

## Vibrational and Normal Coordinate Analysis of Pyrazinamide

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A normal coordinate analysis on pyrazinamide has been carried out with a systematic set of symmetry coordinates following Wilson's F-G matrix method. The potential constant evaluated for the molecule is found to be in good agreement with literature values thereby confirming the vibrational assignments. 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 has been evaluated.

**Key Words:** Normal coordinate analysis, FTIR and laser Raman spectra, Pyrazinamide.

### INTRODUCTION

Pyrazinamide is chemically pyrazine-2-carboxamide. It is used as antitubercular. The increasing interest in the spectroscopic studies of N-heterocyclic molecules is mainly due to their biological and pharmaceutical importance<sup>1, 2</sup>. An extensive work has been carried out by several investigators on the title compound and its derivatives in recent years<sup>3–6</sup>. The characteristic vibrational frequencies of this drug have been identified and assigned on the basis of their relative intensity, characteristic positions and correlation of vibrational bands of related compounds. The properties of this compound like storage condition, solubility and interaction with other trace elements were studied in detail<sup>7</sup>. However, no attempt has been made on normal coordinate analysis calculation. Therefore, the present work is devoted to making use of infrared and Raman spectroscopy methods in the structural elucidations of pyrazinamide. A systematic set of symmetry coordinates has been constructed on the basis of  $C_s$  symmetry and a normal coordinate analysis has been carried out; the potential energy distribution has been evaluated.

### EXPERIMENTAL

The pure sample of pyrazinamide was obtained from Sigma Chemical Company, USA and used as such. The FTIR spectrum of the sample was recorded using Bruker IFS 66V FTIR spectrometer in the region 4000–400  $\text{cm}^{-1}$  and the

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laser Raman spectrum has been recorded in the region 4000–100  $\text{cm}^{-1}$  using Dilor Z 24 laser Raman spectrometer using 647.1 nm krypton ion laser at RSIC Chennai. The infrared and laser Raman spectra are presented in Figs. 1 and 2 respectively.

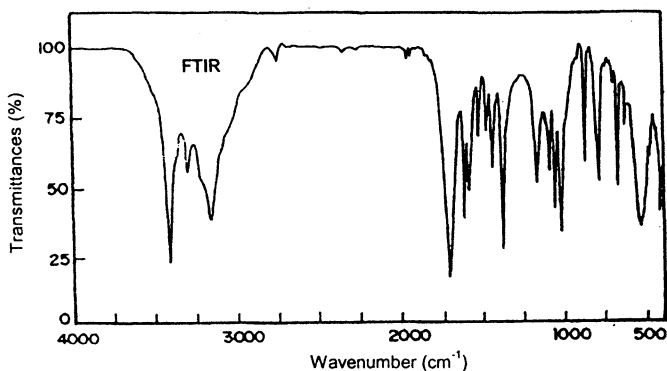


Fig. 1. FT-IR spectrum of pyrazinamide

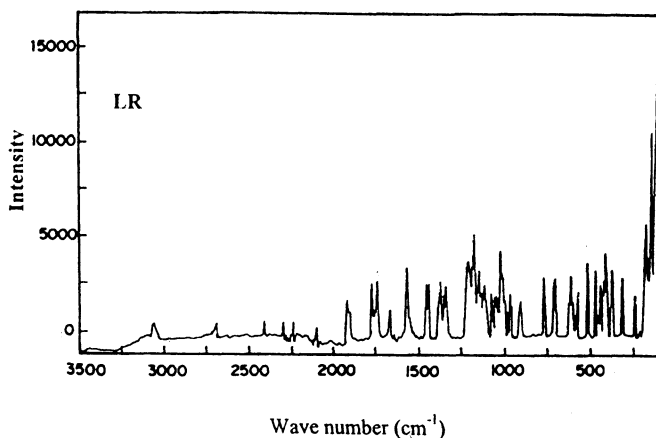


Fig. 2. Laser Raman spectrum of pyrazinamide

### Normal coordinate analysis

Pyrazinamide has 36 fundamental modes of vibration under  $C_s$  symmetry point group which are distributed as  $\Gamma_{\text{vib}} = 24A' + 12A''$ ; all the fundamentals are active both in the infrared and Raman spectra. In the present work only 27 modes are considered. The structure, orientation of the principal axes and the nomenclature of the parameters of the pyrazinamide molecule are shown in Fig. 3. A set of symmetry coordinates has been arrived at using the knowledge of projection operator and the character table pertaining to the  $C_s$  point group symmetry. The symmetry coordinates thus obtained are as follows:

**A' Species**

$$\begin{aligned}
 S_1 &= (1/\sqrt{2})[\Delta r_1 + \Delta r_2] \\
 S_2 &= (1/2)[\Delta R_1 + \Delta R_2 + \Delta R_3 + \Delta R_4] \\
 S_3 &= (1/\sqrt{3})[\Delta d_1 + \Delta d_2 + \Delta d_3] \\
 S_4 &= \Delta D \\
 S_5 &= \Delta a \\
 S_6 &= \Delta A \\
 S_7 &= (1/\sqrt{2})[\Delta b_1 + \Delta b_2] \\
 S_8 &= \Delta \delta \\
 S_9 &= \Delta \sigma \\
 S_{10} &= (1/\sqrt{2})[\Delta \chi_1 + \Delta \chi_2] \\
 S_{11} &= (1/2)[\Delta \alpha_1 + \Delta \alpha_2 + \Delta \alpha_3 + \Delta \alpha_4] \\
 S_{12} &= (1/\sqrt{2})[\Delta \beta_1 + \Delta \beta_2] \\
 S_{13} &= (1/\sqrt{3})[\Delta \gamma_1 + \Delta \gamma_2 + \Delta \gamma_3] \\
 S_{14} &= (1/\sqrt{3})[\Delta \theta_1 + \Delta \theta_2 + \Delta \theta_3] \\
 S_{15} &= \Delta \omega
 \end{aligned}$$

**A'' Species**

$$\begin{aligned}
 S_{16} &= (1/\sqrt{2})[\Delta r_1 - \Delta r_2] \\
 S_{17} &= (1/2)[\Delta R_1 - \Delta R_2 - \Delta R_3 - \Delta R_4] \\
 S_{18} &= (1/\sqrt{6})[2\Delta d_1 - \Delta d_2 - \Delta d_3] \\
 S_{19} &= (1/\sqrt{2})[\Delta b_1 - \Delta b_2] \\
 S_{20} &= \Delta \phi \\
 S_{21} &= \Delta \Psi \\
 S_{22} &= \Delta \epsilon \\
 S_{23} &= (1/\sqrt{2})[\Delta \chi_1 - \Delta \chi_2] \\
 S_{24} &= (1/2)[\Delta \alpha_1 - \Delta \alpha_2 - \Delta \alpha_3 - \Delta \alpha_4] \\
 S_{25} &= (1/\sqrt{2})[\Delta \beta_1 - \Delta \beta_2] \\
 S_{26} &= (1/\sqrt{6})[2\Delta \gamma_1 - \Delta \gamma_2 - \Delta \gamma_3] \\
 S_{27} &= (1/\sqrt{6})[2\Delta \theta_1 - \Delta \theta_2 - \Delta \theta_3]
 \end{aligned}$$

where  $\Delta$ 's represent changes in the corresponding bond distances and bond angles. The required structural data were taken from literature<sup>6</sup>.

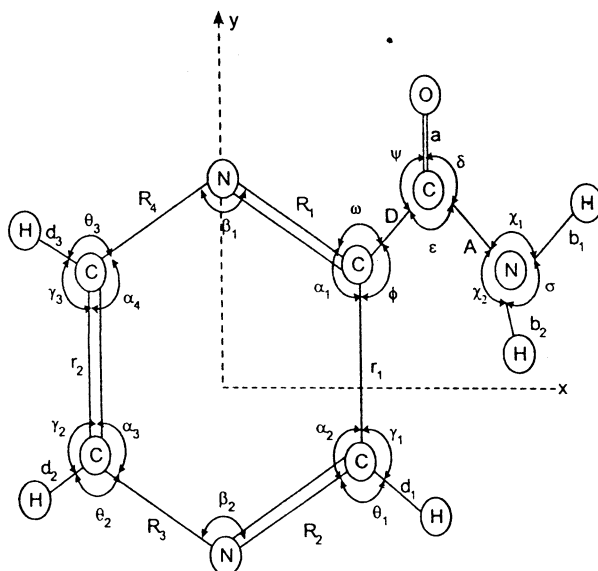


Fig. 3. Structure, nomenclature of parameters and the orientation of the principal axes of pyrazinamide

## RESULTS AND DISCUSSION

A normal coordinate analysis for pyrazinamide has been carried out using the observed frequencies from the FTIR and laser Raman spectra. The evaluation of force constants has been made on the basis of general valence force field by

applying Wilson's F-G matrix method<sup>8</sup>, the method of kinetic constants has been used to solve the secular equation. The correctness of the assignment has been verified by evaluating the potential energy distribution using the relation  $\%PED = L_{ij}^2 F_{ij} / \lambda_j$ . The observed frequencies along with the assignment, calculated force constants and potential energy distribution are presented in Table-1.

The initial set of force constants for the allopurinol were taken from the molecules of similar environment<sup>9, 10</sup> and they were subsequently refined using successive approximate technique. The force constants evaluated for this molecules are compared with earlier work. A brief discussion of the vibrational frequencies, force constants, and potential energy distribution corresponding to various modes appearing in different regions are given below.

**C=O Stretching:** Primary amides have a very strong band due to the C=O stretching vibration at  $1670\text{ cm}^{-1}$  in the solid phase. The corresponding mode in the present study appears at  $1650\text{ cm}^{-1}$  ( $\nu_5$ ) in FTIR and  $1670\text{ cm}^{-1}$  in laser Raman spectra find support from the assignment made by earlier workers in related molecules. The force constant for this vibration is found to be  $11.490 \times 10^2\text{ N/m}$  and the calculated frequency is about 95%.

**C—H Stretching:** The heteroaromatic structure shows the presence of C—H stretching vibrations in the region  $3100\text{--}3000\text{ cm}^{-1}$  for asymmetric stretching and  $2990\text{--}2850\text{ cm}^{-1}$  for symmetric stretching. In the present work, the band observed at  $2850\text{ cm}^{-1}$  ( $\nu_3$ ) in infrared and  $2852\text{ cm}^{-1}$  in laser Raman is assigned to C—H symmetric stretching. The band observed at  $3020\text{ cm}^{-1}$  ( $\nu_{18}$ ) in infrared and  $3018\text{ cm}^{-1}$  in laser Raman has been assigned to C—H asymmetric stretching. The force constant for symmetric C—H stretching is found to be  $5.490 \times 10^2\text{ N/m}$  for symmetric stretching vibration and  $6.290 \times 10^2\text{ N/m}$  for asymmetric vibration. The calculated potential energy distribution is 98 and 99% for symmetric and asymmetric stretching respectively.

**N—H Stretching:** The band due to N—H stretching vibrations<sup>13</sup> occurs in the region  $3300\text{--}3000\text{ cm}^{-1}$ . In the present work the band observed at  $3010\text{ cm}^{-1}$  ( $\nu_7$ ) in FTIR and  $3020\text{ cm}^{-1}$  in laser Raman is assigned to N—H symmetric stretching. The bands observed at  $3162\text{ cm}^{-1}$  ( $\nu_{19}$ ) in FTIR and  $3160\text{ cm}^{-1}$  in laser Raman are assigned to N—H asymmetric stretching. The calculated force constants for this vibrations are found to be in the characteristic range and they contribute the maximum to potential energy distribution.

**C—NH<sub>2</sub> stretching:** C—NH<sub>2</sub> stretching vibrations give generally strong bands in the region<sup>14</sup>  $1330\text{--}1250\text{ cm}^{-1}$ . In the present work the band observed at  $1320\text{ cm}^{-1}$  ( $\nu_6$ ) is assigned to C—NH<sub>2</sub> stretching vibration. The force constant for this vibration is found to be  $5.290 \times 10^2\text{ N/m}$  and the potential energy distribution for this mode is about 65%.

**C—C—C bending:** The C—C—C bending bands always occur below  $600\text{ cm}^{-1}$ . Isopropyl benzenes<sup>15</sup> have a medium intensity absorption band in the region  $545\text{--}520\text{ cm}^{-1}$ . In the present work the strong band observed at  $539\text{ cm}^{-1}$  ( $\nu_{20}$ ) is assigned to C—C—C bending. The force constant evaluated for this bending vibration is found to be  $0.5980 \times 10^2\text{ N/m}$  and the potential energy distribution for this mode is about 53%.

TABLE-1  
VIBRATIONAL ASSIGNMENT, FORCE CONSTANT AND PED VALUES OF  
PYRAZINAMIDE

Symmetry coordinate	Frequency ( $\text{cm}^{-1}$ )		Assignments	Symmetrised force constant ( $10^2 \text{ N/M}$ )	PED (%)
	FTIR	Laser Raman			
<b>A' Species</b>					
S <sub>1</sub>	1438 m	1440 s	ring C—C sym stretching	6.7090	93
S <sub>2</sub>	960 w	960 m	ring C—N sym stretching	12.6900	99
S <sub>3</sub>	2850 m	2852 w	C—H stretching	5.4900	98
S <sub>4</sub>	760 w	773 s	C—C stretching	6.9800	98
S <sub>5</sub>	1650 vs	1670 w	C=O stretching	11.4900	95
S <sub>6</sub>	1320 m	—	C—NH <sub>2</sub> stretching	5.2900	65
S <sub>7</sub>	3010 m	3020 w	sym N—H stretching	6.4900	99
S <sub>8</sub>	619 w	614 s	N—C=O bending	0.3490	20
S <sub>9</sub>	1524 w	1520 m	NH <sub>2</sub> bending	0.3498	48
S <sub>10</sub>	786 s	784 w	C—N—H sym bending	0.1490	10
S <sub>11</sub>	410 w	412 vs	C—C=N sym bending	0.3490	10
S <sub>12</sub>	432 w	430 m	C—N—C sym bending	0.4490	99
S <sub>13</sub>	670 s	—	C—C—H sym bending	0.4480	98
S <sub>14</sub>	1420 w	1420 m	N—C—H sym bending	0.3749	15
S <sub>15</sub>	520 m	515 s	C—C—N bending	0.3490	32
<b>A'' Species</b>					
S <sub>16</sub>	1610 s	1615 w	ring C—C asym stretching	6.9800	77
S <sub>17</sub>	1478 w	1470 m	ring C—N asym stretching	13.6900	99
S <sub>18</sub>	3020 m	3018 w	C—H asym stretching	6.2900	99
S <sub>19</sub>	3162 s	3160 w	N—H asym stretching	7.1900	99
S <sub>20</sub>	539 s	—	C—C—C bending	0.5980	53
S <sub>21</sub>	476 w	471 s	C—C=O bending	0.3980	36
S <sub>22</sub>	490 m	—	C—C—N bending	0.4190	37
S <sub>23</sub>	1378 s	1371 w	C—N—H asym bending	0.5980	53
S <sub>24</sub>	431 w	—	C—C=N asym bending	0.3902	91
S <sub>25</sub>	446 w	443 m	C—N—C asym bending	1.4900	10
S <sub>26</sub>	701 w	713 m	C—C—H asym bending	0.6980	99
S <sub>27</sub>	1462 w	1460 m	N—C—H asym bending	0.5490	10

**C—C—H bending:** The C—H deformation frequencies in benzene derivatives are found to occur in the region 700–600  $\text{cm}^{-1}$ . In the present molecule, the band observed at 670  $\text{cm}^{-1}$  ( $\nu_{13}$ ) and 701  $\text{cm}^{-1}$  ( $\nu_{26}$ ) is assigned to C—C—H symmetric and asymmetric bending respectively. The calculated force constants are found to be in the characteristic range and they contribute the maximum to potential energy distribution.

## Conclusion

Infrared and laser Raman investigations have been carried out successfully on pyrazinamide on the basis of  $C_s$  point group symmetry. All the characteristic vibrations observed in the spectra are correlated with the characters and properties of  $C_s$  system. The molecular constants are found to be in good agreement with those reported in literature, thereby forming the structure of pyrazinamide. The potential energy distribution evaluated for the normal modes of vibration give further support to the present assignments.

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