

The Molecular Structure and Dynamics of 2-aminopyridine-3-carboxylic Acid by X-ray Diffraction at 100K, Inelastic Neutron Scattering, Infrared, Raman Spectroscopy and from *First Principles* Calculations

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Abstract

The molecular structure of 2-aminopyridine-3-carboxylic acid was studied by single crystal X-ray diffraction at 100K and inelastic neutron spectroscopy (INS) at 20K. Infrared and Raman spectra at 293K were also recorded. Molecular geometries and frequencies were calculated for solid state at local density approximation LDA and general gradient approximation GGA methods. The theoretical frequencies were compared with those observed on the INS, infrared and Raman spectral patterns.

1. Introduction

In contrast to the aliphatic aminoacids which in majority exhibit zwitterionic structures, N-heterocyclic aminoacids show a variety of hydrogen configurations. For example, no transfer of a proton has been reported in the molecule of 3-aminopyridine-2-carboxylic acid. Its molecules interact via rather weak hydrogen bonds [1-3]. Dimeric molecular units formed by two acid molecules bridged by O-H...O bonds are observed in the structure of 3-aminobenzenecarboxylic acid [4, 5]. On the other hand, an X-ray crystallographic study of 2-aminopyridine-3-carboxylic acid revealed a transfer of the proton from the carboxylic group to the hetero-ring nitrogen atom. A zwitterionic molecule is formed in this way [6]. For this reason, as a successive step in our research on aminoacids by Inelastic Neutron Spectroscopy (INS) a combined study of the molecular structure of the latter compound by X-ray diffraction, INS, IR and Raman spectroscopy supplemented by DFT calculations was undertaken.

Many previous experiments have shown that the INS method is particularly useful in the studies of organic compounds in which low frequency molecular vibrations due to hydrogen atoms play significant role [7]. All transitions are observed on INS spectral patterns, since the selection rules are not obeyed in this case. Due to the scattering cross sections of relevant nuclei and the amplitudes of vibrations, low frequency modes produce fairly strong peaks observed on the INS spectral patterns.

2. Experiments and computations

A commercial polycrystalline sample (ALDRICH) of the title compound was used for INS and Raman measurements. Single crystals for the X-ray crystallographic study were obtained by recrystallisation from aqueous solution at room temperature.

Single crystal X-ray diffraction data were collected at 100(2) K using KUMA KM4 (MoK α) four-circle diffractometer operating in $\omega - 2\theta$ mode. The temperature of the sample crystal was maintained using a Oxford Cryogenic Cooler attached to the diffractometer. Intensities of three standard reflections were monitored every 200 reflections.

Unit cell dimensions and deviations were obtained by least-squares fit to 35 reflections ($12^\circ \leq 2\theta \leq 30^\circ$). Reflections were processed using profile analysis and corrected for Lorentz and polarization effects. No absorption correction. All atoms were located by direct method. Final least squares refinement on F^2 was done on positional parameters of all atoms, anisotropic temperature factors of all non H-atoms and isotropic temperature factors of hydrogen atoms. Atom location and refinement were performed using SHELX97 program package [8]. The refinement parameters are shown in Table 1. The 2-aminopyridine-3-carboxylic acid molecule is presented in Fig.1. Packing of molecules in the unit cell is shown in Fig. 2.

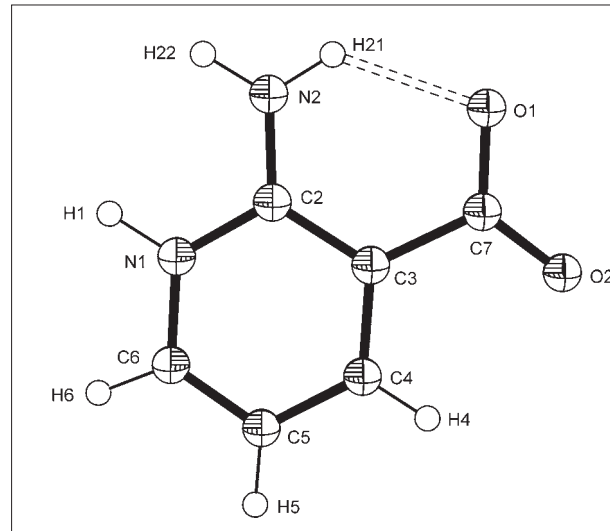


Fig. 1: The molecule of 2-aminopyridine-3-carboxylic acid with atom labeling scheme

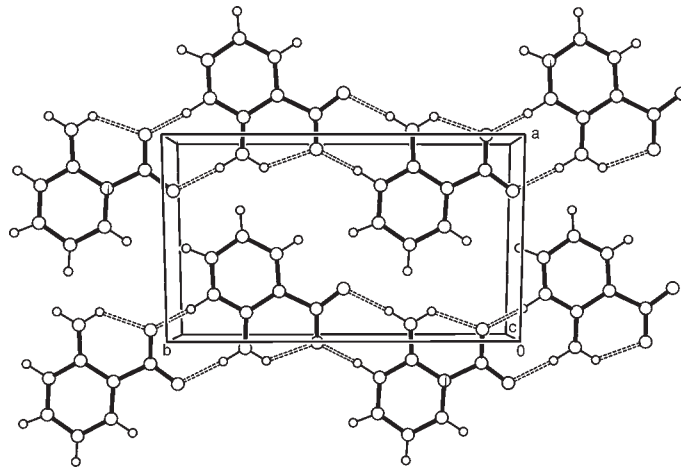


Fig. 2: The molecule of 2-aminopyridine-3-carboxylic acid with atom labeling scheme

Neutron scattering data collection was carried out at the pulsed reactor IBR-2 in JINR, Dubna using the inverted time-of-flight spectrometer NERA-PR [9]. The temperature of the sample was maintained at 20(2) K. The spectra were converted from neutron per channel to $S(Q,\omega)$ function per energy transfer. In the energy transfer range from 5 to 100 meV the relative INS resolution was about 3%. The $S(Q,\omega)$ against energy transfer range

is shown in Fig.3. The structure of the sample could be controlled in the temperature range from 20 K to 300 K because the NERA-PR spectrometer can record simultaneously powder diffraction patterns of the sample in this temperature range.

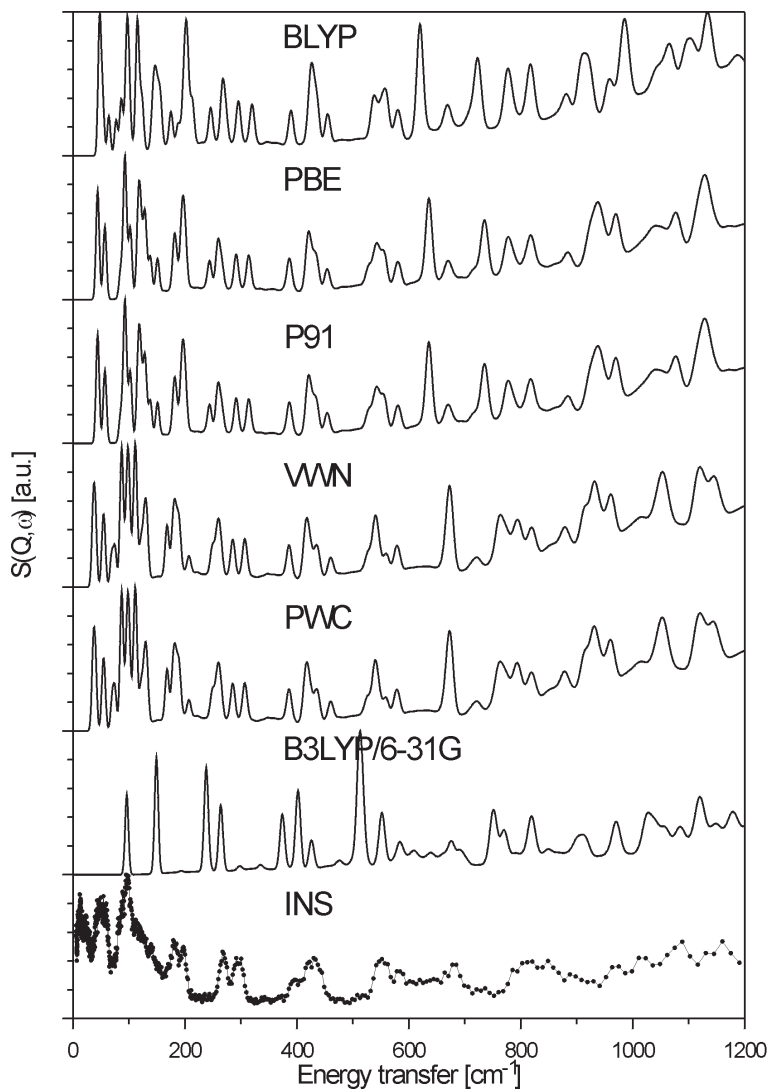


Fig. 3: Experimental and calculated INS spectra of 2-aminopyridine-3-carboxylic acid

The IR spectra were recorded at room temperature in either KBr discs or for Nujol and Fluorolube suspension using either KBr or CsI plates on a FT-IR Bruker IFS 113V spectrometer with a resolution of 2 cm^{-1} . The Raman spectrum of the powder sample was recorded on a Nicolet Magna 860 FT Raman spectrometer. Diode pumped Nd:YAG laser with a power of ca. 200 mW, was the exciting source. The back scattering geometry was applied. The resolution was set up at 2 cm^{-1} . 512 scans were measured. These spectra are presented on Fig.4.

The total energy optimization and the harmonic force field calculations have been performed using the DMol3 program [10, 11] as a part of Materials Studio package [12]. The results have been obtained for solid 2-aminopyridine-3-carboxylic acid within the local density approximation (LDA) at PWC [13] and VWN [14] functionals and within generalized gradient approximation (GGA) at PW91 (Perdew-Wang generalized gradient

approximation [13]), PBE (Perdew-Burke-Ernzerhof correlation [15]) and BLYP (Becke exchange [16] plus Lee-Yang-Parr correlation [17]) functionals. Calculations have been performed using DNP basis set as implemented in DMol3. For the system of 64 atoms in crystallographic unit cell has been obtained 189 frequency modes, in which, 168 describe normal vibrations of four molecules and 21 describe a translation and rotation modes.

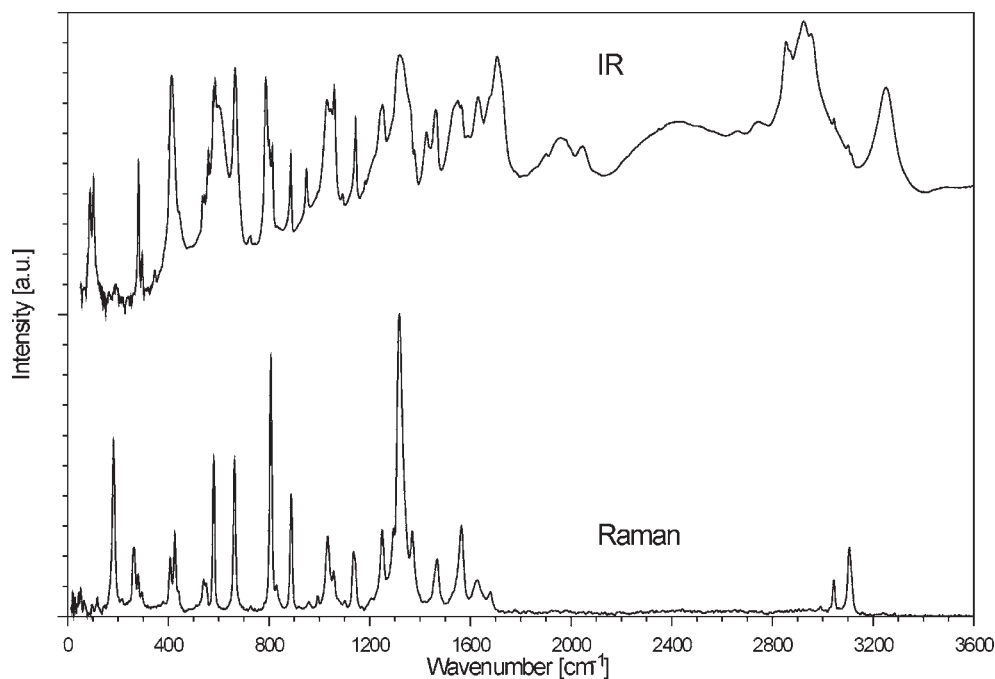


Fig. 4: IR and Raman spectra of 2-aminopyridine-3-carboxylic acid

In addition, the geometries and frequencies for isolated 2-aminopyridine-3-carboxylic acid molecule have been calculated using Gaussian 98 program [18] at B3LYP level. However, calculations at this level with basis sets above 6-31G do not reproduce the shape of the molecule, they yield the forms in which hydrogen from amino group is transferred to carboxyl group. Therefore, they were not used in further consideration.

The observed and calculated molecular parameters are presented in Tables 2 and 3. Table 4 lists the frequencies calculated within LDA(pwc) functional for the solid and for the isolated acid molecule. They are compared with the observed frequencies from INS, IR and Raman spectroscopy data and their assignments.

Inelastic neutron scattering spectra (including overtones, combinations and interaction with lattice modes) were calculated from mass weighted normal vibrational coordinates using auntieCLIMAX program [19] adapted to the parameters of the NERA-PR spectrometer. The calculated INS spectra are presented on Fig. 3.

3. Results and discussion

An interesting feature of the title molecule is its zwitterionic structure in which the carboxylic proton is transferred not to the amino group but to the hetero-ring nitrogen atom. Fig.1 shows the molecule with atom labeling scheme. This configuration produces intermolecular hydrogen bonds in which amino group and hetero-ring nitrogen atoms act as donors and the carboxylate oxygen atoms in adjacent acid molecules act as acceptors giving rise to a catenated pattern. Intramolecular hydrogen bond is also operating between the amino nitrogen and carboxylate oxygen atom of the same molecule. Fig.2. shows the

packing diagram of the title compound. The pyridine ring of the title molecule is almost planar (r.m.s. 0.0129(1)Å). The dihedral angles between the hetero-ring plane and the carboxylate and amino group planes are 5.6(1)° and 2.3(1)°, respectively.

| | |
|---|--|
| Empirical formula | C ₆ H ₆ N ₂ O ₂ |
| Formula weight | 138.13 |
| Color/shape | colourless/rectangular block |
| Temperature | 100(2)K |
| Wavelength (MoK _α), Å | 0.71073 |
| Crystal system | monoclinic |
| Space group | P2 ₁ /c |
| Unit cell dimension | a=7.4022(15) Å b=12.1414(24) Å c=6.7800(14) Å β = 108.73(3)° V=577.07 Å ³ |
| Z | 4 |
| Calculated density, gcm ⁻³ | 1.590 |
| μ (MoK _α), mm ⁻¹ | 0.12 |
| F(000) | 288.0 |
| Crystal size, mm ³ | 0.20x0.21x0.40 |
| θ _{min} , θ _{max} , deg | 2.52, 30.08 |
| Index range | -9 ≤ h ≤ 9, -17 ≤ k ≤ 0, -9 ≤ l ≤ 0 |
| Total data | 1588 |
| Observed data [I > 4σ(I)] | 1212 |
| R _{int} | 0.0310 |
| Method of structure solution | Direct |
| Method of structure refinement | Full-matrix least squares on F ² |
| No. of parameters | 116 |
| Goodness-of-fit on F ² | 1.116 |
| Final R1 [I > 4σ(I)] | 0.0448 |
| Final wR2 index | 0.1593 |
| Completeness to θ=30.08° | 0.994 |
| Largest diff. peak and hole (e/Å ³) | 0.59, -0.44 |
| SHELX-97 weight parameters (A, B) | 0.1128, 0.07 |

Table 1: Crystal data and structure refinement details for 2-amino-3-carboxylic acid

Tables 2 and 3 list the optimized geometries for the molecule of the title compound in a crystal lattice compared with the experimental data. An inspection of the tables reveals that the adopted calculation methods yield very reasonable results, in particular in the case of bond distances for which the R² values are close to 1.00. It is very important to notice a very good agreement between calculated and observed of intra and intermolecular hydrogen bond lengths.

Fig.3 shows at the bottom the INS spectrum taken at 20K. Above it, the spectra calculated using the B3LYP/6-31G level and LDA and GGA functionals are displayed. IR and Raman spectra are presented on Fig.4. Observed frequencies from INS, IR and

| Coordinates | Experimental | LDA | | GGA | | |
|----------------|--------------|----------|----------|----------|----------|----------|
| | | PWC | VWN | P91 | PBE | BLYP |
| C(2)-C(3) | 1.430 | 1.429 | 1.429 | 1.435 | 1.436 | 1.438 |
| C(3)-C(4) | 1.377 | 1.379 | 1.379 | 1.386 | 1.389 | 1.388 |
| C(4)-C(5) | 1.406 | 1.398 | 1.397 | 1.405 | 1.406 | 1.409 |
| C(5)-C(6) | 1.365 | 1.371 | 1.370 | 1.374 | 1.376 | 1.374 |
| C(6)-N(1) | 1.350 | 1.342 | 1.342 | 1.350 | 1.351 | 1.357 |
| N(1)-C(2) | 1.358 | 1.361 | 1.361 | 1.368 | 1.369 | 1.374 |
| C(2)-N(2) | 1.325 | 1.321 | 1.321 | 1.328 | 1.328 | 1.333 |
| C(3)-C(7) | 1.512 | 1.494 | 1.494 | 1.506 | 1.508 | 1.512 |
| C(7)-O(1) | 1.268 | 1.279 | 1.279 | 1.284 | 1.286 | 1.288 |
| C(7)-O(2) | 1.246 | 1.255 | 1.255 | 1.261 | 1.262 | 1.266 |
| N(2)... O(1) | 2.650 | 2.638 | 2.638 | 2.645 | 1.264 | 2.649 |
| N(1)... O(1) | 2.647 | 2.629 | 2.629 | 2.654 | 2.660 | 2.680 |
| N(2)... O(2) | 2.795 | 2.739 | 2.739 | 2.753 | 2.753 | 2.768 |
| R ² | | 0.999625 | 0.999624 | 0.999623 | 0.999542 | 0.999489 |

Table 2: Experimental and calculated bonds distances in the molecule of 2-aminopyridine-3-carboxylic acid

| Coordinates | Experimental | LDA | | GGA | | |
|----------------|--------------|----------|----------|----------|----------|----------|
| | | PWC | VWN | P91 | PBE | BLYP |
| C(2)-C(3)-C(4) | 118.5 | 118.3 | 118.3 | 118.2 | 118.1 | 118.3 |
| C(3)-C(4)-C(5) | 121.5 | 121.5 | 121.5 | 121.5 | 121.5 | 121.5 |
| C(4)-C(5)-C(6) | 117.9 | 118.0 | 118.0 | 118.3 | 118.3 | 118.4 |
| C(5)-C(6)-N(1) | 121.1 | 121.2 | 121.2 | 121.0 | 121.0 | 120.8 |
| C(6)-N(1)-C(2) | 123.0 | 121.7 | 122.7 | 123.0 | 122.9 | 122.8 |
| N(1)-C(2)-C(3) | 117.9 | 118.1 | 118.1 | 118.1 | 118.1 | 118.0 |
| N(2)-C(2)-N(1) | 117.8 | 118.3 | 118.3 | 118.1 | 118.1 | 118.1 |
| N(2)-C(2)-C(3) | 124.3 | 123.6 | 123.6 | 123.8 | 123.8 | 123.8 |
| C(7)-C(3)-C(2) | 121.7 | 122.4 | 122.4 | 122.0 | 122.0 | 121.8 |
| C(7)-C(3)-C(4) | 119.8 | 119.4 | 119.4 | 119.8 | 119.9 | 120.0 |
| O(1)-C(7)-O(2) | 125.7 | 125.0 | 125.0 | 125.4 | 125.5 | 125.4 |
| O(1)-C(7)-C(3) | 117.3 | 117.2 | 117.2 | 117.2 | 117.2 | 117.4 |
| O(2)-C(7)-C(3) | 117.0 | 117.8 | 117.8 | 117.4 | 117.3 | 117.2 |
| R ² | | 0.979059 | 0.979059 | 0.992833 | 0.992304 | 0.994823 |

Table 3: Experimental and calculated bond angles in the molecule of 2-aminopyridine-3-carboxylic acid

Raman spectra, as well as calculated ones for LDA(pwc) functional and their approximate assignments are collected in Table 4.

An analysis of INS spectra displayed on Fig.3 shows that the spectra generated using the calculations for a solid considerably better fit the experimental data than those calculated for an isolated molecule. The calculations performed for the solid take into account the intermolecular interactions, in particular, the influence of hydrogen bonds interactions on the dynamical properties of the title compound. Broad bands observed

| Approximate assignments | Calculated LDA-PWC(dnp) | Experimental | | |
|---|-------------------------|-------------------|---------|-------|
| | | INS | IR | Raman |
| Translations and rotations | 36-207, 21 modes | Massive up to 220 | | |
| CO _{2tors.} | 87, 88, 112, 113 | 97 | 88, 102 | |
| Ring tors. | 168, 180, 183, 190 | 182, 197 | | 182 |
| Ring tors. | 249, 258, 260, 264 | 269 | | 263 |
| C-CO _{2bend.} | 286, 286, 306, 308 | 295 | 281 | 279 |
| C-NH _{2bend.} , Ring def., C-CO _{2str.} | 386, 387, 420, 435 | 396 | 295 | 294 |
| Ring tors. | 415, 416, 420, 426 | 422 | 414 | 407 |
| C-NH _{2bend.} , CO _{2rock.} | 437, 439, 461, 461 | 432 | 443 | 425 |
| N-H...O _{out of plane} | 527, 540, 541, 548 | | 535 | 540 |
| CO _{2rock.} , C-NH _{2bend.} | 539, 540, 560, 560 | 553 | 558 | 549 |
| C-NH _{2wagg.} | 576, 579, 580, 582 | 586 | 586 | 579 |
| Ring def. | 664, 668, 669, 670 | 668 | 663 | 662 |
| C-CO _{2wagg.} | 673, 675, 759, 764 | 684 | | |
| Ring def. | 717, 721, 722, 724 | | 721 | |
| N-H _{wagg.} | 772, 778, 790, 797 | 791 | 789 | |
| CO _{2wagg.} | 801, 806, 814, 815 | 816 | 807 | 807 |
| CO _{2bend.} | 819, 820, 823, 823 | 852 | | 829 |
| C-H _{wagg.} | 878, 878, 880, 881 | 892 | 883 | 888 |
| Ring def. | 914, 915, 929, 930 | | | 918 |
| C-H _{wagg.} | 932, 933, 942, 947 | | 948 | 956 |
| C-H _{wagg.} | 961, 961, 962, 962 | | | 994 |
| Ring str. | 1042, 1044, 1061, 1066 | | 1033 | 1034 |
| NH _{2rock.} , Ring str. | 1053, 1054, 1054, 1056 | | 1054 | 1057 |
| N-H...O _{out of plane} | 1114, 1115, 1117, 1119 | | | 1102 |
| NH _{2rock.} , C-CO _{2str.} | 1127, 1127, 1143, 1144 | | 1140 | 1135 |
| C-H _{bend.} | 1147, 1152, 1152, 1156 | | | |
| NH _{2bend.} , CO _{2sym.} | 1237, 1239, 1246, 1254 | | 1247 | 1249 |
| C-H _{bend.} | 1296, 1297, 1301, 1304 | | | 1295 |
| Ring str., CO _{2str.sym.} | 1335, 1339, 1352, 1361 | | 1321 | 1320 |
| CO _{2str.sym.} , C-H _{bend.} | 1408, 1409, 1416, 1418 | | | 1369 |
| Ring str. | 1436, 1439, 1441, 1442 | | 1425 | |
| C-H _{bend.} | 1469, 1476, 1480, 1482 | | 1461 | 1467 |
| N-H _{bend.} , C-NH _{2str} | 1558, 1559, 1562, 1563 | | 1562 | 1564 |
| Ring str. | 1578, 1584, 1585, 1588 | | | |
| Ring str. | 1589, 1597, 1599, 1600 | | | |
| CO _{2str.asym.} , C-NH _{2str} | 1630, 1630, 1631, 1633 | | 1630 | 1628 |
| Ring str., CO _{2str.asym.} | 1695, 1700, 1704, 1728 | | 1706 | 1680 |
| N-H...O _{str.} | 2257, 2258, 2277, 2340 | | 1960 | |
| N-H...O _{str.} | 2811, 2814, 2830, 2868 | | 2431 | |

Table 4: Approximate assignments for calculated and experimental frequency modes for 2-aminopyridine-3-carboxylic acid

on the IR spectrum (Fig.4) can be assigned to the stretching vibrations of intramolecular N-H...O ($\sim 1960\text{ cm}^{-1}$) and the intermolecular ($\sim 2431\text{ cm}^{-1}$) hydrogen bonds. The data collected in Table 4 show also that the frequencies calculated for a solid agree well with those obtained from the experiment. It can be noticed that the translation and rotation modes calculated for the solid can be assigned to lattice vibrations observed on the INS spectrum.

4. Acknowledgments

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