Spectral investigation and normal coordinate analysis of piperazine

S Gunasekaran & B Anita
Spectrophysics Research Laboratory, Pachaiyappa's College, Chennai 600 030
E-mail: anitabharathan@yahoo.com

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Piperazine is a secondary amine with the molecular formula C₄N₂H₁₂. A normal coordinate analysis (NCA) has been carried out on this molecule with a systematic set of symmetry coordinates following Wilson’s F-G matrix method based on D₂h point group symmetry. The frequency assignments in the FTIR and FTR spectra have been presented. A reasonable set of potential constants evaluated for this molecule has been compared with those of related molecules and are in the characteristic range. The potential energy distribution has been evaluated using the vibrational spectral data. The potential energy distribution value obtained reflects the correctness of the assignment made.

Keywords: FTIR, FTR spectra, Normal coordinate analysis, Potential energy distribution

1 Introduction

Worm infestation is one of the major public health problems in tropical countries like India. Some 300 million people worldwide are chronically infected with soil-transmitted helminthes and schistosomes¹. The most common parasites found in India are roundworms, hookworms, tapeworms and filarial worms. Piperazine (C₄N₂H₁₂) is a potent anthelmintic used in the therapy of ascariasis (roundworm) and oxyuriasis (threadworm) infestations. The piperazines were originally named because of their chemical similarity with piperadine, a constituent of piperine in the black pepper plant (Piper nigrum). Piperazine owes its anthelmintic activity to its ability to produce flaccid paralysis of the muscles of the parasite². The parasites expelled as a result of drug action are paralysed, but not dead. This eliminates the danger of worm migration and absorption of the autolysis products of parasites.

Vibrational spectroscopy has significant contributions towards the studies of structure and physico-chemical properties of molecular systems like trifluoromethyl benzene derivatives, poly vinylidene fluoride and pyridines³⁶. Recently vibrational spectral analysis and normal coordinate analysis of N- heterocyclic compounds have been carried out by many workers because of their considerable pharmaceutical importance⁷⁹. In the present study, the vibrational spectral techniques like Fourier Transform Infrared (FTIR) and Raman spectroscopy have been used to perform a vibrational analysis on the compound piperazine. Using normal coordinate analysis the potential energy constants have been evaluated on the basis of general valence force-field, applying Wilson’s F-G matrix method. From the structural point of view, piperazine molecule belongs to D₂h point group symmetry, as the amine group is considered to lie in the plane containing the hetero-aromatic ring. In order 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 calculated. The structure of the title compound, the orientation of the principal axis and nomenclature of parameters are given in Fig. 1.

2 Experimental Details

The FTIR spectrum was recorded using Bruker IFS 66V spectrophotometer in the region 4000-450 cm⁻¹ by KBr pellet method. The FTRaman spectrum was recorded using Bruker FRA 106 FTRaman spectrophotometer equipped with 647 nm krypton ion laser instrument in the region 3000-500 cm⁻¹. FTIR and FTR spectrometers have a resolution of 0.1 cm. They have the facilities of signal averaging, signal enhancement and baseline correction. Other spectral manipulations are also possible with multi-tasking OPUS software on the dedicated PC Intel 4. The vibrational spectra of piperazine are presented in
3 Normal Co-ordinate Analysis

Piperazine has 42 fundamental modes of vibration under $D_{2h}$ symmetry. They are distributed as $\Gamma_{\text{vib}} = 7A_{1g} + 6B_{1g} + 4B_{1u} + 4B_{2g} + 5B_{2u} + 6B_{3g} + 5B_{3u}$. However, due to the complexity of the structure of the molecule only 25 modes of vibrations are considered in the present work. Also, the vibrations belonging to Au species are not active in both infra-red and Raman and are not considered in the current work. Since the molecule has a centre of symmetry, it obeys the rule of mutual exclusion. So, the Raman active vibrations are infra-red inactive and vice-versa. The molecular parameters have been taken from Sutton table and are presented in Table 1. With the help of internal co-ordinates, a set of symmetry co-ordinates have been constructed systematically from the sets of equivalent internal co-ordinates using projection operators. The symmetry co-ordinates for the specific modes of vibration taken into consideration in the present work are as follows:

Fig. 1—Structure, orientation of the principal axis and nomenclature of parameters of piperazine

Fig. 2. The Raman spectrum of the molecule in the region 3450 to 3100 cm$^{-1}$ in expanded form is shown in Fig. 3.
Fig. 3—Raman spectrum of piperazine in the region 3450 cm\(^{-1}\) – 3100 cm\(^{-1}\) (Expanded chart)

### Table 1—Molecular parameters of piperazine

<table>
<thead>
<tr>
<th>Bond Length (Å)</th>
<th>Bond angle(°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nature</td>
<td>Symbol</td>
</tr>
<tr>
<td>N – H</td>
<td>r</td>
</tr>
<tr>
<td>C – C</td>
<td>a</td>
</tr>
<tr>
<td>C – N</td>
<td>b</td>
</tr>
</tbody>
</table>

### A\(_{1g}\) species:

\[ S_1 = 1/\sqrt{2}(\Delta r_1 + \Delta r_2) \]
\[ S_2 = 1/\sqrt{2}(\Delta \alpha_1 + \Delta \alpha_2) \]
\[ S_3 = 1/\sqrt{2}(\Delta \delta_1 + \Delta \delta_2) \]
\[ S_4 = 1/\sqrt{2}(\Delta \delta_1 + \Delta \delta_2 + \Delta \delta_3 + \Delta \delta_4 + \Delta \delta_5 + \Delta \delta_6 + \Delta \delta_7 + \Delta \delta_8) \]
\[ S_5 = 1/2(\Delta \alpha_1 + \Delta \alpha_2 + \Delta \alpha_3 + \Delta \alpha_4) \]

### B\(_{1u}\) species:

\[ S_{11} = 1/2(\Delta \alpha_1 - \Delta \alpha_2) \]
\[ S_{12} = 1/\sqrt{8}(\Delta d_1 - \Delta d_2 - \Delta d_3 - \Delta d_4 + \Delta d_5 - \Delta d_6 - \Delta d_7 + \Delta d_8) \]
\[ S_{13} = 1/2(\Delta \beta_1 + \Delta \beta_2 - \Delta \beta_3 - \Delta \beta_4) \]

### B\(_{2g}\) species:

\[ S_{14} = 1/2(\Delta \delta_1 - \Delta \delta_2 - \Delta \delta_3 + \Delta \delta_4) \]
\[ S_{15} = 1/2(\Delta \phi_1 - \Delta \phi_2 - \Delta \phi_3 + \Delta \phi_4) \]
\[ S_{16} = 1/2(\Delta \alpha_1 + \Delta \alpha_2 - \Delta \alpha_3 - \Delta \alpha_4) \]

### B\(_{2u}\) species:

\[ S_{17} = 1/2(\Delta \delta_1 - \Delta \delta_2 + \Delta \delta_3 - \Delta \delta_4) \]
\[ S_{18} = 1/2(\Delta \phi_1 + \Delta \phi_2 + \Delta \phi_3 + \Delta \phi_4) \]
\[ S_{19} = 1/2(\Delta \alpha_1 - \Delta \alpha_2 + \Delta \alpha_3 + \Delta \alpha_4) \]

### B\(_{3g}\) species:

\[ S_{20} = 1/2(\Delta \delta_1 + \Delta \delta_2 + \Delta \delta_3 - \Delta \delta_4) \]
\[ S_{21} = 1/2(\Delta \phi_1 + \Delta \phi_2 - \Delta \phi_3 + \Delta \phi_4) \]
\[ S_{22} = 1/2(\Delta \alpha_1 + \Delta \alpha_2 - \Delta \alpha_3 + \Delta \alpha_4) \]

### B\(_{3u}\) species:

\[ S_{23} = 1/2(\Delta \delta_1 - \Delta \delta_2) \]

3.1 Method of kinetic constants

The complex random internal motions of a vibrating molecule are the result of the superposition of relatively simple vibratory motions known as normal vibrations or normal modes of vibration of the molecule. Each of these has its own fixed frequency. There are qualitative ways of determining the number of normal modes of each symmetry type which will arise in the molecule as a whole and in each set of equivalent internal co-ordinates. It is aimed to
determine how the frequencies of these vibrations, obtained experimentally, are related to the masses of the atoms, the bond angles, bond lengths and also to the force constants of the individual bonds and interbond angles. For this purpose, the Wilson’s $F-G$ matrix method is adopted. All of the required relations are combined in the master equation, $|F G - \lambda E| = 0$, in which $F$, $G$ and $E$ are matrices and the left hand side of the equation is a determinant. $F$ is a matrix of force constants, which brings the potential energies of the vibrations into the equation. $G$ is calculated from the relation $G = B \mu B^T$, $B$ being the matrix formed using the vectors evaluated from the expression for symmetry co-ordinates, $\mu$ is a diagonal matrix of the reciprocal masses of the atoms in the molecule. Since $G$ matrix involves the masses and spatial relationships of the atoms, it brings the kinetic energies into the equation. $E$ is the unit matrix, and $\lambda$ which brings the frequency $\nu$ into the equation, is defined by $\lambda = 4T \nu^2$. To determine the value of $F$, the method of kinetic constants is used, which relates the off-diagonal elements of the $F$-matrix to its diagonal elements through the relation, $F_{ij}/F_{jj} = K_{ij}/K_{jj}$ ($i < j$, $i = j = 1, 2, 3\ldots$). Here, only the diagonal force constants have been calculated for the molecule. The initial set of force constants have been taken from related molecules. The calculation begins with a conjectural assignment of the peaks in the vibrational spectra. The frequency assignment is then verified by evaluating the potential energy distribution using the relation, $PED = F_{ij}/\lambda_i$. Here, $PED$ is the contribution of the frequency $\nu$ to the potential energy and $F_{ij}$ is the potential constant pertaining to that vibration and $\lambda_i$ is the corresponding linear transformation matrix element.

### 3.2 Vibrational analysis of piperazine

The infrared and Raman spectra of the molecule contain a number of bands of varying intensity at specific wave numbers. The vibrational analysis of the molecule helps us to decide which of the vibrational modes give rise to each of the observed band. Generally, amines often exhibit a number of peaks when examined as pressed discs, due to a reaction with the dispersing agent and the formation of amine hydrohalides. The vibrational spectra of piperazine also contain a number of peaks for which assignments have been made on the basis of band position, shape and intensity, in correlation with the vibrational bands of structurally related molecules.

**C-H stretching** — The hetero-aromatic compounds and its derivatives are structurally very close to benzene. The C-H stretching vibrations of aromatic and hetero-aromatic structures occur in the region 2800-3100 cm$^{-1}$. This permits the ready identification of the structure. Also, in this region the bands are not much affected due to the nature and position of the substituents. In secondary and tertiary amines, the symmetrical CH$_2$ stretching frequency of the CH$_2$ group next to nitrogen atom, in addition to being intensified, becomes lower in frequency, appearing near 2800 cm$^{-1}$. Sundaraganesan et al. have assigned 3 bands for CH vibration at 3111, 3051 and 3048 cm$^{-1}$ in their study of 5-bromo-2-nitropyridine, while these bands have been traced at 3062 and 3022 cm$^{-1}$ in the case of 2, 3, 5 tri-iodobenzoic acid by Mohd Chaman et al. Hence, for piperazine, the CH stretching bands of strong intensity have been assigned to the wave numbers 3087, 2987, 2914, 2853 and 2750 cm$^{-1}$. In the Raman spectrum, the peaks due to this vibration are located at 2918, 2833 and 2771 cm$^{-1}$.

**C-C stretching** — The ring C-C stretching vibrations occur in the region 1625-1430 cm$^{-1}$. For aromatic six-membered rings, e.g., benzenes and pyridines, there are 2 or 3 bands in the region due to skeletal vibrations, the strongest usually being at about 1500 cm$^{-1}$. Earlier workers have reported a band at 1061 cm$^{-1}$ due to C-C stretching in isoniazid. In the present work, the frequencies 1120 and 1055 cm$^{-1}$ are assigned to asymmetric and symmetric C-C stretching modes, while their Raman counterpart can be located at 1120 and 1049 cm$^{-1}$ with strong intensity.

**N-H stretching** — The molecule under consideration is a secondary amine and hence N-H stretching vibrations are possible. Heteroaromatics containing N-H groups show N-H stretching absorption in the region 3500-3220 cm$^{-1}$. The position of absorption within this region depends upon the degree of hydrogen bonding between the atoms and hence upon the physical state of the sample or polarity of the sample. In general bands due to N-H stretching vibration are sharper and weaker, and do not occur in as wide a range as those due to the OH stretching vibration. The symmetric and asymmetric N-H stretching vibrations of the molecule piperazine are assigned to 3207 cm$^{-1}$ and 3406 cm$^{-1}$ respectively, in line with values reported by earlier workers.
The corresponding symmetric stretching band in FTRaman spectra is traced at 3223 cm\(^{-1}\), as seen in the expanded chart (Fig. 3).

**C-N stretching** — The identification of C-N stretching frequency is a difficult task, since, in this region there is a possibility of mixing of bands. Silverstein et al.\(^{18}\) have assigned C-N stretching absorption in the region 1342-1266 cm\(^{-1}\). The absorption appears at higher frequencies than the corresponding absorption of aliphatic amines because the force constant of the C-N bond is increased by resonance with the ring. Gunasekaran et al.\(^{19}\) have assigned the IR bands observed at 1315 and 1342 cm\(^{-1}\) to C-N symmetric and asymmetric stretching vibrations in their normal coordinate analysis on diazepam and the bands at 1375-250 cm\(^{-1}\) have been assigned to C-N stretching vibration for 5-bromo-2-nitro pyridine by Sundaraganesan et al.\(^{13}\). Using the above as reference, the bands of medium intensity at 1323, 1268 and 1218 cm\(^{-1}\) and have been assigned to asymmetric C-N stretching, while that at 1199 cm\(^{-1}\) has been assigned to symmetric C-N

<table>
<thead>
<tr>
<th>Normal modes</th>
<th>Frequency (cm(^{-1}))</th>
<th>Band assignment</th>
<th>Force constant (10^2 N/m)</th>
<th>PED%</th>
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<tbody>
<tr>
<td>(\text{v}_1)</td>
<td>3207(vs)</td>
<td>3223(s)</td>
<td>N-H symm. Stretching</td>
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<td>(\text{v}_2)</td>
<td>1199(m)</td>
<td>1186(m)</td>
<td>C-C symm. Stretching</td>
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<td>(\text{v}_3)</td>
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<td>1049(w)</td>
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<td>C-H symm. Stretching</td>
<td>4.8613</td>
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<td>(\text{v}_5)</td>
<td>474(m)</td>
<td>424(w)</td>
<td>CNC deformation</td>
<td>1.0572</td>
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<tr>
<td>(\text{v}_6)</td>
<td>1360(s)</td>
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<td>(\text{v}_7)</td>
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<td>(\text{v}_{10})</td>
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<td>1448(vw)</td>
<td>CH(_2) deformation</td>
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<td>C-N asymm. Stretching</td>
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<tr>
<td>(\text{v}_{13})</td>
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<td>-</td>
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<td>5.0318</td>
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<tr>
<td>(\text{v}_{14})</td>
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<td>1120(vw)</td>
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<td>-</td>
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<td>(\text{v}_{16})</td>
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<td>-</td>
<td>CH(_2) deformation</td>
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<td>1294(s)</td>
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<td>2912(s)</td>
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<td>CNH asymm. Bending</td>
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<tr>
<td>(\text{v}_{20})</td>
<td>669(vw)</td>
<td>-</td>
<td>CCN deformation</td>
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<tr>
<td>(\text{v}_{21})</td>
<td>2853(vs)</td>
<td>2833(m)</td>
<td>C-H asymm. Stretching</td>
<td>4.4612</td>
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<tr>
<td>(\text{v}_{22})</td>
<td>612(w)</td>
<td>-</td>
<td>CCN deformation</td>
<td>0.8866</td>
</tr>
<tr>
<td>(\text{v}_{23})</td>
<td>502(m)</td>
<td>-</td>
<td>CNC deformation</td>
<td>0.8964</td>
</tr>
<tr>
<td>(\text{v}_{24})</td>
<td>456(w)</td>
<td>461(w)</td>
<td>CCN deformation</td>
<td>1.3254</td>
</tr>
<tr>
<td>(\text{v}_{25})</td>
<td>1364(s)</td>
<td>-</td>
<td>CH(_2) deformation</td>
<td>0.5413</td>
</tr>
</tbody>
</table>

vs - very strong; s – strong; m – medium; w – weak; vw - very weak.
stretching for the title compound. In Raman spectrum the C-N bands appear at 1186, 1120 and 1049 cm\(^{-1}\).

**Deformation vibrations** — For piperazine, the strong peaks observed at 1556, 1510 and 1490 cm\(^{-1}\) is due to asymmetric CNH deformation vibration. The symmetric CNH deformation vibration is assigned to 1475 cm\(^{-1}\) in the FTIR spectrum. In Raman spectrum the bands for the same vibration appear at 1448 cm\(^{-1}\). In making the assignments for CNH deformation vibrations, guidance has been taken from the results discussed by previous authors\(^{19,20}\). Generally, strong bands in the region 560 cm\(^{-1}\) and 500 cm\(^{-1}\) are due to the CO\(_2\) or CCN group deformation vibrations. In the present investigation, the bands of medium to weak intensity at 669, 612, 601 and 565 cm\(^{-1}\) are assigned to CCN deformation vibrations.

**4 Results and Discussion**

Normal coordinate analysis of piperazine under \(D_{2h}\) symmetry has been carried out by applying Wilson’s \(F-G\) matrix method, using the vibrational frequencies observed in FTIR and FTRaman spectra. The normal modes of vibration, calculated force constants and the corresponding PED values are presented in Table 2. The force constants of the N-H stretching vibration of the compound is found to be 6.06 \(\times 10^2\) N/m, as expected and the C-N stretching mode of vibration shows a force constant around 5 \(\times 10^2\) N/m as reported in literature\(^{15}\). Both the vibrations contribute to a PED of more than 90%. The force constant obtained for C-C asymmetric stretching vibrations are found to be 5.1 \(\times 10^2\) N/m and their contribution to PED is 98\%. Their symmetric counterpart contributes to a PED value of 97% with a force constant equal to 4.9634 \(\times 10^2\) N/m, as reported in literature\(^{19,21}\).

In addition to the above stretching vibrations, the force constants for bending vibrations have also been evaluated. CNH and CNC bending vibrations have force constants of 1.3349 \(\times 10^2\) and 0.9012 \(\times 10^2\) N/m which are in agreement with reported values\(^{7,18}\).

**5 Conclusions**

A satisfactory vibrational band assignment has been made for the molecule piperazine using FTIR and FTRaman spectra. A systematic set of symmetry coordinates has been constructed and the force constants have been evaluated using Wilson’s \(F-G\) matrix method. Further, to check whether the chosen set of vibrational frequencies contribute to the maximum value of potential energy associated with the normal coordinates of the molecule, the PED has also been evaluated. It is observed that the potential energy distribution of the fundamental vibrations is satisfactory, confirming the frequency assignment of the molecule.

**References**

10. Sutton L E, Table of Inter Atomic Bond distances and Bond Angles in Molecules and Ions, (Chemical Society, London), 1956.