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Vibrational spectra and normal coordinate analysis of isoniazid

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Abstract : Isoniazid is a isonicotinc acid hydrazide and its molecular formula is $C_6H_7N_3O$. It is an antimycobacterial drug and regarded as the most effective agent in the treatment of tuberculosis disease. Also, it is a commonly used medication for Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS) patients. In the present investigation, a normal coordinate analysis has been carried out for the molecule of the title compound using fundamental vibrations observed in FTIR and laser Raman spectra on the basis of C_s point group symmetry using Wilson's F-G matrix method. The orthonormal symmetry coordinates have been constructed and a systematic set of potential constants have been computed. The vibrational modes are classified into A' and A'' irreducible representations. The 45 fundamental modes of vibration of isoniazid are distributed to these symmetry species as $\Gamma_{vib} = 31\ A' + 14\ A''$. In the present investigation, only 25 normal modes of vibration are considered such as 15 A' vibrations and 10 A'' vibrations.

1. Introduction

An extensive work has been carried out by several investigators on the title compound in the recent past [1–4]. Recently, normal coordinate analysis was carried out by Nakkeeran [1] by considering NH_2 as a point mass. The FTIR and laser Raman spectra of isoniazid and its related compounds have been investigated [2] and vibrational assignments were made. Krishnakumar et al [3] have made a spectral and normal coordinate analysis of 2,4-dinitrophenyl hydrazine in analogy with the molecule of the title compound. Recently, frequency assignments have been made [4] on pharmaceutical active compounds like isokin, pyraldin and rifampin using FTIR and laser Raman spectroscopic measurements and the results obtained were briefly discussed. The present investigation has been undertaken to provide a satisfactory vibrational analysis of isoniazid through FTIR and laser Raman spectroscopy by taking NH_2 group vibrations individually. To check whether the chosen set of vibrational frequencies contribute maximum to the potential energy associated with the normal coordinates of the molecule, the potential energy distribution have been evaluated.

2. Experimental

The pure samples of isoniazid in solid phase were procured from SISCO-CHEM industries, Mumbai. The FTIR spectrum of the sample has been recorded in evacuation mode over the range 4000–500 cm^{-1} using KBr pellet on Bruker IFS–66 V spectrophotometer and the laser Raman spectrum has been analysed over the region 4000–50 cm^{-1} using DILOR Z-24 laser Raman spectrophotometer using krypton-ion laser source at Sophisticated Analytical Instrument Facility, IIT, Chennai, India. Both the spectra have been recorded at 303 K. The frequencies of all the sharp bands are accurate to ±1 cm^{-1}. A spectral width of 4.29 cm^{-1} was used and spectra were measured with a scanning speed of 1.87 cm^{-1} per minute. The FTIR and laser Raman spectra are

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presented in Figures 1 and 2 respectively. The observed frequencies along with the assignments are summarised in Table 1.

3. Theoretical consideration

The structure, nomenclature of parameters and the orientation of the principal axes of isoniazid molecule [5]

$\Gamma_{vib} = 31A' + 14A''$. In view of the complexity of the structure of molecule, only limited modes of vibration are considered for normal coordinate analysis. However, 25 significant vibrational modes have been considered in the present study, which are distributed as $15A'$ vibrations and $10A''$ vibrations.
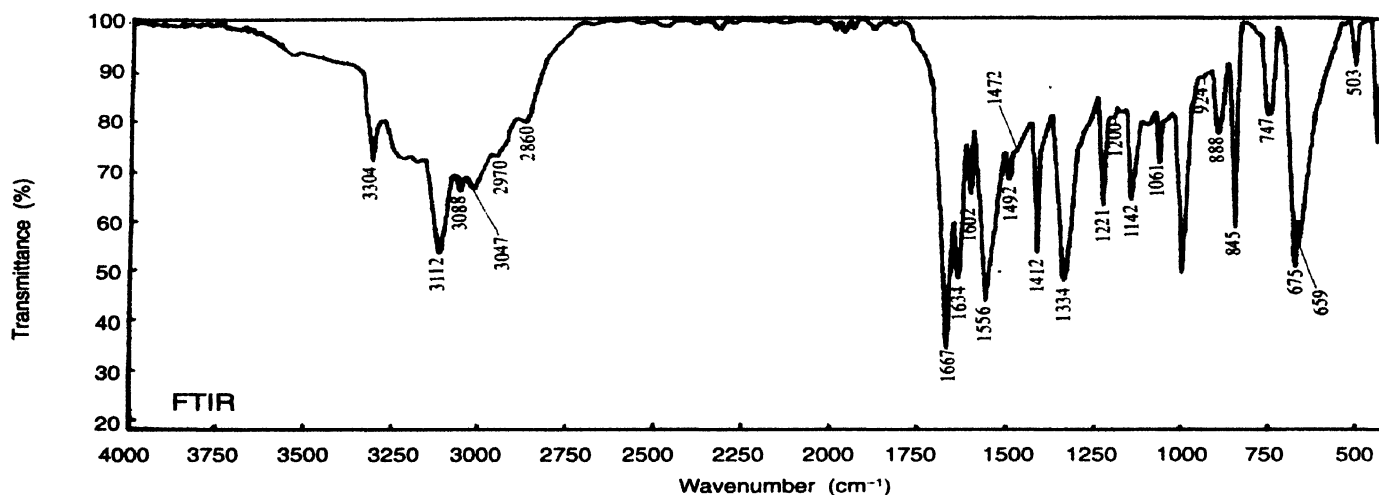

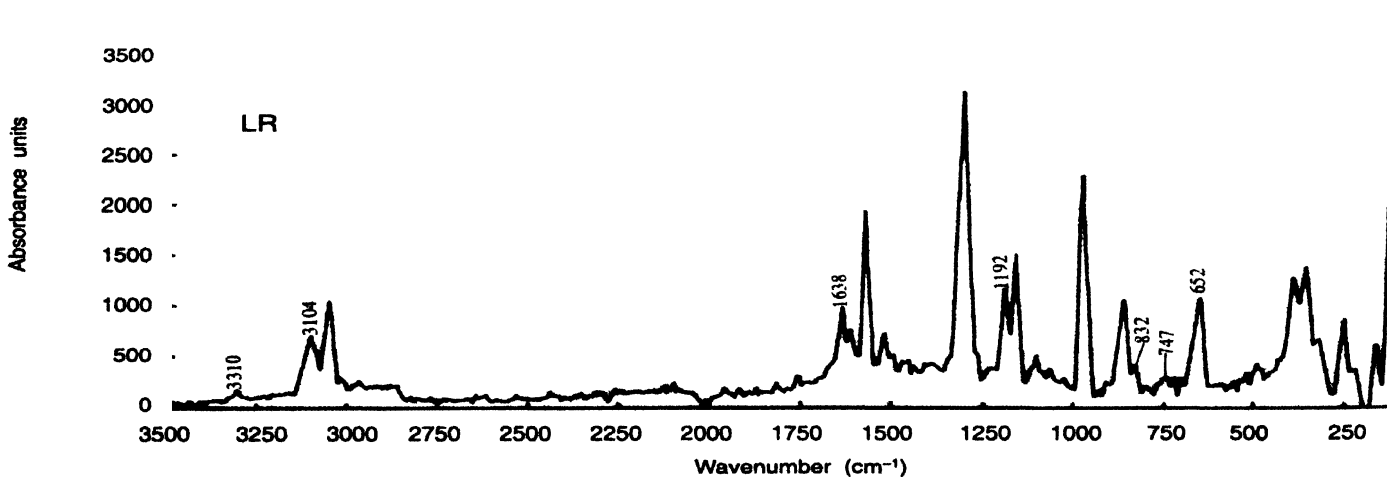Figure 1. FTIR spectrum of isoniazid.

Figure 2. LR spectrum of isoniazid.

is as shown in Figure 3. By applying the principles of group theory, the IR and Raman activity of the vibrational modes and the number of vibrations belonging to each symmetry species have been calculated. From the structural point of view, isoniazid molecule belonging to C_s point group symmetry. The 45 fundamental modes of vibrations of isoniazid are distributed to two symmetry species as

Symmetry coordinates :

Using the internal coordinates, a systematic set of symmetry coordinates were constructed and are given below :

A′ species :

$S_1 = 1/2 \ [\Delta r_1 + \Delta r_2 + \Delta r_3 + \Delta r_4]$,

Table 1. Vibrational assignment, force constant and PED values of isoniazid.

| Symmetry coordinate	Frequency (cm⁻¹) FTIR	LR	Assignment	Symmetrised force constant (× 10² N/m)	PED%
A' species :					
ν_1	1412 (s)		C $\equiv$ C ring sym. stretching	9.7062	88
ν_2	1602 (ms)		C=N ring sym. stretching	13.3960	74
ν_3	2860 (m)		C–H sym. stretching	4.9634	99
ν_4	1061 (m)		C–C sym. streching	5.7367	98
ν_5	1667 (vs)		C=O sym. stretching	11.3970	75
ν_6	1334 (s)		C–N stretching	5.0624	70
ν_7	3304 (m)	3310 (vw)	N–H sym. stretching	6.0669	99
ν_8	1142 (vs)		N–N stretching in NH₂ group	6.1127	56
ν_9	3088 (m)		N–H sym.stretching in NH₂ group	5.9481	99
ν_{10}	503 (vw)		C–C–C ring sym. bending	0.5445	45
ν_{11}	924 (w)		C–C–N ring sym. bending	0.3722	40
ν_{12}	845 (ms)	832 (vw)	C–C–H ring sym. bending	0.4061	37
ν_{13}	747 (w)	747 (vw)	C–C–C bending	0.5583	30
ν_{14}	675 (s)		C–C=O bending	0.7960	28
ν_{15}	1492 (m)		H–N–N bending	0.2966	22
A'' species :					
ν_{16}	1472 (m)		C $\equiv$ C ring asym. stretching	9.7611	98
ν_{17}	1634 (s)		C $\equiv$ C ring asym. stretching	9.8103	99
ν_{18}	1667 (vs)		C=N ring asym. stretching	13.4105	96
ν_{19}	2970 (m)		C–H ring asym. stretching	5.0212	99
ν_{20}	3047 (ms)		C–H ring asym. stretching	5.0416	98
ν_{21}	3112 (m)	3104 (w)	N–H asym.stretching in NH₂ group	6.0102	98
ν_{22}	659 (s)	652 (m)	C–C–C ring asym. bending	0.5500	42
ν_{23}	1200 (w)	1192 (m)	C–C–H ring asym. bending	0.4105	55
ν_{24}	1221 (ms)		C–C–H ring asym. bending	0.4214	63
ν_{25}	1634 (s)	1638 (w)	H–N–N asym. bending	0.3053	20
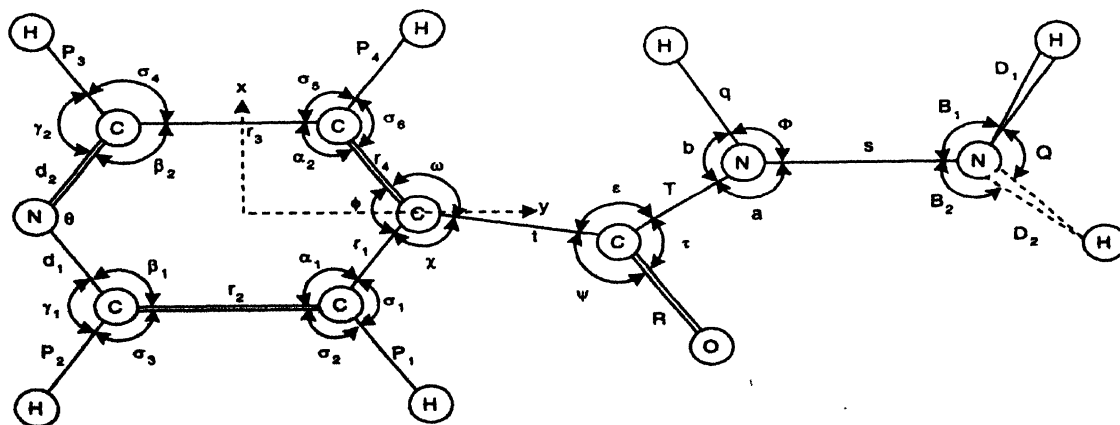
Figure 3. Structure, nomenclature of parameters and the orientation of the principal axes of isoniazid.

$S_2 = 1/\sqrt{2} [\Delta d_1 + \Delta d_2]$,

$S_3 = 1/2[\Delta P_1 + \Delta P_2 + \Delta P_3 + \Delta P_4]$,

$S_4 = \Delta t$,

$S_5 = \Delta R$,

$S_6 = \Delta T$,

$S_7 = \Delta q$,

$S_8 = \Delta s$,

$S_9 = 1/\sqrt{2}[\Delta D_1 + \Delta D_2]$,

$S_{10} = 1/\sqrt{2}[\Delta \alpha_1 + \Delta \alpha_2]$,

$S_{11} = 1/\sqrt{2}[\Delta \beta_1 + \Delta \beta_2]$,

$S_{12} = 1/\sqrt{6}[\Delta \sigma_1 + \Delta \sigma_2 + \Delta \sigma_3 + \Delta \sigma_4 + \Delta \sigma_5 + \Delta \sigma_6]$,

$S_{13} = \Delta \omega$

$S_{14} = \Delta \psi$,

$S_{15} = \Delta \Phi$.

A'' species :

$S_{16} = 1/2[\Delta r_1 - \Delta r_2 - \Delta r_3 + \Delta r_4]$,

$S_{17} = 1/2[\Delta r_1 - \Delta r_2 + \Delta r_3 + \Delta r_4]$,

$S_{18} = 1/\sqrt{2}[\Delta d_1 - \Delta d_2]$,

$S_{19} = 1/2[\Delta P_1 - \Delta P_2 - \Delta P_3 + \Delta P_4]$,

$S_{20} = 1/2 [\Delta P_1 - \Delta P_2 + \Delta P_3 - \Delta P_4]$,

$S_{21} = 1/\sqrt{2} [\Delta D_1 - \Delta D_2]$,

$S_{22} = 1/\sqrt{2} [\Delta \alpha_1 - \Delta \alpha_2]$,

$S_{23} = 1/\sqrt{6} [\Delta \sigma_1 - \Delta \sigma_2 + \Delta \sigma_3 - \Delta \sigma_4 + \Delta \sigma_5 - \Delta \sigma_6]$,

$S_{24} = 1/\sqrt{12} [\Delta \sigma_1 - 2\Delta \sigma_2 + \Delta \sigma_3 + \Delta \sigma_4$
$\qquad\qquad - 2\Delta \sigma_5 + \Delta \sigma_6]$,

$S_{25} = 1/\sqrt{2}[\Delta B_1 - \Delta B_2]$.

where Δ's represent the corresponding change in bond distances and bond angles. The structural data for this title compound were taken from Sutton table [6].

4. Normal coordinate analysis

A normal coordinate analysis for isoniazid has been carried out using the vibrational frequencies observed in FTIR and Laser Raman spectra. The evaluation of force constants is made using general valance force field by applying Wilson's F-G matrix method. The initial set of force constants were taken from the related molecules. In the present work, only the off diagonal force constants have been calculated. The force constants obtained in the present investigation for f_{C-H}, f_{N-H}, f_{C-C}, $f_{C=C}$, $f_{C=O}$, $f_{C=N}$ are in good agreement with the literature values. The potential energy associated with the normal coordinates of the molecules has been calculated using the relation

PED $= F_{ij}L_{ij}^2/\lambda_j$. The calculated force constants and the percentage of potential energy distribution (PED) for fundamental vibrations are presented in Table 1.

The hetero aromatic structure shows the presence of C–H stretching vibrations in the region 3100–3000 cm^{-1}, which is the characteristic region for ready identification of this structure. Hence, the FTIR bands observed at 2860 cm^{-1} (v_3) , 2970 cm^{-1} (v_{19}) and 3047 cm^{-1} (v_{20}) are assigned to C–H stretching vibrations. The force constants for C–H vibrations are found to be 4.9634×10^2 N/m for symmetric stretching vibration and 5.0212×10^2 N/m and 5.0416×10^2 N/m for asymmetric vibration respectively. The calculated PED values are about 99%, 99% and 98% for these vibrations respectively.

The C–C stretching vibrations show absorptions [7] in the region 1260–700 cm^{-1}. Accordingly the band observed at 1061 cm^{-1} has been assigned to C–C stretching. The force constant for this vibration is found to be 5.7367×10^2 N/m and the calculated PED is about 98%. The strong bands due to C=O stretching occur in the region 1870–1540 cm^{-1}. Absorption in the region particularly characteristic for substituted benzene compounds and usually indicates the number of ring substituents. Hence, a strong band observed at 1667 cm^{-1} (v_5) in FTIR is assigned to C=O stretching mode. The calculated force constant and PED for this vibration is determined to be 11.3970×10^2 N/m and 75% respectively.

The ring $C \doteq C$ and C=N stretching vibrations are observed in the regions 1615–1575cm^{-1} and 1520–1465cm^{-1}. Thiazoles, iminocarbonates show the C=N stretching vibrations in the 1689–1471 cm^{-1} region [8]. The intensity of the C=N stretch is variable, it is usually more intense than the $C \doteq C$ stretch. Accordingly, bands observed at 1412 cm^{-1} (v_1), 1472 cm^{-1} (v_{16}), and 1634 cm^{-1} (v_{17}) in FTIR are assigned to $C \doteq C$ vibrations and 1602 cm^{-1}(v_2) and 1667 cm^{-1} (v_{18}) in FTIR are assigned to C=N vibrations, respectively. The force constants for $C \doteq C$ and C=N bonds are found to be in the characteristic range and they contribute the maximum to PED.

The identification of the C–N stretching frequency in the side chain is a rather difficult task since there are problems for identifying from other vibrations. Panday et al [9] assigned C–N stretching band at 1368 cm^{-1} in benzemides. Hence, the FTIR band observed at 1334 cm^{-1} (v_6) is assigned C–N stretching mode. The value of force constant is found to be 5.06240×10^2 N/m and the PED for this mode is about 70%.

The molecule under consideration possesses only one NH_2 group and hence one expects one symmetric and one asymmetric N–H stretching vibrations. In all the primary aromatic amines, the N–H stretching frequency occurs [10] in the region 3300–3500 cm^{-1}. Hence, the band observed at 3088 cm^{-1} (v_6) is assigned to N–H symmetric vibration and 3112 cm^{-1} (v_{21}) is assigned to N–H asymmetric vibration. The force constant is found to be about 6.0 × 10^2 N/m for these vibrations and they contribute the maximum to PED.

Primary amides and secondary amides shows a band or bands at 1650–1515 cm^{-1} region [11] primarily due to NH_2 or NH bending. These bending vibrations are observed in characteristic range. The absorption at 1142 m^{-1} (v_8) in FTIR are assigned to N–N stretching in NH_2 group [1].

The C–H deformation frequencies in benzene derivatives are expected to arise from 1298 cm^{-1}, 1128 cm^{-1}, 1170 cm^{-1} and 1035 cm^{-1} modes (in plane hydrogen bending) and 1016 cm^{-1}, 849 cm^{-1}, 671 cm^{-1} and 985 cm^{-1} modes (out-of-plane hydrogen bending) of benzene. In the present investigation, frequencies at 1200 cm^{-1} (v_{23}) and 1221 cm^{-1} (v_{24}) have been assigned to C–H in-plane bending and 845 cm^{-1} (v_{12}) assigning to C–H out of plane bending. The strong band at 659 cm^{-1} (v_{22}) weak band at 503 cm^{-1} (v_{10}) in FTIR are assigned to C–C bending vibrations and they are in good agreement with the literature value [11]. The normal coordinate analysis helps in assigned the bands observed at 924 (v_{11}) cm^{-1} to C–C–N bending vibrations. The band observed at 675 cm^{-1} (v_{14}) is assigned to C–C=O bending mode. The bands observed at 1492 cm^{-1} (v_{15}) and 1634 cm^{-1} (v_{25}) are assigned to H–N–N bending vibrations.

5. Conclusion

A normal coordinate analysis has been carried out, based on the measurements taken from the FTIR and laser Raman spectra. Thus, the evaluated force constants and their agreement with the earlier works [1,3] for related compounds confirm the validity of the frequency assignment. The calculated PED is used to check whether the chosen set of assignments contribute maximum to the potential energy associated with normal coordinate of the molecules.

References

[1] C Nakkeeran *PhD Thesis* (Bharathidasan University, India) (1997)

[2] S R Varadhan *PhD Thesis* (University of Madras, India) (1997)

[3] V Krishnakumar, K Parasuraman and A Natarajan *Indian J. Pure Appl. Phy.* **36** 171 (1998)

[4] M Parasuraman *PhD Thesis* (University of Madras, India) (2001)

[5] L H Jensen *J. Amer. Chem. Soc.* **76** 4663 (1954)

[6] L E Sutton *The Interatomic Bond Distances and Bond Angles in Molecules and Ions* (London : Chemical Society) (1956)

[7] G Socrates *Infrared Characteristic Group Frequencies* (New York : John Wiley) (1980)

[8] M Silverstein Clayton, G Bassler and C Morrill *Spectrometric Identification of Organic Compounds* (New York : John Wiley) 4th edn. (1981)

[9] K S Panday, B P Asthaman and P C Mishra *Spectrochim. Acta* **A49** 53 (1993)

[10] L J Bellamy *The Infrared Spectra of Complex Molecules* Vol.2 (London : Chapman and Hall) (1959)

[11] D K Mukherjee, P K Sinkar and S C Sinkar *Indian J. Phys* **18** 537 (1965)