

FTIR, FT Raman spectra and normal coordinate analysis of hydralazine

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Hydralazine ($C_8H_8N_4.HCl$) is chemically known as 1-hydrazinophthalazine mono hydrochloride. It is used as an anti-hypertensive agent. In the present investigation, normal coordinate analysis has been carried out for the molecule of the title compound using fundamental modes of vibration observed in infrared and Raman spectroscopy. The vibrational modes are classified into A' and A'' irreducible representations and are distributed as $\Gamma_{vib}=35 A'+19 A''$ based on C_s point group symmetry associated with the structures. In the present work, only 18 A' and 12 A'' normal modes are considered due to complexity of the molecule. A systematic set of orthonormal symmetry co-ordinates has been constructed. Wilson's F-G matrix method has been adopted for the normal coordinate analysis. A satisfactory vibrational band assignment has been made by using the FTIR and FT Raman spectra of the compounds.

Keywords: Fourier transform infrared spectrum, Fourier transform Raman spectrum, Hydralazine, Normal coordinate analysis, Potential energy distribution

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1 Introduction

Hydralazine is a centrally acting anti-hypertensive agent, finds use in the treatment of all grades of hypertension. It is also known to act peripherally, partly by blocking alpha-adrenergic receptors and partly by decreasing vascular reactivity^{1,2}. An extensive work has been carried out on the title compound and its derivatives in the recent years³. 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 present investigation has been undertaken to provide a satisfactory vibrational analysis of hydralazine through FTIR & FT Raman spectroscopy. 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 distributions have been evaluated.

2 Experimental Details

The pure sample of hydralazine was obtained from Hi-media Chemicals, Mumbai and used as such. The

FT-IR spectrum of the compound is recorded in the region $4000-400\text{ cm}^{-1}$ in evacuation mode using KBr pellet technique (solid phase) with 4.0 cm^{-1} resolution. The FT Raman spectrum is recorded in the region $4000-100\text{ cm}^{-1}$ in purge mode using YAG laser of 200 mw. Both the spectra are recorded using BRUKER IFS 66V FTIR spectrophotometer at Sophisticated Instrumentation Analysis Facility, Indian Institute of Technology, Chennai, India. The FTIR and FT Raman spectra are presented in Figs 1 & 2, respectively.

3 Normal Coordinate Analysis

Hydralazine has 54 fundamental modes of vibration under C_s symmetry point group which are distributed as $\Gamma_{vib}=35A'+19A''$, all the fundamental modes of vibration are active both in Raman and infrared spectra. Of 35 modes of vibrations, only 18 are considered in A' species and only 12 in A'' species. The structure, orientation of the principle axes and the nomenclature of the parameters of the hydralazine molecule are shown in Fig. 3. The molecular parameters are taken from Sutton's Table 4 and are given in Table 1.

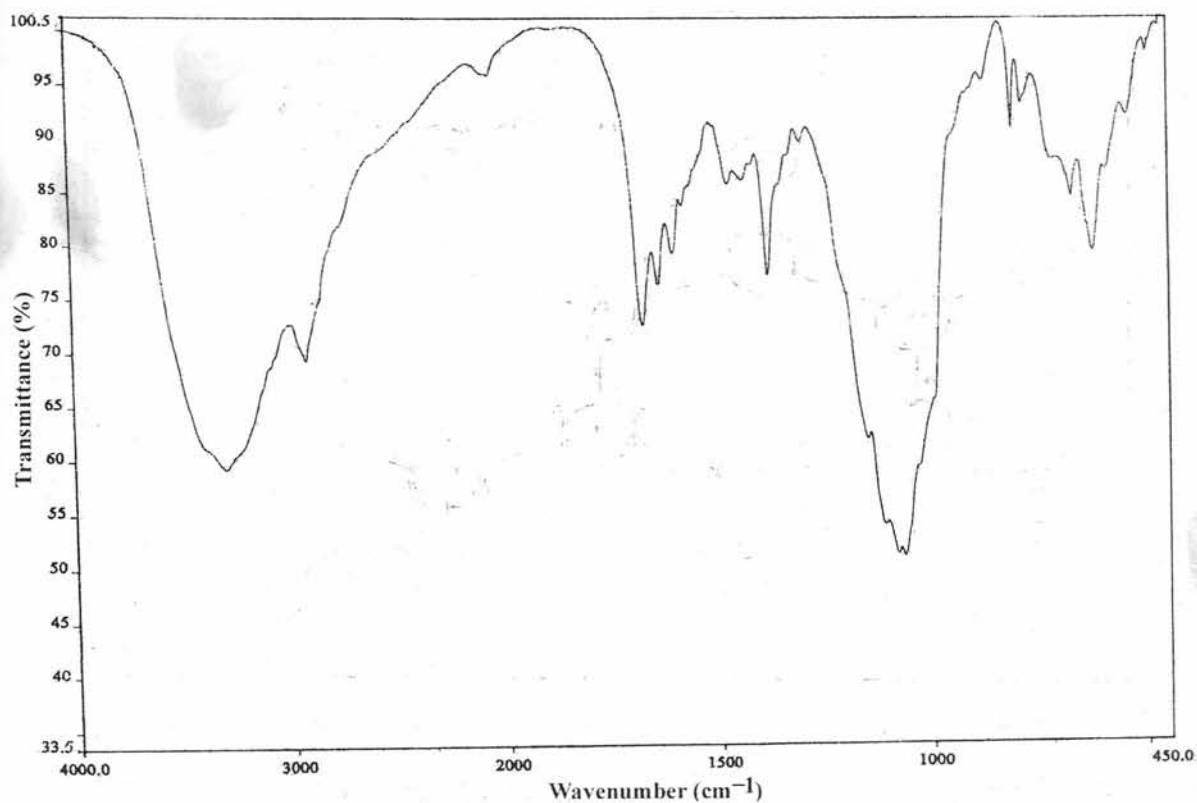


Fig. 1—FTIR spectrum of hydralazine

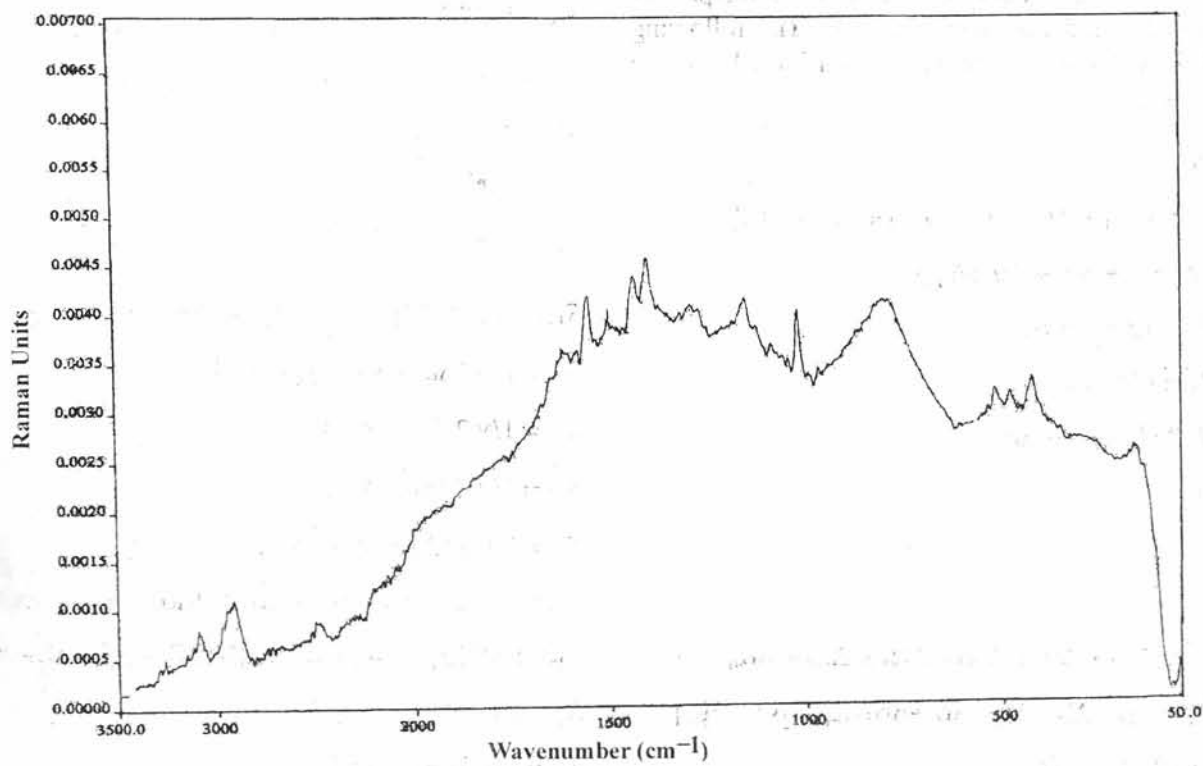


Fig. 2—FT Raman spectrum of hydralazine

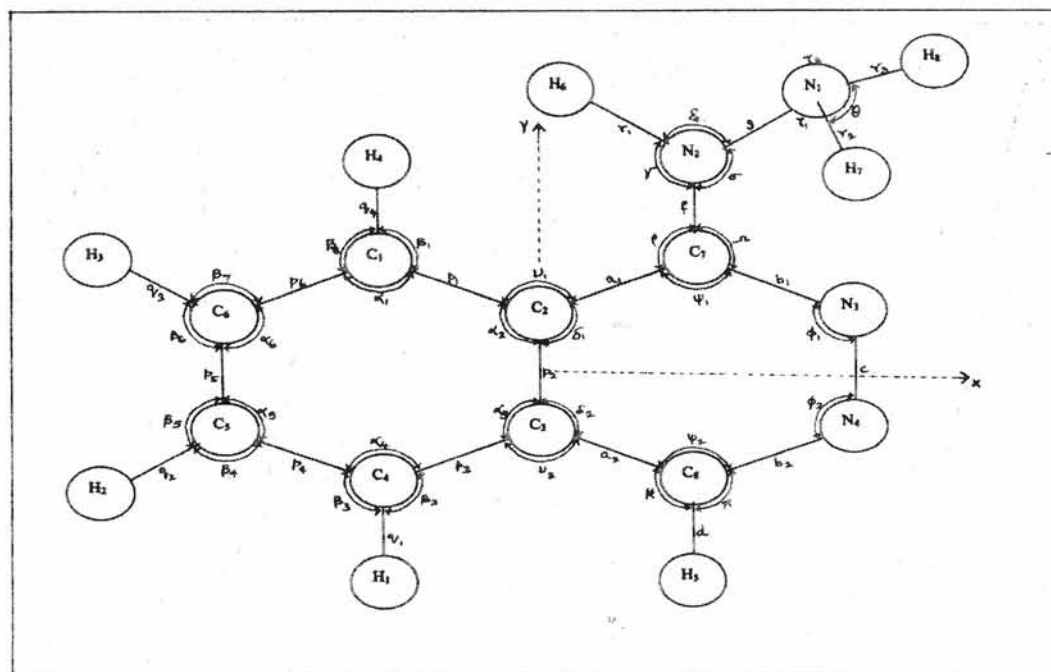


Fig. 3—Structure, nomenclature of parameters and the orientation of the principal axes of hydralazine

3.1 Symmetry co-ordinates

The orthonormal set of symmetry coordinates for the molecule under study is constructed using the internal coordinates with the knowledge of the projection operator and the character table. The following are the symmetry coordinates considered in the present work.

A' species

$$S_1 = 1/\sqrt{6} [\Delta p_1 + \Delta p_2 + \Delta p_3 + \Delta p_4 + \Delta p_5 + \Delta p_6]$$

$$S_2 = 1/2 [\Delta q_1 + \Delta q_2 + \Delta q_3 + \Delta q_4]$$

$$S_3 = 1/\sqrt{2} [\Delta a_1 + \Delta a_2]$$

$$S_4 = 1/\sqrt{2} [\Delta b_1 + \Delta b_2]$$

$$S_5 = 1/\sqrt{3} [\Delta r_1 + \Delta r_2 + \Delta r_3]$$

$$S_6 = \Delta f$$

$$S_7 = \Delta d$$

$$S_8 = \Delta s$$

$$S_9 = 1/\sqrt{6} [\Delta \alpha_1 + \Delta \alpha_2 + \Delta \alpha_3 + \Delta \alpha_4 + \Delta \alpha_5 + \Delta \alpha_6]$$

$$S_{10} = 1/\sqrt{8} [\Delta \beta_1 + \Delta \beta_2 + \Delta \beta_3 + \Delta \beta_4 + \Delta \beta_5 + \Delta \beta_6 + \Delta \beta_7 + \Delta \beta_8]$$

$$S_{11} = 1/\sqrt{2} [\Delta v_1 + \Delta v_2]$$

$$S_{12} = 1/\sqrt{2} [\Delta \delta_1 + \Delta \delta_2]$$

$$S_{13} = 1/\sqrt{2} [\Delta \Psi_1 + \Delta \Psi_2]$$

$$S_{14} = 1/\sqrt{2} [\Delta \phi_1 + \Delta \phi_2]$$

$$S_{15} = 1/\sqrt{2} [\Delta \tau_1 + \Delta \tau_2]$$

$$S_{16} = \Delta \theta$$

$$S_{17} = \Delta \sigma$$

$$S_{18} = \Delta \pi$$

A'' Species

$$S_{19} = 1/\sqrt{12} [2\Delta p_1 - \Delta p_2 - \Delta p_3 + 2\Delta p_4 - \Delta p_5 - \Delta p_6]$$

$$S_{20} = 1/2 [\Delta q_1 - \Delta q_2 - \Delta q_3 + \Delta q_4]$$

$$S_{21} = 1/\sqrt{2} [\Delta a_1 - \Delta a_2]$$

$$S_{22} = 1/\sqrt{2} [\Delta b_1 - \Delta b_2]$$

$$S_{23} = 1/\sqrt{6} [2\Delta r_1 - \Delta r_2 - \Delta r_3]$$

$$S_{24} = 1/\sqrt{12} [2\Delta \alpha_1 - \Delta \alpha_2 - \Delta \alpha_3 + 2\Delta \alpha_4 - \Delta \alpha_5 - \Delta \alpha_6]$$

$$S_{25} = 1/\sqrt{8} [\Delta \beta_1 - \Delta \beta_2 - \Delta \beta_3 + \Delta \beta_4 + \Delta \beta_5 - \Delta \beta_6 - \Delta \beta_7 + \Delta \beta_8]$$

$$S_{26} = 1/\sqrt{2} [\Delta v_1 - \Delta v_2]$$

$$S_{27} = 1/\sqrt{2} [\Delta \delta_1 - \Delta \delta_2]$$

$$S_{28} = 1/\sqrt{2} [\Delta \Psi_1 - \Delta \Psi_2]$$

Table 1—Molecular parameters of hydralazine

Nature of bond	Description	Molecular parameters of hydralazine length / bond angle Å
C ₁ -C ₂	<i>p</i> ₁	1.420
C ₁ -C ₆	<i>p</i> ₆	1.420
C ₁ -H ₄	<i>q</i> ₄	1.100
C ₂ -C ₃	<i>p</i> ₂	1.420
C ₂ -C ₇	<i>a</i> ₁	1.418
C ₃ -C ₄	<i>p</i> ₃	1.419
C ₃ -C ₈	<i>a</i> ₂	1.420
C ₄ -H ₁	<i>q</i> ₁	1.100
C ₄ -C ₅	<i>p</i> ₄	1.420
C ₅ -C ₆	<i>p</i> ₅	1.421
C ₅ -H ₂	<i>q</i> ₂	1.100
C ₆ -H ₃	<i>q</i> ₃	1.100
C ₇ -N ₂	<i>f</i>	1.358
C ₇ -N ₃	<i>b</i> ₁	1.360
C ₈ -N ₄	<i>b</i> ₂	1.360
C ₈ -H ₅	<i>d</i>	1.113
N ₃ -N ₄	<i>c</i>	1.562
N ₁ -N ₂	<i>s</i>	1.352
N ₂ -H ₆	<i>r</i> ₁	1.050
N ₁ -H ₇	<i>r</i> ₂	1.020
N ₁ -H ₈	<i>r</i> ₃	1.020
C ₁ -C ₂ -C ₃	α_2	120.0°
C ₂ -C ₁ -H ₄	β_1	119.8°
C ₄ -C ₂ -C ₃	α_3	120.1°
C ₃ -C ₄ -H ₁	β_2	119.9°
C ₅ -C ₄ -H ₁	β_3	119.8°
C ₃ -C ₄ -C ₅	α_4	120.0°
C ₄ -C ₅ -H ₂	β_4	119.6°
C ₄ -C ₅ -C ₆	α_5	119.9°
C ₆ -C ₅ -H ₂	β_5	120.0°
C ₅ -C ₆ -H ₃	β_6	119.8°
C ₅ -C ₆ -C ₁	α_6	120.0°
C ₆ -C ₁ -C ₂	α_1	120.0°
C ₁ -C ₆ -H ₄	β_7	119.9°
C ₆ -C ₁ -H ₄	β_8	119.8°
C ₁ -C ₂ -C ₇	ν_1	119.9°
C ₄ -C ₃ -C ₈	ν_2	120.2°
N ₃ -C ₇ -N ₂	Ω	122.9°
C ₇ -N ₂ -H ₆	γ	118.6°
N ₂ -N ₁ -H ₇	τ_1	120.6°
N ₂ -N ₁ -H ₈	τ_2	120.6°
C ₂ -C ₇ -N ₃	ψ_1	116.7°
C ₃ -C ₈ -N ₄	ψ_2	116.8°
C ₇ -N ₃ -N ₄	ϕ_1	120.9°
C ₈ -N ₄ -N ₃	ϕ_2	120.9°

$$S_{29} = 1/\sqrt{2} [\Delta\phi_1 - \Delta\phi_2]$$

$$S_{30} = 1/\sqrt{2} [\Delta\tau_1 - \Delta\tau_2]$$

where Δ 's represent the corresponding changes in bond distances and bond angles.

3.2 FTIR & FT Raman spectra and vibrational band assignment

The molecule under study is a system of two heterocyclic ring system, the vibrational frequency assignment of the compound is done using the vibrational frequencies of benzene, pyridine, and pyrimidine as guidelines. A satisfactory assignment of the fundamental vibrations has been made according to the position, shape, nature and relative intensity. The qualitative investigation on the vibrational band assignments derived from FTIR & FT Raman spectra for hydralazine is presented in this paper. The vibrational spectral frequencies of hydralazine are presented in Table 2.

C-H vibrations—The hetero aromatic structure shows the presence of C-H stretching vibrations⁵ in the region 3100-3000 cm⁻¹ for asymmetric stretching and 2990-2900 cm⁻¹ for symmetric stretching modes of vibration. Hetero cyclic compound's C-H vibration absorption bands are usually weak. In many cases, it is too weak for detection. In the present work, the bands observed at 2921 and 3000 cm⁻¹ are assigned to C-H symmetric and C-H asymmetric stretching vibrations, respectively.

C-C ring stretching—Benzene has two doubly degenerate modes and two non-degenerate modes of vibrations due to stretching of C-C bonds. The ring C-C stretching vibrations⁶ occur in the region 1625-1430 cm⁻¹. In the present work, the bands observed at 1465 and 1540 cm⁻¹ in the FTIR spectrum and the bands at 1463 and 1539 cm⁻¹ in FT Raman spectrum are assigned to ring C-C symmetric and asymmetric stretching vibrations, respectively.

C=N stretching—In the vibrational spectra of 2,3,4-substituted pyrazole-5 Zerbi *et al.*⁷ identified stretching frequencies of C=N in the range 1680-1570 cm⁻¹. Referring to the above work, the band observed at 1596 and 1668 cm⁻¹ in FTIR spectrum and the bands at 1602 and 1670 cm⁻¹ in the FT Raman spectrum of hydralazine are assigned to C=N symmetric stretching and asymmetric modes of vibration.

N-H stretching—The band due to N-H stretching vibrations occur in the region⁸ 3450-3250 cm⁻¹. In the

Table 2—Vibrational spectral assignments, potential constants (10^2 N/m) and PED values of hydralazine

Symmetry	Frequency cm^{-1}		Band assignment	Force Constant (10^2 N/m)	PED %
coordinate	FTIR	FT Raman			
A' species					
S_1	1465 (s)	1463 (s)	ring C-C symmetric stretching	9.8966	89
S_2	2921 (m)	2915 (m)	C-H symmetric stretching	5.9313	97
S_3	1430 (m)	1420 (s)	C-C symmetric stretching of pyridazine	9.7495	88
S_4	1596 (s)	1602 (m)	C=N symmetric stretching	14.8596	83
S_5	3304 (m)	3301 (w)	N-H stretching	6.9497	96
S_6	1289 (s)	1278 (m)	C-N Stretching	12.7509	99
S_7	2911 (ms)	1385 (s)	C-H stretching	5.8426	96
S_8	1373 (m)	540 (w)	N-N stretching	6.3745	81
S_9	543 (s)	473 (m)	C-C=C symmetric bending	0.9479	58
S_{10}	1067 (s)	490 (m)	C-H symmetric bending	0.8558	96
S_{11}	528 (m)	463 (s)	C-C=C bending	0.8499	54
S_{12}	481 (w)	1586 (ms)	C-C-C bending	0.8387	54
S_{13}	496 (m)	701 (w)	C-C=N symmetric bending	0.6365	43
S_{14}	465 (s)	971 (m)	C=N-N symmetric bending	0.4454	47
S_{15}	1345 (w)	1539 (vs)	N-N-H symmetric bending	0.5396	39
S_{16}	1580 (ms)	3012 (m)	H-N-H bending	0.5517	41
S_{17}	692 (m)	1670 (w)	C-N-N bending	0.8482	46
S_{18}	960 (m)	3405 (w)	H-C=N symmetric bending	0.9625	52
A'' species		669 (w)	ring C-C asymmetric stretching	9.9401	84
S_{19}	1540 (s)	589 (m)	C-H asymmetric stretching	6.2522	99
S_{20}	3000 (m)	501 (s)	C-C asymmetric stretching	9.8906	83
S_{21}	1526 (ms)	1490 (s)	C=N asymmetric stretching	14.9044	88
S_{22}	1668 (m)		N-H asymmetric stretching	7.0567	96
S_{23}	3411 (w)		C-C=C asymmetric bending	0.8654	52
S_{24}	614 (s)		C-H asymmetric bending	0.9248	87
S_{25}	1135 (m)		C-C=C bending	0.8633	51
S_{26}	659 (s)		C-C-C bending	0.8196	53
S_{27}	645 (m)		C-C=N asymmetric bending	0.6149	77
S_{28}	585(m)		C=N-N asymmetric bending	0.4181	39
S_{29}	501 (s)		N-N-H asymmetric bending	0.5153	43
S_{30}	1498 (m)				

vs - very strong; s - strong; m - medium; ms-medium strong; w - weak

present work, the bands appear in the region $3304\text{--}3411\text{ cm}^{-1}$ are assigned to N-H symmetric and asymmetric modes of vibrations, respectively.

C-N stretching—Silverstien *et al*⁹, assigned C-N stretching absorption in the region $1342\text{--}1266\text{ cm}^{-1}$. The spectra of benzene and pyridyl substituted compounds shows the band in the region $1260\text{--}1210\text{ cm}^{-1}$. In analogy with the previous work, the b and appears at 1289 cm^{-1} in the FTIR spectrum and the b and at 1278 cm^{-1} in the FT Raman spectrum of hydralazine is assigned to C-N stretching vibration, respectively.

N-N stretching—In the vibrational analysis of hydrazine and similar compounds, the band due to N-N stretching vibration¹⁰ is identified at 1380 cm^{-1} . Hence, the bands observed at 1373 cm^{-1} in FTIR spectrum and at 1385 cm^{-1} in FT Raman spectrum are

assigned to N-N stretching mode of vibration, respectively, in the present work.

C-H bending—The C-H deformation frequencies in benzene and its derivatives¹¹ are found to occur in the region $1200\text{--}1050\text{ cm}^{-1}$. In the present work, the bands observed at 1135 cm^{-1} and 1065 cm^{-1} in the FTIR spectrum of hydralazine are assigned to C-H bending, respectively.

N-N-H bending—Usually primary amides and secondary amides show a band or bands in the region $1515\text{--}1350\text{ cm}^{-1}$ primarily due to N-H bending¹². In the present investigation, the bands appear at 1345 and 1498 cm^{-1} are assigned to N-N-H symmetric and asymmetric modes of bending vibrations respectively.

C-C=N bending—Normally, the deformation modes¹³ of C-C=N occur in the region $600\text{ cm}^{-1}\text{--}480\text{ cm}^{-1}$. Hence, in the present study, the bands appear at

496 and 585 cm^{-1} in FTIR spectrum, the bands at 490 and 589 cm^{-1} in FT Raman spectrum of hydralazine are assigned to C-C=N bending modes of vibration, respectively.

H-C=N bending—In the vibrational analysis of xanthine and its derivatives, Gunasekaran *et al.*¹⁴ assigned H-C=N absorption at 970 cm^{-1} . In analogy with the previous work, the band appears at 960 cm^{-1} is assigned to H-C=N bending mode of vibration, respectively.

3.3 Method of kinetic constants

The method of kinetic constants has been successfully employed by many researchers^{15,16} for the structural elucidation of different types of molecules. The determination of the symmetry force constants involved in the secular equation from the n_i vibrational frequencies has remained a mathematically unsolved problem. Therefore, any useful attempt to evaluate all the symmetry force constants associated with a problem of order $n_i > 1$ should involve the incorporation of at least $n_i(n_i-1)/2$ additional data other than n_i frequencies. The method of kinetic constants relates the off-diagonal elements of the force constant matrix F , to its diagonal elements through the relation¹⁴

$$\frac{F_{ij}}{F_{jj}} = \frac{K_{ij}}{K_{jj}}, \quad [i < j, i=j=1, 2, 3, \dots]$$

3.4 Potential energy distribution

Once the G and F matrices are obtained the secular equation $[FG - \lambda E] = 0$ has to be solved, where $\lambda = 4\pi^2 C^2 v^2$, and v is the frequency assigned with the particular symmetry coordinate and E is the unitary matrix. The knowledge of the transformation matrix L (L is the transformation matrix obtained by $LL^T = G$) and the kinetic energy matrix K (G^{-1}) leads to the solution of the secular equation due to Wilson yielding the elements of the force constant matrix F . The frequency assignment is verified by evaluating the potential energy distribution using the relation

$$\text{PED} = \frac{F_{ij} L_{ij}^2}{\lambda_j}$$

where PED is the contribution to the potential energy of vibration of the symmetry coordinate whose frequency is v_j , F_{ij} the force constant and L_{ij} , the L -matrix elements. The secular equation has been solved by fixing the initial set of force constants which are taken from the related molecules like

benzene, pyridine, pyrimidine, quinoline, etc.^{14,17}. This set of force constants has been subsequently refined till the convergence takes place by giving suitable increments without fixing any of the force constants by iteration method using computer. In the present work, only the diagonal force constants have been considered.

4 Results and Discussion

Wilson's F-G matrix method has been successfully employed in the normal coordinate analysis of hydralazine. The potential energy distribution for the fundamental modes of vibrations is given in Table 1 and the force constants are summarised. The correctness of the frequency assignments has been checked by the PED calculation and it is seen that the PED calculation of all the fundamental vibrations is satisfactory. This is supportive of the frequency assignment and hence the structure. The force constants of N-H stretching vibration of the compound are found to be around 6.9×10^2 N/m as expected and they contribute PED values of more than 96%. The symmetric and asymmetric C=N vibrations of the molecule show a force constant around 14.8×10^2 and 14.9×10^2 N/m, respectively, contributing to the PED value of more than 83%.

A PED value of around 87% is found to be calculated for C-C stretching vibrations whose frequency is assigned around 1436 cm^{-1} . The force constant of C-H stretching vibration is found to be around 5.9×10^2 N/m and it contributes PED value around 98%. Apart from these major stretching vibrations, the compounds also have a number of bending vibrations. The force constants for these vibrations have been evaluated to be around $0.8-1.2 \times 10^2$ N/m as expected and contribute to the PED values of 40-60%.

5 Conclusion

Thus, a complete vibrational band assignment of hydralazine has been carried out using infrared and Raman spectra on the basis of C_s point group symmetry. A systematic set of symmetry coordinates has been constructed and the potential force constants have been calculated.

The PED calculations regarding the normal modes of vibration provide a strong support for the frequency assignment on the highly complex molecule.

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