Interaction Study of Lysine-Phenylalanine Dipeptide With Water Molecule

Soniya,K

(12PPH011)

Thesis submitted to

Avinashilingam Institute for Home Science and Higher Education for Women

Coimbatore – 641 043

In partial fulfilment of the requirements for the Degree of

Master of Science in Physics

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31.3.14
Signature of the Head of the department

31.3.14
Signature of the Supervisor

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SONIYA . K

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CHAPTER 1

INTRODUCTION

1.1 BIOMOLECULES:

Living cells are very large molecules, such as proteins, nucleic acids, and polysaccharides. These molecules are larger by many powers of ten than the smaller molecules from which they are built. Hundreds or thousands of these smaller molecules, or monomers, are linked to produce macromolecules, called polymers. Bio-molecules are made up of six elements –carbon, hydrogen, oxygen, nitrogen, sulphur, and phosphorus. Central to these bio molecules is carbon, which has the unique property of being able to bond to itself in long chains and have self –bonding because it allows many different compounds to be formed by mere rearrangement of the existing skeleton, not by having to reduce the compound to its different elements and then resynthesize from scratch [1].

1.2 PROTEINS:

Protein is the complex organic nitrogenous substances found in the cells of the living beings and are most abundant intracellular macro-molecules. Proteins are essential to cell structure and cell-function. The proteins with catalytic activity are largely responsible for determining the phenotype or properties of a cell in a particular environment. Generally proteins are colourless and insoluble in water, alcohol and ether. It is denatured by heat or treatment with mineral acids and hydrolyzed by enzymic treatment or by mineral acids. The resultant products are the constituent amino acid residues and subjected to complete hydrolysis, proteins yield some twenty different types of nitrogenous compounds called amino acids. These amino acids constitute the building blocks of proteins which are essentially organic compounds consisting of amino as well as acidic groups. All amino acids constituting a protein molecule are α types since the amino group is present on the α-Carbon atom, the carbon next to the carboxyl carbon.

1.3 AMINO ACIDS:

Amino acids are carboxylic acids having an amino group and naturally occurring prevalent amino acids are α-amino acids. In which 'amino' functional group is present at α-carbon.

In general, all amino acids have an amino (-NH2) group, carboxylic (-COOH) group, and a hydrogen atom attached to carbon along with a side chain as shown in **fig 1.1**. Amino acids differ in their side chains is shown in the **table 1.1**. The variation in the nature of side chain imparts characteristic properties to amino acids. Amino acids form polymers known as peptides and proteins.

Though a large number of amino acids (more than 500) exist in nature, however, proteins in all living organisms mainly consists of twenty amino acids. Protein molecule may contain several hundreds or thousands of amino acid units joined in different combinations. Amino acid contains an amine and carboxylic group, it exhibits both acidic as well as basic behaviour[2].

1.4 STEREOISOMERISM OF AMINO ACIDS:

Stereoisomer's have the same molecular formula and the same structure but differ only in spatial configuration. Stereoisomerism of amino acids are of two types namely :

1. Geometrical and
2. Optical.

Geometrical isomers arise from peculiar geometry of compounds having a double bond within the carbon chain. Optical isomers differ from each other in the disposition of the various atoms or groups of atoms in space around the asymmetric carbon atom. Two amino acids in which, one will be having general structure and the other will be an enantiomer or mirror image isomer of the first compound is shown in fig 1.2. When the carboxylic group is written in the right in the projection formula and the amino group is below the α- carbon atom, is an L-amino acid. All the amino acid in protein contain L-form. Bacteria and antibodies contain D-form.

1.5 CLASSIFICATION OF AMINO ACIDS:

Amino acids are classified

1) Based on the chemical reactions they undergo in solution form as

a) Acidic b) Basic c) Neutral

2) Based on their nutritional importance as

a) Essential b) Semi-essential c) Non-essential

1.5.1 CLASSIFICATION BASED ON CHEMICAL NATURE:

ACIDIC AMINO ACIDS: The side chain of acidic amino acids contain either carboxylic or carboxyamide group.

Examples are: Aspartic acid, Glutamic and Asparagines.

BASIC AMINO ACIDS: The side chain of basic amino acids have a basic group of amino or an imidazole ring. Examples are: Asginine, Lysine, Hydroxylysine and Histidine.

NEUTRAL AMINO ACIDS: The larger number of amino acids belongs to neutral amino acids. These neutral amino acids are further classified as:

a) ALIPHATIC NEUTRAL AMINO ACIDS: The side chain of these amino acids contains either hydrogen, or an alkyl group, or hydroxyalkyl group. Examples of aliphatic neutral amino acids are Glysine, Alanine, Valine, Leusine, Isoleusine, Serine and Threonine.

b) AROMATIC NEUTRAL AMINO ACIDS: Aromatic amino acids have side chain of an aromatic ring. For example: Phenylalanine and Tyrosine.

c) SULFUR CONTAINING NEUTRAL AMINO ACIDS: The side chain of these amino acids contains thiol group (-SH) such as in cysteine or methylthio group (-SH3) such as in methionine, or a disulphide linkage such as in cysteine.

d) HETEROCYCLIC NEUTRAL AMINO ACIDS: Heterocyclic group such as indole or pyridine belongs to the side chain of Heterocyclic neutral amino acids. For example: Tryptophan, Proline and Hydroxyl proline.

1.5.2 CLASSIFICATION BASED ON NUTRITION IMPORTANCE:

a) ESSENTIAL AMINO ACIDS: The amino acids that are not synthesised by body are required to be taken externally through diet, termed as essential amino-acids.Valine,Leusine,Isoleusine,Phenylalanine,Threonine,Tryptophan,Methionine and Lysine are some of the essential amino acids.

The amount of these amino acids required by our body is 1.1-0.25g per day. These amino acids are synthesized industrially and added to food stuff.

b) SEMI-ESSENTIAL AMINO ACIDS: These amino acids are not synthesised in human body in sufficient amount during growth.Such amino acids are essential in pregnant women, lactating mothers and in growing children. These amino acids have an important role as growth promoting nutrients. Arginine and histidine fall under this category.

c) NON-ESSENTIAL AMINO ACIDS: These amino acids are synthesised by human body from other materials through a series of biochemical reactions and are not consumed through diet. Ten amino acids have been classified under this category namely:Alanine, Asparagine, Aspartate, Glutamine, Glutamate, Glysine, Proline, Serine, Tyrosine and Cysteine.

1.6 PROPERTIES:

Amino acids exhibit the following properties:

a) They are colourless crystalline substances and have high melting point.

b) Highly soluble in water as compared to other polar solvents.

c) Large dipole moment and high dielectric constant value[2].

1.6.1 STRUCTURE OF PROTEIN:

Protein structure is the biomolecular structure of a protein molecule. Proteins are polymers – specifically polypeptides -sequences formed from various L-α-amino acids. Each unit of a protein is called an amino acid residue because it is the residue of every amino acid that forms the protein by losing a water molecule is shown in fig 1.3. By convention, a chain under 40 residues is often identified as a peptide, rather than a protein. To perform their biological function, proteins fold into one or more specific spatial conformations, driven by a number of non-covalent interactions such as hydrogen bonding, ionic interactions, Van der Waals forces, and hydrophobic packing..

A protein undergo reversible structural changes in performing its biological function. The alternative structures of the same protein are referred to as different conformations, and transitions between them are called conformational changes.

There are four distinct levels of protein structure,namely.,

(1) Primary structure
(2) Secondary structure
(3) Tertiary structure
(4) Quaternary structure

(1) Primary structure:

The primary structure of a protein is the linear sequence of amino acids in the polypeptide chain. The primary structure is held together by covalent bonds such as peptide bonds, which are made during the process of protein biosynthesis or translation. The two ends of the polypeptide chain are referred to as the carboxyl terminus (C-terminus) and the amino terminus (N-terminus) based on the nature of the free group on each extremity.The primary structure of a protein is determined by the gene corresponding to the protein. A specific sequence of nucleotides in DNA is transcribed into mRNA, which is read by the ribosome in a process called translation. The sequence of amino acids was discovered by Frederick Sanger. The sequence of a protein is unique to that protein, and defines the structure and function of the protein.

(2) Secondary structure:

Secondary structure refers to highly regular local sub-structures. Two main types of secondary structure, the alpha helix and the beta strand or beta sheets. These secondary structures are defined by patterns of hydrogen bonds between the main-chain peptide groups. They have a regular geometry, being constrained to specific values of the dihedral angles ψ and φ on the Ramachandran plot. Both the alpha helix and the beta sheet represent a way of saturating all the hydrogen bond donors and acceptors in the peptide backbone. Some parts of the protein are ordered but do not form any regular structures. Several sequential secondary structures may form a "supersecondary unit".

(3) Tertiary structure:

Tertiary structure refers to the three-dimensional structure of a single, double, or triple bonded protein molecule. The alpha-helixes and beta pleated-sheets are folded into a compact globular structure. The folding is driven by the non-specific hydrophobic interactions, the burial of hydrophobic residues from water, but the structure is stable only when the parts of a protein domain are locked into place by specific tertiary interactions, such as salt bridges, hydrogen bonds, and the tight packing of side chains and disulfide bonds. The disulfide bonds are extremely rare in cytosolic proteins, since the cytosol (intracellular fluid) is generally a reducing environment.

(4)Quaternary structure:

Quaternary structure is the three-dimensional structure of a multi-subunit protein and how the subunits fit together. The quaternary structure is stabilized by the same non-covalent interactions and disulfide bonds as the tertiary structure. Complexes of two or more polypeptides (i.e. multiple subunits) are called multimers. Specifically it would be called a dimer if it contains two subunits, a trimer if it contains three subunits, a tetramer if it contains four subunits, and a pentamer if it contains five subunits. The subunits are frequently related to one another by symmetry operations, such as a 2-fold axis in a dimer. Multimers made up of identical subunits are referred to with a prefix of "homo-" (e.g. a homotetramer) and those made up of different subunits are referred to with a prefix of "hetero-", for example, a heterotetramer, such as the two alpha and two beta chains of hemoglobin.

1.7 PEPTIDE BOND:

Amino acids are covalently bonded together in chains by peptide bonds. Peptide bonds are formed between the carboxyl group of one amino acid and the amino group of the next amino acid. Peptide bond formation occur in a condensation reaction involves loss of water molecule shown in fig 1.3. The amide bonds between the adjacent amino acid are known as the peptide bond and the chain formed is known as the peptide chain.

By elimination of a water molecule, two amino acids form a “Dipeptide” and their link is a (-CO-NH_) peptide bond, three amino acid linked together form “Tripeptide” and a short chain of few amino acids is known as “Oligopeptide”(oligo=few). According to the properties of their side-chains, amino acid engage into different bonds which are fundamental for recognition of other biomolecules.

1.7.1 CHEMICAL BOND:

Protein synthesis is a multiple dehydration process. The net structure of a protein becomes possible as a result of linking together of various amino acid units. The union of this amino acid to each other forming a chain and also among various amino acid residues of different chains involves various types of chemical bonds.

1.7.2 COVALENT BOND:

The covalent bond is the classical electron pair and forms the bond between two carbon atoms. It is a strong bond and have directional properties. The covalent bond is usually formed from two electrons, one from each atom participating in the bond as shown in fig 1.5. The electron forming the bond tends to be partly localised in the region between the two atoms joined by the bond. The spins of the two electrons in the bond are antiparallel. The binding of molecular hydrogen is a simple example of a covalent bond[3].

1.7.3 HYDROGEN BOND:

The attraction between the positive end of one dipole and the negative end of the neighbouring dipole forms clusters or large aggregates of molecules. On cooling crystallization may take place. The mechanism of bond formation involves the attraction of a hydrogen atom to two strongly electro negative atom. These bonds are called hydrogen bonds and have directional property as shown in **fig 1.6.**

They hydrogen bond is an important part of the interaction between H2O molecules and is responsible together with the electrostatic attraction of the electric dipole moments for the striking physical properties of water and ice[3].

1.7.4 WATER MOLECULE:

Water is a highly soluble substance and an exceedingly effective solvent. It is a compound that has a high dielectric constant, which is a measure of a solvent's ability to overcome the attraction between a dissolved cation and an anion. The dielectric constant is defined as the ability to oppose the electrical attraction between ions of opposite charge. The force of attraction between two oppositely charged ions is less in solvents that have high dielectric constants, relative to solvents that have low dielectric constants.

The polarity of water molecules makes them mutually attractive, as well as attractive to ionic and other polar substances.

PHYSICAL PROPERTIES OF WATER:

A. Water is a polar molecule.
B. Hydrophilic substances dissolve in water.
C. The hydrophobic effect causes non-polar substances to aggregate in water.
D. Water moves by osmosis and solutes move by diffusion.

CHEMICAL PROPERTIES OF WATER:

A. Water ionizes to form H^+ and OH^-.
B. Acids and bases alter the PH.
C. Buffers resist changes in PH.

1.8 PHENYLALANINE:

Phenylalanine is a benzenoid amino acids and have widespread distribution closely resembles tyrosine in structure shown in fig 1.7 [5]. Phenylalanine, an essential amino acid, is a derivative of alanine with a phenyl substituent on the β carbon. Phenylalanine is quite hydrophobic and not soluble in water. It cannot be formed in animals because of its aromatic ring.The function of phenylalanine is converted to tyrosine by ingestion of tyrosine can reduce the dietary requirement of phenylalanine. This phenomenon is referred to as "sparing action" of tyrosine on phenylalanine[6].

The predominant metabolism of phenylalanine occurs through tyrosine. During the course of degradation, phenylalanine and tyrosine are converted to metabolites which can serve as precursors for the synthesis of glucose and fat. Hence, these amino acids are both glucogenic and ketogenic.

Due to its hydrophobicity, phenylalanine is nearly always found buried within a protein. The π electrons of the phenyl ring can stack with other aromatic systems and often do within folded proteins adding to the stability of the structure.

1.9 LYSINE:

Lysine is an essential amino acid and generally abundant in animal proteins. Lysine can be found in plant proteins, such as corn and wheat. Some of the lysine residues are hydroxylysine, methyl lysine or acetyl lysine[5]. These derivatives are hydrolysed to liberate free lysine. Ionic charges are provided by protonation of the amino group of the carbon. It is nutritionally important and cannot be synthesised by higher animals. Pulses contain good amount of lysine whereas cereals lack in it. Lysine is a ketogenic amino acid and are not methylated; hence it cannot be a substrate for carnitine formation. Because of diamino-mono carboxylic acids, lysine is mostly found exposed on the surface of a protein structure shown in fig 1.6.

1.10 OBJECTIVE OF THE PRESENT WORK:

The main objective of the present study is,

- To optimize the structure of lysine and phenylalanine and its interaction with water.
- To study the energetical parameters and the geometrical parameters.
- To find the stability of lysine and phenylalanine using different theoretical methods.
- To confirm the optimized structure through frequency calculation.

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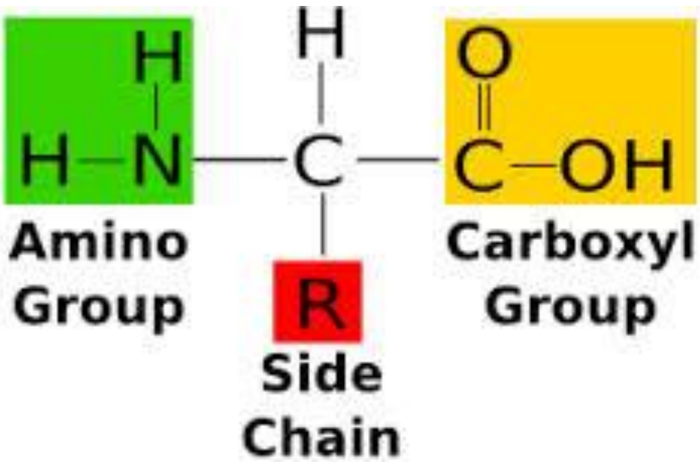


Fig 1.1 GENERAL STRUCTURE OF AMINO ACID

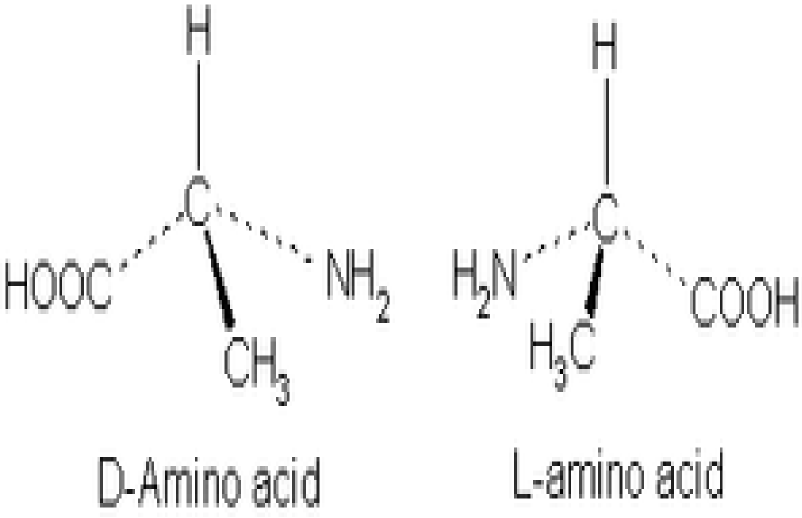


Fig 1.2 STERIOISOMERISM OF AMINO ACID

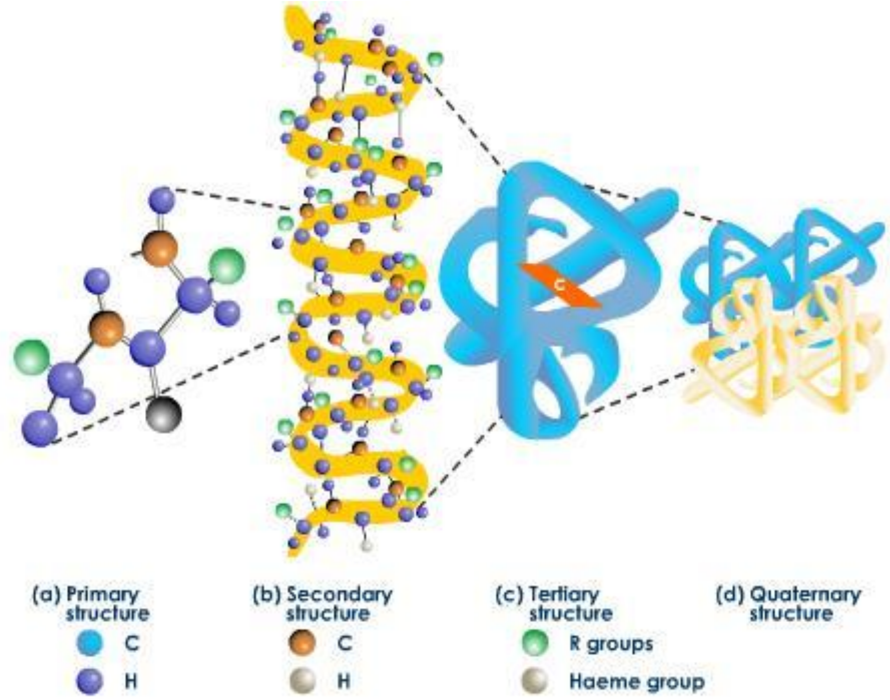


Fig 1.3 STRUCTURE OF PROTEIN

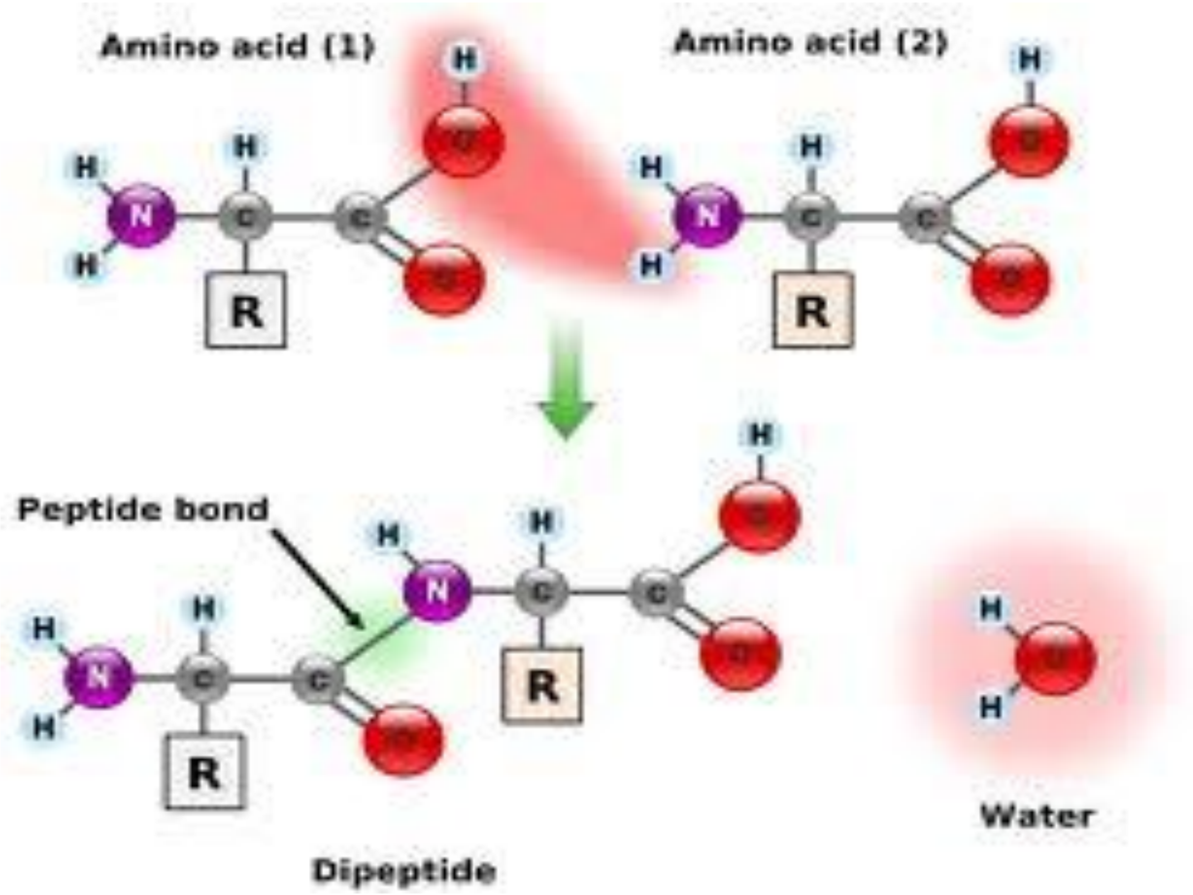


Fig 1.4 PEPTIDE BOND

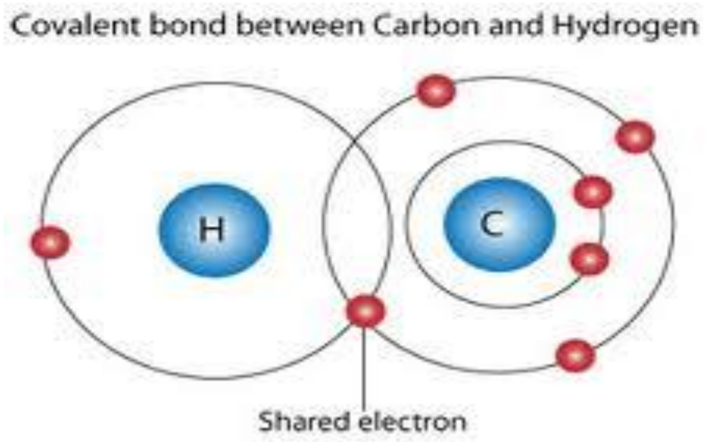


Fig 1.5 COVALENT BOND

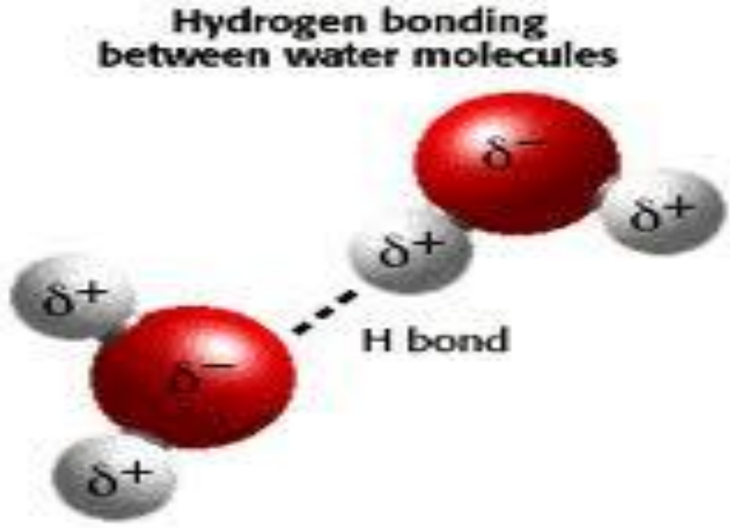


Fig 1.6 HYDROGEN BOND

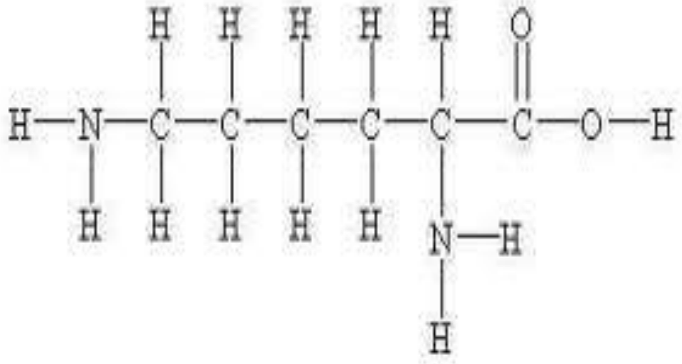


Fig 1.7 STRUCTURE OF LYSINE

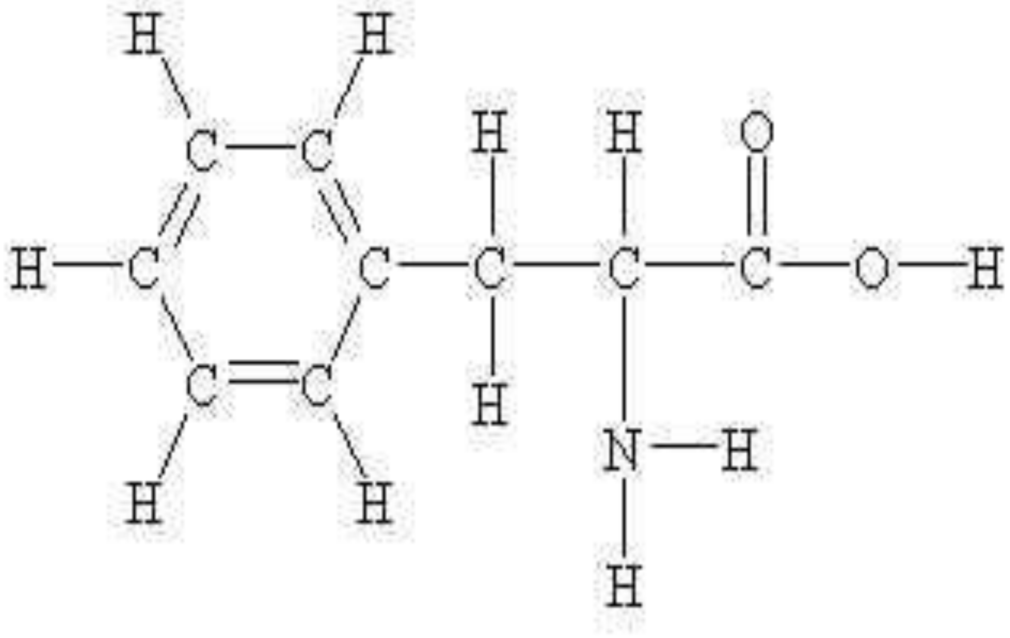
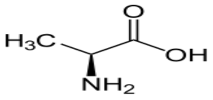
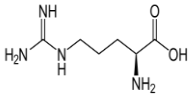
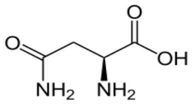
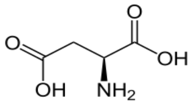
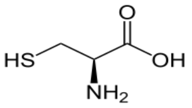
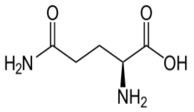
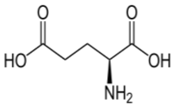
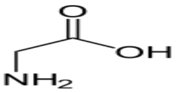
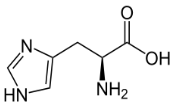
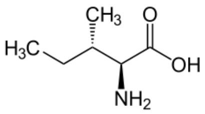
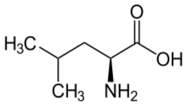
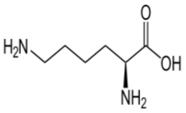
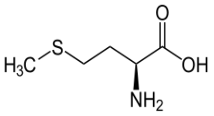
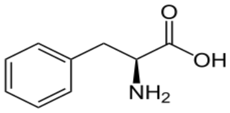
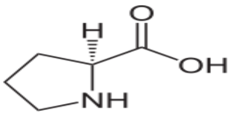
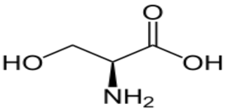
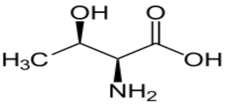
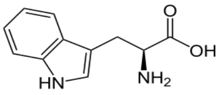
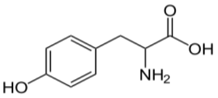
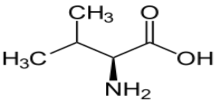


Fig 1.8 STRUCTURE OF PHENYLALANINE

TABLE (1.1): TYPES OF AMINO ACIDS:

Amino acid	**Abbreviations**		**Molecular formula**	**Structure**	**Linear Formula**
Alanine	Ala	A	$C_3H_7NO_2$		CH3-CH(NH2)-COOH
Arginine	Arg	R	$C_6H_{14}N_4O_2$		HN=C(NH2)-NH-(CH2)3-CH(NH2)-COOH
Asparagine	Asn	N	$C_4H_8N_2O_3$		H2N-CO-CH2-CH(NH2)-COOH
Aspartic acid	Asp	D	$C_4H_7NO_4$		HOOC-CH2-CH(NH2)-COOH
Cysteine	Cys	C	$C_3H_7NO_2S$		HS-CH2-CH(NH2)-COOH
Glutamine	Gln	Q	$C_5H_{10}N_2O_3$		H2N-CO-(CH2)2-CH(NH2)-COOH
Glutamic acid	Glu	E	$C_5H_9NO_4$		HOOC-(CH2)2-CH(NH2)-COOH
Glycine	Gly	G	$C_2H_5NO_2$		NH2-CH2-COOH
Histidine	His	H	$C_6H_9N_3O_2$		NH-CH=N-CH=C-CH2-CH(NH2)-COOH
Isoleucine	Ile	I	$C_6H_{13}NO_2$		CH3-CH2-CH(CH3)-CH(NH2)-COOH
Leucine	Leu	L	$C_6H_{13}NO_2$		(CH3)2-CH-CH2-CH(NH2)-COOH

Lysine	Lys	K	$C_6H_{14}N_2O_2$		H2N-(CH2)4-CH(NH2)-COOH
Methionine	Met	M	$C_5H_{11}NO_2S$		CH3-S-(CH2)2-CH(NH2)-COOH
Phenylalanine	Phe	F	$C_9H_{11}NO_2$		Ph-CH2-CH(NH2)-COOH
Proline	Pro	P	$C_5H_9NO_2$		NH-(CH2)3-CH-COOH
Serine	Ser	S	$C_3H_7NO_3$		HO-CH2-CH(NH2)-COOH
Threonine	Thr	T	$C_4H_9NO_3$		CH3-CH(OH)-CH(NH2)-COOH
Tryptophan	Trp	W	$C_{11}H_{12}N_2O_2$		Ph-NH-CH=C-CH2-CH(NH2)-COOH
Tyrosine	Tyr	Y	$C_9H_{11}NO_3$		HO-Ph-CH2-CH(NH2)-COOH
Valine	Val	V	$C_5H_{11}NO_2$		(CH3)2-CH-CH(NH2)-COOH

REVIEW OF LITERATURE

CHAPTER 2

REVIEW OF LITERATURE

INTRODUCTION:

Review of the related literature is an essential part of research project. The research carried out on topics related to the theoretical study of lysine and phenylalanine. Lysine interact with phenylalanine to form dipeptides and it interacts with water. In this literature, the geometrical parameters of lysine and phenylalanine and its interaction with water were investigated using HF/DFT theory.

1. Kang Wang et al., (2013) investigated the Taxus Canadensis phenylalanine aminomutase (TsPAM) catalyze the isomerisation of (S)-α-phenylalanine to the (R)-β-isomer. The active site of TsPAM contains the signature 5-methylene-3,5-dihydroimidazol-4-one (MIO) prosthesis, observed in the ammonia lyase class of enzymes. There are two plausible mechanism for MIO-dependent enzymes,i.e., the amino-MIO adduct mechanism and the Friedel-crafts-type reaction mechanism. Due to this mechanistic uncertainty, the phenylalanine aminomutase mechanism was investigated by using density functional methods. The calculation results indicate that (1) the reaction prefers the amino-MIOadduct mechanism where the 2,3-amine shift process contains six elementary steps; (2) the ammonia elimination step proceeds through an E2 mechanism; (3) a single C1-Cα bond rotation of 180^0 in the cinnamate skeleton occurs in the active site prior to the rebinding of NH2 group to thecinnamate.this explains the stereochemistry of the TsPAM reaction product, contrary to those of the PαPAM and SgTAM enzymes. Based on the calculations, the roles of important residues in the active site were also elucidated.

2. Chimankar,O.P et al., (2011) investigated the ultrasonic studies in liquids are great use in understanding the nature and strength of molecular interaction. The ultrasonic studies of biological materials in aqueous medium are ionized. Lysine is a necessary building block for all protein in the body and plays a major role in calcium absorption; building muscle protein; recovering from surgery or sports injuries; and the body's production of harmones, enzymes and antibodies. Adenosine is important in biochemical processes, such as energy transfer-as adenosine triphosphate (ATP) and adenosine triphosphate(ADP) and as well as in signal transductions cyclic adenosine monophosphate. This increase in hydrogen bonding with increase in lysine concentration as solvent is reflected in increased by hypochromacity thus indicating stronger solute-solvent interaction with higher concentration. Therefore this study of molecular interaction in between lysine, adenosine and water provides significant information about compatibility of water and biomaterials.

3. Schoenebeck F et al., (2009) studied the dipeptide cyclo[(S)-His-(S)-Phe] 1, first applied by inoue et al. In 1981, catalyzes the hydrocyanation of aromatic aldehydes very efficiently. Enantioselectiveautoinduction has been reported for the process. It employe QM (density functional theory and MP2), molecular mechanics(MM), and molecular dynamics (MD) methods to (i) derive a mechanistic picture for catalysis and (ii) reveal the origin of stereochemistry and autoinduction. A dimer is proposed to be the catalytic species, in which one imidazole group is essential for the delivery of the nucleophile and the second imidazole group acts as an acid, accompanied with pi-interaction for most favourable substrate binding. MD studies indicate stability of the dimer only in non-polar media, which is consistent with need of the experimental (heterogeneous) reaction conditions to achieve high enantioselectiveties. DFT and MP2 results suggest the incorporation of the product cynohydrin via extended edge-to-face pi-interaction over three aromatic units. Transition states derived shows good agreement with experimental findings and enantioselectivities.

4.Rozman, Marko et al., (2006) investigated the gas interaction of LysH+ with D2O in order to elucidate the H/D exchange reaction mechanism and possibility of water assisted ion-zwitterion structure formation. The proceed of the interaction is modelled by DFT calculations. Potential energy profiles for: the perturbation from ion-molecule to ion-zwitterion structure, the “flip-flop” and the “dridging” mechanism are presented. Analysis of H/D exchange kinetics results for LysH+ with D2O and CD3OD measured in a fourier transform ion cyclotron resonance (FTICR) mass spectrometer agree with ion-molecule structure of LysH+. Both experimental and theoretical findings suggest that during interaction of LysH+ with D2O isotopic exchange,the water assisted conformational change from ion-molecule into ion-zwitterion structure.

5. N. Khebichat et al., (2006) studied the L,L-Phe-Leu-Cu(II), L,L-Phe-Met-Cu(II), and L,L-Met-Phe-Cu(II) systems using molecular modelling. The results shows good agreement with the potentiometric studies, and there is significant increase in stability of copper complexes,when an aromatic residues is located in C-terminal (compared to the L,L-dipeptides containing the same amino acid residues), this phenomenon is attributed to the interaction between the d-orbital of copper and the π-electrons of the aromatic ring.

6. Dolores Troitino et al .,(2006) performed a study on the hydrogen-bonded dimmers of uracil, cysteine, lysine and phenylalanine by density functional theory (DFT), at the B3LYP/6-311++G** level, the most stable hydrogen-bonded dimmers involved NH and CO groups in uracil and N1-methyluracil, and the carboxylic groups in amino acids. Hydrogen bond energies were found to be between -33.8 and -21.8 kj mol^{-1} for uracil and between -33.7 and -32.1 kj mol^{-1} for the amino acids, indicating that relatively strong hydrogen bonds formed. He also studied the hetero-association between uracils and amino acids at the same level of calculations hydrogen-bonded heterodimers involving those groups which are active in self-associations were found. Dimer formation energies between uracil and the three aminoacids were similar, to that a preferential interaction of uracil with a particular partner is not evident at this level of structural complexity. The nature of the uracil donor group regulates the process of association as observed from a comparison of the energies. Self-association of uracil is favoured over hetero-association with amino acid when N1H is the donor group, but hetero-association is predominant when NH3 is a donor group.

7. Hugosson HW et al., (2005) performed a study on molecular dynamics on the zwitterionic form of the dipeptide glysine-alanine in water, with focus on the salvation and electrostatic properties using a range of theoretical methods, from purely classical force fields, through mixed quantum mechanical/molecular mechanical simulations, to fully quantum mechanical Car-parrinello calculations. The studies show that the salvation pattern is similar for all methods used for most atoms in the dipeptide, but differ substantially for some groups; namely the carboxy and aminoterminii, and the backbone amide NH group. There is implication in other theoretical studies of peptides and proteins with charged –NH(3) (+) and –CO(2) (-) side chains solvated in water. Hybrid quantum mechanical/molecular mechanical simulation successfully reproduce the salvation patterns from the fully quantum mechanical simulations.

8. T Yalsin,A G Harrison et al., (1996) studied the protonated lysine fragments primarily by elimination of the epsilon-amino group as ammonia to form an ion of m/z 130 and to minor extent by elimination of H2O to form an ion of m/z 129. Protonated lysine derivatives such as lysine beta-naphthylamide and H-Lys-Gly-OH show more pronounced formation of m/z 129 while protonated derivatives such as N alpha-Ac-Lys-X(X=OH, OMe, NHMe) and H-Gly-Lys-X(X=OH, NHCH2COOH) also show formation of m/z 129 in both metastable ion and collision-induced fragmentation. In both the latter systems m/z 129 is formed by sequential loss of HX followed by loss of ketene for the N-acetyl derivatives or the glycine residue for the N-glycyl derivatives. It is concluded that this lactam is formed from the lysine derivatives by interaction of amino group of the lysine side-chain with the lysine carbonyl function as HX departs. Protonated N alpha-methyllysine and N alpha-dimethyllysine fragment by elimination of CH3NH2 and (CH3)2NH. Both the protonated alpha-amino-epsilon-caprolactam and protonated pipecolic acid ions fragment primarily to[C5H10N]+(m/z 84), a low mass ion observed in the spectra of lysine-containing peptides.

9. Douglas J. Tobias et al.,(1991) studied the acetyl and methyl amide blocked alanine amino acid,alanine dipeptide is used as a model in theoretical studies of backbone conformational equilibria in proteins. To evaluate the solvent effects on the conformational equilibrium of the dipeptide, molecular dynamics simulation is used with holonomic backbone dihederal angle constraints and thermodynamic perturbation theory to calculate free energy profile along paths connecting four important conformations of the dipeptide in the gas phase and in water. It is found that the extended β conformation is the most stable in the gas phase and in water. The C_{7ax} conformation (seven-membered ring closed by a hydrogen bond with axial methyl group) is less stable than the β conformation by 2.4 kcal/mol in the gas phase and 3.6 kcal/mol in water. The right-and left-handed α helical conformations,$\alpha_R$and $\alpha_{L,}$ are less stable than the β conformation by 9.1 and 11.6 kcal/mol, in the gas phase. In aqueous solution the α_R and α_L conformations are less stable than the β conformation by only 0.2 and 4.1 kcal/mol. It is determined the energetic and entropic contributions to the free energies to explain the relative stabilities of the dipeptide conformations in terms of differences in peptide-peptide and peptide-solvent interaction.

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METHODOLOGY

CHAPTER 3

METHODOLOGY

3.1 INTRODUCTION:

Quantum chemistry has long promised to become a major tool for the study of molecular properties and reaction mechanisms. The fundamental methods of quantum chemistry date back to the earliest days of quantum mechanics in the first decades of the twentieth century. Quantum mechanics is the theoretical frame work within which it has been found possible to describe, correlate and predict the behavior of vast range of physical system, from elementary particles, through nuclei, atoms and radiation, to molecules and solids. Modern molecular physics includes the quantum mechanical explanation of the several kinds of chemical bonding between the atom in a molecules, the quantization of the vibrational, rotational and electronic motion of the molecules, the phenomena arising from intermolecular forces. Quantum chemistry has developed into an indispensable part of modern chemistry and molecular physics over the last 50 years. It provides the concepts and ideas that are central to our modern understanding of chemical systems. Quantum chemistry is considered to be a quantitative tool, capable of producing numerical results that agree quantitatively with the true or exact results, to within some estimated uncertainty.

There are mainly four methods in quantum chemistry to calculate the molecular properties of polyatomic molecules. They are,

(1) Semi empirical methods
(2) Ab initio methods
(3) Density functional methods
(4) Molecular mechanics methods

3.2 AB INITIO METHODS:

The programs used in computational chemistry are based on many different quantum-chemical methods that solve the molecular schrodinger equation associated with the molecular Hamiltonian. Methods that do not include any empirical parameters in their equations being derived directly from theoretical principles, with no inclusion of experimental data-are called ab initio methods. This does not imply that the solution is an exact one; all are approximate quantum mechanical calculations. It means that a particular approximation is rigorously defined on first principles (quantum theory) and then solved within an error margin that is qualitatively known beforehand. If numerical iterative methods have to be employed, the aim is to iterate until full machine accuracy is obtained. The simplest type of ab initio electronic structure calculation is the Hartree-Fock (HF) scheme, in which the coulombic electron-electron repulsion is not specifically taken into account. Only its average effect is included in the calculation. As the basis set size is increased the energy and wave function tend to a limit called the Hartree-Fock limit. Many types of calculations, known as post-Hartree-Fock methods, begin with a Hartree-Fock calculation and subsequently correct for electron-electron repulsion, reffered to also as electronic correlation. As these methods are pushed to the limit, they approach the exact solution of the non-relativistic schrodinger equation. The Hartree-Fock wave function is a single configuration or determinant. In some cases, particularly for bond breaking processes, this is quite inadequate.

3.3 SEMI – EMPIRICAL METHODS:

Semi – empirical quantum chemistry methods are based on the Hartree-Fock formalism, but make many approximations and obtain some parameters from empirical data and are very important in computational chemistry for treating large molecules where the full Hartree-Fock method without the approximations is too expensive. The use of empirical parameters appears to allow some inclusion of correlation effects into the methods. Semi-empirical methods are called empirical methods where the two/-electrons part of the Hamiltonian is not explicitly included.

3.4 HARTREE-FOCK EQUATION:

The starting point of the Hartree-fock procedure for helium is as the two-electron wave function as a product of orbitals, i.e.,

$$\Psi (r_1, r_2) = \phi(r_1)\,\phi(r_2) \tag{3.1}$$

According to Eq. 3.1, the probability diatribution of electron 2 is $\phi^*(r_2)\phi(r_2)dr_2$. We interpret this probability distribution classically as a charge density, and so the potential energy that electron 1 experiences at the point r_1 due to electron 2 is

$$U_1^{eff}(r_1) = \int dr_2\, \phi^*(r_2)\, \frac{1}{r12}\, \phi(r_2) \qquad (3.2)$$

Where the subscript eff emphasizes that $U_1^{eff}(r_1)$ is an effective, or average, potential. We now define an effective one-electron Hamiltonian operator by

$$\hat{H}_1^{eff}(r_1) = -\tfrac{1}{2}\nabla_1^2 - \frac{Z}{r1} + U_1^{eff}(r_1) \qquad (3.3)$$

The schrödinger equation corresponding to this effective Hamiltonian is

$$\hat{H}_1^{eff}(r_1)\, \phi(r_1) = \varepsilon_1 \phi(r_1) \qquad (3.4)$$

Equation 3.4 is the Hartree-Fock equation for helium atom. The solution to Eq 3.4 gives the best orbital wave function for helium.

Although we have deduced Eq 3.4 by a physical argument and possible to derive Eq 3.4 directly by applying the variational principle to the energy of a helium atom:

$$E = \iint dr_1 dr_2 \phi^*(r_1)\phi^*(r_2)\hat{H}\phi(r_1)\phi(r_2) \qquad (3.5)$$

Substituting $\hat{H}$ into Eq, 3.5, we get

$$E = I_1 + I_2 \text{ And}$$

$$J_{12} = \iint dr_1\ dr_2\, \phi^*(r_1)\phi^*(r_2)\frac{1}{r_{12}}\phi(r_1)\ \phi(r_2) \qquad (3.6)$$

The integral J_{12} here is called a coulomb integral. Equation 3.4 can be obtained by minimizing E with respect to ϕ.

Because $\hat{H}_1^{eff}$ in 3.4 is spherically symmetric, we write

$$\Phi(r) = R(r)\ Y\frac{m}{l}(\theta,\phi) \qquad (3.7)$$

Where R(r) is a radial function to be determined and $Y\frac{m}{l}(\theta,\phi)$ is a spherical harmonic. If Eq, 3.7 is substituted into Eq, 3.4.and obtained as

$$\left[-\frac{1}{2r_1^2}\frac{d}{dr_1}\left(r_1^2\frac{d}{dr_1}\right)-\frac{Z}{r_1}+\frac{l(l+1)}{2r_1^2}+U_1^{eff}(r_1)\right]\mathrm{R}(r_1)=\varepsilon R(r_1) \qquad (3.8)$$

The method of solving an equation Eq. (3.8) is by the self-consistent field method. We first guess the form of ϕ(r) and using ϕ(r) to evaluate $U_1^{eff}r_1$ by Eq. (3.2) and then solve Eq. (3.8) for a new $\phi(r_1)$. Usually, after one cycle, the ϕ(r) is used as input and $\phi(r_1)$ obtained as output differ. ϕ(r) is used as input by calculating $U_1^{eff}r_1$ with this new ϕ(r) and then solve Eq. (3.8) for a newer $\phi(r_1)$. This cyclic process is continued until the ϕ(r) used as input and the ϕ(r) obtained from Eq. (3.8) are sufficiently close, or are self-consistent. The orbitals obtained by this method are the Hartree-Fock orbitals.

In practice, one uses linear combinations of Slater orbitals for ϕ(r), varying the parameters in each Slater orbital and the number of Slater orbitals used until convergence is obtained. The method using linear combination of Slater orbitals in Hartree-Fock calculations was developed by Professor C. Roothaan, of the university of Chicago. The Hartree-Fock-Roothaan procedure is widely used for the calculation of atomic orbitals.

3.4.1THE HARTREE-FOCK LIMIT:

It should be apparent that different choices of basis set will produce different SCF wave functions and energies. If we do an SCF calculation on some molecule, using a minimal basis set and obtain a total electronic energy E_1, and a double-ζ basis and do a new SCF calculation, we will obtain an energy E_2 that normally will be lower than E_1. If we now add polarization functions and repeat the SCF procedure and find E_3 to be lower than E_2. In continuation, adding new functions in bonds and elsewhere, always increasing the capabilities of our basis set, but always requiring that the basis describe MO, in a single determinental wave function. The electronic energy will decrease with each basis set and become very slight for any improvement; ie., the energy will approach a limiting value as the basis set approaches mathematical completeness. This limiting energy value is the lowest that are achieved for a single determinantal wave function called the Hartree-Fock energy. The MO, that correspond to this limit are called Hartree-Fock orbitals, and the determinant is called the HF wave function.

Sometimes the term restricted Hartree-Fock(RHF) is used to emphasize the wave function is restricted to be a single determinantal function for a configuration wherein electrons of α spin occupy the same space orbitals as do the electrons of β spin. When this restriction is relaxed, and different orbitals are allowed for electrons with different spins, and have an unrestricted Hartree-Fock (UHF) calculation. This refinement is most likely to be important when the numbers of α- and β- spin electrons differ.

3.5 KOHN-SHAM THEORY:

The foundation for the use of DFT methods in computational chemistry is the introduction of orbitals, as suggested by Kohn-sham. The main flaw in orbital- free models is the poor representation of the kinetic energy, and the idea in the KS formalism is to split the kinetic energy functional into two parts, one which is calculated exactly, and a small correction term. The orbital re-introduced, thereby increasing the complexity from 3 to 3N variables, and that electron correlation re-emerges as a separate term. The KS model is closely related to the HF method, sharing identical formulas for the kinetic, electron-nuclear and coulomb electron-electron energies.

The division of the electron kinetic energy is into two parts, with the major contribution being equivalent to the HF kinetic energy. Assume for the moment a Hamiltonian operator of the form in equation (1) with $0 \leq \lambda \leq 1$.

$$H_\lambda = T + V_{ext}(\lambda) + \lambda V_{ee} \qquad (3.9)$$

The external potential operator V_{ext} is equal to the V_{ee} for $\lambda = 1$, but for intermediate λ values, it is assumed that $V_{ext}(\lambda)$ is adjusted such that the same density is obtained for $\lambda=1$ (the real system). For $\lambda=0$ case , the electrons are non interacting, and the exact solution to the schordinger equation is given as a slater determinant composed of (molecular) orbitals, ϕ_i, and the exact kinetic energy functional is given in equation (3.10)

$$T_S = \sum_{i=1}^{N_{elec}} < i \left| -\frac{1}{2}\nabla^2 \right| i > \qquad (3.10)$$

The subscript S denotes that it is the kinetic energy calculated from the slater determinant. The $\lambda=1$ case corresponds to interacting electrons, and eq (3.10) is an approximation to the real kinetic energy, but a substantial improvement over the TF formula,

$$K_\rho[\rho] = -C_X \int \rho^{4/3}(r)dr$$

$$C_F = \frac{3}{10}\,(3\pi^2)^{2/3}$$

Another way of justifying the use of eq. (3.10) for calculating the kinetic energy is by reference to natural orbitals. The exact kinetic energy can be calculated from the natural orbitals arising from the exact density matrix.

$$T\,[\rho_{\text{exact}}] = \sum_{i=1}^{\infty} n_i \; < \frac{N_0}{i} \left| -\frac{1}{2}\nabla^2 \right| \frac{N_0}{i} >$$

$$\rho_{\text{exact}} = \sum_{i=1}^{\infty} n_i \left|\frac{\mathrm{N}_0}{\mathrm{i}}\right|^2 \tag{3.11}$$

$$\mathrm{N}_{\text{elec}} = \sum_{i=1}^{\infty} n_i$$

The orbital occupation numbers n_i (eigen values of the density values) will be between 0 &1, corresponding to the number of electrons in the (spin) orbital. Representing the exact density will require an infinite number of natural orbitals, with the N_{elec} first having occupation numbers close to 1, and the remaining close to 0. Since the exact density matrix is not known, an (approximate) density can be written in terms of a set of auxiliary one-electron functions, i.e.,orbitals.

$$\rho_{approx} = \sum_{i=1}^{N_{elec}} |i|^2 \tag{3.12}$$

This corresponds to eq.(3.11) with occupation numbers of exactly 1 or 0. The “missing” kinetic energy from eq.(3.10) is due to the occupation numbers deviating from being exactly 1 or 0. Since the occupation numbers of an HF (single-determinant) wave function are also exactly 1 or 0, the missing kinetic energy can also be considered as the (kinetic) correlation energy.

The key of kohn-sham theory is to calculate the kinetic energy under the assumption of non-interacting electrons (in the same sense that HF orbitals in wave mechanics describe non-interacting electrons) for eq. (3.10). In reality, the electrons are interacting, and eq. (3.10) does not provide the total kinetic energy. However, just as HF theory provides 99% of the correct answer, the difference between the exact kinetic energy and that calculated by assuming non-interacting orbitals is small. The remaining kinetic energy is absorbed into an exchange-correlation term, and a general DFT energy expression can be written as in eq. (3.13)

$$E_{DFT}\,[\rho]=T_S[\rho]+E_{ne}[\rho]+J[\rho]+E_{XC}[\rho] \qquad (3.13)$$

By equating E_{DFT} to the exact energy, this expression defines E_{XC}, is the part that remains after subtraction of the non-interacting kinetic energy, E_{ne} and J potential energy terms as

$$E_{xc}[\rho]=(T[\rho]-T_S[\rho])+(E_{ee}[\rho]-J[\rho]) \qquad (3.14)$$

The first paranthesis in eq. (3.14) are considered as the kinetic correlation energy, while the last contains both potential correlation and exchange energy.

The task in devolping orbital-free models is to derive approximations to the kinetic, exchange and correlation energy functionals, while the corresponding task in kohn-sham theory is to derive approximations to the exchange-correlation energy function only. The exchange-correlation energy is roughly a factor of 10 smaller than the kinetic energy, kohn-sham theory is much less sensitive to the inaccuracies in the functional(s) than orbital-free theory. While orbital-free theory is a true density functional theory, khon-sham methods are independent particle models, analogous to Hartree Fock theory, but are still much less complicated than many particle wave function models.

3.6 DENSITY FUNCTIONAL THEORY METHOD:

The wave function ψ for an n-electron molecule is a function of 3n spatial coordinates and n spin coordinates. From ψ we can produce the molecule's spin-free electron density function,$\rho(1)$, by integrating $\psi^{*}\,\psi$ overall of the spin coordinates and all the space coordinates except those for our of the electrons:

$$\rho(1)=\int|\psi(1,2,\dots\dots.N)|^2 d\omega_1 d\tau_2 \dots.d\tau_n \qquad (3.15)$$

Which is a function of only the three spatial coordinates.

In 1964, Hohenberg and Kohn made a connection between the ground state energy,(Eo), and the ground state density function (ρ_o) for a system.

For a system having n electrons and N nuclei, the Hamiltonian operator for the electronic energy is

$$H=-\frac{1}{2}\sum_{i=1}^{n}\nabla_i^2+\sum_{i=1}^{n}\sum_{\alpha=1}^{N}-\frac{Z_\alpha}{r_{i\alpha}}+\sum_{i=1}^{n-1}\sum_{j=i+1}^{n}\frac{1}{r_{ij}} \quad (3.16)$$

The first and last term are written if there is known number of electrons present, but the middle term depends on $\sum_{\alpha=1}^{N}-\frac{Z_\alpha}{r_{i\alpha}}$, which is a function of nuclear charges and locations. This quantity is called the external potential, symbolized v_{ext} (r), because it results from the presence of fields produced by particles not included in the group of electrons.

Hohenberg and Kohn were able to prove that there is a uniqueness relation between ρ_o and the external potential: No two external potential could give the same ρ_o . This raises the possibility that to work backwards from ρ_o to find Vext (r) and Eo. Using ab initio methods,we get an accurate Eo and ψ_0, and from ψ_0 we calculate T_o, V_{neo}, V_{eeo}, and all the other properties of interest for the system.

There is no generally applicable procedure known for getting from ρ_o to V_{ext} (r). V_{ext}(r) is a functional of ρ_o, which we symbolize V_{ext} (r), but don't know the functional relationship. Then Hamiltonian operator, by uniqueness theorem have led to the current goal of density functional theory.

A Subsequent relation proved by Hohenberg and Kohn indicated a way to proceed and proved that an approximate density function, when subjected to the (unknown) procedure that relates the exact ρ_o to the exact E_0: $E_{0,approx} \geq E_0$, so a variational bond exists. Unknown process referred to here is that assumes V_{ext}(r) to be the same for the analysis of ρ_o and $\rho_{o,approx}$, which means that the same nuclear frame work applies in both cases.

If a procedure were known for finding E from ρ ,then the existence of a variational bound would allow a variational procedure analogous to what applied earlier. One would start with a trail ρ, calculate its energy, and vary ρ to locate the ρ that gives the lowest energy.

In analogy to wave function methods, the functional that connects E to ρ, E[ρ] are separated into an electronic kinetic energy contribution, T[ρ], a contribution due to nuclear- electron attractions, E_{ne}[ρ], and the electron electron repulsion, E_{ee}[ρ]. The latter term is further decomposed into coulomb and exchange terms, J[ρ] and K[ρ]. Both the nuclear –electron attraction and the interelectronic coulomb terms are easily written in terms of the density using their classical expressions as in wave function methods. For an accurate treatment of the electronic kinetic energy term, differentiate a wave function, and led to the practice first proposed by kohn and sham of expressing density in terms of one- electron orbitals ф. These orbitals serve two purposes and allow us to calculate a value of the kinetic energy within a single slater determinant framework similar to Hartree – Fock theory,

$$T_S = \sum_{i=1}^{n} < i \left| -\frac{1}{2}\nabla^2 \right| i > \qquad (3.17)$$

And to obtain the electron density, defined in terms of these Kohn-sham orbitals as

$$\rho_s = \sum_{i}^{n} |i|^2 \qquad (3.18)$$

the final DFT energy expression is then written as,

$$E_{DFT}[\rho] = T_S[\rho] + E_{ne}[\rho] + J[\rho] + E_{XC}[\rho]$$

3.7 THE BASIS SET:

All of the molecular orbital calculations make use of some types of atomic wave functions that generally describe a single electron. The basis set is the set of one-electron wave function that is combined to give the molecular wave function. The minimal set is the set that incorporates only the orbital actually populated by electrons. Slater-type orbital (STO) having the form

$$\Psi(r) = r^{n-1} e^{-(Z-s)r/n}, \qquad (3.19)$$

Where s is the screening constants, n is a number that varies with the type of orbital, and Z is the nuclear charge, are widely used. Using one STO wave function for each nucleus and constructing molecular wave functions by taking liner combinations of the atomic orbitals, the molecular calculation is referred to as the minimal basis set calculation. The quantity (Z - s) is replaced by ζ (Zeta) to give functions written in the form

$$\Psi(r) = r^{n-1} e^{-\zeta . r/n} \qquad (3.20)$$

The wave functions of this type are referred to as single ζ STO functions. An additional modification involves representing each atomic wave function by two STO wave functions, the wave functions are referred to as double ζ functions. Within the framework of double ζ wave functions, there are several variations in parameterizations that have been developed.

Another type of function used to represent atomic wave function is known as a Gaussian. Gaussian functions, which are in the form $\psi(r) = exp\,(-\alpha r^2)$ where α is an adjustable (best-fit) parameter, are combined as linear combinations in order to approximate the STO functions. The motivation for this is that computations of the integrals involved in the quantum mechanical calculations are greatly facilitated. The linear combination of Gaussian functions is referred to contracted Gaussian function or Gaussian type orbitals (GTO). All of these and manipulations of STO and GTO are to provide approximations to the radial portions of the atomic functions, and the complete wave functions are obtained by making use of the spherical harmonics, $Y_{l,m}\,(\theta, \emptyset)$, to provide the angular dependence.

When each STO is represented by a linear combination of three Gaussian functions, the result is known as STO-3G. Other combinations of wave functions lead to the 6-31G designation in which each STO is represented as a linear combination of six Gaussian functions. Further, each STO representing valence shell orbitals is a double ζ function with the inner part represented by a linear combination of three Gaussian functions and the outer by one such function.

3.8 BOND STRENGTH:

Bond strength is the degree to which each atom joined to another in a chemical bond contributes to the valency of the other system.

3.8.1 BOND LENGTH:

The distance between centres of bonded atoms are called bond lengths, or bond distances. Bond lengths vary depending on many factors, in general, they are very consistent. The bond order affects the bond length, and of the same order for the same pair of atoms in various molecules are consistent. The bond lengths ranges from the shortest of 74pm for H-H to 200pm for large atoms, and the bond energies depends on bond order and lengths.

3.8.2 BOND ANGLE:

The average angle between the orbitals of the central atom containing the bonding electron pairs in the molecules is known as bond angle between the atoms. The unit of bond angle is either degree or minute or second. This gives the distribution of orbital's around the central atom in a molecule. Therefore bond angle determines the shape of a molecule.

3.8.3 BOND ENERGY:

When a chemical reaction occurs, molecules bonds are broken and other bonds are formed to make different molecules. For example, the bonds of two water molecules are broken to form hydrogen and oxygen.

$$\mathbf{2H2O \rightarrow 2H_2 + O_2}$$

Bonds do not break and form spontaneously- an energy change is required. The energy input required to break a bond known as bond energy.When a bond is strong, there is a higher bond energy because it takes more energy to break a strong bond. This correlates with bond order and bond length. When the bond order is higher, bond length is shorter, and the shorter the bond length means a greater the bond energy because of its increased electric attraction.

3.9 CHEMICAL POTENTIAL:

Chemical potential is an important thermodynamic property and have an important application in thermodynamics, physical chemistry, biological fluid mechanics and other realms. It is a measure of the escaping tendency of an electron cloud and constant, throughout all space for ground state of the system. If a plot of E vs N for any system is drawn then,μ is simply the instantaneous slope of such a curve and designated as

$$\mu = \left[\frac{\partial E}{\partial N}\right]_{V(r)} \tag{3.21}$$

Where E is the energy, N is the number of electron and V is the potential due to the fixed nuclei.

Chemical potential can also be defined as:

$$\mu = (\text{-I/A}) / 2 \tag{3.22}$$

Where I is the ionization potential ($-E_{HOMO}$) and A is the electron affinity (E_{LUMO}).

HOMO = Highest Occupied Orbital

LUMO = Lowest Unoccupied Orbital.

3.9.1 CHEMICAL HARDNESS:

The chemical hardness of an atom or a molecule is defined as the second derivative of the energy E with respect to the number of electrons N at constant external potential and temperature.

$$2\eta = \left(\frac{\partial^2 E}{\partial N^2}\right)_{V(r)} \qquad (3.23)$$

To obtain the other approximation to η it is useful to correlate χ and η with molecular orbital theory. Fortunately, it turns out that they are completely compatible from Koopmans theorem

$$I = (-E_{HOMO})$$

$$A = (-E_{LUMO})$$

$$\eta = (E_{LUMO} - E_{HOMO}) / 2 \qquad (3.24)$$

The gap between the HOMO and LUMO is equal to 2η. The hardness of an atom or a molecule is the reciprocal of the respective softness (S) ie., $\eta = 1/2s$.

COMPUTATIONAL DETAILS OF THE PRESENT STUDY:

- In the present work the molecular structure of lysine and phenylalanine and its interaction with water were fully optimized using Hartree Fock method in HF/6-31G basis set and Density Functional Theory at B3LYP/6-31G levels of theory.
- All the calculations were performed using Gaussian 09 packages.
- The vibrational frequency calculation has been performed using HF in the basis set 6-31G and DFT theory in the basis set 6-31G.
- The bond length, bond angle, energy, dipole moment, molecular vibrations, chemical reactivity parameters have been calculated using the above levels of theory

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RESULT AND DISCUSSION

CHAPTER IV

RESULTS AND DISCUSSION

4.1 INTRODUCTION:

Amino acids, the backbone of proteins are an attracting target for computational chemists due to their variety of intermolecular interactions and conformational flexibilities. The interest in the structure and spectra of the amino acids, stems from atleast three reasons (1) the search for the origin and sign of life in cool interstellar space, which can be aided by careful laboratory investigations of the structures and the related signals of these biomolecules; (2) the desire to establish the intrinsic tautomeric and conformational energetic and the underlying potential energy surfaces and hyper surfaces of these species which probably determine the characteristics of polypeptides and proteins; and (3) to stimulate and provide vital data for the development of better more efficient and or reliable computational methods, whether they are empirical or non-empirical in nature. The experimental and theoretical studies on the conformational behaviour of the amino acids are not straightforward procedure. The different dipole moments of the stable rotamers and intra molecular interactions complicate the determination of the relative stabilities. The joint analysis of electron diffraction and microwave data can provide a reasonable molecular structure for the different conformations of amino acids. Aromatic amino acids are essential to higher animals including humans. Phenylalanine contain phenyl ring and classified as non-polar. The phenolic hydroxyl group of this amino acid is more acidic and vary depending on its environment.Lysine is also an essential amino acid contain imidazole ring and supplied through the diet in humans. The present study has been made to explain the structure and spectroscopic values of dipeptide phenylalanine with lysine and the effect of explicit inclusion of water molecule attached to dipeptide.

4.2 GEOMETRICAL STRUCTURE OPTIMIZATION:

The structure of lysine with phenylalanine dipeptide is optimized with Gaussian 09 package by using ab initio method HF/6-31G and density functional theory B3LYP/6-31G. Then the dipeptide (lysine+phenylalanine) is interacted with water and optimized by using the same level of theories. The optimized structures of (Lys+phe) and lys+phe(H_2O) at HF/6-31G and B3LYP/6-31G level of theories are shown in **Fig (4.1), (4.2), (4.3)** and **(4.4).** The geometrical parameters such as bond length, bond angle, chemical hardness, chemical potential, chemical softness and dipole moment were calculated at the same level of theory.

4.2.1 HYDROGEN BONDING:

The hydrogen bond is the most important factor in the structure, which conforms the optimized structure of lys+phe (H_2O). An intermolecular hydrogen bond is formed between (O1-H24.....O4) having the length of 1.90154(Å) at HF/6-31G level of theory. Lys+phe (H_2O) forms an intermolecular hydrogen bond (O-H....O) with the length of 2.06630(Å)(O4-H25...O1), 2.16159(Å)(O4-H24....O2) and 2.15636 (Å) (H24-O4...H15) at B3LYP/6-31G level of theory.

4.3 GEOMETRICAL PARAMETERS:

The geometrical parameters such as bond length and bond angle, energy and dipole moment are calculated from the optimized structure of lys+phe and lys+phe (H_2O) at HF/6-31G and B3LYP/6-31G methods.

4.3.1 BOND LENGTH AND BOND ANGLE:

(LYS + PHE):

The bond length of N2-H10 obtained by the ab initio method and density functional theory are 0.99496 (Å) and 1.01253 (Å) and the bond length of C6-H8 are 1.0843 (Å) and 1.09784 (Å) at HF/6-31G and B3LYP/6-31G level of theories in lys + phe. In the ab initio method the bond length of Hydroxyl (O3-H23) is found to be 0.95124 (Å) similar at B3LYP/6-31G level of theory the above bond length is found to be 0.98222 (Å) which is shown in the **Table 4.1.** The bond angles H11-N2-H10, C6-N2-H11, N2-C6-H8, C5-C6-H9, C1-C2=O1, N3-C2=O1, at ab initio method are 112.772^0, 115.815^0, 107.781^0, 109.204^0, 122.589^0, 121.644^0 and at density functional theory the bond angle values are 112.088^0, 114.776^0, 107.662^0, 108.687^0, 123.153^0,122.830^0 respectively is shown in **Table 4.2 .**

LYS + PHE (H2O):

In lys + phe (H_2O) the bond length of N2-H10 obtained are 0.99529 (Å) and 1.01266 (Å) and the bond length of C-H are 1.09105 (Å) and 1.10772 (Å) at HF/6-31G and B3LYP/6-31G level of theories is shown in **Table 4.1.** The bond angles H11-N2-H10, C6-N2-H11, N2-C6-

H8, C5-C6-H9, C1-C2=O1, N3-C2=O1 are 112.707^0, 115.326^0, 107.828^0, 108.969^0, 122.794^0, 121.076^0 for HF/6-31G and at B3LYP/6-31G the bond angle values are 111.993^0, 114.704^0, 107.675^0, 122.773^0, 122.645^0 is shown in the **Table 4.2.**

4.3.2 DIPOLE MOMENT AND ENERGY:

The dipole moment is the first derivative of energy with respect to an applied electric field. The dipole moment and energy were calculated for lys+phe and lys+phe (H2O) at HF/6-31G and B3LYP/6-31G level of theories and tabulated in **Table (4.7)** and **(4.8).**

The dipole moment (μ) for lys + phe is 7.7105 (Debye) and 5.5173 (Debye) at HF/6-31G and B3LYP/6-31G level of theories and for lys + phe (H2O) is 6.9737 (Debye) and 7.6773(Debye) at HF/6-31G and B3LYP/6-31G level of theories. The energy value of lys + phe is -968.9608 (a.u) and -975.1118 (a.u) at HF/6-31G and B3LYP/6-31G level of theories and for lys + phe (H2O) is -1044.9463 (a.u) and -1051.5162 (a.u) at HF/6-31G and B3LYP/6-31G level of theories respectively. The dipole moment on comparison with the ab initio and Density functional theory it seems to be higher in HF/6-31G for Lys + Phe and high in B3LYP/6-31G for Lys + Phe (H2O). The energy value is found to be higher in Lys+Phe when compared to Lys+Phe (H2O) in both HF/6-31G and B3LYP/6-31G level of theories.

4.4 MOLECULAR VIBRATION:

A molecule vibration occurs when atoms in a molecule are in periodic motion while the molecule as a whole has constant translation and rotational motion. The frequency of the periodic motion is known as a vibrational frequency, and the typical frequencies of vibrations range from less than 10^{12} to approximately 10^{14} Hz.

Stretching vibration : In this type of vibration, the atoms move only along the bond axis, so that the bond length increases or decreases at regular intervals but the atom remains in the same bond axis. In stretching vibrations bond angles change.

Type of stretching vibration: there are of two types

- **Symmetrical stretching:** In this type of stretching with respect to a particular atom, other two atoms in a molecule move in the same direction.

- **Asymmetric stretching:** In this type of stretching one atoms departs from the central atom, while the other atoms approaches the central atom.

Bending or Deforming vibrations: This type of vibrations consist of a change in bond angle between bonds with a common atom or the movement of a group of atoms with respect to the remainder of the molecule without movement of the atoms in the group with respect one another. Various type of bonding vibration are: scissoring, rocking, wagging and twisting. Twisting and rocking vibrations(tortional) involve a change in bond angle with respect to a set of co-ordinates arbitrarily set up within the molecule.

- **Scissoring:** The two atoms move towards and away from each other with deformation of the valency angle (in plane bonding).
- **Wagging:** In wagging, the structural unit swings back and forth out of the plane of the molecule consist of plane bonding.
- **Twisting:** In this type one of the atoms moves up the plane while the other moves down in the plane with respect to the central atom consist of plane bending.
- **Rocking:** Rocking is the in plane bending of the atom in a molecule.

The frequency mode of vibration for lys+phe and for lys+phe (H2O) were observed and tabulated using HF/6-31G of Hartree Fock method and B3LYP/6-31G level at density functional theory in **Table (4.3) and (4.4).**

NH_2 vibrations:

(Lys+phe):

Amino group of NH_2 (H10-N2-H11),(H13-N1-H12) group exists in lys+phe molecule. The vibrations of the NH_2 amino group have symmetric stretching, asymmetric stretching, scissoring, rocking and wagging. Asymmetric stretching is found for (H10-N2-H11) and (H13-N1-H12) at the frequencies of 3901.68 cm^{-1},3879.34 cm^{-1} at HF/6-31G and 3652.04 cm^{-1}, 3631.46 cm^{-1} at B3LYP/6-31G. Symmetric stretching is obtained at 3785.29 cm^{-1}(H10-N2-H11), 3762.89 cm^{-1}(H13-N1-H12) at HF/6-31G and 3535.49 cm^{-1}(H13-N1-H12), 3514.91 cm^{-1}(H13-N1-H12) at B3LYP/6-31G. The computed values at 1854.18 cm^{-1}(H13-N1-H12),1846.66 cm^{-1}(H10-N2-H11) and 1711.05 cm^{-1}(H13-N1-H12),1709.27 cm^{-1}(H10-

N2-H11) are assigned to scissoring vibration at HF/6-31G and B3LYP/6-31G level of theory. The value found at 690.74 cm^{-1}(H11-N2-H10) in HF/6-31G is assigned to wagging vibration is shown in **Table (4.3).**

Lys+phe (H2O):

Amino group of NH_2 in lys+phe (H2O) is seen to have asymmetric stretching at 3896.50cm^{-1}, (H10-N2-H11) 3877.07 cm^{-1}(H13-N1-H12) at HF/6-31G and 3650.37 cm^{-1}(H10-N2-H11), 3625.58 cm^{-1}(H13-N1-H12) at B3LYP/6-31G. The values obtained for symmetric stretching are 3780.58 cm^{1}(H10-N2-H11),3761.27 cm^{-1} (H13-N1-H12)and 3524.15 cm^{-1}(H10-N2-H11), 3510.38 cm^{-1} (H13-N1-H12) at HF/6-31G and B3LYP/6-31G level of theory. The computed values at 1851.30 cm^{-1}(H13-N1-H12),1845.87 cm^{-1} (H10-N2-H11) and 1711.57 cm^{-1}(H13-N1-H12),1709.27 cm^{-1} (H10-N2-H11) are assigned to scissoring vibration at both HF/6-31G and B3LYP/6-31G methods. Rocking vibration occur at the values of 1218.48 cm^{-1} (H10-N2-H11) at HF/6-31G and 1448.85 cm^{-1} (H10-N2-H11) at B3LYP/6-31G level of theory is shown in the **Table (4.4).**

OH, NH vibrations:

(Lys+phe):

The lys+phe molecule of stretching vibrations are observed for O3-H25 in the range of 4030.01 cm^{-1} in HF/6-31G and 3586.52 cm^{-1} in B3LYP/6-31G. The theoretically computed values of N3-H14 stretching are found at 3842.32 cm^{-1} and 3481.06 cm^{-1} in HF/6-31G and B3LYP/6-31G level is shown in **Table (4.3).**

Lys+phe (H2O):

The stretching vibration of lys+phe (H2O) for O3-H25 is in the range of 4033.67 cm^{-1} in HF/6-31G and 3587.92 cm^{-1} in B3LYP/6-31G. The value found for N3-H14 stretching in HF/6-31G and B3LYP/6-31G are 3834.38 cm^{-1} and 3490.03 cm^{-1} is shown in the **Table (4.4).**

CH_2 vibrations:(Lys+phe):

The CH_2 vibrations in lys+phe gives rise to asymmetric stretching at (H3-C3-H2) found at the frequencies of 3225.31 cm^{-1} at HF/6-31G and 3067.89 cm^{-1} at B3LYP/6-31G. Symmetric stretching of the lys+phe compound is observed at 3180.11 cm^{-1}(H3-C3-H2), 3168.79 cm^{-1}

(H7-C5-H6) and 3023.27 cm^{-1}(H3-C3-H2), 3015.13 cm^{-1} (H7-C5-H6) at HF/6-31G and B3LYP/6-31G level. Scissoring vibration is obtained at 1684.78 cm^{-1}(H8-C6-H9), 1684.78 cm^{-1} (H7-C5-H6) at HF/6-31G and 1565.91 cm^{-1}(H8-C6-H9),1538.15 cm^{-1} (H7-C5-H6) at B3LYP/6-31G. The theoretically computed values of Rocking falls in the range of 1492.58 cm^{-1}(H8-C6-H9) ,1675.82 cm^{-1} (H16-C9-H17) at HF/6-31G and 3117.57 cm^{-1}(H8-C6-H9),1519.93 cm^{-1} (H16-C9-H17) at B3LYP/6-31G. In this present work, the Wagging vibrations observed at 1522.97 cm^{-1}(H16-C9-H17), 1541.89 cm^{-1}(H4-C4-H5),1510.96 cm^{-1} (H8-C6-H9) and 1509.60 cm^{-1} (H3-C3-H2) at HF/6-31G level of theory is shown in **Table (4.3).**

Lys+phe (H2O):

In lys+phe (H2O), asymmetric stretching values are found at 3242.00 cm^{-1}(H7-C5-H6),3236.74 cm^{-1} (H17-C9-H16) at HF/6-31G and 3077.03 cm^{-1}(H7-C5-H6) ,3064.86 cm^{-1} (H17-C9-H16) at B3LYP/6-31G. The observed values of symmetric stretching for (H2-C3-H3) is found to be 3186.38 cm^{-1} and 3024.64 cm^{-1} at HF/6-31G and B3LYP/6-31G. The theoretically computed values of scissoring falls in the range of 1666.94 cm^{-1}(H5-C4-H4) ,1655.60 cm^{-1}(H16-C9-H17) and 1554.87 cm^{-1}(H5-C4-H4),1519.44 cm^{-1}(H16-C9-H17) at HF/6-31G and B3LYP/6-31G level of theory. The value found for Rocking vibration is 1218.48 cm^{-1}(H11-N2-H10), 1231.02 cm^{-1}(H3-C3-H2) at HF/6-31G and 1448.85 cm^{-1},792.49 cm^{-1} at B3LYP/6-31G. The band appeared for (H2-C3-H3) at 1484.15 cm^{-1} and 1288.43 cm^{-1} are Twisting vibrations in HF/6-31G and B3LYP/6-31G methods is shown in **Table (4.4).**

Benzene Ring:

The computed values at 3391.05 cm^{-1} and 3230.42 cm^{-1} are assigned to stretching vibrations by both HF/6-31G and B3LYP/6-31G methods in Lys+Phe. The stretching vibrations are found to be 3391.75 cm^{-1} and 3225.11 cm^{-1} at Lys+Phe (H2O).

4.5 SPECTROSCOPIC ANALYSIS OF PRESENT STUDY:

The variation in the frequency significantly alters the intensity of the spectrum. The IR and Raman spectra obtained for (lys + phe) and for lys + phe (H2O) is optimized at HF/6-31G and B3LYP/6-31G level of theories are shown in **graph (4.1), (4.2), (4.3), (4.4)** respectively.

Lys + phe:

The vibrational spectra of lys + phe have 126 modes of vibration on both HF/6-31G and B3LYP/6-31G level of theories. The strongest peak in the IR spectrum at ab initio and Density functional theory are 1675.817cm^{-1}(H16-C9-H17) and 1519.9331 cm^{-1} (H16-C9-H17) having the vibrational mode of 95 and 91 that corresponds to scissoring of H16-C9-H17 and Rocking of H16-C9-H17 in HF/6-31G and B3LYP/6-31G level of theories. The second strongest peak is 690.7398 cm^{-1}(H11-N2-H10) and 1265.3765 cm^{-1} (H12-N1-H13) with the mode of vibration 34 and 74 that attributed to the Wagging and Rocking at ab initio and Density functional level of theories. The highest peak in the Raman spectrum at ab initio theory is 3391.0478 cm^{-1} (benzene ring) having the vibrational mode of 120 that attributed to stretching are tabulated in the **Table (4.1).**

Lys + phe (H2O):

The vibrational spectra of lys + phe (H2O) have 135 modes of vibration on both HF/6-31G and B3LYP/6-31G level of theories. The highest peak in the IR spectrum at ab initio and Density function theory are 1683.9396 cm^{-1} (H8-C6-H9) and 1519.4426 cm^{-1} (H16-C9-H17) having the vibrational mode of 102 and 97 that corresponds to scissoring on both level of theories. The second strongest peak is 3920.6698 cm^{-1} (H24-O4-H25) and 625.3458cm^{-1} (H13-N1-H2) with the mode of vibration 133 and 37 that attributed to the symmetric stretching and wagging at HF/6-31G and B3LYP/6-31G level of theories is shown in **Table 4.2**. The highest peak in the Raman spectrum at HF/6-31G level of theory is 3391.7513 cm^{-1} (benezene ring) having the vibrational mode 127 that corresponds to stretching.

4.6 CHEMICAL REACTIVITY:

The chemical reactivity parameters are important tools to study the stability of molecular system. The values of chemical potential, chemical hardness, chemical softness of lys+phe and lys+phe (H2O) are calculated at HF/6-31G level and B3LYP/6-31G level of theory.

4.6.1 CHEMICAL POTENTIAL AND CHEMICAL HARDNESS:

Lys + Phe:

Chemical potential and chemical hardness are important tools to study the stability of the molecular system, which have been calculated at HF/6-31G and B3LYP/6-31G level of theory for the lys + phe is given in **Table 4.5**. These two parameters of a molecular system are the first and second derivatives of energy with respect to the number of electrons. The chemical potential of lys + phe is -0.234315 ev and -0.114725 ev at ab initio and density functional theory respectively. The value of chemical hardness at HF/6-31G and B3LYP/6-31G level of theory are given as 0.234315 ev and 0.114725 ev respectively is shown in **Table 4.5**. The chemical potential is found to be negative and it means that the molecule is stable. The hardness signifies the resistance towards the deformation of electron cloud of chemical system under small perturbation encountered during the chemical process.

Lys + Phe (H2O):

The chemical potential of Lys + Phe (H2O) is -0.234525 ev and -0.009632 ev at HF/6-31G and B3LYP/6-31G theory. The value of chemical hardness at HF/6-31G and B3LYP/6-31G level of theory are as 0.234525 ev and 0.09632 ev respectively is shown in **Table 4.6**. It is seem that chemical potential is high in B3LYP/6-31G theory than the HF/6-31G theory and the chemical hardness is high in HF/6-31G level of theory when compared to the density functional theory.

4.6.2 CHEMICAL SOFTNESS:

In ab initio method the chemical softness value is 2.13387 ev and in density functional theory its value is 4.35824 ev, in Lys + Phe which are shown in **Table 4.7**. In the Lys+Phe (H2O) the chemical softness is 2.1319688 ev and 5.1910299 ev at HF/6-31G and B3LYP/6-31G level of theories is shown in **Table 4.8** . The value of chemical softness is found to be higher in density functional theory when compared to ab initio method in both HF/6-31G and B3LYP/6-31G level of theories. Soft systems are large and highly polarisable, while hard systems are relatively small and much less polarisable.

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FIGURES AND TABLES

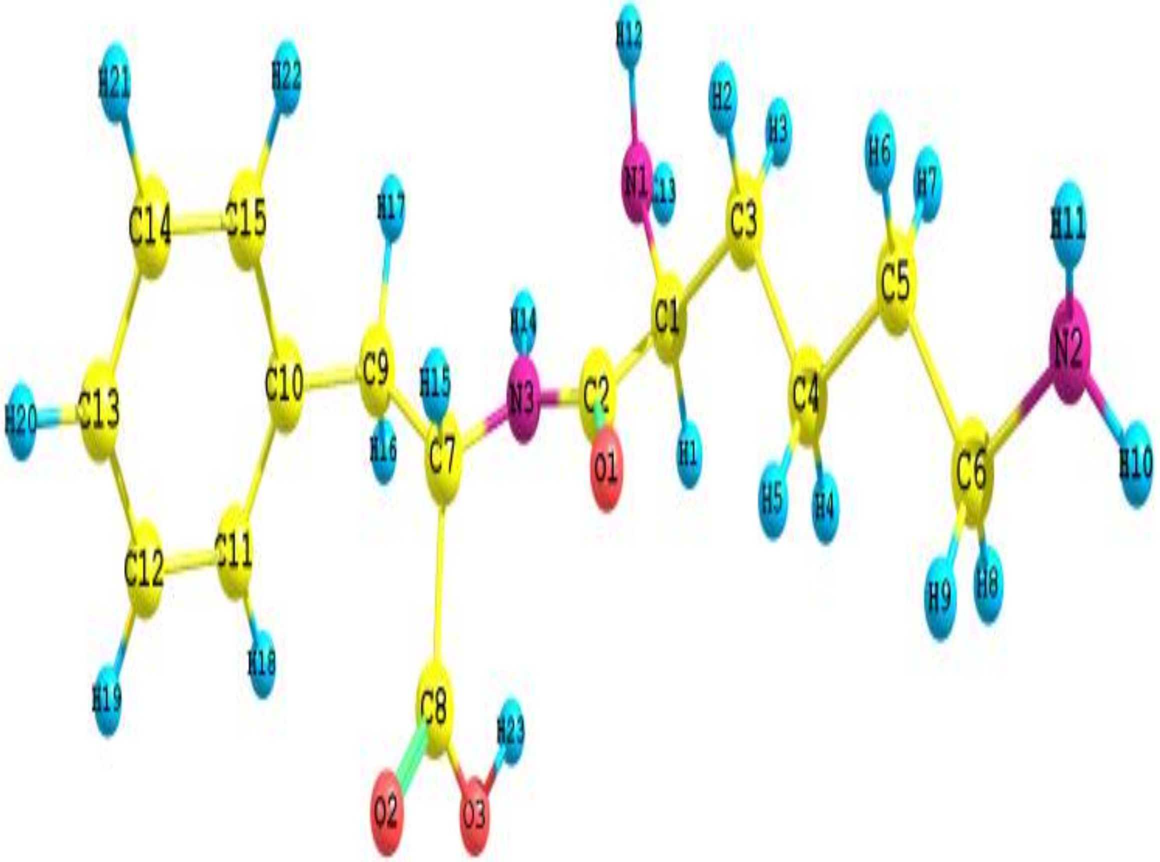


Fig 4.1 THE OPTIMIZED STRUCTURE OF LYS + PHE AT HF/6-31G LEVEL OF THEORY

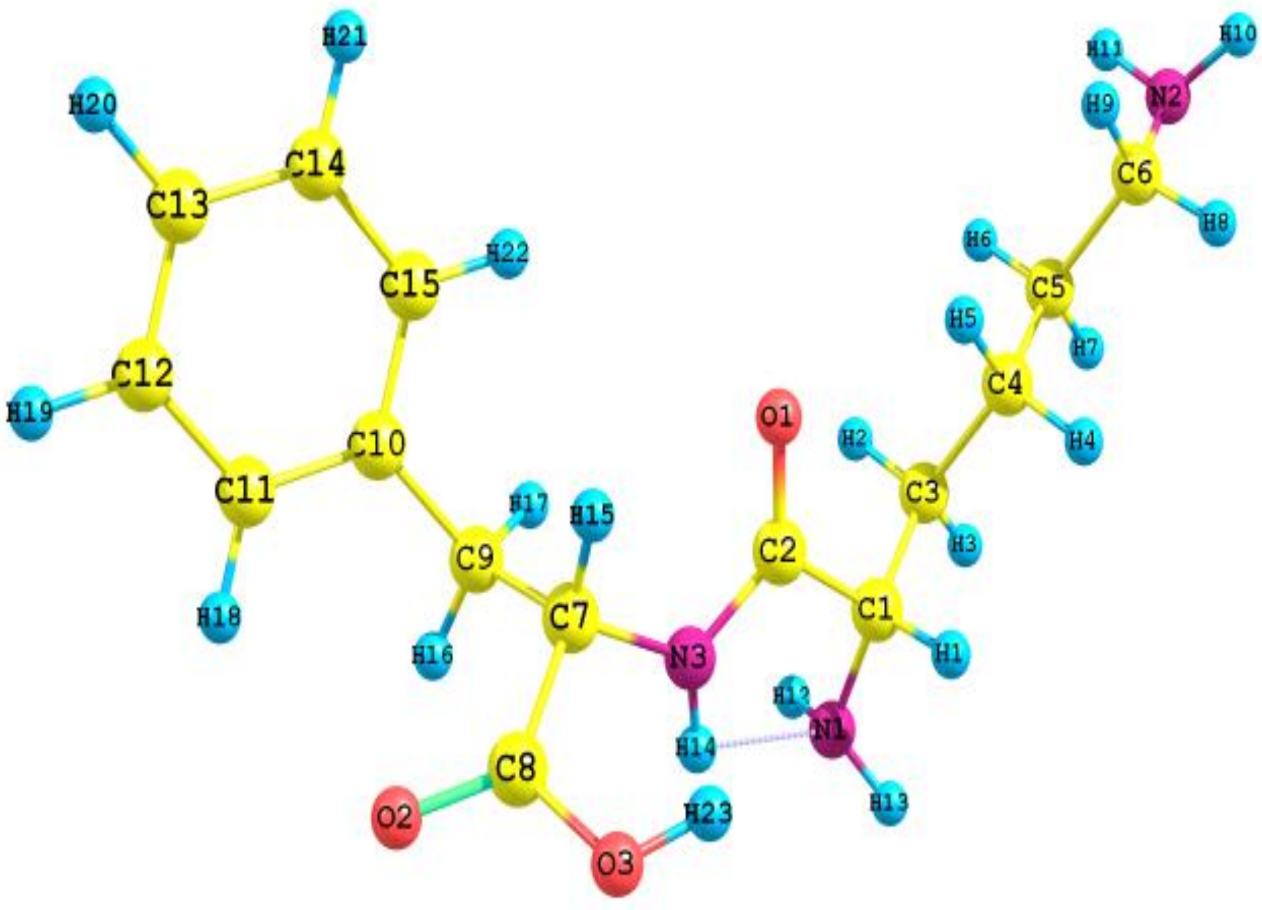


Fig 4.2 THE OPTIMIZED STRUCTURE OF LYS + PHE AT B3LYP/6-31G LEVEL OF THEORY

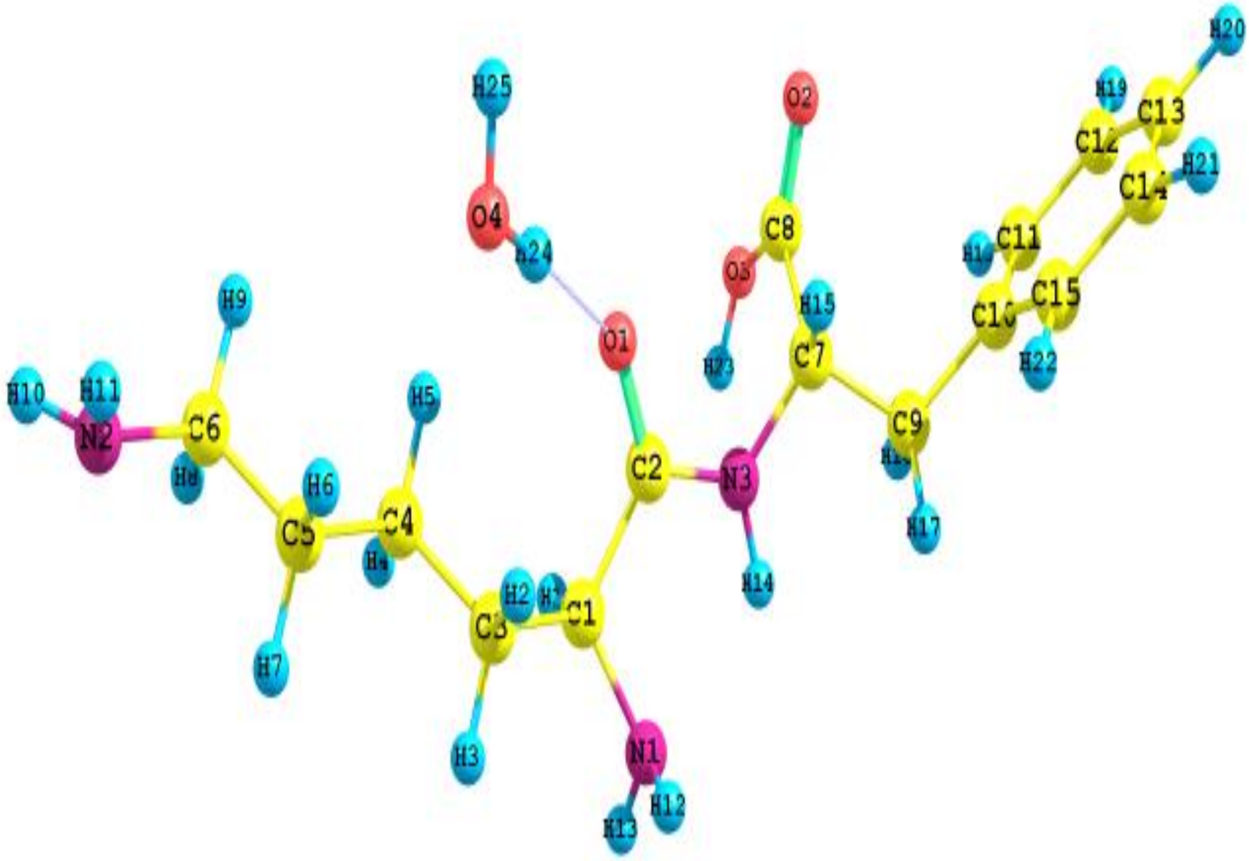


Fig 4.3 THE OPTIMIZED STRUCTURE OF LYS + PHE (H20) AT HF/6-31G LEVEL OF THEORY

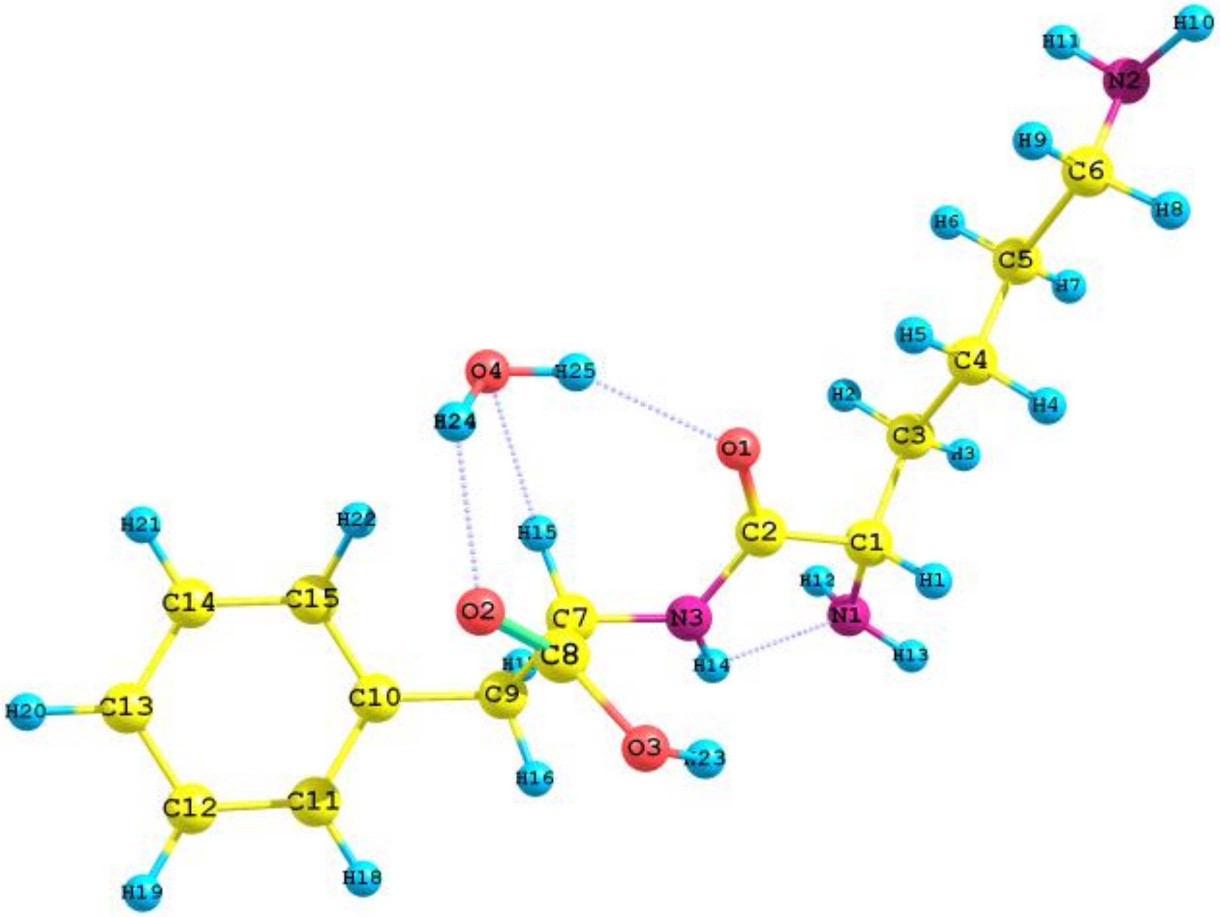
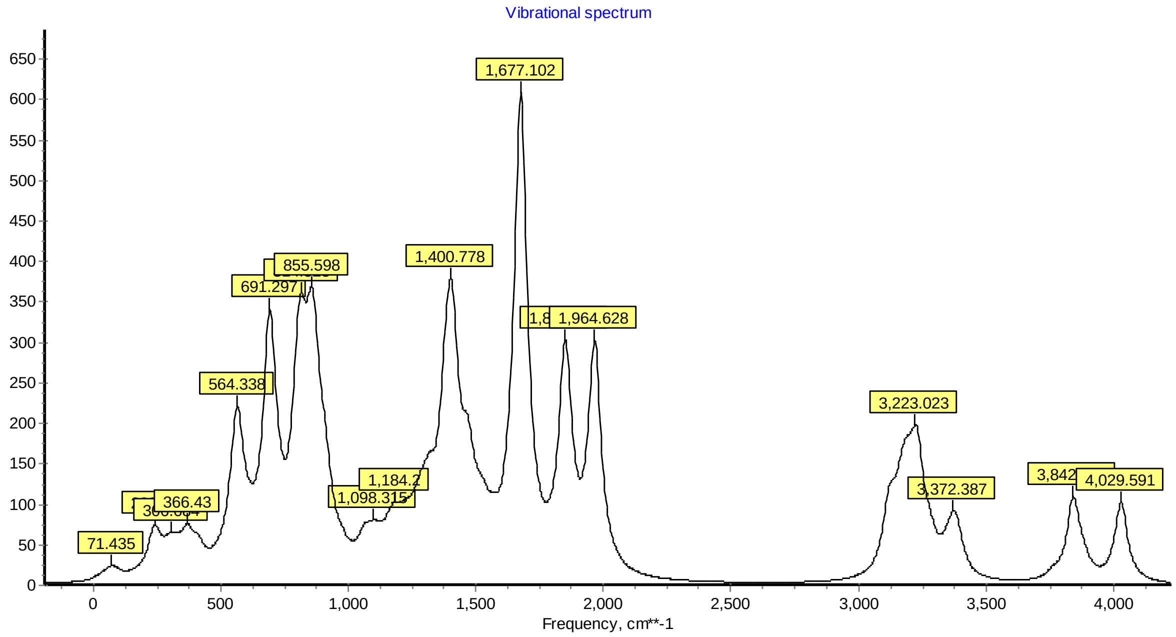
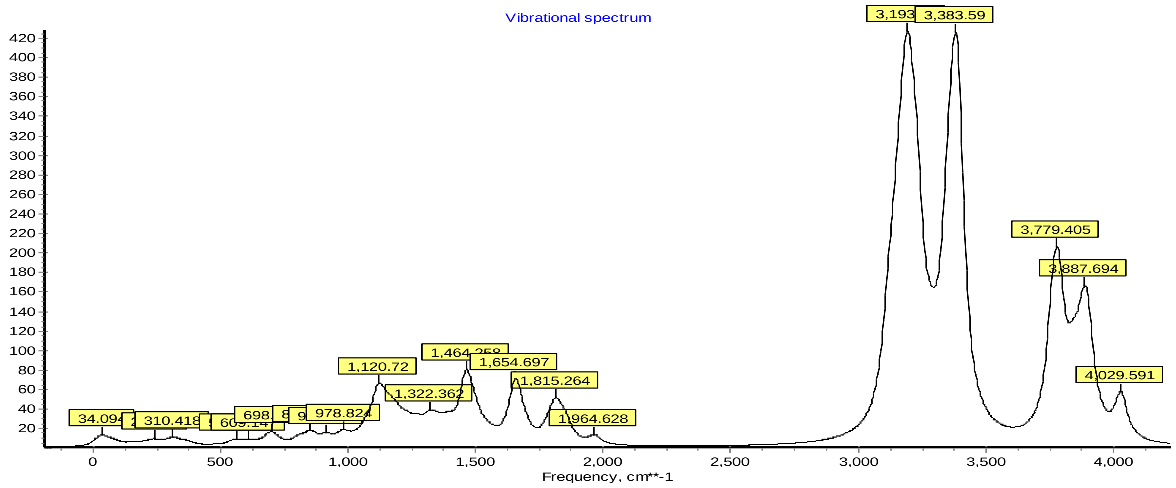


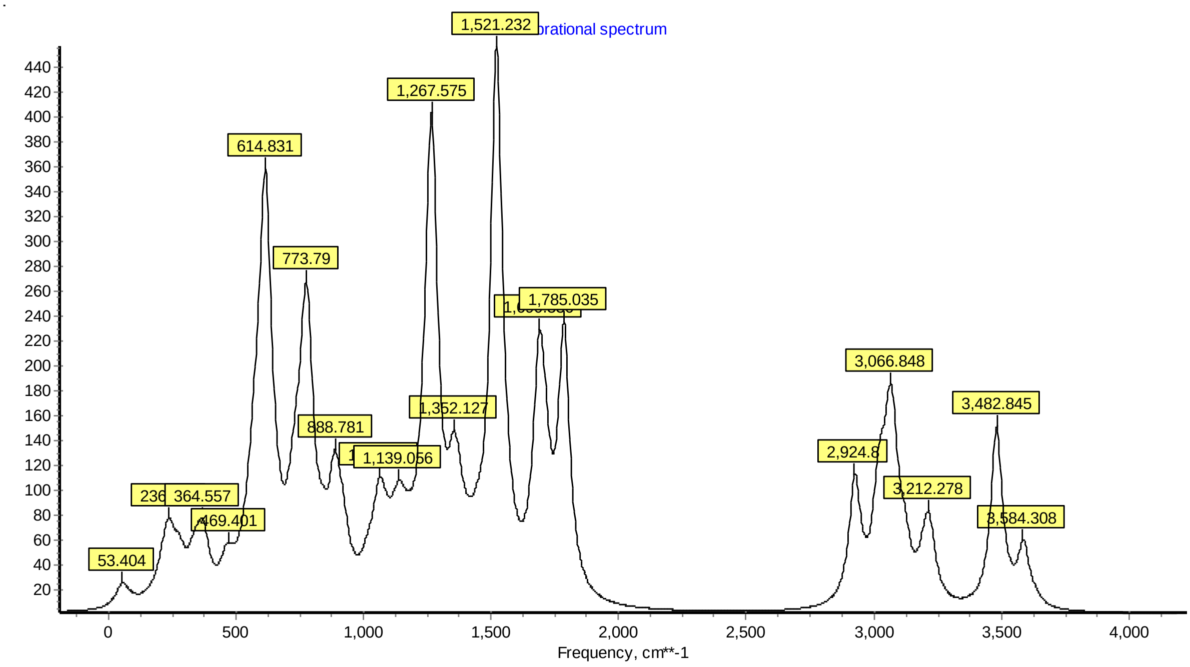
Fig 4.4 THE OPTIMIZED STRUCTURE OF LYS + PHE (H20) AT B3LYP/6-31G LEVEL OF THEORY



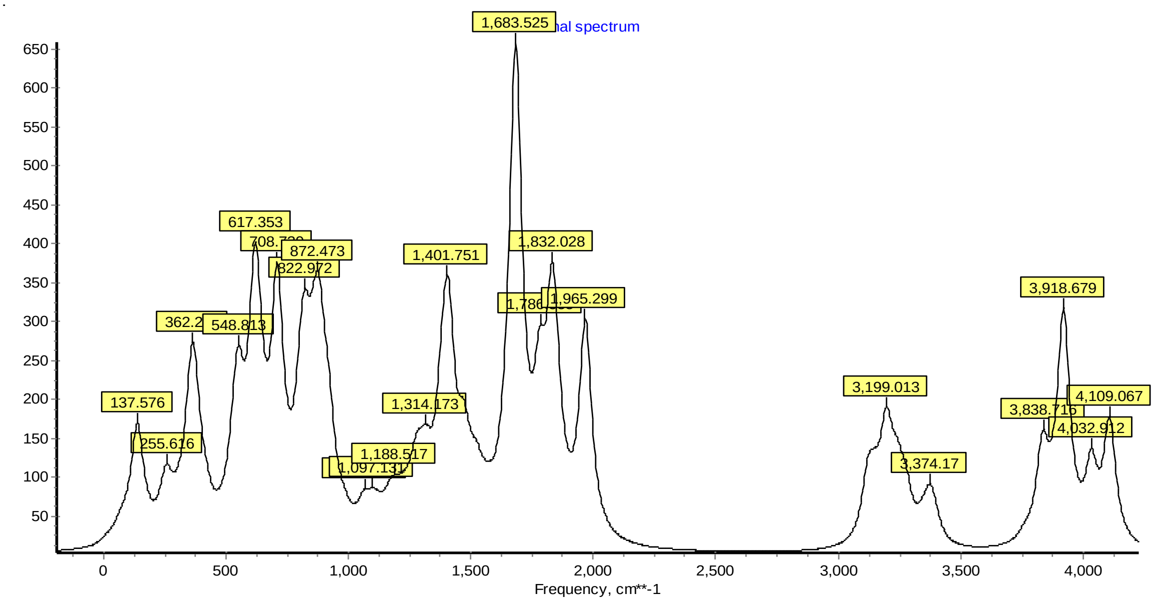
Graph 4.1: A graph between wavenumber (vs) IR intensity for Lys +Phe at HF/6-31G level of theory



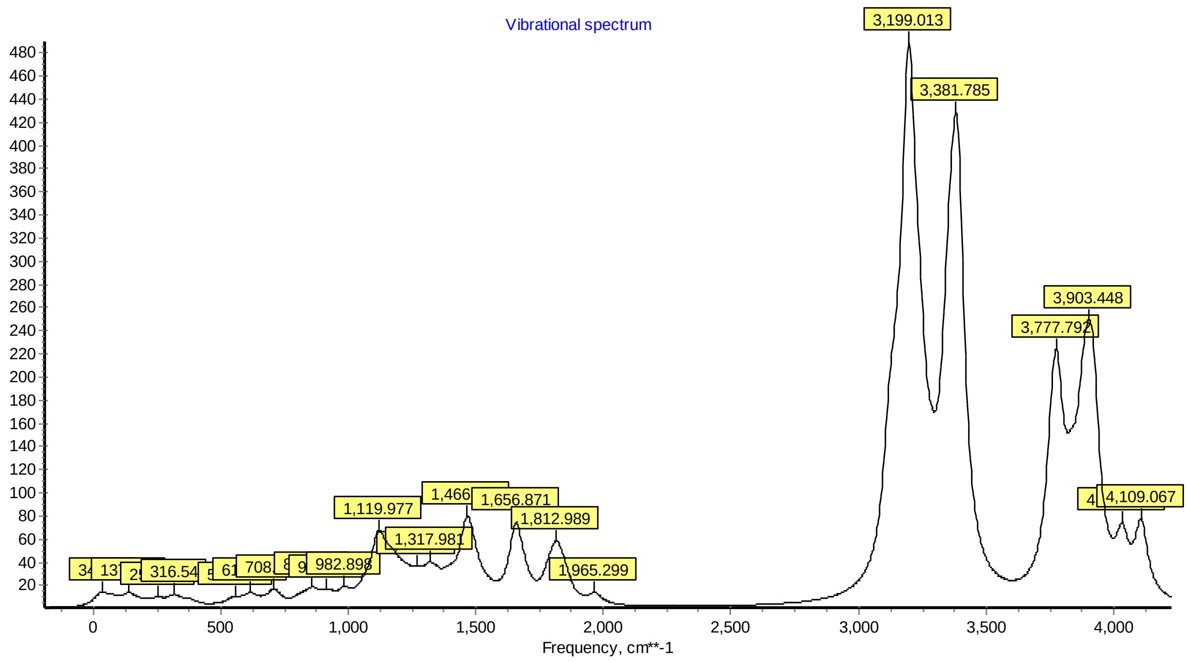
Graph 4.2: A graph between wavenumber (vs) Raman intensity for Lys + Phe at HF/6-31G level of theory



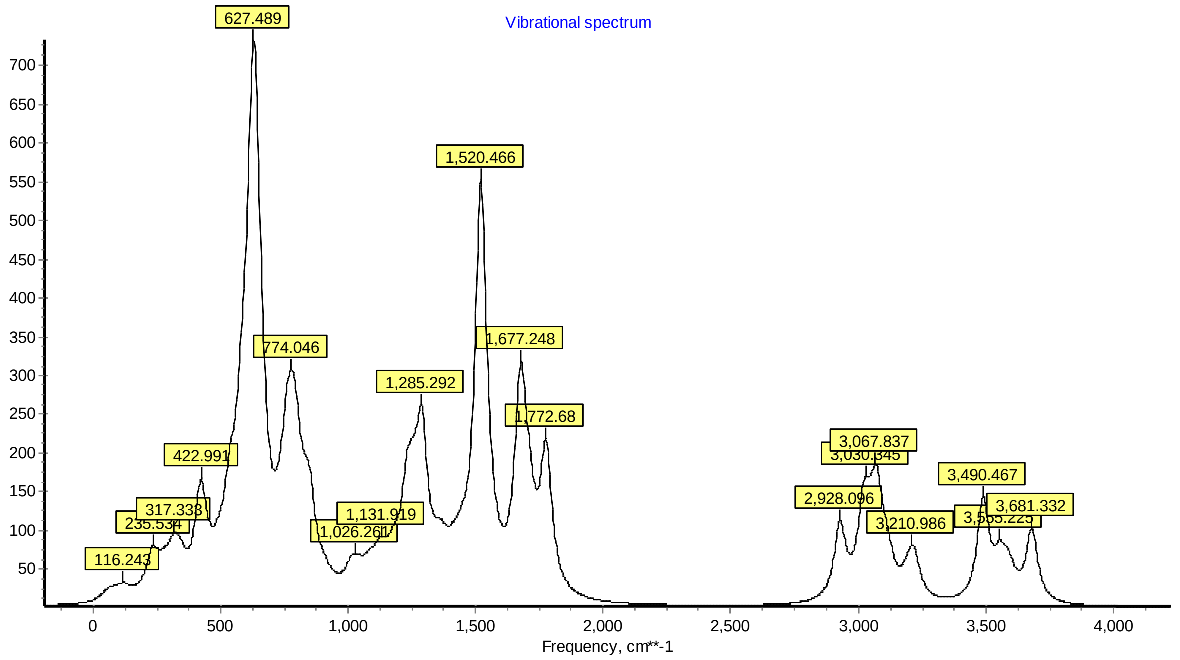
Graph 4.3: A graph between wavenumber (vs) IR intensity for Lys + Phe at B3LYP/6-31G level of theory



Graph 4.4: A graph between wavenumber (vs) IR intensity for Lys + Phe (H2O) at HF/6-31G level of theory



Graph 4.5: A graph between wavenumber (vs) Raman intensity for Lys + Phe (H2O) at HF/6-31G level of theory



Graph 4.6: A graph between wavenumber (vs) IR intensity for Lys + Phe (H2O) at B3LYP/6-31G level of theory

Table 4.1: BOND LENGTH (Å) OF (LYS+ PHE) AND LYS + PHE (H2O) OPTIMZED AT HF/6-31G AND B3LYP/6-31G LEVEL OF THEORY.

BOND LENGTH	HF/6-31G		B3LYP/6-31G	
PARAMETERS	LYS + PHE (Å)	LYS + PHE (H2O) (Å)	LYS + PHE (Å)	LYS + PHE (H2O) (Å)
N2-H10	0.99496	0.99529	1.01253	1.01266
N2-H11	0.99603	0.99638	1.01387	1.01403
N2-C6	1.45476	1.45554	1.46457	1.46481
C6-H9	1.09117	1.09105	1.10796	1.10772
C6-H8	1.08433	1.08490	1.09784	1.09781
C6-H5	1.52784	1.52712	1.53592	1.53592
C5-H6	1.08846	1.08523	1.10178	1.09817
C5-H7	1.08545	1.08592	1.09813	1.10161
C5-C4	1.53218	1.53120	1.53824	1.53838
C4-H5	1.08141	1.08191	1.09470	1.09465
C4-H4	1.08950	1.08988	1.10207	1.10197
C4-C3	1.53375	1.53437	1.54069	1.54068
C3-H2	1.08609	1.08487	1.09963	1.09947
C3-H3	1.08685	1.08631	1.09980	1.09978

C3-C1	**1.54018**	**1.54150**	**1.54776**	**1.54815**
C1-H1	**1.08658**	**1.08668**	**1.09988**	**1.09988**
C1-N1	**1.46269**	**1.46269**	**1.47936**	**1.48068**
N1-H13	**0.99613**	**0.99629**	**1.01373**	**1.01415**
N1-H12	**0.99877**	**0.99896**	**1.01694**	**1.01738**
C1-C2	**1.52621**	**1.52591**	**1.54216**	**1.53920**
C2=O1	**1.22682**	**1.23247**	**1.25214**	**1.25614**
C2-N3	**1.35864**	**1.35147**	**1.37258**	**1.36700**
N3-H14	**0.99581**	**0.99638**	**1.02045**	**1.01967**
N3-C7	**1.45529**	**1.45676**	**1.46750**	**1.46752**
C7-H15	**1.07932**	**1.07929**	**1.09890**	**1.09349**
C7-C9	**1.54994**	**1.54925**	**1.55247**	**1.54901**
C9-H17	**1.08514**	**1.08514**	**1.09603**	**1.10023**
C9-H16	**1.08559**	**1.08546**	**1.09483**	**1.09860**
C7-C8	**1.52162**	**1.52099**	**1.53168**	**1.53442**
C8-O3	**1.35479**	**1.35512**	**1.37930**	**1.37610**

C8=O2	**1.20205**	**1.20149**	**1.22647**	**1.22916**
O3-H23	**0.95124**	**0.95104**	**0.98222**	**0.98195**
C9-C10	**1.51228**	**1.51227**	**1.51939**	**1.52000**
C10-C11	**1.39003**	**1.39016**	**1.40376**	**1.40401**
C11-H18	**1.07376**	**1.07388**	**1.08437**	**1.08691**
C11-C12	**1.38742**	**1.38740**	**1.39961**	**1.39927**
C12-H19	**1.07278**	**1.07272**	**1.08564**	**1.08555**
C12-C13	**1.38618**	**1.38623**	**1.39954**	**1.39831**
C13-H20	**1.07287**	**1.07282**	**1.08563**	**1.08540**
C13-C14	**1.38793**	**1.38793**	**1.40041**	**1.40022**
C14-H21	**1.07305**	**1.07298**	**1.08575**	**1.08534**
C14-C15	**1.38577**	**1.38582**	**1.39841**	**1.39833**
C15-H22	**1.07487**	**1.07486**	**1.08740**	**1.08605**
C10-C15	**1.39251**	**1.39244**	**1.40691**	**1.40706**
O1-H24	**-**	**1.90154**	**-**	**2.06630**
H24-O4	**-**	**0.95618**	**-**	**0.98225**
O4-H25	**-**	**0.94875**	**-**	**0.98071**

Table 4.2: BOND ANGLE (in degrees) OF LYS+PHE AND LYS+PHE (H2O) OPTIMZED AT HF/6-31G AND B3LYP/6-31G LEVEL OF THEORY.

BOND ANGLE	HF/6-31G		B3LYP/6-31G	
PARAMETERS	LYS + PHE	LYS + PHE (H20)	LYS + PHE	LYS + PHE (H2O)
H11-N2-H10	112.772	112.707	112.088	111.993
C6-N2-H11	115.815	115.326	114.776	114.704
C6-N2-H10	116.247	116.110	115.365	115.276
N2-C6-H8	107.781	107.828	107.662	107.675
N2-C6-H9	112.950	112.868	113.880	113.878
H8-C6-H9	106.730	108.939	106.412	106.435
C5-C6-H9	109.204	108.969	108.687	108.696
C5-C6-N2	110.769	110.503	110.918	110.877
C6-C5-H7	108.272	108.364	108.260	108.259
H7-C5-H6	106.673	107.551	106.528	106.554
C4-C5-C6	112.802	112.719	112.802	112.855
C5-C4-H4	109.091	109.637	109.135	109.176
H5-C4-H4	107.160	107.198	106.953	106.915
C3-C4-H5	109.375	109.727	108.934	109.020

C3-C4-C5	**112.096**	**111.971**	**112.436**	**112.406**
C4-C3-H3	**108.778**	**108.685**	**108.939**	**108.906**
H2-C3-C1	**109.312**	**109.857**	**109.067**	**109.098**
C3-C1-H1	**108.367**	**108.342**	**108.140**	**108.168**
H1-C1-N1	**106.653**	**106.619**	**106.608**	**106.651**
C1-N1-H13	**114.943**	**114.749**	**114.209**	**113.909**
C1-N1-H12	**114.769**	**114.609**	**113.457**	**113.178**
H12-N1-H13	**111.616**	**111.464**	**110.891**	**110.662**
C1-C2=O1	**122.589**	**122.794**	**123.153**	**122.773**
C1-C2-N3	**115.722**	**116.085**	**113.988**	**114.559**
N3-C2=O1	**121.644**	**121.076**	**122.830**	**122.645**
H14-N3-C2	**115.697**	**115.552**	**113.770**	**114.203**
H14-N3-C7	**120.185**	**120.230**	**122.281**	**122.808**
C7-N3-C2	**121.716**	**121.949**	**121.278**	**121.051**

H15-C7-N3	**110.137**	**110.204**	**105.384**	**109.047**
C9-C7-N3	**108.186**	**108.109**	**113.670**	**109.718**
H15-C7-C8	**106.317**	**106.279**	**108.020**	**105.369**
C7-C8=O2	**123.233**	**123.213**	**124.860**	**123.706**
C7-C8-O3	**115.828**	**115.852**	**114.770**	**115.859**
O2=C8-O3	**120.787**	**120.785**	**120.364**	**120.415**
C8-O3-H23	**114.680**	**115.127**	**110.842**	**110.728**
H16-C9-H17	**106.968**	**106.981**	**107.822**	**106.763**
C7-C9-H16	**108.813**	**108.844**	**109.299**	**109.341**
C7-C9-H17	**106.757**	**106.867**	**106.676**	**106.411**
H17-C9-C10	**109.200**	**109.273**	**109.003**	**109.791**
H16-C9-C10	**109.993**	**110.005**	**110.485**	**109.354**
C9-C10-C11	**121.095**	**121.028**	**121.606**	**119.672**
C10-C11-H18	**119.814**	**119.837**	**119.301**	**119.480**
H18-C11-C12	**119.524**	**119.523**	**120.210**	**119.652**

H19-C12-C11	**119.723**	**119.728**	**119.671**	**119.798**
H19-C12-C13	**120.129**	**120.134**	**120.057**	**120.233**
C12-C13-H20	**120.184**	**120.174**	**120.182**	**120.218**
H20-C13-C14	**120.155**	**120.145**	**120.154**	**120.189**
C13-C14-H21	**120.114**	**120.117**	**120.132**	**120.059**
H21-C14-C15	**119.856**	**119.853**	**119.821**	**119.455**
C14-C15-H22	**119.527**	**119.528**	**119.998**	**119.102**
H22-C15-C10	**119.720**	**119.747**	**119.343**	**120.598**
C9-C10-C15	**120.154**	**120.182**	**119.510**	**121.489**
C10-C11-C12	**120.659**	**120.638**	**120.473**	**120.868**
C11-C12-C13	**120.147**	**120.138**	**120.272**	**119.968**
C12-C13-C14	**119.661**	**119.681**	**119.664**	**119.592**
C13-C14-C15	**120.029**	**120.030**	**120.047**	**120.485**
C14-C15-C10	**120.753**	**120.725**	**120.658**	**120.277**
C15-C10-C11	**118.749**	**118.788**	**118.884**	**118.808**
H24-O4-H25	**-**	**111.651**	**-**	**107.519**

Table 4.3: FREQUENCY MODE OF VIBRATION OF LYS + PHE OPTIMIZED AT HF/6-31G AND B3LYP/6-31G LEVEL OF THEORY

FREQUENCY MODE OF VIBRATION	PARAMETERS	#HF/6-31G (cm^{-1})	B3LYP/6-31G (cm^{-1})
STRETCHING	O3-H25	4030.01	3586.52
	N3-H14	3842.32	3481.06
	Benzene Ring	3391.05	3230.42
	C7-H15	3197.81	3038.95
ASYMMETRIC	H10-N2-H11	3901.68	3652.04
	H13-N1-H12	3879.34	3631.46
	H3-C3-H2	3225.31	3067.89
SYMMETRIC	H10-N2-H11	3785.29	3535.49
	H13-N1-H12	3762.89	3514.91
	H3-C3-H2	3180.11	3023.27
	H7-C5-H6	3168.79	3015.13
SCISSORING	H13-N1-H12	1854.18	1711.05
	H10-N2-H11	1846.66	1709.27
	H8-C6-H9	1684.78	1565.91
	H7-C5-H6	1654.15	1538.15
ROCKING	H8-C6-H9	1492.58	3117.57
	H16-C9-H17	1675.82	1519.93
WAGGING	H16-C9-H17	1522.97	-
	H4-C4-H5	1541.89	-
	H8-C6-H9	1570.96	-
	H3-C3-H2	1509.60	-
	H11-N2-H10	690.74	-

Table 4.4: FREQUENCY MODE OF VIBRATION OF LYS + PHE (H2O) OPTIMIZED AT HF/6-31G AND B3LYP/6-31G LEVEL OF THEORY

FREQUENCY MODE OF VIBRATION	PARAMETERS	#HF/6-31G (cm^{-1})	B3LYP/6-31G (cm^{-1})
STRETCHING	O3-H25	4033.67	3587.92
	N3-H14	3834.38	3490.03
	Benzene Ring	3391.75	3225.11
	C7-H15	3291.57	3102.95
ASSYMMETRIC	H25-O4-H24	4109.50	3681.28
	H10-N2-H11	3896.50	3650.37
	H13-N1-H12	3877.07	3625.58
	H7-C5-H6	3242.00	3077.03
	H17-C9-H16	3236.74	3064.86
SYMMETRIC	H24-O4-H25	3920.67	3554.27
	H10-N2-H11	3780.58	3524.15
	H13-N1-H12	3761.27	3510.38
	H2-C3-H3	3186.38	3024.64
	H25-O4-H24	1779.59	1775.35
	H13-N1-H12	1851.30	1711.57
SCISSORING	H10-N2-H11	1845.87	1709.27
	H5-C4-H4	1666.94	1554.87
	H16-C9-H17	1655.60	1519.44
ROCKING	H11-N2-H10	1218.48	1448.85
	H3-C3-H2	792.49	792.49
TWISTING	H2-C3-H3	1484.15	1288.43

Table 4.5: ENERGY (a.u), DIPOLE MOMENT (μ), CHEMICAL POTENTIAL (μ), CHEMICAL HARDNESS (η), CHEMICAL SOFTNESS (S) OF LYS + PHE OPTIMIZED AT HF/6-31G AND B3LYP/6-31G LEVEL OF THEORY:

PARAMETERS	#HF/6-31G	B3LYP/6-31G
ENERGY(a.u)	-968.960809045	-975.111871073
DIPOLE MOMENT	7.7105	5.5173
CHEMICALPOTENTIAL(μ)	-0.234315	-0.114725
CHEMICAL HARDNESS(η)	0.234315	0.114725
CHEMICAL SOFTNESS(S)	2.13387	4.35824

Table 4.6: ENERGY (a.u), DIPOLE MOMENT (μ), CHEMICAL POTENTIAL (μ), CHEMICAL HARDNESS (η), CHEMICAL SOFTNESS (S) OF LYS + PHE (H2O) OPTIMIZED AT HF/6-31G AND B3LYP/6-31G LEVEL OF THEORY:

PARAMETERS	#HF/6-31G	B3LYP/6-31G
ENERGY(a.u)	-1044.94630875	-1051.51621333
DIPOLE MOMENT	6.9737	7.6773
CHEMICALPOTENTIAL(μ)	-0.234525	-0.09632
CHEMICAL HARDNESS(η)	0.234525	0.09632
CHEMICAL SOFTNESS(S)	2.1319688	5.1910299

SUMMARY AND CONCLUSION

CHAPTER V

SUMMARY AND CONCLUSION

The structure of lysine + phenylalanine, lysine + phenylalanine (H2O) were optimized using HF/6-31G level of theory of ab initio method and B3LYP/6-31G level of theory of density function method. The geometrical parameters such as bond length, bond angle, chemical potential, chemical hardness, chemical softness, dipole moment and energy of the molecules were calculated. It is observed that the energy of the water molecules effects the geometry of the lysine + phenylalanine and there is decrease in energy with increase in number of water molecules. The calculated vibrational frequency shows that all the optimized structures are in local minima. The chemical softness are large and highly polarisable, while chemical hardness are relatively small and much less polarisable.