Chapter-1

INTRODUCTION
This thesis is mainly concerned with the study of molecular structures and vibrational assignments of heterosubstituted-4-Bromomethycoumarins, 6-Methoxy-4-bromomethylcoumarin and 2-Iodopyridine by using the experimental techniques of IR and Raman spectroscopy combined with theoretical molecular orbital (MO) and normal mode calculations. In this Chapter an attempt will be made to present the theory of IR and Raman spectroscopy except a qualitatively through a short discussion of the basic elements. We will also present an overview of the studies on similar molecular systems, and motivations for selecting our compounds. Chapter-2 will deal with the method of preparation of the compounds; the details of IR and Raman measurements; the basics of theoretical molecular orbital (MO) and normal mode calculations. Chapter-3 will present IR and Raman spectral measurements, structures and assignments for 6- and 7-Methyl-4-bromomethylcoumarins. In a similar way, in Chapter-4, we will discuss 6-Chloro- and 7-Chloro-4-bromomethylcoumarins; in Chapter-5, 7, 8-Benzo and 5, 6-Benzo-4-bromomethylcoumarins; in Chapter-6, 6-Methoxy-4-bromomethylcoumarin; in Chapter-7, 6-Methoxy-azidomethylcoumarin; and finally, in Chapter-8, 2-Iodopyridine.

1.1 Theoretical background:

The measurement and interpretation of the molecular vibrational spectrum is of fundamental importance that may very well be correlated with physical, chemical and biological processes. The study of vibrational spectra throws light on the identification of chemical functional groups, the molecular energy, molecular structures, and relative concentrations of two or more components, molecular conformation, force-fields, thermodynamic properties, rotational isomerism, tautomerism, and the nature of hydrogen bonding [1].
Vibrational Spectroscopy is the study of the measurement and theoretical interpretation of molecular vibrational spectra [2]. Typically, a beam of radiation from a source such as heat source or a laser is passed through a sample, and the radiation absorbed or scattered by the sample is measured. Thus the resulting spectrum will show bands characterized by the characteristic frequencies and intensities, arising from molecular transitions between different vibrational states. Each molecular spectrum shows the characteristic frequencies and intensities corresponding to vibrational motions of chemical units or functional groups. [1-2]. Modern methods of spectroscopy, both experimental and theoretical, in different regions of electromagnetic spectrum have provided the spectroscopist with an indispensable tool for the investigation of molecular spectra and structures which may very well correlated with a host of molecular phenomena. Depending on the information sought, we can choose an appropriate method. Understanding of the vibrational structures of the molecule enables us to understand its physical as well as chemical properties and even biological properties [2].

A molecule is considered as an assembly of many atoms and the total molecular energy is the sum of the translational energy, rotational energy, vibrational energy, and electronic energy. For a first approximation these energy contributions can be treated separately. Electronic energy transitions normally give rise to vibrational bands in the ultraviolet and visible regions of the electromagnetic spectrum. Pure rotation gives rise to rotational lines in the microwave region. Molecular vibrations give rise to bands throughout most of the Near Infrared (NIR) and Mid Infrared regions (MIR) of the spectrum. We are interested in the Mid Infrared region (4000-100 cm\(^{-1}\)) where the vibrational transitions occur. Vibrational spectra can be utilized directly as molecular 'finger prints' to identify the chemical constituents of the
molecule. A study of molecular vibrations gives a dynamic picture of the molecule, unlike a static picture given by the X-ray diffraction method. A wide range of compounds in different phases like solids (crystals / powder), liquids, solutions, gases, and films can be used in the study. The information contained in vibrational spectrum help in the elucidation of molecular structure, intra- and inter-molecular forces in condensed phases and the nature of the chemical bond (i.e. ionic, valence or the hydrogen bonding).

The two methods, Infrared and Raman spectroscopies, are widely used and both yield the complementary types of information. For a complete vibrational analysis both the methods should necessarily be used. It is not an exaggeration to say that both IR and Raman are the most powerful physical methods employed by the vibrational spectroscopist because other physical techniques like X-ray diffraction and electron diffraction methods give only structural information of molecules from intricate analysis which is very time consuming process. In attempting to account for the observed vibrational spectrum (Infrared or Raman spectrum) we have to consider a simple model [3-4]. In this model, the molecules are made up of atoms that are loosely held together by bonds as weightless springs obeying Hooke's law. The atoms may be electrically polarized by an external electrical field as in the beam of light and both polarizibility and electric dipole moment depend upon the relative motion of the atoms. According to classical electrodynamics, the rotational motion causes radiation (emission or absorption) if and only if the molecule has permanent electric dipole moment. If the vibrational motion alters the electric dipole moment during the vibration, then the vibrating molecule can emit or absorb the radiation. The fundamental requirement for infrared activity, leading to absorption or emission of infrared radiation is that there must be a net change in the electric dipole moment
during the vibration of the molecule. Similarly, we can explain the Raman effect using classical theory as the induced dipole moment due to an incident light for a vibrating molecule will depend up on the orientation of the molecule and relative position of its atoms and for Raman activity the net change in bond polarizability must occur. Since the molecular configuration changes periodically because of vibrational motions the scattered radiation is modulated by the vibrational frequencies equal to the sum and to the differences of the incident frequency and the frequencies of molecular vibrations in addition to incident frequency. However, the classical theory fails to explain the intensities observed in the spectrum of real molecules, which quantum theory explains satisfactorily. The quantum picture of the Raman effect is that a photon of energy $h\nu_0$ comes up to a molecule in a given vibrational state $n''$, causing a transition to another higher vibrational energy level $n'$ differing in energy by an amount $h\nu_{n''-n'}$. This amount of energy is subtracted from the incident photon’s energy so that the emitted or scattered photon then has the energy $h\nu_0 \pm h\nu_{n''-n'}$ and therefore has the vibrational frequencies $\nu_0 \pm \nu_{n''-n'}$ on either side of the incident frequency $\nu_0$. Since in general more molecules are in the lower than in higher vibrational energy states so that there will be more cases in which the photon gives up some of its energy giving rise to stronger Stokes lines ($h\nu_0 - h\nu_{n''-n'}$) than the weaker Anti-Stokes lines ($h\nu_0 + h\nu_{n''-n'}$) [4].

A molecule with $N$ number of atoms possesses $3N-6$ vibrational degrees of freedom, known as normal modes of vibration (for a linear molecule, the number of modes is $3N-5$). A pure vibrational spectrum shows bands arising due to the transitions between the adjacent vibrational states. The frequencies arising due to these transitions are referred to as fundamental normal modes of vibration or simply fundamentals. The integral multiples of the fundamental vibrations are called
overtones. Two fundamentals or a fundamental and an overtone may interact to give sum or difference of these two frequencies. They are called combination bands [4]. These overtones and combination bands correspond to transitions between states other than adjacent ones, and arise due to the effect of anharmonicity of vibrations. Both overtone and combination bands are generally weak in intensity. The normal modes of vibration have symmetry properties characterized by symmetry point group to which the molecule belongs and hence the normal modes break up into sets; each set corresponds to a symmetry species or type [4]. Conversely, each symmetry species describes the symmetry properties of normal modes. The normal modes which have same frequencies are said to be degenerate and which have different frequencies are said to be non-degenerate. For example, benzene has ten non-degenerate modes and twenty degenerate modes [3]. The calculation of the number of normal modes for a given molecule will be discussed later.

1.2 Selection Rules

According to the theory of Infrared Spectroscopy, not all of the normal modes of vibration can be excited by the infrared radiation. The vibrational transitions which produce a spectrum are governed by certain Selection Rules [4].

1.2.1 Selection Rule for Infrared Transitions:

For a fundamental transition to occur by absorption or emission of infrared radiation, say, \( v'' \rightarrow v' \) (where \( v'' \) is the lower vibrational state and \( v' \) is the higher vibrational state), the transition moment integrals of the form: \( \int \psi_\nu^* M_x \psi_\nu' \, dt \), \( \int \psi_\nu^* M_y \psi_\nu' \, dt \) and \( \int \psi_\nu^* M_z \psi_\nu' \, dt \), where \( \psi_\nu^* \) is the wave function for the higher vibrational state, and \( \psi_\nu' \) is the wave function for the lower state involved in the transition, must be nonzero; the \( M_x \), \( M_y \) and \( M_z \) are the components of the molecular electric dipole moment. If any one of these three components is nonzero, then the
transition moment integral is nonzero and the transition is allowed. By the symmetry considerations we can determine whether the transition moment integral is zero or nonzero, and hence whether the transitions is allowed or forbidden. If one of the products, say, $\psi_{\nu}M_{\alpha}\psi_{\nu}$ in the transition moment integral is not totally symmetric under any symmetry operation of the point group to which the molecule belongs, then the integral will be zero. This leads to a very simple rule for the activity of fundamentals in infrared absorption.

"A fundamental transition will be infrared active (that is, gives rise to an IR band) only when there is at least one component of the dipole moment, $M$, that has the same species as the product $\psi_{\nu}\psi_{\nu}$." [1].

1.2.2 Selection rule for Raman Transitions:

For a fundamental transition to occur by Raman scattering of radiation the transition moment integral must be nonzero as for IR transitions. The transition moment integrals are of the form: $\int\psi_{\nu}\alpha\psi_{\nu}\,d\tau$ where $\alpha$ represents the polarizability of the molecule and it is a tensor of second rank having nine Cartesian components ($\alpha_{xx}, \alpha_{yy}, \alpha_{zz}, \alpha_{xy}, \ldots$). The symmetry species of these components are usually shown in the character tables for different symmetry point groups. The selection rule for Raman transition is similar as for IR transitions:

"A fundamental transition will be Raman active (that is, gives rise to a Raman shift) if the product $\psi_{\nu}\psi_{\nu}$ has the same species as at least one of the six components $\alpha_{xx}, \alpha_{yy}, \ldots$ of the polarizability tensor $\alpha$" [1]. Thus, for both IR and Raman transitions, the vibrational quantum numbers of the vibrational states change by $\Delta \nu = \nu' - \nu'' = \pm 1$. However, any observed spectrum shows, in addition to bands corresponding to fundamentals, bands due to overtones and combinations as a result
of anharmonicity of normal modes. Thus the additional selection rules are: $\Delta \nu = \pm 2, \pm 3, \ldots$.

1.3 Normal Modes of Vibration:

In a diatomic molecule the two nuclei are joined by a single bond much like two mass points joined by a spring. Thus the molecule has a single mode of vibration, that is to say, the two nuclei move back and forth along the bond with a characteristic vibrational stretching frequency determined by the stiffness of bond oscillator and masses. However, as we have seen a polyatomic molecule has a large number of normal modes (3N-6 or 3N-5) breaking up into stretching, bending, torsional, wagging and rocking vibrations with characteristic frequencies and symmetry properties. In the theory of molecular vibrations for small amplitudes, each normal mode is best described in terms of a normal coordinate which is a linear combination of internal coordinates (i.e. coordinates refer to changes in bond lengths, bond angles, etc). There will be as many normal coordinates as there are normal modes. Thus, for a given molecule, group theoretical considerations enable us to calculate a priori the number of normal modes (or normal coordinates) of each symmetry type or symmetry species. In the theory of matrix representation of symmetry point groups as discussed in the Group Theory, symmetry species refer to a definite small number of non-equivalent irreducible representations possible (matrices of smaller dimensions) for each point group. Further, it is possible to determine, again a priori, which of the normal modes are IR modes or IR active and which are Raman active, including the degeneracy of modes [1, 4]. Since the method of calculating the normal modes of each symmetry species is straightforward we do not wish to give the details here except the results for Coumarin and Pyridine as examples.
As the Coumarin, shown in Fig 1.1 (a), belongs to C₅ point group, the fifty five normal modes break up into 31 A'+ 14 A", where there are thirty one symmetric or in-plane vibrations and fourteen antisymmetric or out-of-plane vibrations. All the modes are both IR and Raman active. Similarly, for Pyridine, shown in Fig 1.1 (b), which belongs to C₂ᵥ point group (with the molecule in the x-y plane, C₂ along y-axis and z-axis normal to the plane), twenty seven normal modes of vibration are distributed as 10 A₁ + 3 A₂ + 5 B₁ + 9 B₂. All but A₂ are both IR and Raman active.

1.4 Group Frequency Correlations:

The structural features of a molecule having functional groups, produce characteristic and reproducible vibrational frequencies in the spectrum. These frequencies are called group frequencies. The group frequency concept is extremely useful as an aid to the interpretation of vibrational spectra. Its main hypothesis is that chemical groups have characteristic frequencies which are affected only by the molecular environment of the group to a slight extent. Over the years, much has been published in terms of the group frequencies which are the key to unlocking the spectra-structure relationships of the associated molecular vibrations [1-4]. For example, the existence of one or more aromatic rings is readily determined from the C-H and C-C ring vibrations. The C-H stretching occurs near 3000 cm⁻¹. The structure of the bands is defined by the number and positions of the C-H bonds around the ring. The same thing applies to the C-H out-of-plane bending vibrations. Similar group frequencies are produced due to substituents on the ring when either H, or C-H are
replaced. The application of this principle is effective as long as normal modes are pure, that is to say, each normal corresponds to a single vibrational frequency of a chemical group. Thus the observed bands are readily assigned to their normal modes on a one-to-one basis. This is valid for small to moderate sized symmetrical molecules. However, as molecules become large and their symmetry lowered, this picture often becomes more complex with coupling of normal modes showing contributions from more than bond oscillators, as will become evident in discussions that follow in subsequent chapters. Nevertheless, a combined application of spectra-structure correlations and normal mode analysis enables us to carry out assignments satisfactorily.

1.5 Overview and Motivations:

Coumarin and its derivatives are indexed in the chemical abstracts as 2H [1]-benzopyran-2-ones. The parent Coumarin can be looked up as arising out of the fusion of benzene ring with the C (5)-C (6) bonds of pyran-2-one.

![Fig 1.2 Standard numbering scheme for pyran-2-one and Coumarin](image)

The numbering adopted for molecular structure is as shown in Fig 1.2 [5]. In Coumarin, C (6) and C (8) are most reactive centers [6]. Wald and Feuer have studied the ability of Coumarin and its derivatives to induce drug metabolizing enzymes by quantum chemical analysis [7]. The dipole moment of Coumarin is $4.51 \times 10^{-18}$ e.s.u [8]. The crystal structure of Coumarin was first reported by S. Ramaswamy in 1941 [9]. Coumarin derivatives are associated with the class of naturally occurring lactones that are found in different food sources such as fruits, herbs, and vegetables [10].
number of derivatives have been identified from natural sources, especially green plants. They are of great interest owing to their vital and diverse role in the fields of biology, medicine, industry, botany and chemistry [11-12]. The Coumarin derivatives or, simply coumarins possess diverse biological properties. The pharmacological and biochemical properties and therapeutic applications of simple Coumarins depend upon the pattern of substitution. Some synthetic modifications of natural Coumarins like acsculamin are of pharmacological importance. The coumarins are extremely variable in structure due to the various types of substitutions in their basic structure which can influence their biological activity. Hence coumarins exhibit important effects in plant biochemistry and physiology, acting as antioxidants, enzyme inhibitors and precursors of toxic substances. Further, these compounds are involved in the actions of plant growth hormones and growth regulators, the control of respiration, photosynthesis, as well as defense against infection. The coumarins have long been recognized to possess anti-inflammatory, antioxidant, anti-allergic, hepatoprotective, anti-thrombotic, antiviral, and anti-carcinogenic activities. The coumarin group consists of molecules of great versatility, containing both natural products and substances used in the pharmaceutical industry as antibiotics, antiviral agents, anticoagulants (for example psoralen, angelicin etc, novobiocin and warfarin), as pesticides, sensitizers in phototherapy as well as in the chemical industry as optical brighteners and laser dyes [13]. Their photochemical properties dominate their utility. Electron donor or acceptor groups or their combinations at positions 4th and 7th of the Coumarin nucleus result in bathochromic shifts whereas extension of the aromatic or conjugated system of the molecule causes pronounced enhancement of fluorescence intensity [14-15]. The derivatives of coumarin belong to the well-known class of chemical substances, many of which are natural compounds displaying biological
activity [16]. Like simple pyrones, the properties of the heterocyclic ring of coumarin are greatly influenced by the presence of substitutents. The Coumarin nucleus has been widely employed as such, affording a number of excellent reagents of substituted bromomethylcoumarins with significant commercial acceptance [13]. Many 4-bromomethylcoumarins like 7-Methoxy-4-bromomethylcoumarin, and its acetoxy analogue 7-Acetoxy-4-bromomethylcoumarin, and 7,8-Benz0-4-bromomethylcoumarin are also reported as fluoregenic reagents [13]. 4-Bromomethylcoumarins have served as fluorescent labels for t-RNA [17-18]. Chlorinated derivatives have been found to be antibacterial [19] and photographic [20] developers. 6-Methyl-4-bromomethylcoumarin, whose vibrational spectroscopy has been reported from our laboratory [12], also belongs to the class of 4-Bromomethylcoumarins that serves as useful precursor in the synthesis of 4-Aryloxyethylcoumarins, 4-Dichloroacetamidomethylcoumarins and 4-2-Benzofuraxylcoumarins [21-23].

As far as the spectroscopic studies of coumarins are concerned, the parent Coumarin and its some derivatives have been subjected to spectroscopic studies [24-26]. Specifically, Thomas Wolff and Helmut Gorner have investigated the photodimerization of the parent Coumarin and a series of 6-Alkyl substituted coumarins in solution by the time resolved UV-visible absorption spectroscopy [27]. Substitution and solvent effects on the photophysical behavior of the Coumarin and its derivatives (that includes methyl, methoxy, chlorine and their combinations) have been reported by Macanita, et al [28]. Ganguly and Bagchi have studied the UV spectrum of Coumarin and its methyl derivatives [29]. While the literature is abound with photochemical and photophysical studies of coumarins, it seems that not much work has been reported on the experimental and theoretical vibrational spectroscopy.
of coumarin derivatives. However, the vibrational spectra of Dihydro-, 6-Methyl-, and 7-Methylcoumarins have been studied [30]. Probably the first report on the Raman spectrum of the Coumarin in the crystalline state is due to Venkateshwaran [31]. This spectrum shows a large number of intense bands including in those regions where they are expected to be weak even in liquid phase. This was followed by a short supplementary report on the low frequency Raman bands assigned to lattice vibrations. The Infrared spectrum of parent Coumarin is reported by Murti and Sheshadri in 1938 [32]. Proton magnetic resonance spectra of Coumarin and its derivatives were reported by Dharmatti et al [33]. Many of the crystallographic data has also been reported in the past to study the intermolecular forces acting which are responsible for the stability of the molecule [34-39]. For example, Parthapratim Munshi and Tayur N. Guru Row have studied C-H....O and C-H....δ interactions in Coumarin, 1-Thiocoumarin, and 3-Acetylcoumarin based on the X-ray diffraction data at 90 K [40].

Pyridine and its derivatives have been the subject of investigations by several workers in the last fifty years [41]. Green et al studied the vibrational spectra of monosubstituted pyridines with fluorine, chlorine and bromine along with deuterated compounds. In a series of studies, Stidham and DiLella assigned the vibrational spectra of several deuterium substituted pyridines including a detailed investigation of Fermi resonance in the region 1595 to 1553 cm\(^{-1}\)[42]. Gabor Pongor et al computed the vibrational frequencies of pyridine at 4-21 Hartree-Fock (HF) level, by the method of Scaled Quantum Mechanical (SQM) force-field [43]. This was the one of the early attempts to compute the harmonic force-field and then the vibrational spectra of pyridine and its deuterated forms by a priori method. In order to aid statistical thermodynamic calculations, Draeger reported complete vibrational assignments...
based on force-field calculations of several deuterated species of pyridine and methylpyridines [44]. Recently, new assignments of the vapor-phase vibrational spectra of pyridine have been reported by T.D. Klots [45]. Arenas et al have recently assigned vibrational spectra of Methylpyridines using the scaled Quantum Mechanical Force Field (SQMFF) calculations [46]. 2-Iodopyridine is a versatile reagent used in Sonogashira and Suzuki coupling reactions [47-49]. Hussein Abdel et al have reported the assignments of IR and the Raman spectra of 2-Fluoro, 2-, 3-Iodopyridines using only "spectra-structure correlation" principles [50]. We therefore reviewed all the assignments of 2-Iodopyridine by measuring IR and Raman spectra; the assignments have been supported by extensive calculations using \emph{ab initio}, density functional and second order perturbation theoretical methods. We have also carried out potential energy distribution (PED), analysis to aid the assignment.