoKα radiation ($\lambda = 0.71073$ Å), and using only ω-scan mode. The empirical absorption corrections were applied by multi-scan via Bruker, SADABS software [16]. The structures were solved by the direct methods and refined by full-matrix least-squares techniques on F^2 using the solution program SHELXS-97 and refined using SHELXL-2014/6. All non-hydrogen atoms were refined with anisotropic displacement parameters. The molecular structure plots were prepared using Mercury CSD 2.4 [17]. The crystal and instrumental parameters used in the unit-cell determination and data collection are summarized in Table 1 for the compounds.

Theoretical calculations

Because of the effective bioactivities of N’-Acetyl propane sulfonic acid hydrazide the three dimensional conformation of the molecule was also determined as it will be able to give important previews about molecular behaviour in gas and solution forms. The molecular geometry optimizations, HOMO, LUMO frontier molecular orbital energy, nonlinear optical (NLO) activity and vibration frequency calculations were performed with the Gaussian 03 W software package by using DFT approaches in addition to the determination of crystal structure [18]. The split valence 6-311++G (d, p) basis set was used for the expansion of the molecular orbital [19]. The geometries were fully optimized without any constraint with the help of an analytical gradient procedure implemented within the Gaussian 03 W program. All the parameters were allowed to relax and all the calculations converged to an optimized geometry which corresponds to a true energy minimum as revealed by the lack of imaginary values in the wave number calculations. The ^{1}H and ^{13}C NMR chemical shifts of the compounds were calculated in $CDCl_3$ using the GIAO