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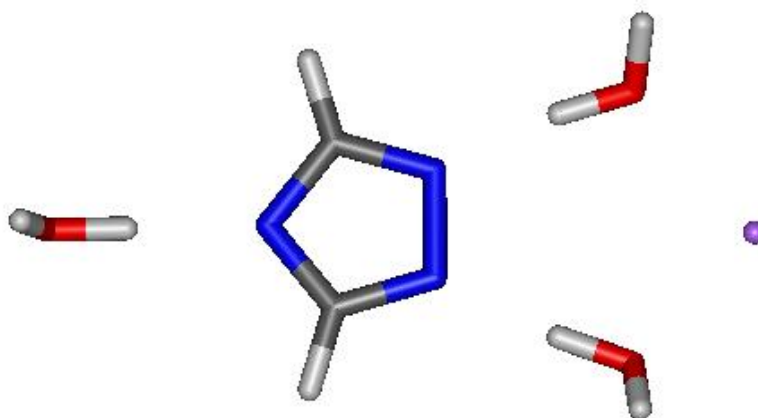


Vibrational spectroscopic study of sodium-1,2,4-triazole, an important intermediate compound in the synthesis of several active substancesFerenc Billes^{*1,3}, Ildikó Ziegler², Hans Mikosch³

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Graphical abstract**Abstract**

The molecular properties, geometric parameters, atomic charges, vibrational spectra of sodium 1,2,4-triazolate were investigated with both experimentally and quantum chemical modeling. During the quantum chemical calculations the possible tautomerism and the aqueous environment were considered since the compound is hygroscopic. The polar environment was modeled as aqueous solvent, and by adding water molecules as structural water. The two kinds of effects were also applied together.

Keywords

Hygroscopic compound, infrared and Raman spectra, tautomers, quantum chemical calculations, modeling effect of wet environment

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1. Introduction

The parent molecule, 1,2,4-triazole is a very important and interesting molecule. It plays important role in the production of active drug substances and is also important from scientific aspects. One can find applications of this molecule in both neutral and anion forms.

El-Azhary et al. [1] reported a detailed analysis of the theoretical (at various levels of theory) and experimental data (by IR and Raman spectroscopy) obtained for 1,2,3-triazole, 1,2,4-triazole and their anions. Billes et al. [2] determined the stable tautomeric forms of the molecule and presented a more correct interpretation of its experimental IR and Raman spectrum by the aid of Pulay's SQM method. The effects of tautomerism on IR spectrum of 1,2,4-triazole was discussed by Aziz et al. [3]. Above the theoretical vibrational spectral data obtained at DFT/B3LYB/6-311++G** level of theory, the authors report the effects of the substitution position of the H atom on triazole in its IR spectrum. Wrzosek et al. [4] interpreted the Surface Enhanced Raman Spectra of 1,2,4-triazole, based on DFT calculations applying the B3LYP/aug-cc-pVTZ and B3LYP/aug-cc-pVTZ-PP levels for stable neutral, anion and cation forms of the molecule.

The aim of this work is to elaborate a model for the simulation of the vibrational spectra of a hygroscopic molecule. For the solution of the problems both experimental and theoretical tools were used. The study of the external polar fields on a molecular ion pair is an essential aim of this work.

Our present work is the continuation of our earlier results presented already on a conference in Keszthely (Hungary) [5].

As already mentioned, we dealt already in a previous work with the vibrational spectroscopy of 1,2,4-triazole [2]. However, the structure and properties of its sodium salt raise different problems. We discuss them in the present work.

By searching the scientific literature, only one article was found presenting X-ray structure data of sodium-1,2,4-triazole (STRZ) [6].

STRZ is a very important compound in the pharmaceutical industry; it is an often used starting material for the production of several active pharmaceutical ingredients (APIs). These APIs are particularly effective against infections of *Candida albicans*, a diploid fungus. *Candidae* live under normal conditions in the gastrointestinal tract and build part of the human gut flora and also in women's vagina. However, if the balance of the gut flora is disturbed, or an acute disease act on the human organism, *Candidae* can predominate over other participants of the gut flora.

Candidae are regarded as reason for several very painful diseases; the effects of Candidae are called candidiasis [7]. Voriconazole [8], Itraconazole [9], and Diflucan (Fluconazole) [10] are three of the well known anti-Candida APIs synthesized on the basis of STRZ (see Fig.1). A new API, Isacuvonazole (see Fig. 1) is just under marketing authorization in Europe and its activity is demonstrated against clinically relevant fungi. [11].

STRZ is also applied in modification of polyvinyl chloride with Na(K) salts of 1,2,4-triazole and 1,2,3-benzotriazole [12], in the modeling of chemical reactions [13]. Some properties of STRZ and its NMR (^1H and ^{13}C) data were published in MOLBASE [14].

The synthesis of 1-Na-1,2,4-triazole was published by Kazhemekaite et al. [15]. It is a very simple reaction. 1-Na-1,2,4,-triazole is the product of the reaction of 1,2,4-triazole with sodium hydroxide.

In the frame of this article quantum chemical modeling was applied for the calculation of some properties of STRZ. Since the compound is hygroscopic, and tautomerism is possible, we considered also these properties in our calculations (see Subsection 4.4). The experimental vibrational spectra were compared with the calculated ones.

2. Experimental

Infrared spectra of the compound were recorded on a Nicolet Magna FT-IR infrared spectrometer with 2 cm^{-1} resolution, in the $4000 - 400\text{ cm}^{-1}$ region, in KBr pellet.

Raman spectra were measured by a Jobin-Yvon LabRAM microprobe using 2 cm^{-1} resolution, in the $4000-100\text{ cm}^{-1}$ region, excited with the 632.8 nm band of a He-Ne laser. The spectra were collected for 20s at a magnification of 100X, 2 scans were accumulated.

3. Calculations

The Gaussian09 program package was applied for our quantum chemical calculations [16]. The DFT Becke3LYP functional [17] was used with the 6-311++G** basis set. This set contains diffuse functions taking into account the structure of the calculated molecules and molecular ensembles. The molecular geometries were optimized NBO atomic natural charges [18] were also computed. The second derivative of the molecular energy function to the Cartesian coordinates provided the vibrational force constants and the vibrational frequencies, infrared and Raman intensities and depolarization ratios. Difficulties arose during the second numerical differentiation of the molecular energy functions to the Cartesian coordinates. If it was necessary, the grid was refined using the INT(GRID=ULTRAFINE) and CPHF(GRID=FINE) options. In some cases the convergence was improved by placing an

individual sphere around some hydrogen atoms (SphereOnH option, United Atom Topological Model) [19]. These calculations run at the Computer Centre of the Vienna University of Technology.

Potential energy distributions (PED) were also calculated using our home made program [20].

The hygroscopic property of the molecule was modeled with two methods. Either the molecules were surrounded with three structural water molecules (resulting in a supermolecule), or the PCM model [21] was used in our calculations for representing the effects of the aqueous continuum (see Fig. 2 for the structures). Finally, the two methods were also combined, i.e. the supermolecule was dipped into the water continuum applying the PCM method. For PCM aqueous environment, the dielectric constant (ϵ) of 78.39 was used.

Internal coordinates were defined, and then normal coordinate analysis was carried out. The calculated frequencies were fitted to the experimental ones through scale factors. Scale factors were chosen for minimizing the deviation between the experimental and the scaled calculated frequencies.

The calculated Raman activities (S_i) were converted to the Raman intensities using the equation [22]

$$I_i = f \frac{(v_0 - v_i)^4}{v_i \left[1 - \exp\left(-\frac{hcv_i}{kT}\right) \right]} S_i \quad (1)$$

where v_0 , T , h , k and c are the experimental excitation wavelength (wavenumber), the temperature of the medium (here 293 K), the Planck's constant, the Boltzmann's constant and the velocity of light in vacuum, respectively. The factor f is an arbitrary constant valid for all vibrational frequencies of the molecule (it is given in cm^3 units, I and S are given in the same intensity units).

4. Results and discussion

The molecule STRZ has two tautomers (Fig. 2): 1STRZ and 4STRZ; they exist in equilibrium. As already mentioned above (Section 3), we studied both. However, beside these forms their supermolecules were also computed, i.e. they were also surrounded with three structural water molecules. These supermolecules are denoted as 1STRZW and 4STRZW, respectively. All of the four mentioned molecular assemblies were studied also by dipping them into aqueous continuum (see below). These forms are denoted with 1STRZA, 4STRZA,

1STRZWA and 4STRZWA, respectively. Since water molecule is part of some of these supermolecules, for comparison the same calculations were also carried out for the isolated water molecule.

4.1. Molecular geometry

The different molecular assemblies mentioned above are shown in Fig 3.

Table 1A presents selections from the optimized molecular parameters under different interactions of the environment for the 1STRZ type molecules, Table 1B contains similarly selected parameters for 4STRZ type ones. The full geometric parameter sets of the optimized molecular structures are shown in the Supplement as Tables S1A and S1B, respectively.

A comparison over the geometric parameters reported for 1STRZ and 1STRZA indicates that the N-Na (1-6, 2-6) distances will be first influenced in a polar environment as modeled here by the PCM approach and that these distances increase and the sodium atom is squeezed out from the direct environment of the triazole ring (see the bold numbers) when the interaction of 1,2,4-triazole with the polar environment increases.

The appearance of the water molecules (1STRZW) and the polar environment around this supermolecule (1STRZWA) cause significant increase of these distances (Table 1A, bold numbers). The N1-N2 distances show some shrinkage under the polar environment.

The presence of three water molecules rearranges the environment of the 1STRZ molecule (see Fig. 3). There are interactions between the atoms of the triazole ring, the sodium ion and the atoms of the water molecules. The polar medium affects these geometric parameters, i.e. interatomic distances, angles and dihedral angles change. The most important changes of parameters are stressed using italics in Table 1A. Both the water molecules and the polar continuum increase essentially the N...H(O) and the Na...O(H) distances.

By investigating the geometric parameters of the 4-Na-1,2,4-triazole tautomers (see Table 1B), one can see that striking changes occur in the geometric parameters of the 4-Na-1,2,4-triazole tautomers, depending on the different position of the sodium ion.

The sodium ion is in direct contact with only one nitrogen atom and with only one water molecule. The sodium atom builds a bridge between the triazole ring and the water molecule, and therefore the position of the Na ion is stabilized. The N1-Na7 and O10-Na7 distances (see Fig 4 for the numbering of the atoms) show only weak influence by the external fields (Tab1B). This is in contrast with the behavior of the N1-Na6 (N2-Na6) or O10-Na6 (O16-Na6) (Fig 4), with their large or very large extension under the effect of the polar fields (Tab 1A).

The studied structures can also be characterized by their symmetry properties. Both 1STRZ and 4STRZ have C_{2v} symmetry. 1STRZWA have C_s symmetry, while 4STRZWA can be classified as C_2 .

4.2. Atomic net charges

The NBO atomic net charges are listed in Tables 2A and 2B for the 1-Na and 4-Na tautomers, respectively.

If the corresponding data in Table 2A are compared, it can be seen that the polar solvent exhibits different effects on the atoms in the triazole ring. The charge of two neighboring nitrogen atoms N1 and N2 (Fig. 4) becomes more positive, while that of N4 atom more negative. The charges of the two carbon atoms, C3 and C5, shift to negative direction, in contrary to the H7 and H8 charges: those increase their positivity. The appearance of the three structural water molecules increases the positivity of all of the ring atoms and also that of H7 and H8.

Inclusion of the solvent effect to the calculation through PCM model in some cases leads to weak but important charge shifts on the atoms of the 1STRZ+3 water supermolecule with respect to those calculated without including this effect (see columns 4, 5 in Table 2A).

The Na ion charges become more positive under effects of all external fields; the effect of the polar solvent is stronger than that of the water molecules. The water molecules of the super molecules are more polarized than in the isolated water molecules (the charge calculated for the oxygen and hydrogens in the isolated molecule using the same quantum chemical method and basis set are, respectively, -0.502 and +0.251 in atomic unit system). The oxygen atoms in the super molecule are more negative compared to those in the isolated H₂O, whereas the hydrogens are more positive. While the charges of the hydrogen atoms are very close to those of the carbons, the nitrogen atoms have relatively quite large negative charge values with respect to the other atoms in the triazole ring (compare e.g. the charges of H9 and H11 or H15 and H17).

The charge relations in the 4-Na tautomer (Table 2B) are different as a consequence of the different position of the sodium ion (Fig. 2). The atomic charges in the water molecule H9-O10-H11 (see also Fig. 4) are far from the triazole ring, its effect is small, and therefore its two hydrogen atoms have the same charge. The two other water molecules “feel” the positive charge of the close N3 and N4 atoms, respectively. The charges of their closer H12 and H15 atoms are more positive than the H14 and H16 atom those are further from the ring nitrogens.

In this way these water molecules become polarized. The positions and the functions of the N3 and N4 atoms are on one side of the triazole ring; on the other side N1 atom it is different. Both the polar environment and the presence of three structural water molecules increase the negative charges of the N3 and N4 but in a different extent. On the contrary, the same effects make the charge of atom N1 less positive, here the solvent effect is the stronger one. These results are in line with those obtained for the water molecule.

4.3. Molecular energies and dipole moments

The *molecular energies* of the investigated structures are given in Tables 3A and 3B, for the 1STRZ and the 4STRZ tautomers, respectively. Besides, also the energy losses, the stabilization energies, are also shown as effect of the increasing polarity of the environment.

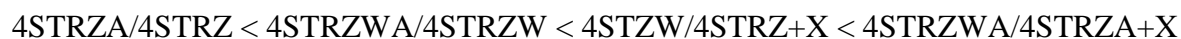
Regarding to the stabilization energies given for the two tautomers, one can conclude that aqueous solution increases the stability of STRZ compounds both in STRZA and in STRZWA molecular assemblies; while the stabilization energies determined for 1STRZ tautomer are lower than those for 4STRZ, the stabilization energies determined for 1STRZ are higher than those of 1STRZW. In case of the other tautomer this relation is the other way around.

Addition of three water molecules (X on tables 3A and 3B) stabilizes all studied structures.

The stabilization energies are listed in Table 3A for the 1STRZ tautomer (X=3H₂O). The order of the studied molecular assemblies based on the absolute values of their stabilization energies is as follows:



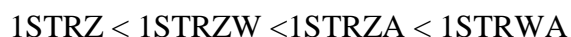
The corresponding data for the 4STRZ tautomer are given in Table 2B, their order is (absolute values):



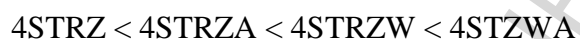
The latter order differs from the previous one. The reason of the deviation is the different structure. The water molecules, the sodium ion and the nitrogens of the triazole ring play substantially different roles in the two tautomers.

Similarly, the molecular *dipole moments* are presented in Tables 3A (1STRZ tautomer) and Table 3B (4STRZ tautomer). Analogously, the order of the molecular assemblies

containing the 1STRZ tautomer as derived from the absolute values of their stabilization energies is as follows:



While, the calculated dipole moments for the 4STRZ tautomer “series” show the order:



The difference in the two sequences consists of change of the orders of STRZW and STRZA dipole moments. The reason of this difference is similar: the different role of the water molecules, the sodium ion and the nitrogens of the triazole ring.

4.4. Tautomeric equilibrium

The equilibrium of the tautomers is presented in Fig. 2. The Gibbs free energy (G) of the studied molecule and its thermal correction are also results of the quantum chemical calculations. Based on these data we tried to calculate the tautomeric equilibrium constants (K), according to eq.(2).

$$\Delta G = RT \ln K \quad (2)$$

Where R is the gas constant (8.314 J/K/mol), the temperature (T) was chosen to be 25°C. We assumed that the equilibrium constant is the ratio of the activity of the 1-Na tautomer (a_1) and the same of the 4-Na tautomer (a_4):

$$K = \frac{a_1}{a_4} \quad (3)$$

The results are presented in Table 4. We follow the equilibrium data. All these results prove the shift of the equilibrium to the direction of the 1-Na tautomer, i.e. this molecular arrangement is more stable energetically than the 4-Na tautomer. However, the effects of the environments are remarkable. In case of the isolated molecules (1-Na-1,2,4-triazole and the same with 3H₂O molecules) the presence of the 1-Na tautomer is practically 100%. However, in case of the dissolved molecular arrangements of 1-Na-1,2,4-triazole, the 4-Na tautomer should be present in about 50%, and about 6% in the solution of the same completed with three water molecules.

These results show the strong effect of the solvent on the equilibrium, massive to the direction of the 1-Na tautomer, and the opposite string direction in case of molecular assemblies containing three structural water molecules.

With these molecular modeling calculations we could observe the different effects on the tautomeric equilibria.

4.5 Vibrational force constants

The vibrational force constant matrices are very spacious. Therefore only their diagonal elements are listed. For better understanding of the physical reason of the force constants also the definitions of the corresponding *internal coordinates* are given. While Tables 5A1 and 5B1 contain data sets for all vibrational modes, Tables 5A2 and 5B2 give them only for selected vibrational modes. Full sets of these data are listed in extended Tables S5A2 and S5B2, in the Supplement.

Table 5A1 refers to 1STRZ and 1STRZA. The solvent effect of caused changes in force constants belonging to all ring stretching coordinates. Essential changes are the increase of the N1-N2 force constant and the decreases of the C3-N4 and N4-C5. This is in harmony with the change of the NBO atomic charges Table 2A. The charges on N1 and N2 show large positive shifts. The N4 charge increases in negative direction, while the C3 and C5 charges change smaller in positive one. The presence of the water molecules causes tensions in the triazole ring reflected in the high diagonal force constant values of the ring stretching and deformation coordinate force constants, see Table 5A2, 1STRZW. The polar solvent decreases these tensions. Compare the data for 1STRZW and 1STRZWA.

The situation for the 4-Na tautomer is different, as already indicated before; while the solvent effect decreases the force constant values of C2-N3, N4-C5 and N3-N4 stretching coordinates, it increases those of N1-C2 and N1-C5 stretching coordinates (see Table 5B1).

This reflects the changes in the charges of the corresponding atomic net charges (Table 2B), the charges of N3 and N4 show negative shifts, while that of N1 shifts in positive direction. The addition of the water molecules, see Table 5B2 results moderated changes in ring the force constants in comparison with the case of the 1-Na tautomer. The aqueous solution brings these diagonal force constants near to the usual values of this type force constants.

4.6 Vibrational spectra

In this subsection the measured infrared and Raman spectra of 1-Na-1,2,4-triazole are presented. Besides, here one can also find all the calculated infrared and Raman spectra for comparison with the measured ones in order to evaluate the reliability of our elaborated model.

The vibrational spectra are more sensible to the dipole moment than the Raman spectra. Therefore the intensities of the infrared spectral bands are also sensitive to the local dipole moments of the internal coordinates participating in the vibrational modes (normal coordinates). Similarly, the applied polar environment has effect on the local dipole moments and, in this way, influences the band intensities. The structural water molecules as parts of the supermolecules have similar influences, and additionally their own spectral bands also appear. The spectra also reflect to the studied molecule – water molecule interactions like band shifts.

The choice of the normal frequencies of the pure sodium-1,2,4-triazole from the wet spectra of the compound is not an easy task. We measured the infrared spectra of a more and a less wet sample and recorded also its Raman spectrum. The high level associations in the wet samples act on the position of the fundamental bands of the dry compound, i.e. the band positions depend on the chemical environment in position, intensity and shape.

The quantum chemical calculations helped in the choice of the normal frequencies from the experimental spectra. We found, the supposed fundamental band positions belonging to the same normal mode are a little different in the recorded spectra. Our choice was the experimental frequency closest to the calculated ones. For the better assignment we used several models for both tautomers of the pure molecule, molecule in aqueous environment, molecule with three water molecules considering the hydrogen bonds and the same in aqueous environment. The calculated potential energy distributions give information about the frequency assignments and character of the individual vibrational modes (Tables 5, 6, 7 and 8).

Fig. 5 shows the infrared spectra of the hygroscopic compound at different humidity levels. The effect of increasing humidity content is well observable. In case of high humidity level the transmittance was close to 0 T% in some spectral regions. It caused difficulties, since we wished to compare the two spectra in absorbance. For this purpose the spectrum of wetter sample was off-set. The original spectrum is shown in transmittance in Fig. 6.

The recorded Raman spectrum of Na-1,2,4-triazole is presented in Fig. 7. Since there are some very intense bands in the spectrum, the most intense bands were resolved in subsets.

Fig. 8 introduces the aqueous solvent effect on the infrared spectra of both studied tautomers in the absence of structural water molecules.

While this effect is in general very small, one can predict a relatively large alteration for the OH stretching band by comparing the Raman spectrum of 1STRZ with that of 1STRZA.

Fig. 9 is the continuation of Fig. 8, it compares the spectra of supermolecules including 3 structural water molecules. A comparison between the spectra of 1STRZW and 1STRZWA indicate that the effect of aqueous solution on the OH stretching vibration of Na-1,2,4-triazole

molecule is very strong, and accordingly, one may predict a significant frequency shift in this relation. Nevertheless, a similar shift is not predicted as the corresponding spectra of the 4-Na tautomer are compared.

Fig. 10 compares the simulated infrared spectra of the four stable molecular structures (molecules/supramolecules) determined for the 1-Na tautomer. As can be seen from this figure, in the presence of the water molecules, the OH stretching bands are the most intense ones and dominate the spectra.

The simulated Raman spectra of the four stable molecular structures (molecules/supramolecules) determined for the 1-Na tautomer are presented in Fig. 11. If these spectra are compared with the corresponding simulated infrared spectra, it can be seen that the frequency shifts are similar, but the intensities predicted for the OH stretching bands in Raman are relatively smaller.

The corresponding spectra for the 4-Na tautomer are shown in Fig. 12. It has been predicted that the solvent effect causes some considerable band shifts in the spectra 4STRZ compared to those of 4STRZA. Differently, the shifts occurred between the OH stretching bands of 4STRZW and 4STRZWA due to the fact that solvent effects are not so large as these ones but the number of the observable bands is considerably lower than those determined for 4STRZ and 4STRZA.

The comparison of the measured infrared spectra (Fig. 5) and the simulated spectra (Fig. 8) show that the 1STRZW and the 1STRZWA absorption bands are similar in the position but not in their intensities. The model spectra reflect to the presence of the water molecules (1STRZW) and also the aqueous solution (1STRZWA). However, around the STRZ molecule more than three water molecules may be present (like in the model in [6]), the number of the OH groups is higher and thus the OH stretching bands are more intense, they are higher and broader.

4.7 Interpretation of the vibrational spectra

The results of the normal coordinate analyses are presented as potential energy distribution under the vibrational modes in Tables 6, 7, 8 and 9.

Table 6A gives insight in the characterization of the 1STRZ normal coordinates. Table 7A contains the same for 1STRA. The comparison of these two Tables shows different interpretations of the measured frequencies, first of all for the following ones located at 1378.6 cm^{-1} ($\nu_{\text{NC}+\beta\text{CH}}$), 1256.8 cm^{-1} ($\nu_{\text{NC}+\beta\text{rg}}$), 995.2 cm^{-1} ($\nu_{\text{NN}+\beta\text{rg}}$). The same experimental

wavenumbers were chosen in both cases and even the same scale factors (see Table 7A1). The results of calculations reflected to the effect of the aqueous solvent.

For complex molecules, the properties of the normal coordinates are given in Tables 8A, and 9A, where only the data of the normal vibrations at higher frequencies are included. On the other hand, the tables SA1, SA2, SB1 and SB2, which include the complete set of the normal vibrations of the same molecules, are presented in the supplementary section for the interested reader.

The presence of the structural water molecules causes interesting effects on the OH stretching vibrations, and these can be seen in Table 8A, where the results of the normal coordinate analysis performed for 1STRW are given.

The OH stretching frequencies of the water molecules show interesting distribution under the normal modes. The OH stretchings of the water molecule far from the sodium ion build independent vibrational modes (H15-O16 and O16-H17). These vibrational modes are characterized by the highest and lowest ν_{OH} frequencies, respectively. The OH stretchings of the two other water molecules far from the triazole ring are coupled (O10-H11 and O13-H14). and have very close frequencies to one another.

It seems the H9-O10 and H12-O13 stretchings disappeared. However, instead of them the N1-H12 and the N2-H9 stretchings dominate in the vibrational mode with 2510.1 cm^{-1} calculated frequency. According to the analysis some deformation modes participate with very low PED but altogether with about 50% participations. N-H interactions seem to be stronger in this normal mode than the missed O-H ones; those participate here with a negligible weight. There exists also another vibrational mode dominated by the stretching vibrations of N1-H12 and N2-H9 bonds; the measured and calculated wavenumbers for this mode 2275.5 and 2275.6 cm^{-1} , respectively.

The supermolecule is compact. Therefore the reasons of the domination of these two modes are the relatively short and consequently relatively strong N1-H12 and N2-H9 hydrogen bonds (consequences of associations). The long H9-O10 and H12-O13 distances are consequences of the mentioned relatively strong hydrogen bonds, electron effect of the nitrogen atoms (see Tables 1A and 2A).

When the vibrational modes of 1STRZWA in Table 9A are investigated, it is seen that the distributions of the OH stretching vibrations in these modes differ from those determined for 1STRZW.

The polar solvent field loosens the compact structure, and thus the N-H distances increase about 0.014 \AA . Instead of the N-H stretching bands, the H9-O10 and H13-O14 stretchings

appear. The stretching frequencies of all OH groups far from the triazole ring have frequencies close to each other. The alterations of those OH vibrations are remarkable which are close to the ring or in connection with it. That demonstrates the strong effect of the ring nitrogens. The ring effect is large on the O16-H15 stretching (more than 300 cm^{-1} shift to lower frequency).

Looking at the two other OH stretching frequencies, the H9-O10 and H13-O14 stretchings are coupled; their frequencies shift about 500 cm^{-1} in comparison of the bulk of the OH stretching bands.

The interpretation of the vibrational modes of the 4-Na tautomer models are shown in Tables 6B, 7B, 8B and 9B for 4STRZ, 4STRZA, 4STRZW and 4STRZWA, respectively.

If the experimental frequencies of the title compound are compared with the theoretical frequencies calculated for 4STRZ and 4STRZA, important differences are determined for the bands observed at 1396.3 , 1136.0 , 886.3 and 878.6 cm^{-1} . The first two ones contain ring stretchings (NC) in large amount and are sensitively reflecting the solvent effect. The two other modes may be affected by ring deformation.

The interpretation of the 4STRZW and 4STRZWA spectra is a nice example of the solvent effect. This is well-illustrated by the comparison of the distribution of the six OH stretchings. The OH stretchings in 4STRZW of the single water molecule close to the sodium ion are mixed in two vibrational modes. These ones have the lowest frequencies among the OH stretching vibrational modes. They are similarly coupled in the spectrum of 4STRZWA, however their frequencies are higher with respect to those of 4STRZW. The OH stretchings of the other two vibrational modes are present in STRZW partly in form of individual vibrational modes of stretchings H15-O16 and H17-O16, respectively, and partly as coupled modes of stretchings H12-O13 and H14-O15.

The situation changes with the appearance of the polar solvent. The OH stretchings close to the triazole ring are mixed to each other similarly. The last ones have the lower frequencies.

It has to be remarked that the asymmetric behavior of the H12-O13-H14 and H15-O16-H17 water molecules in the 4STRZW model is striking and although it can be traced from other quantum chemical results as well – it is the most striking exactly here. The geometry optimization resulted in with a bond length value of 1.857 \AA for the N4-H15 bond while a higher one (2.072 \AA) for the N3-H12, even though these two values were supposed to be nearly equal before.

5. Conclusions

The interpretation of vibrational spectra of a hygroscopic compound, namely sodium-1,2,4-triazolate raises problems since besides the uncertainty of the measurement due to undefined quantity of the humidity, a tautomeric equilibrium also may exist.

The effect of humidity was observed from one side by measuring infrared spectra of samples with different humidity content and then observing the shifts in locations and intensity changes of the OH stretching bands. On the other side four models were applied with increasing polarity effects for getting acquainted with the properties of the wet compound. Quantum chemical calculations were carried out for these simulations. These results proved the increasing environmental polarity shift on the molecular properties in the direction of the properties of a wet title molecule.

According to our results the equilibrium calculations proved the massive preference of the 1-Na tautomer. However, the polar solvent increases the presence of the 4-Na tautomer in comparison to those cases where the polar solvent was not considered.

Important interaction was evidenced between the water molecules and the Na-1,2,4-triazole molecule through increase of the dipole moments and the decrease of the molecular energies of the supermolecules in case of the Na-1,2,4-triazole molecule + 3H₂O system. The directions of the changes in the atomic net charges confirm the previous conclusions.

The interpretation of the vibrational spectra of the supermolecules serves with a deeper insight into the hydration effect of polar molecules.

The interpretation of the role of the different water interactions was successful on the properties of the Na⁺ - water – 1,2,4-triazole ion system and the suitability of the evolved model is clearly evidenced by the good agreement of the measured and calculated vibrational spectra.

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References

- [1] A. A. El-Azhary, H. U. Suter, J. Kubelka, *J. Phys. Chem. A*, 102 (1998) 620–629.
- [2] F. Billes, H. Endrédi, G. Keresztury, *J. Mol. Struct. - (Theochem)* 530 (2000) 183–200.

- [3] S- G. Aziz, S. A. Elroby, A. Alyoubi, O. I. Osman, & R. Hilal, *J Mol. Model.*, 20 (2014) 2078,1-15.
- [4] B. Wrzosek, J. Cukras and J. Bukowska, *J. Raman Spectrosc.* 43 (2012) 1010-1017.
- [5] I. Mohammed-Ziegler, F. Billes: The effect of aqueous medium on the vibrational spectra of 1,2,4-triazolylsodium, *Women Chemists and Innovation Conference, Keszthely, 19-22 October 2010* (<http://www.women-in-chemistry2010.mke.org.hu/scientific-programme>).
- [6] Jing-cai Yao, Xue-lan Mei, Kai Jiang, Yan-ge Li, Lu-fang Ma, *Inorg. Chem. Comm.* 12 (2009) 941–944.
- [7] J.J. Bernman: *Fungi (Part V.)*, pp. 181-212. In: J.J. Bernman: *Taxonomic Guide to Infectious Diseases: Understanding the Biologic Classes of Pathogenic Organisms*, 1st Ed., Academic Press, Amsterdam, New York, Tokyo, 2012.
- [8] *European Pharmacopoeia 8.0: Monograph for Voriconazole*, Council of Europe, Strasbourg, (2014) 3548-3550.
- [9] CIS-itraconazole crystalline forms and related processes, pharmaceutical compositions and methods, patent US 7078526 B2. and *European Pharmacopoeia 8.0: Monograph for Itraconazole*, Council of Europe, Strasbourg, (2014) 2548-2549.
- [10] Process for preparing monohydrate and crystal modifications of fluconazole, patent US 7094904 B2. and *European Pharmacopoeia 8.0: Monograph for Fluconazole*, Council of Europe, Strasbourg, (2014) 2245-2246.
- [11] M.A. Pfaller, S.A. Messer, P.R. Rhomberg, R.N. Jones, M. Castanheira, *J. Clin. Microbiol.*, 51(8) (2013) 2608-2616.
- [12] T. G. Ermakova, N. P. Kuznetsova, L. I. Volkova, and G. F. Myachina, *Russ. J. of Appl. Chem.*, 82 (2009) 488–491 and *Zhurnal Prikladnoi Khimii*, 82 (2009)494-497.
- [13] H. Grénman, T. Salmi, P. Mäki-Arvela, J. Wärnä, K. Eränen, *Org. Process Res. Dev.*, 7 (2003) 942–950.
- [14] <http://www.molbase.com>
- [15] M. Kazhemekaite, A Yuodvirsis, A. Vertarene, *Chem. Heterocyclic Comp.*, 34 (1998) 252-253.
- [16] Gaussian 09, Revision A.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima,

Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.

[17] A. D. Becke, *J. Chem. Phys.* 98 (1993) 5648–5652.

[18] A. E. Reed, R. B. Weinstock, F. J. Weinhold, *J. Chem. Phys.* 83 (1985) 735–746; A. E. Reed, F. J. Weinhold, L. A. Curtiss, *Chem. Rev.* 88 (1988) 899–926.

[19] Gaussian Technical Support, http://www.gaussian.com/g_tech/1.htm .

[20] F. Billes, unpublished result.

[21] M. Cossi, G. Scalmani, N. Rega and V. Barone, *J. Chem. Phys.*, 117 (2002) 43-54.

[22] G. Keresztury, S. Holly, G. Besenyi, J. Varga, A. Wang, J. R. Durig, *Spectrochim Acta Part A*, 49 (1993) 2007-2026.

Figures

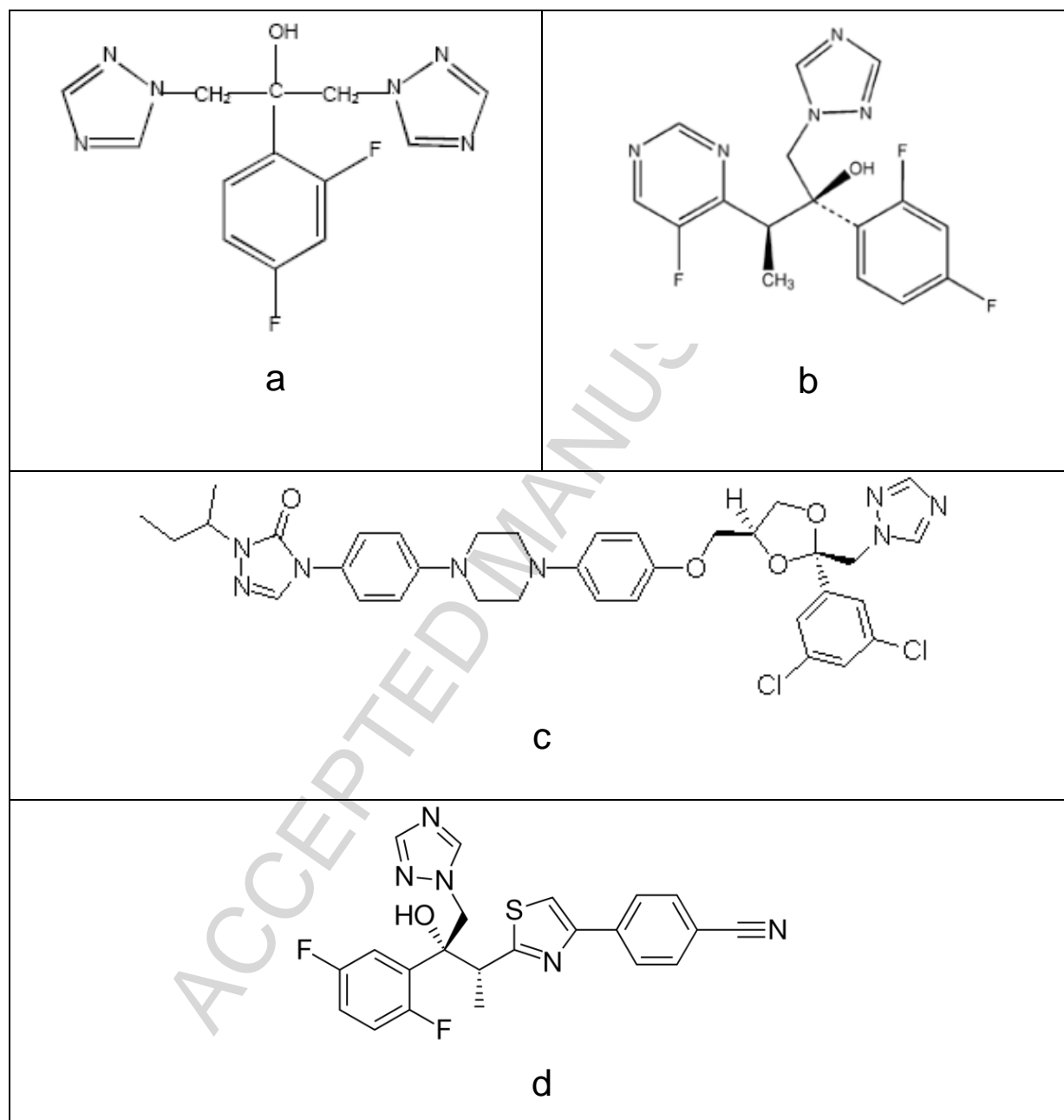


Fig. 1 Anti-Candida active pharmaceutical ingredients; a: diflucan, b: voriconazole, c: itraconazole, d: isavuconazole

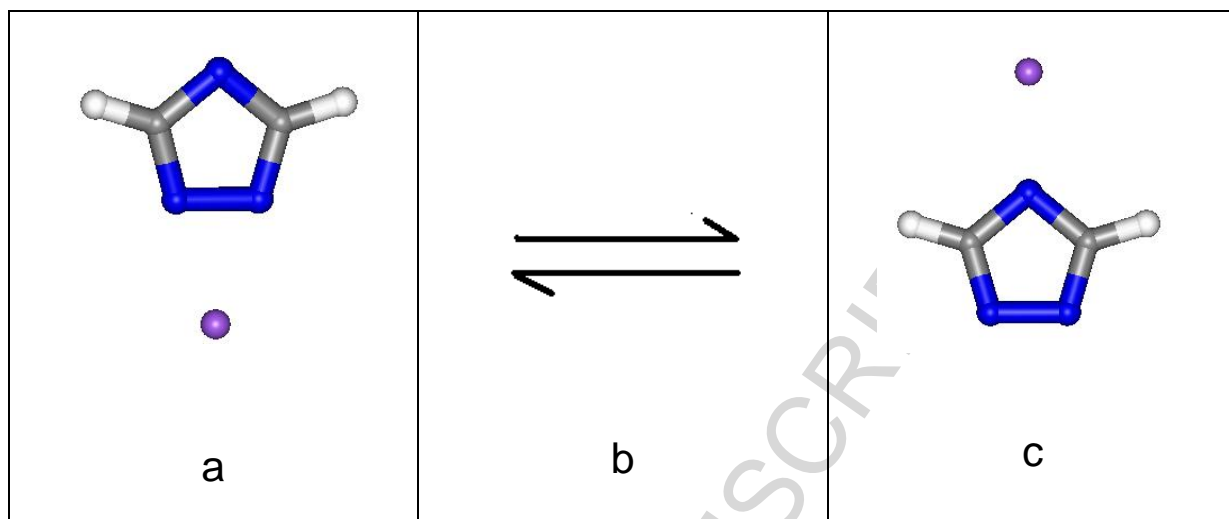


Fig. 2 Tautomeric equilibrium: a: 1STRZ, b: arrows, c: 4STRZ

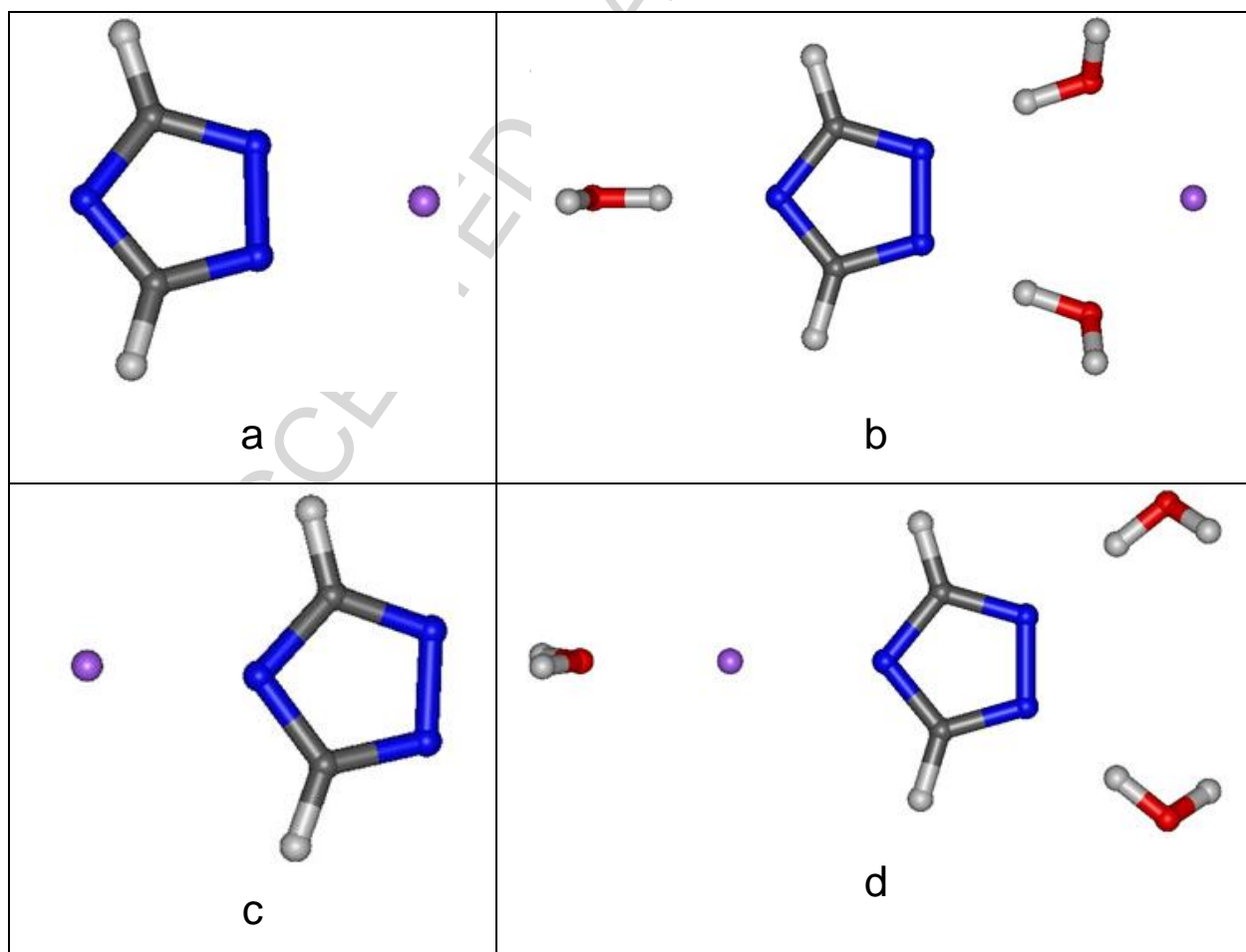


Fig. 3 Optimized molecular structures: a: 1STRZ/1STRZA, b: 1STRZW/1STRZWA
c: 4STRZ/4STRZA, d: 4STRZW/4STRZWA

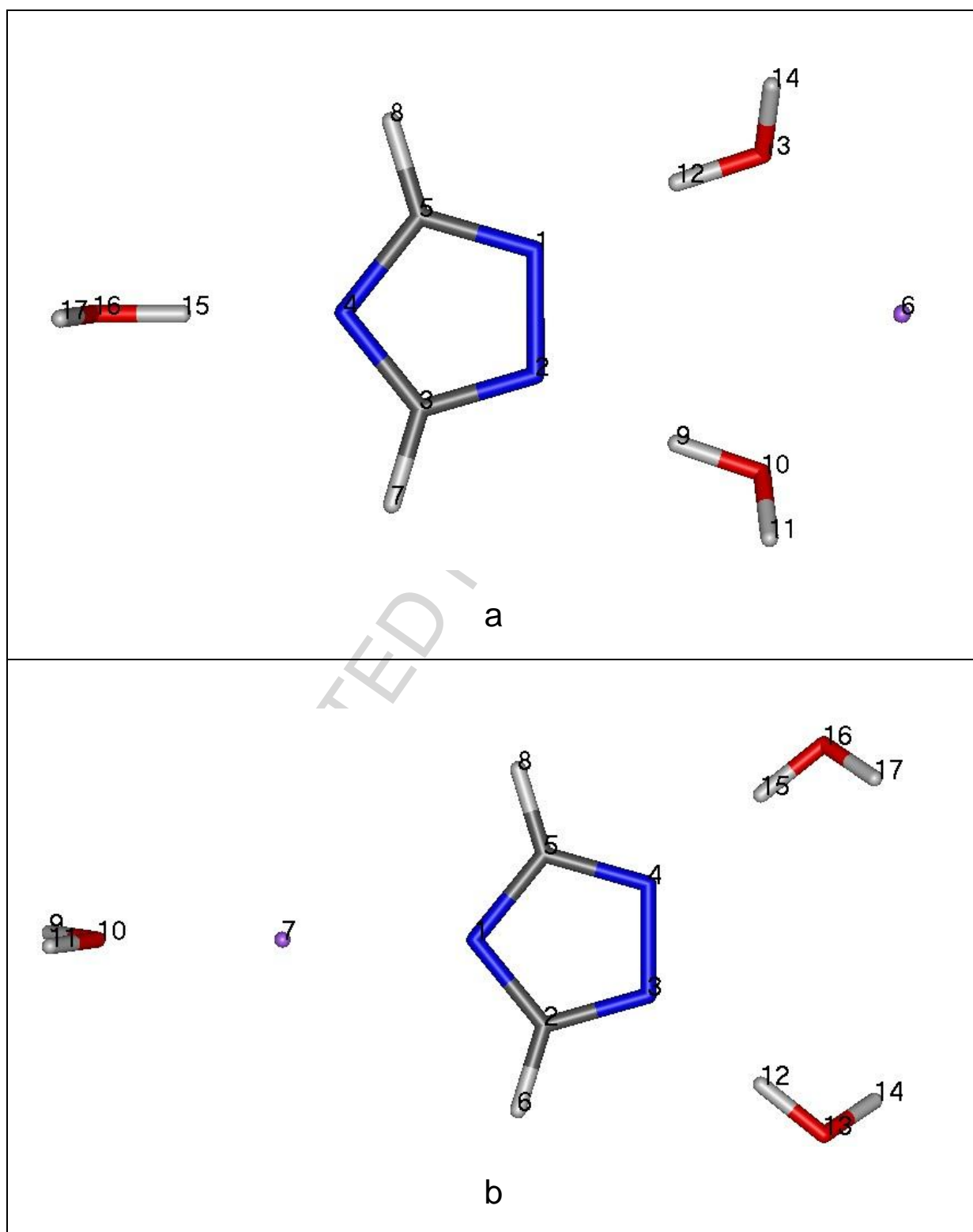


Fig. 4 a: Optimized structure of supermolecule 1-Na-1,2,4,-triazole with three water molecules;
b: optimized structure of supermolecule 4-Na-1,2,4-triazole with three water molecules.

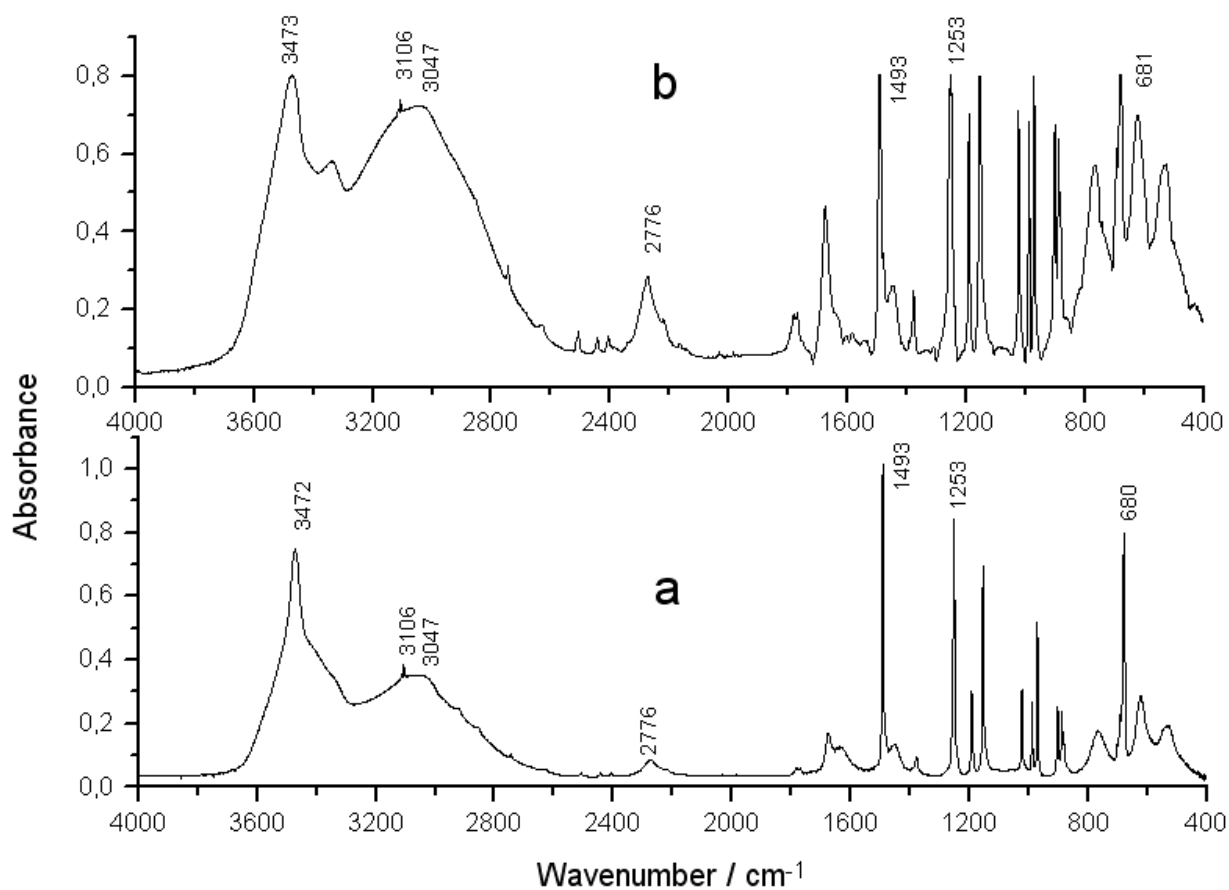


Fig. 5 Measured infrared spectra of wet 1-Na-1,2,4-triazolate: a: spectrum of less wet compound, b: spectrum of wetter compound

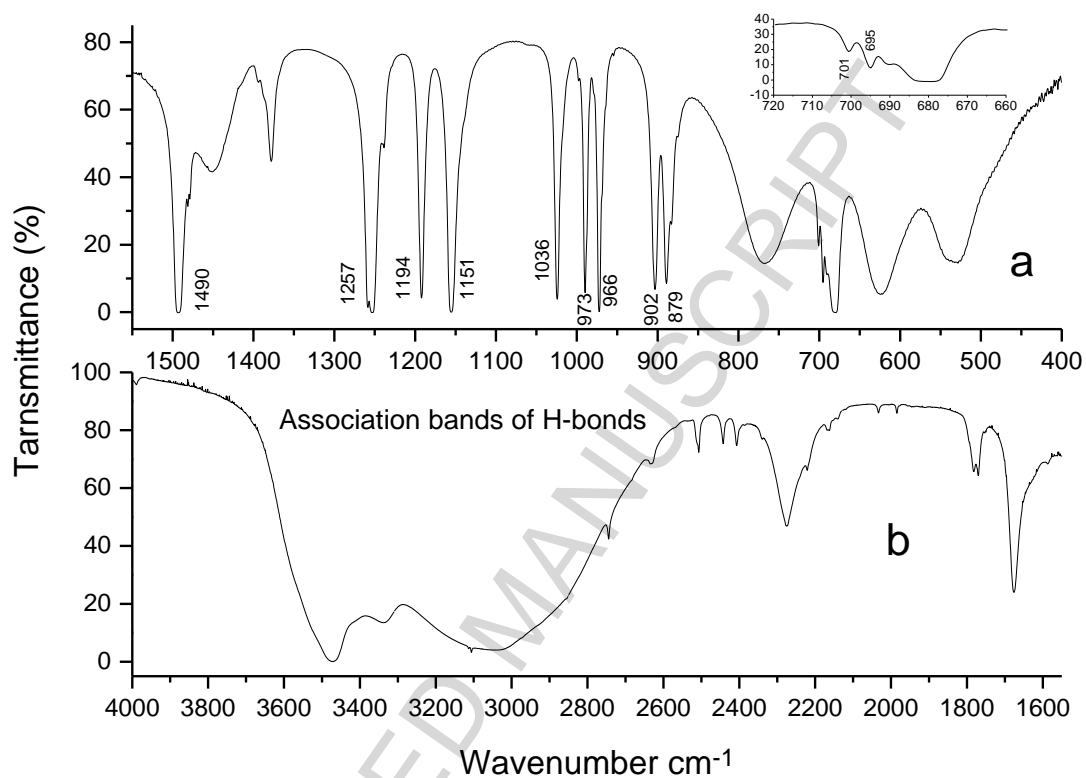


Fig. 6 Original infrared spectrum of more wet sodium-1,2,4-triazole, a: 1550-400 cm^{-1} , b: 4000-1550 cm^{-1} .

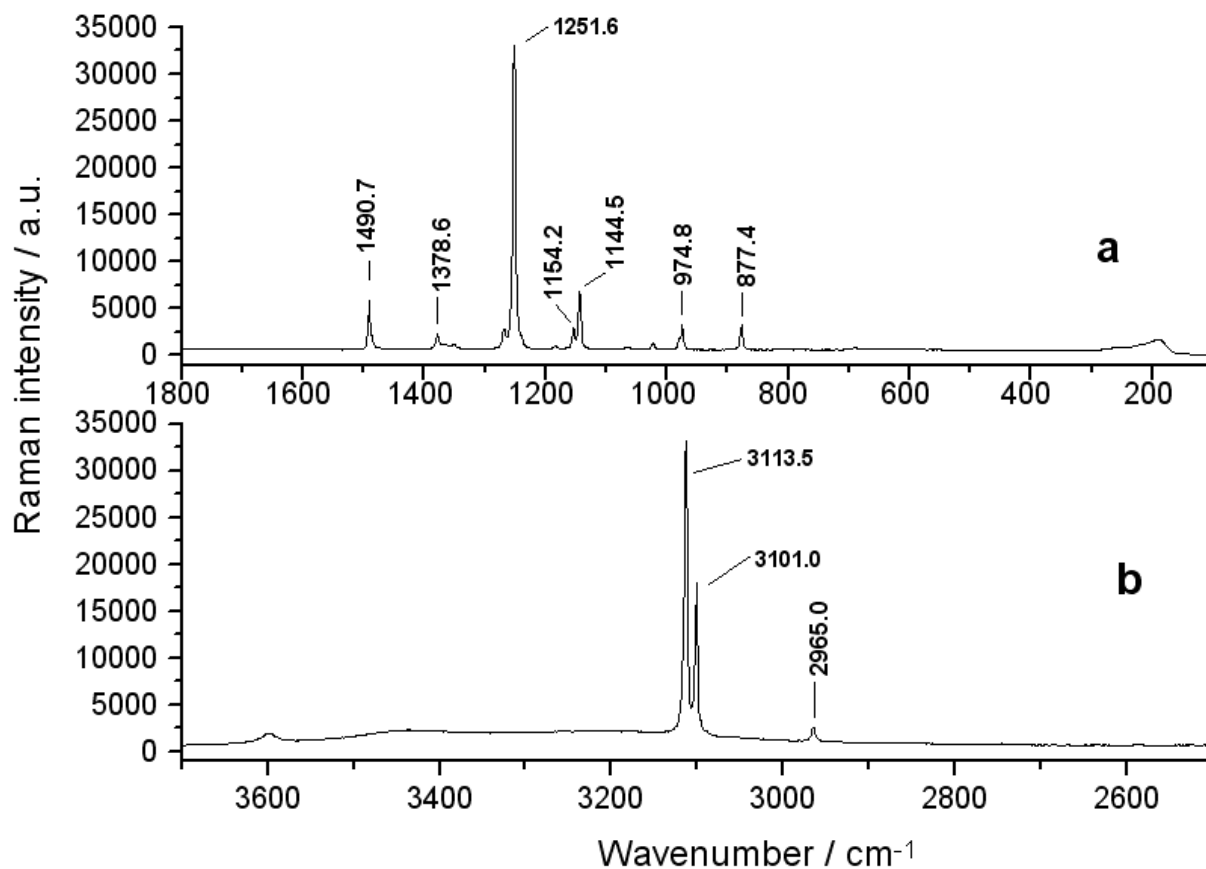


Fig. 7 Raman spectrum of sodium-1,2,4,-triazole, a: 1800-100 cm^{-1} , b: 3700-2500 cm^{-1} .

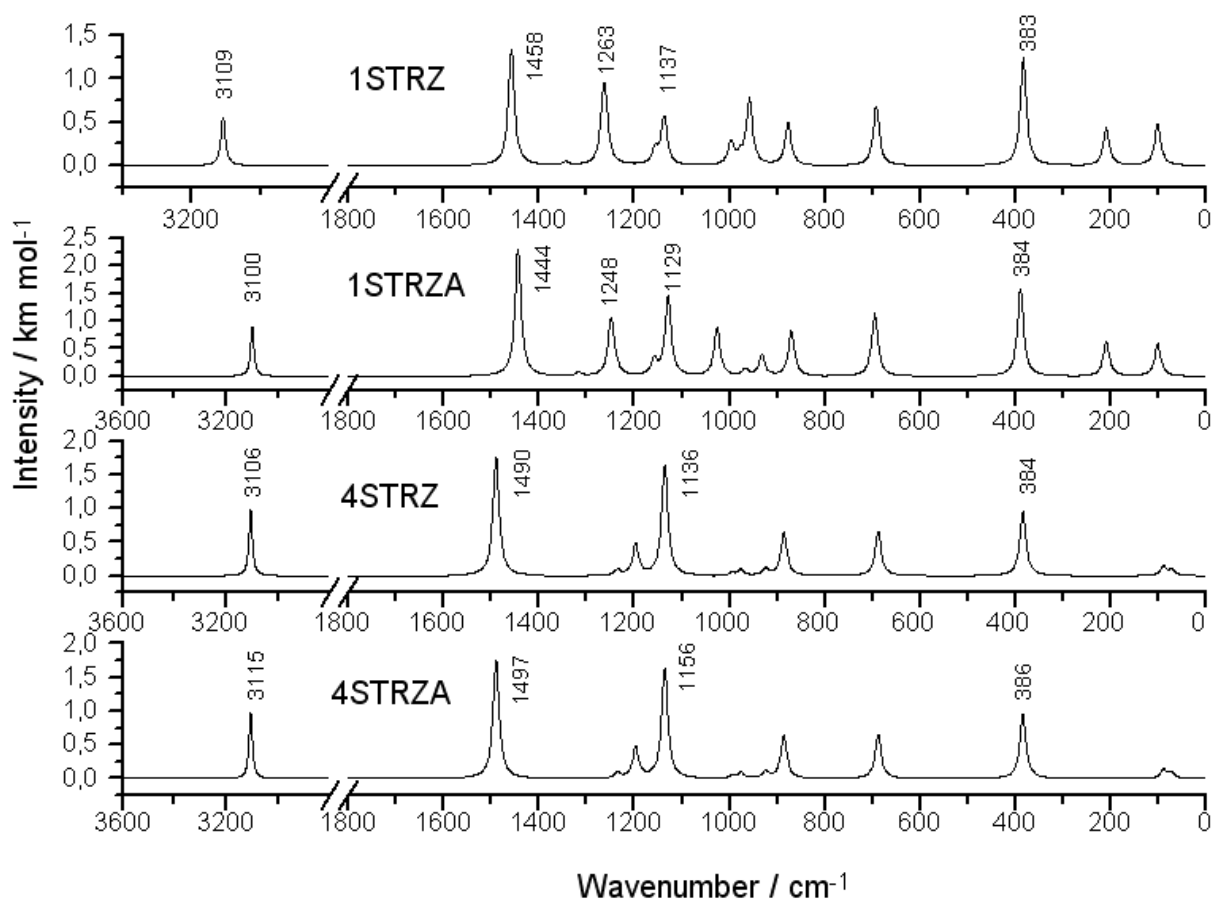


Fig. 8 Tautomerism and solvent effect on simulated infrared spectra of Na-1,2,4-triazoles 1.

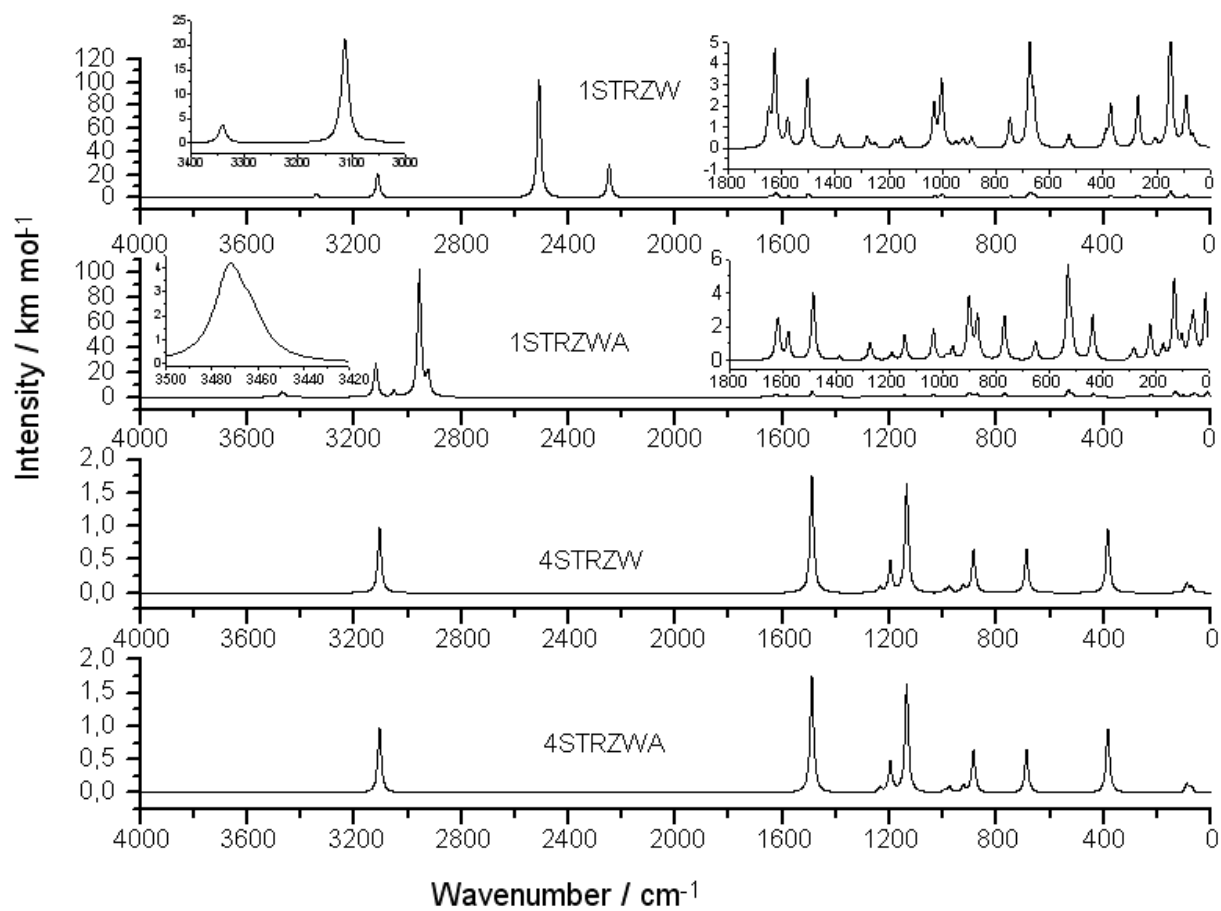


Fig. 9 Tautomerism and water solvent effect on simulated infrared spectra of Na-1,2,4-triazoles 2.

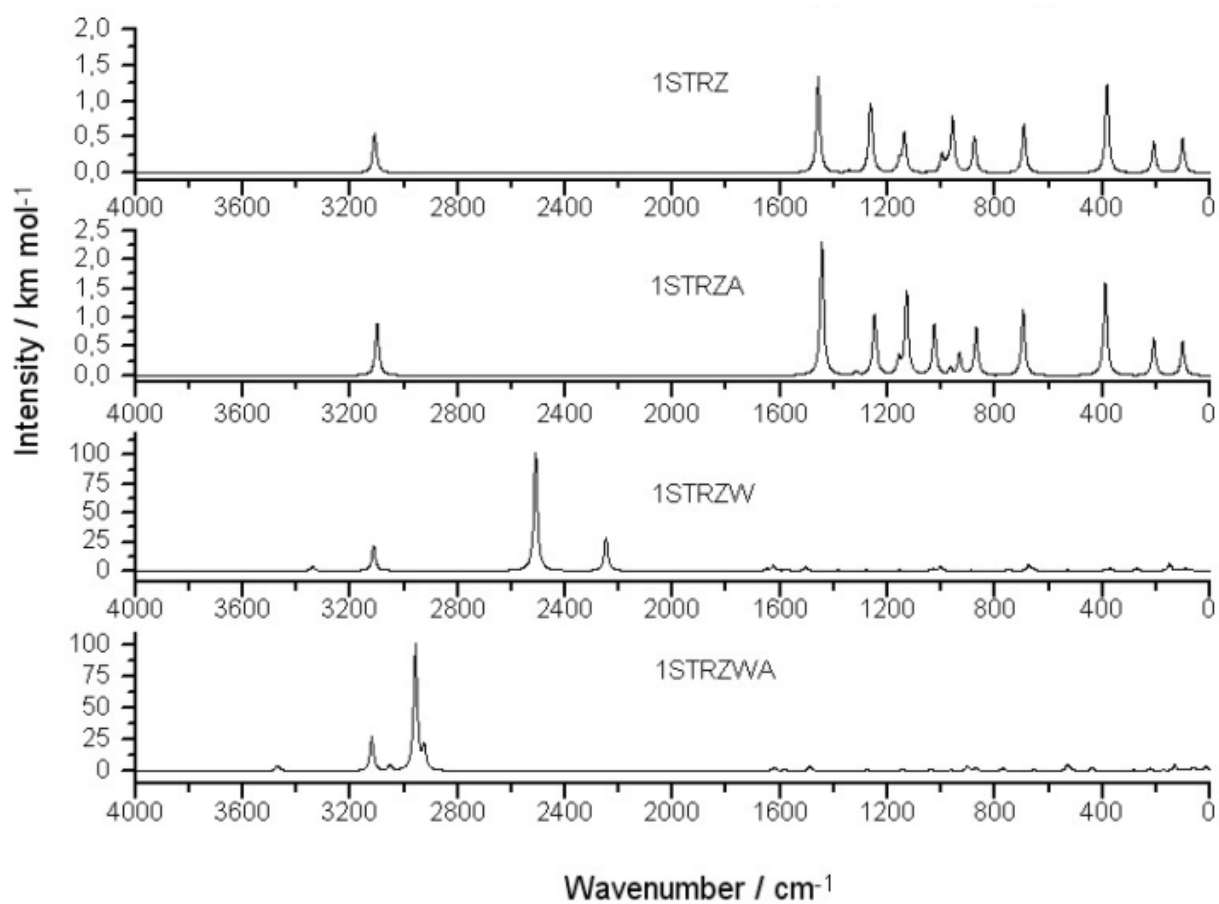


Fig. 10 Tautomerism and water molecule effect on simulated infrared spectra on 1-Na-1,2,4-triazole

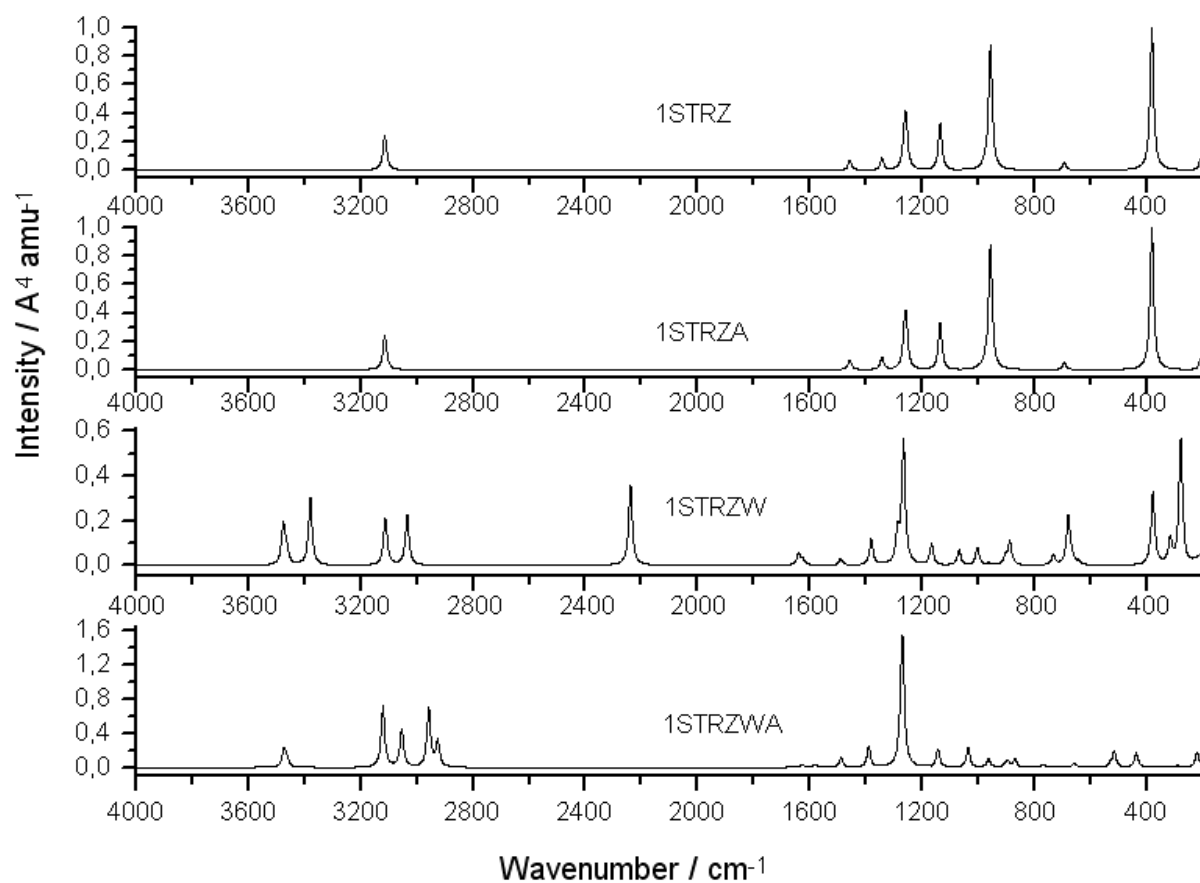


Fig. 11 Solvent effect on simulated Raman spectra of 1-Na-1,2,4-triazole

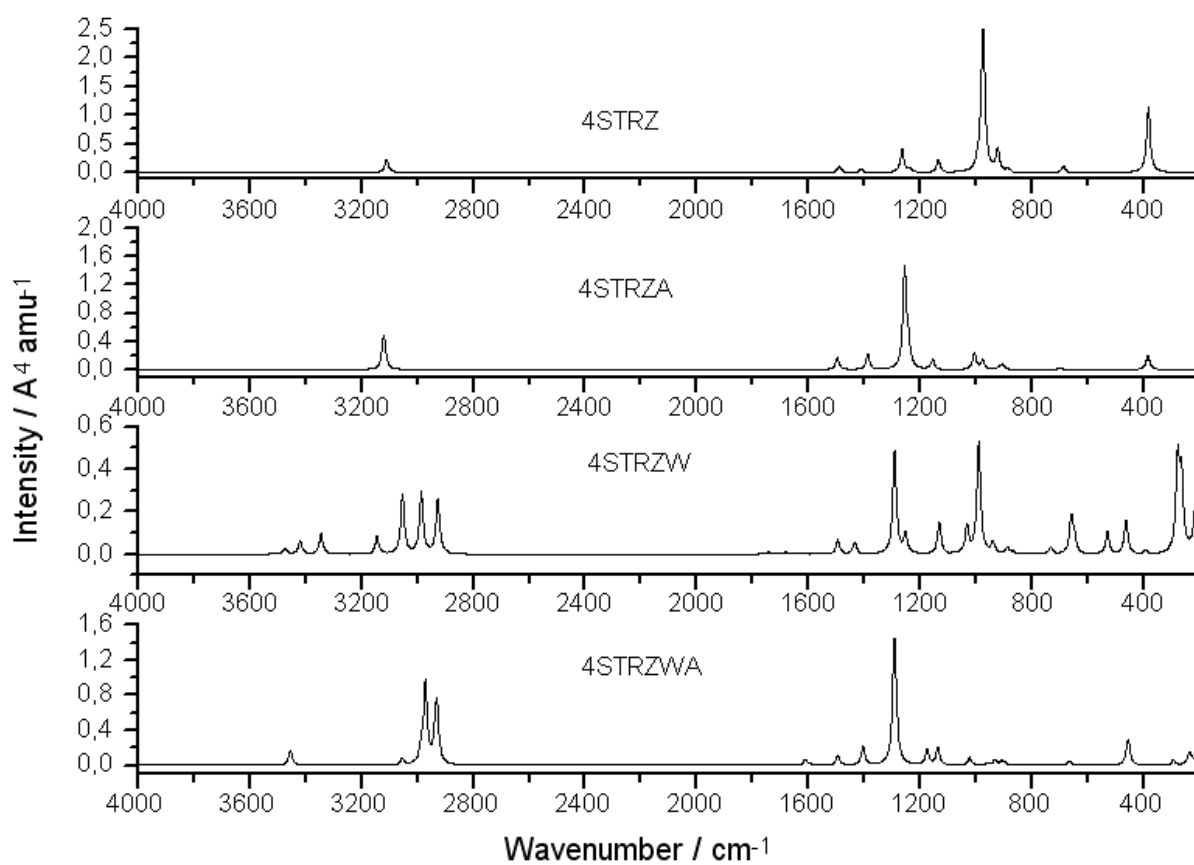


Fig. 12 Solvent effect on simulated Raman spectra of 4-Na-1,2,4-triazole

Tables

Table 1A				
Geometric parameters of 1-Na-1,2,4-triazole (selection) ^a				
Parameter ^{b,c}	1STRZ	1STRZA	1STRZW	1STRZWA
r(1,2)	1.394	1.381	<i>1.371</i>	<i>1.372</i>
r(1,5)	1.331	1.332	1.331	1.329
r(1,6)	2.206	2.414	3.473	4.154
r(2,3)	1.331	1.331	1.331	1.329
r(2,6)	2.206	2.413	3.473	4.154
r(3,4)	1.344	1.351	1.344	1.351
r(3,7)	1.081	1.082	1.080	1.080
r(4,5)	1.344	1.351	1.344	1.351
r(5,8)	1.081	1.082	1.080	1.080
φ(2,1,5)	105.1	105.4	105.7	105.9
φ(1,2,3)	105.1	105.4	105.7	105.9
φ(2,3,4)	114.0	113.9	113.3	113.2
φ(2,3,7)	122.4	122.5	122.9	123.0
φ(4,3,7)	123.6	123.6	123.8	123.9
φ(3,4,5)	101.9	101.4	102.1	101.9
φ(1,5,4)	114.0	113.9	113.3	113.2
φ(1,5,8)	122.4	122.5	122.9	123.0
φ(4,5,8)	123.6	123.6	123.8	123.9
r(1,12)			<i>1.594</i>	<i>1.739</i>
r(2,9)			<i>1.594</i>	<i>1.739</i>
r(4,15)			<i>1.907</i>	<i>1.807</i>
r(6,10)			<i>2.151</i>	<i>2.307</i>
r(6,13)			<i>2.151</i>	<i>2.306</i>
r(9,10)			<i>1.036</i>	<i>1.000</i>
r(10,11)			0.958	0.962
r(12,13)			1.036	1.000
r(15,16)			0.980	0.991
φ(2,1,12)			121.4	115.0
φ(5,1,12)			132.9	139.1
φ(1,2,9)			121.4	115.0
φ(3,2,9)			132.9	139.1
φ(10,6,13)			120.4	94.9
φ(6,10,9)			100.1	116.5
φ(6,10,11)			<i>151.3</i>	<i>129.1</i>
φ(6,13,12)			100.1	116.5
φ(6,13,14)			<i>151.3</i>	<i>129.4</i>

^aSee the full table in the Supplement as Table S1A.
^br: distances (angstroms); φ: in-plane angles (degrees);
bold numbers: large changes in distances, italics: large
numbers: large changes in distances; italics: large changes

in deformations;

for the numbering of atoms see Fig. 4.

^c1STRZ: isolated molecule, 1STRZA: in aqueous solution,

1STRZW: with three water molecules,

1STRZWA: the same in aqueous solution.

Table 1B

Geometric parameters of 4-Na-1,2,4-triazole (selection) ^a				
Parameter ^b	4STRZ ^c	4STRZA	4STRZW	4STRZWA
r (1,2)	1.366	1.355	1.363	1.352
r (1,5)	1.366	1.355	1.36	1.352
r (1,7)	2.167	2.367	2.209	2.382
r (2,3)	1.319	1.33	1.319	1.329
r (2,6)	1.082	1.082	1.081	1.081
r (3,4)	1.375	1.379	1.371	1.372
r (4,5)	1.319	1.33	1.321	1.329
r (5,8)	1.082	1.082	1.081	1.081
φ (2,1,5)	100.7	101.1	101.1	101.6
φ (2,1,7)	129.7	129.4	128.4	129.2
φ (5,1,7)	129.7	129.4	130.0	129.2
φ (1,2,3)	113.6	113.8	113.5	113.4
φ (1,2,6)	123.5	123.4	123.8	123.8
φ (3,2,6)	122.9	122.8	122.7	122.8
φ (2,3,4)	106.0	105.6	105.9	105.8
φ (3,4,5)	106.0	105.6	106.3	105.8
φ (1,5,4)	113.6	113.8	113.2	113.4
φ (1,5,8)	123.5	123.4	123.9	123.8
φ (4,5,8)	122.9	122.8	122.9	122.8
r (3,12)			2.071	1.792
r (4,15)			1.857	1.792
r (7,10)			2.286	2.329
r (9,10)			0.964	0.963
r (10,11)			0.963	0.963
r (12,13)			0.972	0.993
r (13,14)			0.969	0.962
r (15,16)			0.985	0.993
r (16,17)			0.961	0.962
φ (2,3,12)			142.5	132.2
φ (4,3,12)			108.4	122.0
φ (3,4,15)			113.1	122.1
φ (5,4,15)			139.6	132.1
φ (7,10,11)			129.2	127.6
φ (9,10,11)			105.6	105.5

φ (3,12,13)			160.9	105.2
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^aSee for the full table in the Supplement as Table S1B.
^br: distances (angstroms); φ : in-plane angles (degrees);
for the numbering of the atoms see Fig. 4.
^c4STRZ: isolated molecule, 4STRZA: molecule in aqueous solution (PCM), 4STRZW: molecule with three water molecules, 4STRZWA: 4STRZW in aqueous solution (PCM).

Atom ^b	1STRZ	1STRZA	1STRZW	1STRZWA ^c
N 1	-0.525	-0.481	-0.437	-0.443
N 2	-0.525	-0.481	-0.437	-0.443
C 3	0.162	0.130	0.188	0.167
N 4	-0.553	-0.629	-0.601	-0.646
C 5	0.162	0.130	0.188	0.167
Na 6	0.922	0.963	0.941	0.972
H 7	0.177	0.182	0.185	0.192
H 8	0.177	0.182	0.185	0.192
H 9			0.497	0.502
O 10			-1.069	-1.035
H 11			0.477	0.476
H 12			0.497	0.502
O 13			-1.069	-1.035
H 14			0.477	0.476
H 15			0.492	0.497
O 16			-0.964	-1.009
H 17			0.441	0.462

^aAtomic charge units.
^bFor the numbering of the atoms see Fig. 4.
^c1STRZ: isolated molecule, 1STRZA: molecule in aqueous solution (PCM);
1STRZW: molecule with three water molecules;
1STRZWA: like 1STRZW but in aqueous solution (PCM)

Atom ^b	4STRZ	4STRZA	4STRZW	4STRZWA ^c
N 1	-0.814	-0.699	-0.766	-0.668
C 2	0.122	0.124	0.148	0.157
N 3	-0.348	-0.445	-0.371	-0.445
N 4	-0.348	-0.445	-0.403	-0.445
C 5	0.122	0.124	0.156	0.157
H 6	0.163	0.180	0.172	0.189
Na 7	0.936	0.979	0.926	0.961
H 8	0.163	0.180	0.172	0.189
H 9			0.493	0.492
O 10			-0.973	-0.976
H 11			0.492	0.492
H 12			0.479	0.494
O 13			-0.979	-1.011
H 14			0.474	0.461
H 15			0.495	0.494
O 16			-0.973	-1.011
H 17			0.448	0.461

^aAtomic charge units.
^bFor the numbering of the atoms see Fig. 4.
^c4STRZ: isolated molecule, 4STRZA: molecule in aqueous solution (PCM);
4STRZW: molecule with three water molecules;
4STRZWA: like 4STRZW but in aqueous solution (PCM)

Form ^a	Molecular energy ^b	Dipole moment ^b
1STRZ	-404.0617878	9.316
1STRZA	-404.1175132	12.549
1STRZW	-633.5037922	11.898
1STRZWA	-633.5558471	18.331
X=3*H2O	-229.37559210	2.158e
Energy differences / kJ/mol		
1STRZA-1STRZ	-146.307	
1STRZW-1STRZ-X	-174.365	

1STRZWA-1STRZA-X	-164.729	
1STRZWA-1STRZW	-136.670	
<p>^a1STRZ: isolated molecule; 1STRZA: molecule in aqueous solution (PCM); 1STRZW: molecule with three water molecules; 1STRZWA: like 1STRZW but in aqueous solution (PCM).</p> <p>^bEnergy in Hartrees, dipole moments in Debyes.</p> <p>^cFor one water molecule.</p>		

Table 3B		
Calculated molecular energies and dipole moments of 4-Na-1,2,4-triazole		
Form ^a	Molecular energy ^b	Dipole moment ^b
4STRZ	-404.0345828	14.285
4STRZA	-404.1165547	18.745
4STRZW	-633.4713288	22.050
4STRZWA	-633.5452611	25.066
X=3*H ₂ O	-229.3755921	2.158 ^c
Energy differences / kJ/mol		
4STRZA-4STRZ	-215.217	
4STRZW-4STRZ-X	-160.560	
4STRZWA-4STRZA-X	-139.452	
4STRZWA-4STRZW	-194.109	
<p>^a4STRZ: isolated molecule; 4STRZA: molecule in aqueous solution (PCM); 4STRZW: molecule with three water molecules; 4STRZWA: like 4STRZW but in aqueous solution (PCM).</p> <p>^bEnergy in Hartrees, dipole moments in Debeys.</p> <p>^cFor one water molecule.</p>		

Table 4	
Calculated equilibrium constants ^a	
Equilibrium (ratio of activities)	Equilibrium constant
1STRZ/4STRZ	4.404E+10
1STRZA/4STRZA	0.9968

1STRZW/4STRZW	3.2809E+12
1SRZWA/4STRZWA	15.8352
^a Calculated with the consideration of the quantum chemically calculated Gibbs free energy and its thermal correction.	

Table 5A1
Definition of internal coordinates and their force constants
1STRZ

Serial number	Internal coordinate ^a	Scale factor	Diagonal force constant ^b	
			1STRZ	1STRZA
1	r (1,2)	1.021	4.783	5.075
2	r (2,3)	0.934	7.146	7.192
3	r (3,4)	0.934	6.715	6.502
4	r (4,5)	0.934	6.715	6.507
5	r (5,1)	0.934	7.143	7.094
6	r (1,6)	1.291	1.754	1.773
7	r (3,7)	0.934	5.306	5.272
8	r (5,8)	0.934	5.304	5.273
9	φ (6,2,1)	1.229	0.943	1.379
	$-\varphi$ (6,1,2)			
10	φ (4,7,3)	0.904	0.457	0.459
	$-\varphi$ (2,7,3)			
11	φ (1,8,5)	0.904	0.457	0.459
	$-\varphi$ (4,8,5)			
12	φ (2,5,1)	0.954	1.939	2.063
	-0.8φ (3,1,2)			
	$+0.3\varphi$ (4,2,3)			
	$+0.3\varphi$ (5,3,4)			
	-0.8φ (4,1,5)			
13	0.7φ (1,3,2)	0.954	1.880	1.930
	-1.1φ (2,4,3)			
	$+1.1\varphi$ (3,5,4)			
	-0.7φ (1,4,5)			
14	ϑ (6,2,5,1)	0.999	0.118	0.129
15	ϑ (7,2,4,3)	1.012	0.434	0.426
16	ϑ (8,1,4,5)	1.012	0.434	0.426
17	-0.8τ (1,2,3,4)	1.009	0.489	0.503
	$+\tau$ (2,3,4,5)			
	-0.8τ (3,4,5,1)			

18	+ 0.3 τ	(4,5,1,2)	1.009	0.467	0.478
	+ 0.3 τ	(5,1,2,3)			
	0.7 τ	(1,2,3,4)			
	+ 0.7 τ	(3,4,5,1)			
	-1.1 τ	(4,5,1,2)			
	+ 1.1 τ	(5,1,2,3)			

^ar: bond stretching, φ : in-plane deformation, ϑ : out-of-plane deformation, τ : torsion; for the numbering of the atoms see Fig. 4.

^bforce constants: units for stretching coordinates 10^8 N/m, for deformation coordinates 10^{-18} Nm. The most important changes are in bolds and in italics.

Table 5A2

Definition of internal coordinates and their force constants 1STRZW (selection)^a

Serial number	Internal coordinate ^b	STRZW		STRZWA	
		Scale factor	Diagonal force constant ^c	Scale factor	Diagonal force constant ^c
1	r (1,2)	0.897	2878.76	0.916	44.767
2	r (2,3)	0.935	628.781	0.972	17.743
3	r (3,4)	0.935	62.777	0.972	7.753
4	r (4,5)	0.935	983.181	0.972	22.742
5	r (5,1)	0.935	138.202	0.972	9.627
6	r (1,6)	0.901	2461.72	0.954	17.978
7	r (3,7)	0.897	5.131	0.894	5.096
8	r (5,8)	0.897	5.131	0.894	5.096
9	φ (4,7,3)	0.933	0.473	0.964	0.488
	$-\varphi$ (2,7,3)				
19	r (9,2)	0.912	1.509	0.935	1.891
20	φ (9,3,2)	0.900	7771.44	0.978	133.149
22	r (10,9)	0.783	34.008	0.92	9.132
23	r (10,6)	0.907	1149.52	0.871	16.31
24	φ (10,2,9)	0.900	1185.26	0.937	16.396
25	r (11,1)	0.727	6.237	0.804	6.741
26	φ (11,9,10)	0.912	0.473	0.937	0.54
28	r (12,1)	0.912	4.542	0.935	1.779
29	φ (12,6,1)	0.900	33701.5	0.978	124.401
31	r (13,12)	0.783	135.241	0.92	8.889
32	r (13,6)	0.907	1123732	0.871	15.145
33	φ (13,1,12)	0.900	5133.22	0.937	15.371
34	r (14,13)	0.727	6.237	0.804	6.742

35	φ (14,12,13)	0.912	0.473	0.937	0.54
37	r (15,4)	0.912	0.218	0.935	0.29
38	φ (15,5,4)	0.900	0.074	0.978	0.108
40	r (16,15)	0.795	5.808	0.92	6.178
41	φ (16,4,15)	0.900	0.071	0.937	0.101
43	r (17,16)	0.805	6.77	0.804	6.696

^aSee the full table in Supplement as Table S5A2.

^br: bond stretching, φ : in-plane deformation, for the numbering of atoms see Fig. 4.

^cForce constants: units for stretching coordinates 10^8 N/m, for deformation coordinates 10^{-18} Nm.

Serial number	Internal coordinate ^a	4STRZ		4STRZA	
		Scale factor	Diagonal force constant ^b	Scale factor	Diagonal force constant ^b
1	r (1,2)	0.964	6.319	0.964	6.611
2	r (2,3)	0.964	7.645	0.964	7.287
3	r (3,4)	0.916	4.711	0.916	4.664
4	r (4,5)	0.964	7.645	0.964	7.287
5	r (5,1)	0.964	6.319	0.964	6.611
6	r (2,6)	0.945	5.296	0.945	5.326
7	r (5,8)	0.945	5.296	0.945	5.326
8	φ (3,6,2)	1.013	0.514	1.013	0.515
	$-\varphi$ (1,6,2)				
9	φ (1,8,5)	1.013	0.514	1.013	0.515
	$-\varphi$ (4,8,5)				
10	φ (2,5,1)	0.902	1.826	0.902	1.805
	-0.8φ (3,1,2)				
	$+0.3\varphi$ (4,2,3)				
	$+0.3\varphi$ (5,3,4)				
	-0.8φ (4,1,5)				
11	0.7φ (1,3,2)	0.902	1.767	0.902	1.841
	-1.1φ (2,4,3)				
	$+1.1\varphi$ (3,5,4)				
	-0.7φ (1,4,5)				
12	ϑ (6,1,3,2)	1.131	0.434	1.131	0.468
13	ϑ (8,1,4,5)	1.131	0.434	1.131	0.468

14	-0.8τ (1,2,3,4) + τ (2,3,4,5) -0.8τ (3,4,5,1) + 0.3τ (4,5,1,2) + 0.3τ (5,1,2,3)	1.014	0.443	1.014	0.456
15	-0.7τ (1,2,3,4) + 0.7τ (3,4,5,1) -1.1τ (4,5,1,2) + 1.1τ (5,1,2,3)	1.014	0.504	1.014	0.512
16	r (1,7)	1.600	1.699	3.800	1.788
17	φ (7,5,1) $-\varphi$ (7,2,1)	1.300	0.064	1.300	0.051
18	ϑ (7,2,5,1)	1.224	0.049	1.224	0.061

^ar: bond stretching, φ : in-plane deformation, ϑ : out-of-plane deformation, τ : torsion;
for the numbering of the atoms see Fig. 4.

^bforce constants: units for stretching coordinates 10^8 N/m, for deformation coordinates 10^{-18} Nm.

Table 5B2

Definition of internal coordinates and values of their force constants (selection)^a

Serial number	Internal coordinate ^b	4STRZW		4STRZWA	
		Scale factor	Diagonal force constant ^b	Scale factor	Diagonal force constant ^c
1	r (1,2)	1.364	6.914	1.017	7.104
2	r (2,3)	1.017	8.203	1.017	7.799
3	r (3,4)	0.949	5.807	0.949	5.129
4	r (4,5)	1.017	8.133	1.017	7.799
5	r (5,1)	1.017	7.081	1.017	7.103
6	r (2,6)	0.827	4.680	0.827	4.701
7	r (5,8)	0.827	4.681	0.827	4.701
8	φ (3,6,2) $-\varphi$ (1,6,2)	0.915	0.467	0.915	0.465
9	φ (1,8,5) $-\varphi$ (4,8,5)	0.915	0.465	0.915	0.465
16	r (1,7)	0.398	0.361	0.398	0.173
17	φ (7,5,1) $-\varphi$ (7,2,1)	0.853	0.051	0.853	0.066
19	r (10,7)	0.764	0.328	0.764	0.271

20	ϕ	(10,1,7)	3.950	0.048	3.950	0.851
22	r	(9,1)	0.614	5.097	0.614	5.103
23	ϕ	(9,7,10)	0.964	0.725	0.964	0.679
25	r	(11,1)	0.614	5.109	0.614	5.107
26	ϕ	(11,7,10)	0.964	0.72	0.964	0.674
28	r	(12,3)	1.230	0,247	1,23	0,393
29	ϕ	(12,2,3)	1,28	1,171	1,280	0,151
31	r	(13,12)	0.862	6.741	0.862	5.705
32	ϕ	(13,3,12)	0.964	0.237	0.964	0.108
34	r	(14,13)	0.801	6.274	0.801	6.668
35	ϕ	(14,12,13)	0.964	0.774	0.964	0.547
37	r	(15,4)	1.230	0.382	1.230	0.392
38	ϕ	(15,5,4)	1.180	1.032	1.280	0.130
40	r	(16,15)	0.862	230	0.862	5.703
41	ϕ	(16,4,15)	0.964	0.216	0.964	0.108
43	r	(17,16)	0.801	6.733	0.801	6.668
44	ϕ	(17,15,16)	0.964	0.574	0.964	0.547

^aSee the full table in Supplement as Table 5SB2.

^br: bond stretching, ϕ : in-plane deformation, for the numbering of atoms see Fig. 4.

^cforce constants: units for stretching coordinates 10^8 N/m, for deformation coordinates 10^{-18} Nm.

Frequencies /cm ⁻¹		PED(type,%) ^{a,b}			
Measured	Calculated				
3115.0	3113.8	v CH	99		
3105.5	3109.5	v CH	99		
1490.2	1457.7	v NC	64	β CH	33
1378.6	1343.8	v NC	66	β CH	28
1256.8	1263.6	v NC	82	β rg	10
1251.6	1258.1	v NC	80		
1150.5	1156.5	v NC	37	β CH	60
1136.0	1136.8	v NN	13	v NC	42
995.2	997.1	v NN	70	β rg	20
973.7	978.4	β rg	83		
966.3	958.1	v NN	13	β rg	70
886.3	882.3	γ CH	96		
878.6	876.8	γ CH	96		
698.5	694.7	γ rg	96		

691.6	691.8	γ rg	96	
384.7	383.5	ν NNa	93	
209.2	209.2	β NNa	93	
101.3	101.3	γ NNa	99	

^aData less than 10% were omitted.

^b ν : stretching; β : in-plane deformation; γ : out-of-plane deformation; rg: ring.

Table 6B

Potential energy distributions under the normal coordinates of 4STRZ

Frequencies /cm ⁻¹		PED(type,%) ^{a,b}	
Measured	Calculated		
3115.0	3110.0	ν CH	99
3105.0	3105.8	ν CH	99
1490.2	1489.9	ν NC	48 β CH 48
1396.3	1412.8	ν NC	68 β CH 29
1256.8	1264.5	ν NC	85
1251.6	1235.5	ν NC	33 β CH 61
1193.9	1196.9	ν NC	88
1136.0	1135.5	ν NC	56 β CH 36
995.2	995.2	ν NN	35 β rg 56
973.7	975.9	ν NN	59 β rg 29
901.2	923.8	β rg	88
886.3	885.5	γ CH	94
878.6	852.6	γ CH	94
698.5	698.6	τ rg	94
691.6	688.3	τ rg	92
384.7	383.8	ν NNa	83
77.8	88.7	β NNa	99
64.9	71.5	γ NNa	99

^aData less than 10% were omitted.

^b ν : stretching; β : in-plane deformation; γ : out-of-plane deformation; rg: ring.

Frequencies /cm ⁻¹		PED(type,%) ^{a,b}			
Measured	Calculated				
3115.0	3104.9	v CH	99		
3105.5	3099.7	v CH	99		
1490.2	1444.0	v NC	58	β CH	39
1378.6	1317.4	v NC	60	β CH	35
1256.8	1249.3	v NC	77	β CH	10
1251.6	1243.0	v NC	81	β rg	11
1150.5	1158.4	v NC	47	β CH	50
1136.0	1128.6	v NN	20	v NC	48 β CH 28
995.2	1025.6	v NN	69	β CH	16
973.7	967.4	β rg	82		
966.3	932.0	β rg	84		
886.3	870.5	γ CH	97		
878.6	867.5	γ CH	95		
698.5	698.2	γ rg	97		
691.6	694.7	γ rg	94		
384.7	389.1	v NNa	75	β NNa	17
209.2	209.2	v NNa	15	β NNa	78
101.3	101.3	γ NNa	97		

^aData less than 10% were omitted.
^bv: stretching; β: in-plane deformation; γ: out-of-plane deformation;
rg: ring.

Frequencies /cm ⁻¹		PED(type,%) ^{a,b}			
Measured	Calculated				
3115.0	3120.4	v CH	99		
3105.5	3115.2	v CH	99		
1490.2	1496.7	v NC	48	β CH	47
1396.3	1387.8	v NC	52	β CH	44
1256.8	1256.1	v NC	90		
1251.6	1242.7	v NC	82		
1193.9	1204.4	v NC	55	β CH	43
1136.0	1155.7	v NC	50	β CH	41

995.2	1007.3	v NN	13	β rg	76
973.7	978.3	v NN	80	β rg	10
901.2	938.1	β rg	90		
886.3	916.8	γ CH	94		
878.6	905.3	γ CH	95		
698.5	703.2	τ rg	95		
691.6	694.4	τ rg	93		
384.7	386.3	v NNa	81	β rg	11
77.8	77.0	γ NNa	96		
64.9	76.7	β NNa	97		

^aData less than 10% were omitted.

^bv: stretching; β: in-plane deformation;
^cγ: out-of-plane deformation; rg: ring.

Frequencies /cm ⁻¹		PED(type,%) ^{b,c,d}							
Measured	Calculated								
3488.8	3482.6	v OHb	98	O16–H17					
3340.2	3340.1	v OHa	98	O10–H11&O13–H14					
3440.2	3340.5	v OHa	95	O10–H11&O13–H14					
3113.5	3112.9	v OHd	95	O15–H16					
3060.8	3063.5	v CH	94						
3060.8	3059.7	v CH	95						
2506.7	2510.1 ^d	β NH	50						
137119	2247.7 ^d	β NH	51						
1641.5	1648.5	β NOH	47						
1626.4	1625.2	β OH	10	β NOH	45				
1586.6	1576.8	β OH	85	β NOH	12				
1492.6	1502.7	v NC	47						
1381.0	1384.6	v NC	21	β rg	22				
1259.5	1280.0	v NC	28	β NH	26				
1253.1	1253.2	v NC	56	β rg	10				
1192.2	1178.8	v NC	16	β CH	12	β rg	14	β NH	14
1155.3	1155.1	v NC	20	β CH	10	β NaN	25		
1024.2	1031.2	β NH	52	β NaN	12				
989.7	1003.1	β rg	40						
972.4	948.7	β NOH	26	v NaN	11				
903.2	941.4	v OHc	11	β NOH	24	v NaO	11		

889.1	922.6	β NaN	26		
882.5	870.1	β NOH	12	β NaN	23
882.5	890.8	γ CH	58		
769.2	747.8	β NH	17	τ OHb	80
680.4	674.6	β NH	49		
624.4	658.5	β NH	50	β OH	10
528.5	535.7	τ rg	54		
528.5	528.2	τ rg	87		

^aSee the full table in the Supplement as Table S8A.

^bData less than 10% were omitted.

^cv: stretching; β : in-plane deformation; γ : out-of-plane deformation; τ : torsion; rg: ring.

^dFor numbering of the atoms see Fig. 4.

^dThe relatively short distances of N(1)-H(12) and N(2)-H(9) have strong influence on these frequency and PED element data, see Tab1A.

Table 8B					
Potential energy distributions under normal coordinates of 4STRZW (higher frequencies) ^a					
Frequencies /cm ⁻¹		PED(type,%) ^{b,c,d}			
Measured	Calculated				
3472.2	3473.2	ν OH	98	O16-H17	
3408.8	3418.5	ν OH	99	O13-H12(88)&O13-H14(11)	
3378.6	3344.3	ν OH	99	O13-H12(11)&O13-H14(88)	
3106.2	3144.4	ν OH	99	H15-O16	
3050.8	3053.0	ν OH	99	O10-H9(47)&O10-H11(52)	
2973.5	2985.9	ν OH	99	O10-H9(52)&O10-H11(47)	
2921.3	2921.9	ν CH	99		
2921.3	2926.7	ν CH	99		
1770.6	1743.6	β OH	73	τ OH	25
1676.6	1681.8	β OH	94		
1626.4	1627.1	β OH	99		
1492.6	1495.3	ν NC	66	β CH	31
1450.7	1435.4	ν NC	84	β CH	13
1259.5	1292.5	ν NC	84	β CH	10
1253.1	1253.4	ν NC	88		
1192.2	1192.3	ν NC	20	β CH	78
1155.3	1133.2	ν NN	12	ν NC	43
1024.2	1033.0	ν NN	69	β CH	12
989.7	991.2	τ OH	75		
972.4	942.8	β rg	79		

903.2	937.2	β rg	83			
889.1	888.4	γ CH	84			
882.5	864.9	γ CH	91			
882.5	869.8	β NaH	14	β OH	49	τ OH 20
769.2	734.5	τ OH	73			
680.4	659.7	τ rg	91			
624.4	649.3	τ rg	88			
528.5	530.7	β OH	37	τ OH	47	
475.6	464.1	β NaH	15	β OH	59	τ OH 10

^aSee the full table in the Supplement as Table S8B.

^bData less than 10% were omitted.

^cv: stretching; β : in-plane deformation; γ : out-of-plane deformation; τ : torsion; rg: ring.

^dFor numbering of the atoms see Fig. 4.

Potential energy distributions under normal coordinates of 1STRZWA (higher frequencies) ^a						
Frequencies /cm ⁻¹			PED(type,%) ^{b,c,d}			
Measured	Calculated					
3472.2	3472.4	v OHa	98	O10-H11		
3472.2	3479.4	v OHa	98	O13-H14		
3472.2	3463.2	v OHa	98	O16-H17		
3106.2	3120.3	v OHb	93	O16-H15		
3050.8	3053.8	v CH	97			
3050.8	3049.7	v CH	99			
2973.5	2956.6	v OHb	93	O10-H9&O13-H12		
2921.3	2925.3	v OHb	93			
1641.5	1628.4	β NH	38	β OH	54	
1626.4	1620.0	β NH	37	β OH	53	
1626.4	1583.0	β OH	98	□		
1492.6	1489.4	v NC	57	β CH	40	
1381	1391.2	v NC	55	β CH	25	
1259.5	1276.4	v NC	69	β NH	13	
1253.1	1270.1	v NC	80			
1192.2	1193.5	v NC	36	β CH	50	
1155.3	1144.6	v NC	50	β CH	36	
1024.2	1037.3	v NN	18	β NH	46	β NaN 10
989.7	988.3	β rg	76			
972.4	964.9	v NN	19	β rg	67	

903.2	903.5	γ CH	88		
889.1	896.0	γ CH	82		
882.5	867.5	β NH	48		
882.5	872.2	β NH	54		
769.2	770.2	β NH	16	τ OH	81
680.4	659.7	τ rg	91		
624.4	652.6	τ rg	93		
528.5	516.5	β OH	52		
528.5	531.0	β OH	54		
475.6	438.3	β OH	92		

^aSee the full table in the Supplement as Table S9A.

^bData less than 10% were omitted.

^c ν : stretching; β : in-plane deformation; γ : out-of-plane deformation; τ : torsion; rg: ring.

^dFor numbering of the atoms see Fig. 4.

Table 9B
Potential energy distributions under normal coordinates of 4STRZWA (higher frequencies)^a

Frequencies /cm ⁻¹		PED(type,%) ^{b,c,d}			
Measured	Calculated				
3472.2	3454.7	ν OH	99	O13–H14(38)&O16–H17(61)	
3472.2	3454.4	ν OH	99	O13–H14(61)&O16–H17(38)	
3050.8	3054.4	ν OH	99	O10–H9(50)&O10–H11(49)	
2973.5	2986.3	ν OH	99	O10–H9(49)&O10–H11(50)	
2973.5	2970.6	ν OH	95	O13–H12(50)&O16–H15(45)	
2921.3	2933.7	ν CH	96		
2921.3	2928.6	ν CH	93		
2921.3	2943.5	ν OH	94	O13–H12(45)&O16–H15(49)	
1626.4	1597.1	β OH	99		
1626.4	1613.9	β OH	97		
1626.4	1611.5	β OH	98		
1492.6	1495.1	ν NC	66	β CH	31
1396.3	1404.7	ν NC	76	β CH	18
1268.7	1293.4	ν NC	80		
1253.1	1286.9	ν NC	86		
1192.2	1195.9	ν NC	17	β CH	57
1187.7	1175.5	ν NN	11	ν NC	19
1155.3	1134.3	ν NC	27	β CH	42
1155.3	1138.3	ν NC	12	β CH	16
				τ OH	20
				τ OH	54
				τ OH	21
				τ OH	63

1017.0	1024.4	ν NN	71	β CH	11	
972.4	932.8	β rg	86			
972.4	960.1	β rg	87			
901.7	910.7	γ CH	93			
901.7	900.1	γ CH	95			
680.4	665.6	τ rg	94			
680.4	661.9	τ rg	90			
475.6	459.8	β OH	91			
475.6	454.9	β OH	90			

^aSee the full table in the Supplement as Table S9A.

^bData less than 10% were omitted.

^c ν : stretching; β : in-plane deformation; γ : out-of-plane deformation; τ : torsion; rg: ring.

^dFor numbering of the atoms see Fig. 4.

Highlights

- Tautomerism and solvent effect of Na-1,2,4-triazole
- Evaluation of the calculated properties: net charges, molecular energies
- Calculation of force constants and potential energy distributions
- Evaluation of the measured and simulated infrared and Raman spectra

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