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An experimental and theoretical vibrational spectra of isoniazide

Ayberk Yilmaz [a], Olcay Bolukbasi [a], Meric Bakiler [b,*]

[a] Istanbul University, Science Faculty, Physics Department, Vezneciler, 34118, Istanbul, Turkey
[b] Mimar Sinan Fine Art University, Physics Department, Besiktas, 34347, Istanbul, Turkey

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Abstract

The molecular structure and vibrational spectra of isoniazide (INH) were calculated by the Density Functional Theory (DFT) method using the B3LYP function with the 6-31++G(d,p) and the Z3PolX basis sets. The representation of the hydrogen bonding effect was achieved with the Polarizable Continuum Model (PCM) including the DFT/B3LYP with the 6-31++G(d,p) basis set. Our calculations were performed with the Gaussian98W package program. The scaled wavenumbers, the modified intensities and the total energy distributions (TED) of the vibrational modes of INH were calculated by using Scale 2.0 program. SQM results showed that the scaling factors were transferable to the similar molecules. The solid phase FT-IR and FT-Raman spectra of INH have been recorded in the range of 4000–450 and 4000–100 cm^{-1}, respectively. The calculated wavenumbers were compared with the corresponding experimental values.

Keywords: DFT calculations; Z3PolX; PCM; SQM; Isoniazide; Vibrational spectra

1. Introduction

Tuberculosis is still one of the most infectious diseases in the world. Although in the United States the infection rate has tremendously declined in the last century, the strains of bacteries resistant to antibiotics have been observed very recently, leading to emergence of tuberculosis once again. INH, which has been widely used in the past, is known to act against mycobacterium tuberculosis, and is still the most widely used drug in antituberculous regimens [1].

The pharmacological activity of the biologically active molecules is inherently related to their chemical structures. In this work, we report a description on the molecular geometry, experimental, and theoretical vibrational spectra of isoniazide molecule. Additionally, the hydrogen bonding and the inter-molecular hydrogen bonding effects on vibrational spectra of the molecule were investigated.

Experimental information on the molecular vibrations was obtained from the FT-IR and FT-Raman spectra measured. In order to determine optimized geometry and a reliable assignment for the observed vibrational spectra of INH molecule, quantum chemical calculations were performed via Density Functional Theory (DFT). We also have performed DFT and DFT with PCM calculations to investigate the intra- and inter-molecular hydrogen bonding effects on the same molecule.

2. Experimental details

INH purchased from Sigma was reagent grade and used without further purification. The solid phase FT-IR spectrum of INH were obtained by a pellet of the powdered sample with KBr. The spectrum were recorded by a Perkin Elmer FT-IR spectrometer in the range of 4000–450 cm^{-1}, where the resolution was set to 4 cm^{-1} with 100 scans. The FT-Raman spectrum of the powdered sample were recorded on a Bruker RFS 100/S FT-Raman instrument equipped with Nd-YAG laser by using 1064 nm excitation. The detector was Ge detector cooled with liquid nitrogen. During the process 100 scans were accumulated. Both

* Corresponding author. Tel.: +90 212 2366936; fax: +90 212 2611121.
E-mail address: mbakiler@msu.edu.tr (M. Bakiler).

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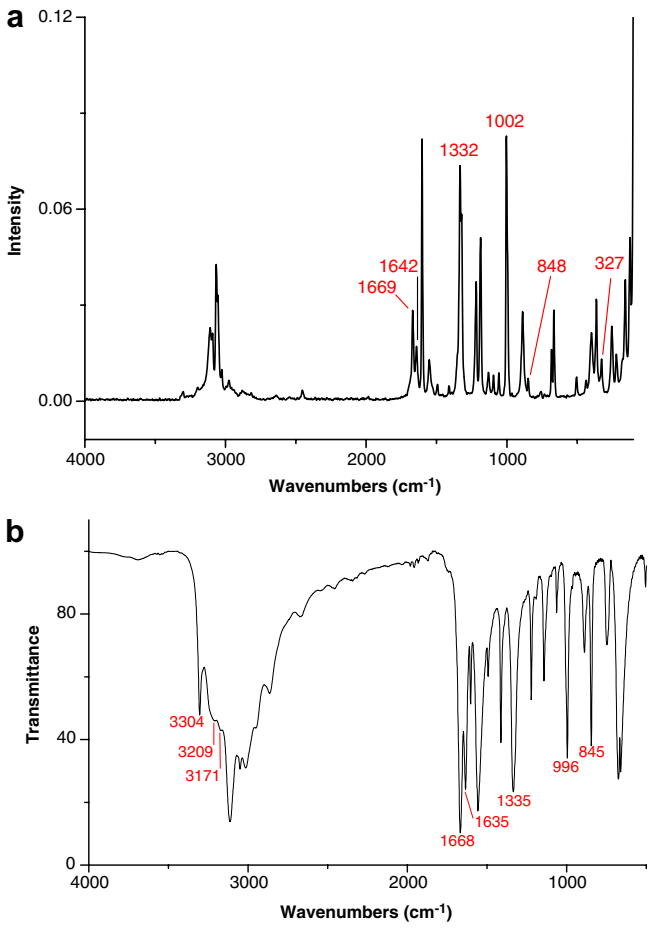

Fig. 1. (a) The experimental FT-Raman spectrum. (b) The experimental FT-IR solid phase spectrum of isoniazide.

FT-IR and FT-Raman spectra shown in Fig. 1, were recorded at room temperature.

3. Computational details

The geometry optimizations and corresponding wavenumbers of INH molecule were calculated at the DFT level with the B3LYP exchange-correlation functional [2,3] in conjunction with the 6-31++G(d,p) basis set and a new highly compact Pol-type basis set Z3PolX [4,5] by using Gaussian 98W program [6].

To investigate the hydrogen bonding effects on INH molecule, as a solvent, water was taken into account during the calculations by using the PCM (Polarizable Continuum Model) at the DFT level with only the B3LYP/6-31++G(d,p) basis set. In order to investigate the influence of the inter-molecular hydrogen bonding effects on the vibrational spectra of INH, we here considered the dimer molecule and performed the associated calculations at the DFT level with the B3LYP/6-31++G(d,p) basis set.

The vibrational modes of the molecule were determined by using the total energy distribution (TED) [7,8]. Vibrational wavenumbers calculated through the B3LYP/

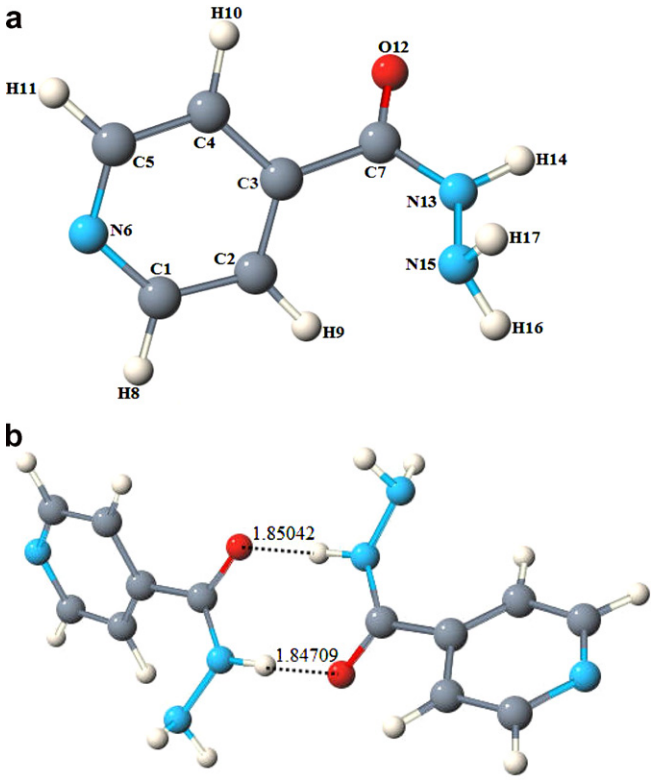

Fig. 2. The atom numbering of (a) free isoniazide molecule and (b) dimer structure of isoniazide.

6-31++G(d,p) basis set were scaled by using the scaled quantum mechanical (SQM) analysis method with the help of Scale 2.0 program [9,10]. The natural internal coordinates recomended by Pulay were used. First, the natural internal coordinates were generated by the FCTINT program [11] then, the force constants matrix, dipole moment, and polarizability derivatives were obtained in the natural internal coordinates by using the same program. In the SQM procedure, the natural internal coordinates were classified into 12 different groups according to their chemical type. The diagonal force constants were scaled by the scaling factors associated with the internal coordinates. On the other hand, the off-diagonal force constants were scaled by the geometric mean of the associated scaling factors. On

Table 1
Scaling factors for isoniazide

Internal coordinates	Scaling factors
X-Y stretching	0.9300
X-H stretching	0.9140
X-Y-Z in plane bending	0.9950
X-Y-H in plane bending	0.9500
CO/CC out of plane bending	0.8300
CH out of plane bending	0.9340
All torsion	0.9350
NH_2 scissoring	0.9130
NH_2 rocking	0.9672
NH_2 wagging	0.8000

H means hydrogen; X, Y, and Z mean first-row heavy atoms C, N, O.