A Computational Investigation on Cysteine

By

Kowsalya,P

(12PPH004)

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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CERTIFIED AS A BONAFIDE RESEARCH WORK

31.3.14

Signature of the Head of the Department

31.3.14

Signature of Supervisor

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KOWSALYA . P

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CHAPTER 1

INTRODUCTION

1.1 BIOMOLECULES

The molecules associated with life are called biomolecules which include carbohydrates, proteins, lipids and nucleic acids. Biomolecules form a cell that comprise living matter **[1]** and is the basic unit of life. All living organisms are composed of cells, either unicellular or multi- cellular. It is the structural and functional unit of all living things. Cells are permeable to small, uncharged molecule like H_2O, CO_2 and O_2. All cells have the same chemical composition. Each cell is an amazing world of several biochemical activities it assimilate nutrients, and convert the nutrients in to energy, and carry out specialized functions and reproduces as necessary **[2].**

1.2 PROTEINS

Protein is a complex organic nitrogenous substances found in the cells of all living beings. All proteins are macromolecules because of their very high molecular weight, which contain carbon, hydrogen, oxygen, nitrogen and some contain phosphorus, sulfur **[11].** It serves as enzymes or as structural components of cells and tissues and it occupies the central position in the architecture and functioning of living matter. Proteins with catalytic activity are largely responsible for determining the phenotype or properties of cell in particular environment. Proteins are intimately connected with all phases of chemical and physical activity that constitutes the life of the cell. Proteins perform a wide variety of regulatory functions, as membrane receptors and transporters. Proteins exhibit a high degree of specificity, a property that maintains the order and complexity of life. They are polymers i.e. chain like molecules produced by joining a number of small units of 20 different species of amino acids called monomers **[3].** Proteins possess free ionic or electrically charged groups that migrate in an electrical field **[11].**

1.3 STRUCTURE OF PROTEINS

Proteins are polymers of L-α-amino acids it is of 3-dimensonal structure. The structure of proteins is classified in to four, based on the degree or complexity of their molecule.

a) Primary Structure,

b) Secondary Structure,

c) Tertiary Structure,

d) Quaternary Structure.

1.3.1 PRIMARY STRUCTURE

The primary structure of a protein refers to the number and sequence of amino acids that constitutes units of the polypeptide chain. The main mode of linkage of the amino acids in protein is the peptide bond which links the α-carboxyl group of one amino acid residue to the α-amino group of the other, as shown in **fig. (1.1)**. the protein may contain more than one amino acid chain **[3].** The primary structure of a protein is largely responsible for its function, and it comprises the identification of constituent amino acids with regard to their quality, quantity and sequence in a protein structure **[5].**

1.3.2 SECONDARY STRUCTURE

The conformation of polypeptide chain by twisting or folding is referred to a secondary structure and the amino acids are located close to each other in the sequence. Based on the nature of hydrogen bonding the secondary structure are of two types.

a) α- helix,

b) β- pleated sheet.

a) α-HELIX

α- Helix is the most common spiral structure of protein **[5]** and has rigid arrangement of polypeptide chains shown in **fig. (1.2)**. Each peptide bond in polypeptide chain participates in intrachain hydrogen bonding. Hydrogen bonding occurs between the carbonyl group of peptide bond and – NH of another peptide bond **[12],** the bond that involved is collectively strong enough to stabilize the structure though they are individually weak. Proteins in hair and wool are belongs to this category.

b) β- PLEATED SHEET

Hydrogen bonding occurs between two polypeptide chains or between two regions of a single chain (inters chain). The β sheet structures are quite common in nature

and are favored by the presence of amino acids, glycine and alanine. Silk and synthetic fibers such as nylon, orlon are belongs to this category. The polypeptide chains in the β-sheet may arranged in parallel or anti-parallel, as shown in **fig. (1.2)**.

1.3.3 TERTIARY STRUCTURE

The tertiary structure of a protein refers to the final 3-dimensional shapes that result from twisting, bending, and folding of protein helix as shown in **fig. (1.3) [13].** It is a compact structure with hydrophobic side chains held interior, while the hydrophilic groups are on the surface of the protein molecule. This type of arrangement ensures the stability of molecule. Hydrogen bond, disulfide bonds, ionic and hydrophobic interactions also contributes the tertiary structure of proteins **[5].**

1.3.4 QUATERNARY STRUCTURE

Complex proteins are often formed from two or more amino acid chains rather than a single amino acid chain. Each chain is a complete protein with a protein with a characteristic of primary, secondary, and tertiary structure **[13].** The quaternary structure refers to the arrangement of protein monomers into an aggregation **[15]** as shown in **fig. (1.3)**. Hydrogen bond, hydrophobic interactions, and electronic interactions contribute to the quaternary structure of proteins.

1.4 AMINO ACIDS

Amino acids are the building blocks of proteins. Each amino acids is a nitrogenous compound having both an acidic carboxyl group (-COOH) and a basic amino group (-NH_2) as shown in **fig. (1.5).** R stands for the different side chains that are different for each amino group. R is simple as H atom,-CH_3 methyl group or more complex structure. The amino acids exist in the ionized form in the biological system as shown in **fig. (1.6).** Amino acids are linked to one another by peptide bonds. The amino group of one amino acids reacts with carboxyl group of another amino acids to form a peptide bond with the generation of water molecule.

1.4.1 STEREOISOMERISM OF AMINO ACIDS

The α-carbon atom in all the amino acids is joined by covalent bonds to form four different groups. The α-carbon of amino acids is asymmetric in which amino acids exists in two optically active forms, having $–NH_2$ group to the right are designated as D forms and $–NH_2$ group to the left as L forms or levorotatory as in **fig.(1.7)**. The amino acids found in proteins are belongs to the L series, it's a naturally occurring amino acids. In few amino acids, α- carbon are symmetric and the same are found in glycine **[3].**

1.5 CLASSIFICATION OF AMINO ACIDS

There are different ways of classifying the amino acids based on the structure, chemical nature, nutritional requirement and metabolic fate. Each amino acid is assigned a 3 letter or 1 letter symbol. These symbols are commonly used to represent the amino acids in protein structure **[5].**

1.5.1 NUTRITIONAL CLASSIFICATION OF AMINO ACIDS

Based on the nutritional requirement amino acids are grouped into three different classes such as.

(a) Essential or Indispensable amino acids,

(b) Semi-Essential amino acids,

(c) Non-Essential or Dispensable amino acids.

a) ESSENTIAL OR INDISPENSABLE AMINO ACIDS

The amino acids which cannot be synthesized by the human body and therefore, need to be supplied through the diet are called essential amino acids. They are required for proper growth and maintenance of the individual. Arginine, valine, histidine, phenylalanine, tryptophan, threonine, lysine, methionine, leucine, isoleucine are the essential amino acids.

b) **SEMI- ESSENTIAL AMINO ACIDS**

The amino acids are not synthesized in human body and found to be insufficient amount during growth. These amino acids have an important role in growth promoting nutrients. Arginine and histidine are the semi- essential amino acids.

c) NON- ESSENTIAL OR DISPENSABLE AMINO ACIDS

The body can synthesize 10 amino acids to meet the biological needs, and are not to be consumed by the diet. Amino acid such as glycine, alanine, asparagine, serine, aspartate, tyrosine, glutamine, glutamate and proline belongs to the same category.

1.5.2 ON THE BASIS OF POLARITY OF THE SIDE CHAIN OR R GROUP

The 20 amino acids could be classified according to the chemical nature of their R groups in to appropriate subclasses as shown in **table (1.14).**

a) Amino acids with non-polar R groups,
b) Amino acids with polar but uncharged R groups
c) Amino acids with negatively charged (acidic) R groups and
d) Amino acids with negatively charged (acidic) R groups.

a) AMINO ACIDS WITH NON-POLAR R GROUP

The R group in this category of amino acids are hydrocarbon and hydrophobic (water hating) in nature. A term used to describe aliphatic and aromatic hydrocarbon compounds or portions of molecules or the chemical groups, that share the property of having only very limited solubility in water**[10].**This group includes five amino acids with aliphatic R groups (alanine ,valine ,leucine, proline, isoleucine), two with aromatic rings and one with sulfur.

b) AMINO ACIDS WITH POLAR BUT UNCHARGED R GROUPS

The R groups of these amino acids are more soluble in water i.e., more hydrophilic than those of the non-polar amino acids because they contain functional groups that form hydrogen bonds with water. The polarities of these amino acids are due to either a hydroxyl group or a sulfhydryl group (cysteine) or an amide group. The R group of glycine, a single hydrogen atom is too small to influence the high degree of polarity of the α-amino and α-carboxyl groups.

c) AMINO ACIDS WITH NEGATIVELY CHARGED (=ACIDIC) R GROUPS:

In this group, amino acids are monoamino di-carboxylic acids i.e. their side chain contains an extra carboxyl group with a dissociable proton. The resulting additional negative charge accounts for the electrochemical behavior of proteins. Aspartic and glutamic acid are the two amino acids which belong to this group.

d) AMINO ACIDS WITH POSITIVELY CHARGED (=BASIC) R GROUPS:

The side chain of amino acid contains an extra amino group are called diamino-monocarboxylic acid which imparts basic properties to them. Lysine, arginine, histidine belongs to these category.

1.6 PROPERTIES OF AMINO ACIDS

1.6.1 PHYSICAL PROPERTIES

The amino acids are colorless crystalline substances and vary from slender needles to thick hexagonal plates (cysteine). Amino acids are tasteless, sweet or bitter. All amino acids except glycine have optical isomers due to the presence of asymmetric α-carbon atom and have high melting points (above 200°c). Densities are result in decomposition and soluble in polar solvents such as water and ethanol, insoluble in non-polar solvents such as benzene and ether. The dipole moment for the amino acids is high **[7].** Some amino acids like tryptophan, tyrosine, histidine and phenylalanine absorb ultraviolet rays at 260-290mμ which enables the identification of property which contain them.

1.6.2 CHEMICAL PROPERTIES

All molecules have both acidic and basic groups might exist as uncharged molecules or ionic form or mixture of both. Amino acids react with both acids and bases. Hence, they are amphoteric in nature. In acid solution, the COO^{-} ion acquires a proton and the amino acid becomes an ammonium salt of the acid. Conversely, in alkaline solution, the NH_3^{+} ion loses a proton and the amino acid becomes an anion of salt. These reactions are of reversible in nature and depend upon the PH of the medium. Hence amino acid serves as buffers and tends to prevent PH changes when acid or base is added **[3].**

1.6.3 ACID – BASE PROPERTIES OF AMINO ACIDS

The most important chemical property of amino acid is the acid – base property. Amino acids are weak polyprotic acids because of their COOH and NH_3^+ groups. The structure of amino acid depends on the pH of the solution.

❖ ZWITTERION OR DIPOLAR ION

The zwitterion contains both carboxyl (COO^-) group and amino (NH_3^+) group. At certain pH amino acids would not migrate to either electrode and exists as neutral zwitterions. This pH is called isoelectric point (pI) or the isoelectric pH. Isoelectric PH is the PH that a molecule exists as a zwitterion and carries no net charge. Thus the molecule is electrically neutral **[5].** Each amino acid has a characteristic PH that carries both positive and negative charges and exists as zwitterion as in **figure1.8**. The pI differs for the different amino acids based on the number and charge of the ionizable groups. Amino acids in the zwitterion form are amphoteric and act as acid as well as bases.

❖ ACIDIC SIDE CHAINS

The amino acid when react with acids convert the carboxyl group (COOH) in to a carboxylate group (COO^-) by deprotonation and it exists as anion as in **fig.(1.8)**. In acidic solution, amino acids exist as positive ions and are attracted towards the cathode. The pH value of anion is high and has a net negative charge.

❖ BASIC SIDE CHAINS

The amino acid reacts with bases converts the ammonium group (NH_3^+) to an amino group (NH_2) through protonation as in **fig. (1.8)**. In basic solution, amino acids exist as positive ions and are attracted towards the cathode. The pH value of cation is low and has a net positive charge. The net charge of an amino acid at any given moment depends on the particular amino acid and the pH N of the medium **[13].**

1.7 TYPES OF BONDS

Several atoms are assembled and held together to form thousands of molecules which participate in the building and function of physical and biological systems. A bond is force which holds two atoms together. The formation of bond between two atoms is due

to some redistribution or regrouping of electrons to form a more stable configuration. Protein synthesis is a multiple dehydration process. The union of amino acids forms a chain and also among various amino acid residues of different chains involves various types of chemical bonds. Protein structure is stabilized by two types of bonds.

a) Covalent bond
b) Non-covalent bond.

1.7.1 COVALENT BOND

A covalent bond is formed between the two combining atoms by the mutual sharing of one, two or three electron pairs between them. By the mutual sharing of electron pair(s) each of the two combining atoms attains stable noble gas configuration. One electron of each electron pair is contributed by one atom while the other electron is contributed by the other atom. Thus combination of both atoms have equal claim on the shared electron pair. Covalent bonds are strong bonds that occur between the atoms that make up a molecule. The cysteine is the sole amino acid, in which side chain forms covalent bonds, yielding Disulfide Bridge with other-CH2-S-S-CH2-A.

1.7.2 NON-COVALENT BOND

A non-covalent bond is a type of chemical bond between macromolecules that does not involve the sharing of pairs of electrons, but rather involves more dispersed variations of electromagnetic interactions. Non covalent interactions are critical in maintaining three dimensional structures of large molecules, such as proteins and nucleic acids and involved in many biological processes in which large molecules bind specifically but transiently to one another.Individual non covalent bond can be divided into four types:

a) Ionic bond,
b) Hydrogen bonds,
c) Hydrophobic interactions and
d) Vander Waals interactions.

a) IONIC BOND OR ELECTROSTATIC BOND

Ionic bonding is the interaction between the acidic and basic groups of the constituent amino acids. The R groups of glutamic acid and aspartic acid contain negatively charged carboxylate groups, and the basic amino acids (arginine, histidine, and lysine) contain positively charged amino groups in the physiological pH range. Thus, these amino acids contribute negatively charged and positively charged side chains to the polypeptide backbone. When two oppositely charged groups are brought close together, electrostatic interactions lead to a strong attraction, resulting in the formation of an electrostatic bond. Ionized groups are found in stabilizing interactions between protein and other molecules. The ionic bond is a weaker one when compared to the hydrogen bond.

b) HYDROGEN BOND

The hydrogen atom is covalently bonded to a strong electronegative and small-sized atom (N_2, O_2 and F_2), the shared electron pair between the hydrogen atom and the strongly electronegative atom lies much more nearer to the electronegative atom. This results in the development of partial ionic character in the covalent bond, with a fractional positive charge on the hydrogen atom and a fractional negative charge on the electronegative atom. The attractive force that binds hydrogen atom of one molecule with electronegative atom of another molecule of the same substance, called hydrogen bond or Hydrogen Bridge because hydrogen atom acts as a bridge between two electronegative atoms. The hydrogen bond is usually denoted by a dotted line as shown in **fig. (1.9), [9]** and important in many biological molecules such as DNA, where it helps to control the possible paring between the two stands of the molecule and in certain ferroelectric crystals **[8].**

- **INTERMOLECULAR HYDROGEN BOND**

Intermolecular hydrogen bonding involves the electrostatic force of attraction between hydrogen atom and an electronegative element of two different molecules **fig. (1.10).**

❖ INTRAMOLECULAR HYDROGEN BOND

Intra molecular hydrogen bond involves the electrostatic force of attraction between hydrogen atom and an electronegative atom, both present in same molecule **fig. (1.11).**

❖ CHARATERISTICS OF HYDROGEN BOND

- Electrostating in nature and consequently, compounds containing hydrogen bonding are partially polar.
- Hydrogen bonds, being weak in nature are readily formed and ruptured.
- High melting and boiling point, due to higher effective molecular mass of the associated molecules **[9].**

c) HYDROBHOBIC INTERACTIONS

These interactions occur between non-polar molecules in the presence of a polar solvent. Several amino acids side chains are, to vary the degrees ofhydrobhobic. The most hydrobhobic of the amino acids side chains are those of alanine, valine, leucine and isoleucine. These amino acids have bulky alkyl side chains with different molecular geomatries. It is a general rule that these residues are found in the interior of protein molecules where they form hydrobhobic core containing very little water. It is belived that the different molecular geomatries of the side chains are important in facilitating close packing of proteins and other biopolymers like β-peptides.

d) VANDER WAALS FORCES

There are both attractive and repulsive van der Waals forces that control protein folding. Attractive van der Waals force involves the interactions among induced dipoles that arise from fluctuations in the charge densities that occur between adjacent uncharged non-bonded atoms. Repulsive Vander walls forces involve the interactions that occur when uncharged non-bonded atoms come very close together but do not induce dipoles. The repulsion is the result of the electron-electron repulsion that occurs as two clouds of electron begins to overlap. Although Vander Waals forces are extremely weak, relative to other forces governing conformation and number of such interactions that occur in large protein, molecules that make them significant to the folding of proteins.

1.8 PEPTIDE BOND

The amino acid units are linked together through the carboxyl and amino groups to produce the primary structure of the protein chain. The bond between two adjacent amino acids is a special type of amide group, in which the hydrogen atom of amino group is replaced by an R radical. Such a substitute amide bond is known as peptide bond as shown in **fig. (1.12).** and the chain thus formed by linking together of many amino acid units called peptide chain. Depending on the number of amino acid molecules composing chain, the peptides are termed as a di-peptide, a tri-peptide and so on **[4].**

1.9 CYSTEINE

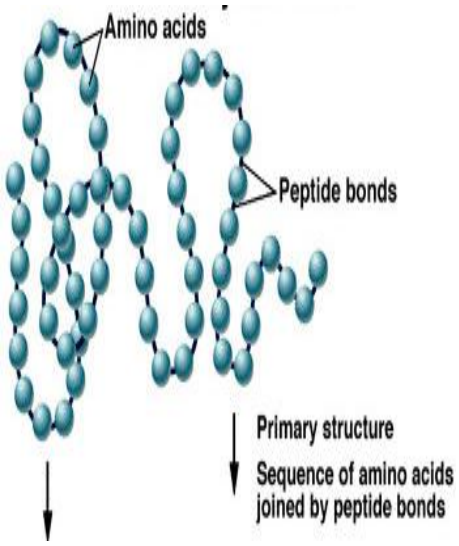
Cysteine (Cys or C) is one of the most reactive α-amino acids with chemical formula HO_2CCH (NH_2) CH2SH found in proteins. It is the sulfur analogue of serine. It contains sulfhydryl (SH) group that is quite reactive and easily dehydrogenated. When it is dehydrogenated (i.e. oxidized), two molecules join to form the amino acid cysteine. The general structure of cysteine is as shown in **fig. (1.13).** Cysteine is a semi-essential amino acid [3] and found to be hydrophilic (polar amino acid with no charge on R group),based largely on the chemical parallel between its thiol group and the hydroxyl groups in the side chains of other polar amino acid. Cysteine is at the center of catalytic site of thiol enzymes serving as a nucleophile and represented as α-amino-β-mercaptopropionate. The cysteine amino acid in zwitteronic, anionic, cationic forms are shown in **fig. 1.14, and1.15.**

1.9.1 ROLE OF CYSTEINE

Cysteine mainly L-enantiomer is a precursor in food, pharmaceutical and personal care industries. It is also used to prevent or for the treatment of cancer, liver diseases, heart diseases, treatment of colitis, respiratory distress syndrome etc., and Food source of cysteine include garlic, onion, broccoli, red peppers, wheat germs etc., Cysteine are manufactured by the body from the amino acid methionine. In the production of cysteine, methionine is converted to S-adenosyl methionine which is converted to homocysteine. Then it reacts with serine and form cysteine. Cysteine appears in white crystal or powder **[5].**

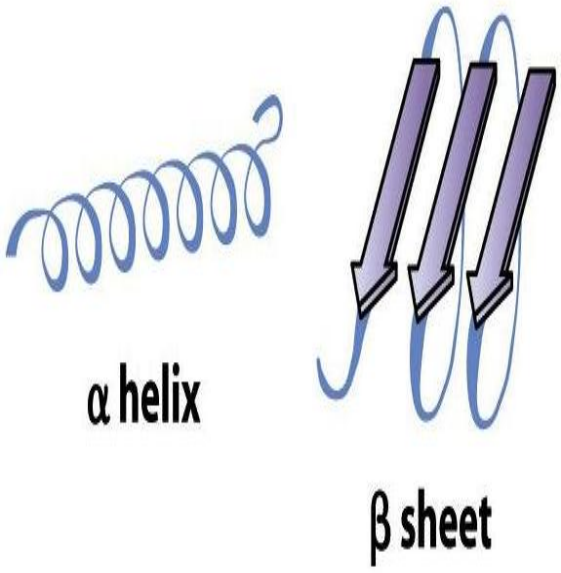
1.10 OBJECTIVE OF THE PRESENT EORK

- To optimize the structure of Cysteine in normal, zwitteronic(CysZW), anionic (CysAN) and cationic (CysCAT)forms.
- To study the energy and geometrical parameters.
- To confirm the optimized structures through frequency calculations.
- To find the stability of different forms of Cysteine using HF and DFT theoretical methods.
- To study the comparison of the geometrical parameters of optimized structures.



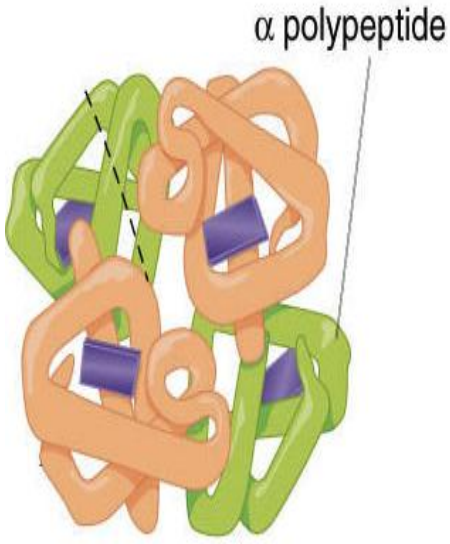
Primary structure

Fig 1.1



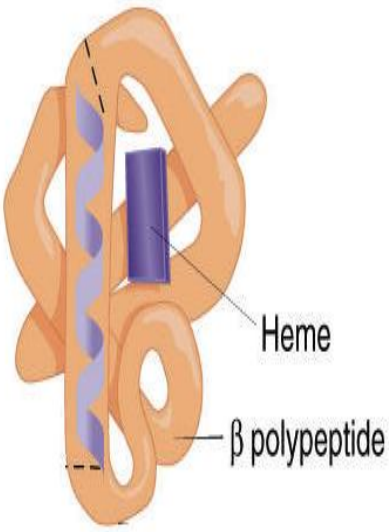
Secondary structure

Fig 1.2



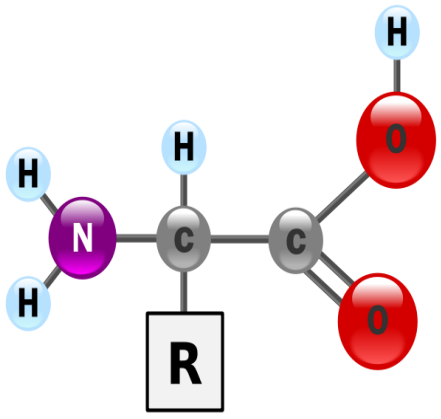
Tertiary structure

Fig 1.3



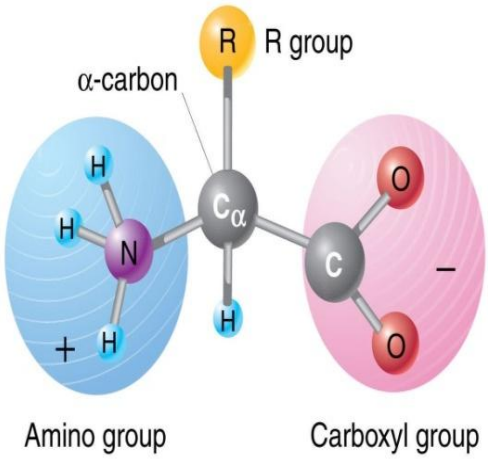
Quaternary structure

Figs 1.4



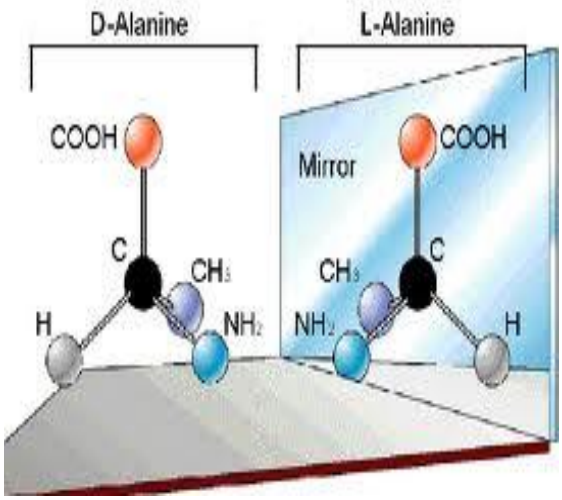
General structure of amino acids

Fig 1.5



Exist as ion

Fig1.6



Stereoisomerism of amino acids

Fig 1.7

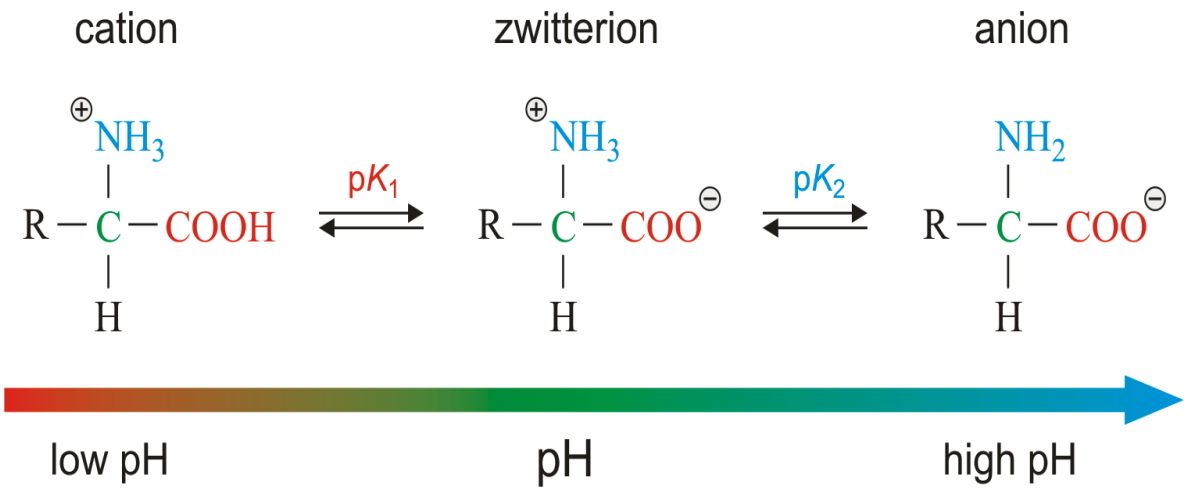


Fig 1.8 Existence of amino acid as cation, zwitterion, anion.

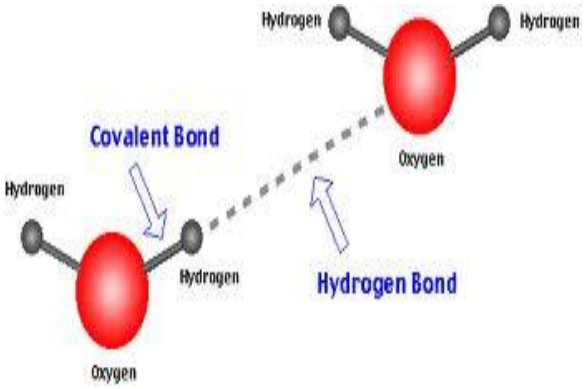


Fig 1.9 Hydrogen bond.

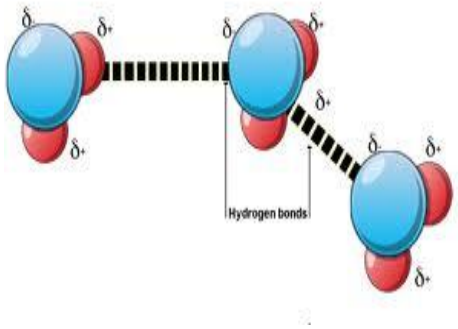


Fig 1.10 Intermolecular Hydrogen bond

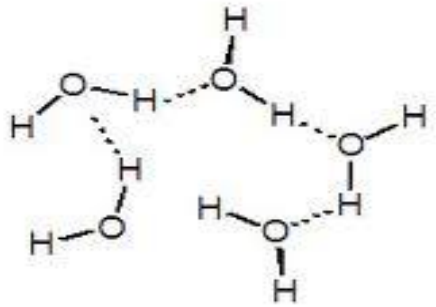


Fig 1.11 Intramolecular Hydrogen bond.

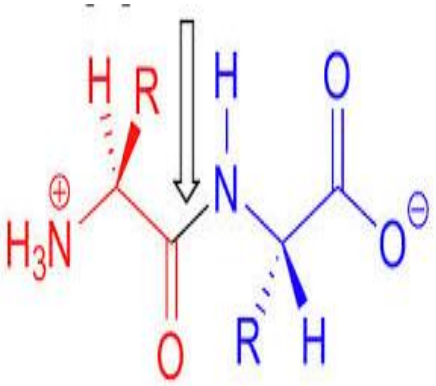


Fig 1.12 Peptide Bond.

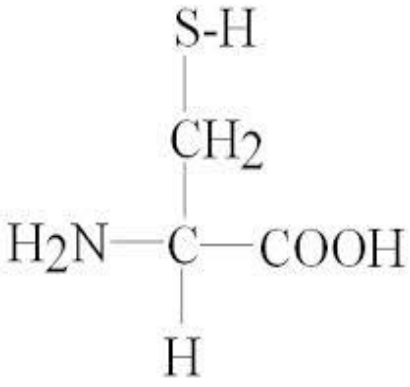
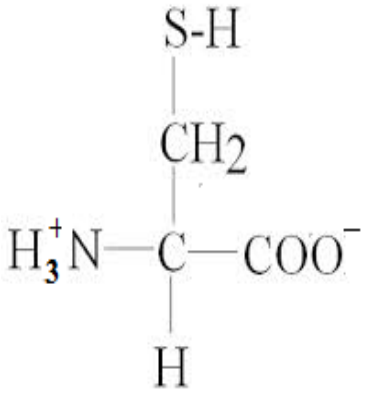
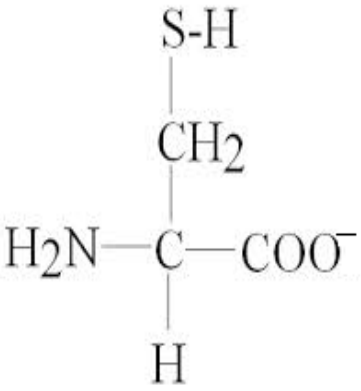


Fig 1.13 Cysteine.



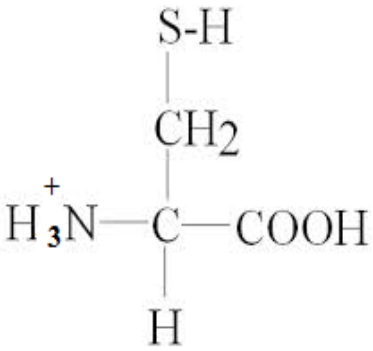
Zwitterion form of cysteine

Fig 1.14.



Anion form of Cysteine (high PH)

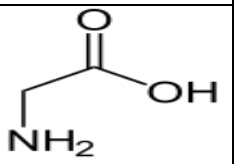
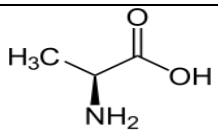
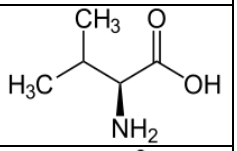
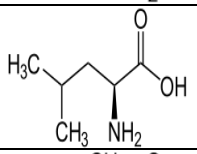
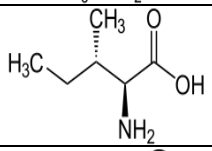
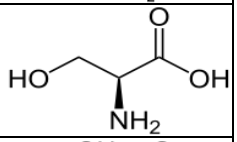
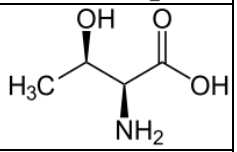
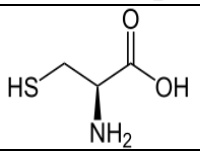
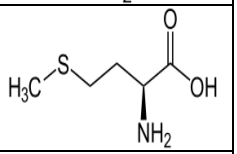
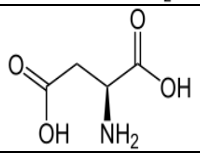
Fig .1.15

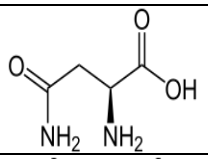
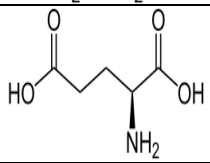
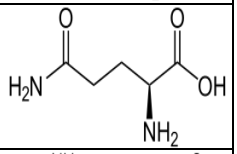
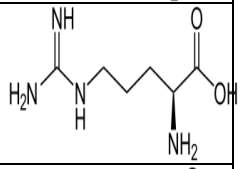
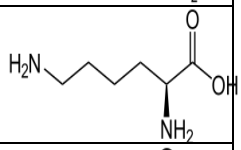
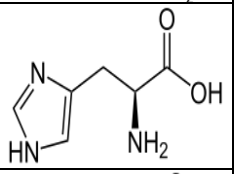
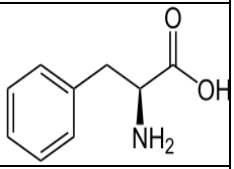
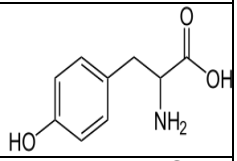
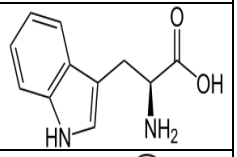
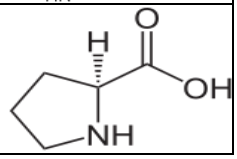


Cation form of cysteine (low PH)

Fig. 1.16

TABLE 1.1 Structures of 20 Amino Acid.

Amino acids	**Abbreviation**	**Molecular Formula**	**Properties**	**Structure**
Glycine	Gly – G	$C_2H_5NO_2$	Aliphatic neutral	
Alanine	Ala – A	$C_3H_7N_1O_2$	Aliphatic hydrophobic Neutral	
Valine	Val – V	$C_5H_{11}N_1O_2$	Aliphatic hydrophobic neutral	
Leucine	Leu – L	$C_6H_{13}N_1O_2$	Aliphatic hydrophobic Neutral	
Isoleucine	Ile – I	$C_6H_{13}N_1O_2$	Aliphatic hydrophobic Neutral	
Serine	Ser – S	$C_3H_7N_1O_3$	Polar hydrophilic Neutral	
Threonine	Thr – T	$C_4H_9N_1O_3$	Polar hydrophobic neutral	
Cysteine	Cys – C	$C_3H_7N_1O_2S_1$	Polar hydrophobic Neutral	
Methionine	Met – M	$C_5H_{11}N_1O_2S_1$	Hydrophobic Neutral	
Aspartic Acid	Asp – D	$C_4H_7N_1O_4$	Polar hydrophilic Charged (-)	

Asparagine	Asn – N	$C_4H_8N_2O_3$	Polar hydrophilic Neutral	
Glutamic Acid	Glu – E	$C_5H_9N_1O_4$	Polar hydrophilic Charged (-)	
Glutamine	Gln – Q	$C_5H_{10}N_2O_3$	Polar hydrophilic Neutral	
Arginine	Arg – R	$C_6H_{14}N_{14}O_2$	Polar hydrophilic Charged (+)	
Lysine	Lys – K	$C_6H_{14}N_2O_2$	Polar hydrophilic Charged (+)	
Histidine	His – H	$C_6H_9N_3O_2$	Aromatic Polar hydrophilic Charged (+)	
Phenylalaine	Phe – F	$C_9H_{11}N_1O_2$	Aromatic hydrophobic Neutral	
Tyrosine	Tyr – Y	$C_9H_{11}N_1O_3$	Aromatic polar hydrophobic	
Tryptophan	Trp – W	$C_{11}H_{12}N_2O_2$	Aromatic hydrophobic Neutral	
Proline	Pro – P	$C_5H_9N_1O_2$	hydrophobic Neutral	

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REVIEW OF LITERATURE

CHAPTER 2

REVIEW OF LITERATURE

2.1 INTRODUCTION

Review of literature is the most essential part of the research. It describes the researches that are carried out related to a computational investigation on cysteine amino acid through various theoretical methods.

2.2 LITERATURE SURVEY

1. Fillmore Freeman et al., (2013) were studied the equilibrium and molecular structures, relative energies of conformers of gaseous cysteine (Cys C, Cys-SH) and gaseous cysteine sulfenic acid (Cys-SOH), and the mechanisms of the reaction of Cys-SOH with 3-hydroxy-5,5-dimethyl -2-cyclohexen-1-one , the enol tautomer of 5,5-dimethyl-1,3-cyclohexadione (dimedone) with MP2 and DFT theory. The structure of the six lowest energy conformers of gaseous Cys-SOH are compared with the six lowest energy conformers of gaseous cysteine (Cys-SH). Their relative stabilities are influenced by many factors such as dispersive effects, electronic effect, electrostatic interactions, hydrogen bonds, inductive effect and non-covalent interactions and the variation in activation barrier have also been discussed.

2. Joshua Watts et al., (2013) have investigated the structures and the thermodynamic stabilities of complexes formed between L-cysteine and Hg (II) ions in neutral aqueous solution by both ab initio and density functional theory. The energies obtained by this method are compared with CCSD (T)/CBS (2, 3) energies. Stable complexes of L-cysteinate and mercury can be formed in 1:1, 2:1, 3:1 and 4:1 ratios. The results indicate that at high cysteinate to Hg (II) ratios high-coordinate complexes can be present but at lower ratios the 2:1 complex should be dominant.

3. Shankar et al., (2010) were studied the interaction of cysteine with metal cation complexes ($Li^{+}Na^{+}$,K^{+},Be^{+},Mg^{+} and Ca^{+}) using DFT (B3LYP) and second order Moller-Plesset perturbation (MP2) theory methods using 6-311++G^{**} basis set. The interactions of

the metal cations at different nucleophilic sites of cysteine conformations were considered. All the metal cations coordinate with cysteine are in a tridentate manner. The metal ion affinity (MIA) and the basis set superposition error (BSSE) corrected interaction energy was also computed for all the complexes. The effect of metal cations on the infrared (IR) stretching vibrational modes of amino N-H bond, side chain thiol group S-H bond, hydroxyl O-H bond, and carbonyl C = O bond in cysteine molecules have also been studied. Then the metal ion-ligand bond and the coordination properties are examined.

4. **Maria Victoria Roux et al., (2010)** were conducted both an experimental and theoretical study of sulfur containing amino acid L-cysteine. The vapor pressure of L-cysteine was measured as function of temperature by the Knudsen effusion mass-loss technique. The standard molar enthalpy of sublimation at T=298.15K, was derived from the Clausis-Clapeyron equation. The standard ab initio molecular orbital calculations at the G3 (MP2)//B3LYP also performed. Enthalpies of formation, using atomization and isodesmic reactions were calculated and compared with experimental data. Detailed inspections of the molecular and electronic structures of the compounds studied were carried out. Finally, bond dissociation enthalpies of S-H, S-S, and C-S bonds, and enthalpies of formation of L-cysteine-derived radicals were also computed.

5. Ralf Steudel et al., (2009) studied that certain sulfur bacteria oxidize thiosulfate enzymatically and the amino acid cysteine play an important role as intermediate in this process. This is because intermediates are hypothetical in nature,2 the structures and then the thermodynamic properties of more than 60 related derivatives of cysteine (CysH) by high level quantum mechanical calculations both in the gas phase and in a polarizable continuum using the PCM method to simulate an aqueous solution was investigated from this. For the smaller species several conformational isomers of similar energy were identified, their relative stabilities are mainly determined by intramolecular hydrogen bonds. In contrast to the thiolate ion $[Cys]^-$,the gaseous anions $[CysS]^-$,$[CysSO_2]^-$, $[CysSO_3]^-$ and $[CysSSO_3]^-$ are most stable as zwitterions containing an NH_3 rather than NH_2 group. The result which obtained was similar to polarizable continuum.

6. **Saumya Tiwari et al., (2009)** have analyzed the vibrational spectrum of the zwitterion (Z) forms of cysteine by considering the full geometry optimization under the bulk solvent effect of aqueous media combined with the solvent effect of up to three specific water molecules. Geometry was performed at the B3LYP/AUG-cc-pVDZ level which was followed by single point energy calculations at the MP2/AUG-cc-pVDZ level of theory in both gas phase and aqueous media. Transition states were located between the N and Z forms of cysteine completed with one to three water molecules and also without any complex water molecule. Two conformers of Z-cysteine are found to have comparable stabilities. The agreement between the experimentally observed and calculated vibrationakl frequencies for Z-cysteine is improved significantly for 22 out of 27 frequencies. Cerain vibrational frequencies have been identified with the help of which the conformers A and B of Z cysteine can be identified.

7. Junfangzhao et al., (2007) have reported the structure and fragmentation pathways of cysteine radical cation [NH_2CH (CH_2SH) COOH] calculated at DFT (B3LYP), 6-311++g (d,p) level basis set. The isomer at the global minimum, captodative-1 has the structure NH_2C (CH_2SH) C $(OH)_2$ and the stability of this ion is attributed to the captodativ effect in which the NH_2 function as a powerful π -electron donor and C $(OH)_2$ as a powerful π– electron acceptor. Two additional transient tautomers one having radical located at C_α and the charge on SH_2 and other one carboxy radical having charge on NH_3 have also been reported and the fragmentation pathways from canonical-1 are also examined.

8. **Blecastro.M et al.,(2005)** were studied the structure and energetic of complexes obtained upon interaction between cysteine and Zn2+,Cd2+,Hg2+and Cu2+ cations using DFT calculations with the 6-311++G** orbital basis set and pseudo potentials for the cations. Different coordination site for metal ions on several cysteine conformers were considered. All metal cations except sulfur are found to be ionic and later considered to be covalent bond when Hg2+ and Cu2+ are involved. The order of metal ion affinity has found to be Cu>Zn>Hg>Cd.

9. **Rosa Di Felice et al., (2002)** have performed the detailed study on the adsorption of the cysteine amino acid on the surface of gold using DFT calculations. Results for different absorption sites and molecular configurations shows that chemisorptions involving S-Au

bonds on Au (111) is favored by staring with either cysteine or cysteine gas phase molecular precursors. The analysis of the electronic properties shows that the hybridization of the P-like S states with the D-like Au states produces both bonding and antibonding occupied orbitals. The bonding orbitals well below the Fermi level contribute to the strong chemisorptions of cysteine on Gold. The calculated molecular orbital gives a measure of the injection barrier at the molecule/electrode junction.

10. **Noguera M et al., (2001)** have been computed the proton affinities and gas-phase basicities of cysteine using DFT approach. The geometry and vibrational frequencies of several conformations of neutral and protonated cysteine have been verified. An intramolecular H bond formed between NH_3 and the carbonylic oxygen on lowest conformations, additional H bonds are also found on cysteine. Good consistency has been found between the computed and the experimental result.

11. **Rauk. A et al.,(1998)** were used the ab initio computations to predict the bond dissociation energies of $^{\alpha}$C-H and other bonds of cysteine, both as free neutral amino acid and as a residue in a model peptide. The latter was intended to mimic the environment in proteins. Transition structures were located for intermolecular and intramolecular H atoms transfer to a thiyl radical from a sulfhydryl group or the $^{\alpha}$C-H. The enthalpic barriers for intermolecular and intramolecular H transfer were also found.

12. **Scott Gronert et al., (1995)** characterize the gas phase conformations of cysteine by high level ab initio methods. A wide range of possible structure was surveyed at the AM1 level, and then the geometries of the unique conformers were refined at the 3-21G*levels. At the highest theoretical level 42 conformers were located for cysteine. Calculation at the MP2/6-31+G*// HF/6-31G* level gives values in good aceord with a series of test calculations at the MP2/6-31+G*// MP2/6-31+G* level. Ab initio rotational constants and dipole moments are reported. The results are compared to previous studies and are analyzed in terms of intramolecular hydrogen- bonding interactions.

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METHODOLOGY

CHAPTER 3

METHODOLOGY

3.1 INTRODUCTION

Quantum Chemistry is based on the postulates of quantum mechanics; it is evident in all branches of chemistry and lies on the border of chemistry and physics. It has a strong and active overlap with the field of atomic physics, molecular physics as well as physical chemistry. Physical chemists use quantum chemistry to calculate thermodynamic properties of gases; to interpret molecular spectra, thereby allowing experimental detection of molecular properties (bond length, bond angle, dipole moments, barrier to internal rotation, energy difference between conformational isomers); to calculate molecular properties theoretically; to calculate properties of transition states in chemical reactions, to understand the intermolecular forces; and to deal with bonding in solids**[1].**

3.2 THEORETICAL METHODS

The presence of several nuclei makes quantum-mechanical calculations harder for polyatomic molecules when compared with diatomic molecules. The electronic wave function of a diatomic molecule is a function of one parameter- the inter nuclear distance. In contrast, the electronic wave function of a polyatomic molecule depends on several parameters- the bond distance, bond angles, and dihedral angles of rotation about single bonds (molecular conformation). The equilibrium bond distances and angles are then found as those values that minimize the electronic energy including nuclear repulsion. The four main approaches to calculate molecular properties are,

a) Ab initio methods,
b) Semi empirical methods,
c) The density functional method and
d) The molecular mechanics method **[2].**

3.3 Ab INITIO METHOD

The Latin term “ab initio” means “from the beginning” or from the first principles”. Within ab-initio simulations, the electrons are treated quantum mechanically and based only theoretical principles, using no experimental data. The numerous methods have the same basic approach, but differ in the mathematical approximations. The approximations made in these cases are usually mathematical in nature, such as using a simpler functional form or getting an approximate solution for a complicated differential equation. A Hartree-Fock SCF calculation seeks the anti summarized products ϕ of one-electron functions that minimizes

$$\int \phi^* \hat{H} \phi \, d\tau,$$

Where $\hat{H}$ is a true Hamiltonian, and is thus an ab initio calculation. The term ab initio should not be interpreted to mean 100% correct. The simplest type of ab initio electronic structure calculation is the Hartree-Fock (HF) scheme. The convergence however is usually not monotonic, and sometimes- for a given propert-aless accurate calculation can give better result (for instance the total energy in the series HF, MP2, MP4...).The drawback of ab initio methods is their cost. They often take enormous amount of computer time memory and disk space.

3.3.1 HARTREE-FOCK METHOD

Hartree-Fock theory is a fundamental of electronic structure theory. It is developed to solve the electronic Schrodinger equation that results from the time-independent Schrodinger equation after invoking the Born-Oppenheimer approximation. It is the basis of molecular orbital (MO) theory, in which each electron’s motion are described by a single-particle function (orbital) which does not depend explicitly on the instantaneous motions of the other electrons. The Huckel MO theory, which takes Hartree - Fock MO theory as an implicit foundation and throws away most of the terms to make it tractable for simple calculations. However, it is important to remember that these orbital are mathematical constructs which only approximate reality. Consider molecules are near to their equilibrium geometry, HF theory often provides a good starting point for more elaborate theoretical methods which are better approximations to the electronic Schrodinger equation (e.g. many body perturbation theory , single-reference configuration

interaction).

Hartree-Fock theory is based on the assumption that the many-electron wave-function of the system can be described by a single Slater determinant made of one-electron molecular orbital. The Hartree-Fock wave function will have the form of a Slater determinant, and that the energy will be given by the usual quantum mechanical expression (assuming the wave function is normalized)

$$E = < \psi |\hat{H}_{el}| \psi > \quad (3.1)$$

3.3.2 HARTREE- FOCK EQUATION

The Hartree-Fock method seeks to approximately solve the electronic Schrodinger equation, and it assumes that the wave function approximated by a single slater determinant made up of one spin orbital per electron. According to the variation theorem that the slater determinant with the lowest energy is as close as to the true wave function for the assumed functional form of a single slater determinant. The Hartree- Fock determines the set of spin orbital which minimize the set of spin orbital which minimize the energy and give us this "best single determinant."

To minimize the Hartree- Fock energy expression with respect to changes in the orbital

$$\phi_i \rightarrow \phi_i + \delta\phi_j$$

Where ϕ is orthonormal.Bylagrange's method of undetermined multipliers

$$\mathcal{L}[\{\phi_i\}] = E_{HF}[\{\phi_i\}] - \sum_{ij} \in_{ij} \left(< i|j > -\delta_{ij} \right) \quad (3.2)$$

$$< i|j > = \int \phi_i^*(x)\phi_j(x)dx \quad (3.3)$$

The Hartree-Fock equations defining the orbital will be

$$h(x_1)\phi_i(x_1) + \sum_{j \neq i} [\int dx_2 |\phi_j(x_2)|^2 r_{12}^{-1}]\phi_j(x_1) -$$

$$\sum_{j \neq i} [\int dx_2 \phi_j^*(x_2)\, \phi_i(x_2) r_{12}^{-1}]\phi_j(x_1) = \epsilon_i \phi_i x_1 \quad (3.4)$$

Where ϵ_i is the energy eigenvalue associated with orbitalϕ_i.

The HF equation are solved numerically or solved in the space spanned by a set of basic functions (HF-Roothan equations). In either case, the solutions depend upon the

orbital.

For initial orbital, HF is called a self- consistent-field (SCF) approach.

The first term of equation (3.4) gives the coulomb interaction of an electron in spin orbital with the average charge distribution of the other electrons. HF is a "mean field" theory. This is called the coulomb term, and it is convenient to define a Coulomb operator as

$$J_i(x_1) = \int dx_2 \, |\phi_j(x_2)|^2 r_{12}^{-1} \tag{3.5}$$

Which gives the average local potential at point X_1 due to the charge distribution from the electron in orbital ϕ_j.

The other term in bracket of equation (3.4) is harder to explain and have a simple classical analog. It arises from the antisymmetry requirement of the wave function. It looks much like coulomb term, except that it switches or exchanges spin orbital (ϕ_i) and (ϕ_j). Hence, it is called exchange term

$$\sum_{j \neq i} [\int dx_2 \phi_j^*(x_2) \, \phi_i(x_2) r_{12}^{-1}] \phi_j(x_1) \tag{3.6}$$

We can define an exchange operator in terms of its action on arbitrary spin orbital ϕ_i.

$$\mathrm{K}_j(x_1)\phi_i(x_1) = \left[\int dx_2 \phi_j^* \, x_2 r_{12}^{-1} \phi_i(x_2)\right) \phi_j(x_1) \tag{3.7}$$

In terms of these coulomb and exchange operators, the HF equations become considerably more compact.

$$[h(x_1) + \sum_{j \neq 1} J_i x_1 - \sum_{j \neq i} \mathrm{K}_j(x_1)] \phi_i(x_1) = \epsilon_i \phi_i(x_1) \tag{3.8}$$

Now it is more clear that the HF equations are eigenvalue equations. Then

$$[J_i(x_1) - \mathrm{K}_i(x_1)] \phi_i \tag{3.9}$$

It is clear that by removing the restrictions j$\neq i$ in the summations, and by introduce a new operator, the Fock operator, as

$$f(x_1) = hx_1 + \sum_j J_j(x_1) - \mathrm{K}_j x_1 \tag{3.10}$$

And now the Hartree-Fock equations are just **[5]**

$$f(x_1)\phi_i(x_1) = \epsilon_i \phi_i(x_1) \tag{3.11}$$

3.4 DENSITY FUNCTIONAL THEORY

Density functional theory is one of the most popular and successful quantum mechanical approaches to matter. **[5]**

The basis for DFT is the proof by Hohenberg and Kohn that the ground-state electronic energy is determined completely by the electron density ρ. In other words there exists one-to-one correspondence between the electron density of a system and the energy. The significance of this is illustrated by comparing to the wave function approach. A wave function for an N electron system contains 3N coordinates, three for each electron (four if spin is included). The electron density is the square of the wave function, integrated over N-1 electron coordinates; the electron density has a same number of variables, independently of the system size. The only problem is that although it has been proven that each different density yields a different ground- state energy, the functional connecting these two quantities is not known. The goal of DFT method is to design functional connecting the electron density with energy.

A function is a prescription for producing a number from a set of variables (coordinates). A wave functions and the electron density are functions, while energy depending on wave function or an electron density is a functional and it is denoted as E[ρ], in which the basic variable is a number, for example f(x) = Sin x is a function of x, in the functional the basic variable is a function and there is one to one correspondence between the variable and the function; the expectation value ($\bar{E}$) of energy, for example,

$$\bar{E}[\Psi\psi] = \frac{\int \Psi\psi^* \hat{H}\psi \Psi d\tau}{\int \Psi\psi^* \psi \Psi \, d\tau} \qquad (3.12)$$

is a function of the wave function ψ.

The advantage with DFT method is that the central quality of interest in its electron density (ρ) which is 3-dimensational quality, in place of wave function (ψ) which is 3N-dimensational, N being the number of electrons.

The electron density (ρ) is defined, for an N-electron system, by integrating the N-electron distribution function P (r_1, r_2 … r_n) over N-1 coordinate as

$$\rho\,(r_1) = N \int \ldots\ldots P\,(r_1, r_2, r_n)\, dr_2, dr_3. .dr_n \qquad (3.13)$$

and represents the number of electron per unit volume at a point r_1, thus integrating to the total number N,

$$\int \rho(r)\, dr = N \tag{3.14}$$

for the N electron wave function, the distribution wave function is given by

$$\rho\,(r_1, r_2 \ldots r_n) = |\,\psi\ (r_1, r_2 \ldots r_n)\,|^2 \tag{3.15}$$

an attempt to use the electron density of a system for calculating electronic energy was made by Thomas and Fermi in 1927 and obtained an expression for energy as a function of electron density without any information about the wave function. An uniform electron gas model is used for kinetic energy and electrostatic (columbic) potential energy. The results obtained by them were far from accurate because neither exchange nor correlated motion of electrons was considered. No molecular binding could be predicted in this method. Hence the Thomas- Fermi model was considered to be of little quantitative significance in atoms or molecules.

3.4.1 HOHENBERG-KOHN THEOREMS

In 1964, Hohenberg and Kohn formally justified the use of electron density as the basic variable in determining the electronic energy which became the foundation of modern electron density functional theory. They proposed two theorems:

HOHENBERG-KOHN THEOREM 1

In non-degenerate ground state of a system, there is a correspondence between external potential (V_{ext}) wave function (ψ) and electron density (ρ) of the system. Hence there exists a density functional in terms of which the electronic energy (E) is formulated. In Schrodinger equation, energy function would contain three terms: the kinetic energy T[ρ], the energy of interaction with external potential $V_{ext}[\rho]$ and the energy due to the electron – electron interaction $V_{ee}[\rho]$, energy is produced due to interaction with external potential

$$E[\rho] = T[\rho] + V_{ext}[\rho] + V_{ee}[\rho] \tag{3.16}$$

For atoms and molecules V_{ext} arises from nuclei-electron attraction; this interaction is trivial given by

$$V_{ext}[\rho] = \int V_{ext} \cdot dr \tag{3.17}$$

Where V_{ex} is nuclei-electron attraction in atoms and molecules. The kinetic energy functional, T [ρ] and electron – electron interaction energy functional, $_{Vee}[\rho]$, together may be called Hohenberg-Kohn functional, $F_{HK}[\rho]$,

$$F_{HK}[\rho] = T[\rho] + V_{ee}[\rho] \quad (3.18)$$

$F_{HK}[\rho]$ is independent of V_{ext} and hence is universal.

If the functional of $F_{HK}[\rho]$ were known, the electronic energy are calculated by substituting $F_{HK}[\rho]$ in the equation (3.16). Unfortunately, explicit form of neither T [P] nor V_{ee} [P] is known.

The interaction energy V_{ee} contains

(i) Classical caulombic repulsion, or Haretree energy V_H,

$$V_H = \frac{1}{2}\sum_i \sum_j \Psi_i^*(1)\Psi_j^*(2)\frac{1}{r}\Psi_i(1)\Psi_j(2)dr_1 dr_2$$

$$= \frac{1}{2}\iint \frac{\rho(1)\rho(2)}{r_{12}} dr_1 dr_2 \quad (3.19)$$

(ii) Non – classical interaction arising due to electron exchange and electron correction, $V_{nci.}$

HOHENBERG-KOHN THEOREM 2

The variation principle holds for the minimization of E[ρ] and gives as

$$P \geq 0 \text{ and } \int \rho(r)\, dr = N,$$

the energy is given by

$$E[\rho] \geq E_0[\rho_0] \quad (3.20)$$

Where E_0 is the true ground state energy and ρ_0, the true density. The minimization results in the equation of

$$\frac{\delta E[\rho]}{\delta \rho} = V_{ext}[\rho] + \frac{\delta F_{HK}[\rho]}{\delta \rho} \quad (3.21)$$

3.4.2 KOHN – SHAM EQUATIONS

Kohn and Sham proposed a way of approximating the universal function $F_{HK}[\rho]$, and separated the kinetic energy function T[ρ] in to the kinetic energy of a hypothetical non-interacting system of electrons $T_s[\rho]$ and an unknown part $T_e[\rho]$ ($T_e[\rho] = T[\rho] - T_s[\rho]$), which contains the correction due to interaction between the electrons in the real system. For non-interacting part, the kinetic energy are known exactly from the 1-practicle

schrodinger equations

$$T_s = \sum_{i=1}^{N} \int \Psi_i \left(-\frac{1}{2}\nabla_i^2\right)\Psi_i \tau \tag{3.22}$$

The functional $F_{HK}[\rho]$ are expressed as

$$F_{HK}[\rho] = T_s[\rho] + V_H[\rho] + E_{xe}[\rho] \tag{3.23}$$

With $E_{xc}[\rho]$, is called exchange-correlation potential defined as

$$E_{xc}[\rho] = (T[\rho] - T_s[\rho]) + (V_{ee}[\rho] - V_H[\rho]) \tag{3.24}$$

$E_{xc}[P]$ contains the difference between the kinetic energies of the real system plus the non-classical part of the electron-electron interaction.

The many electron problem is again mapped onto an effective 1-electron problem and all unknown terms are merged into the exchange-correlation part. The 1-particle wave functions (orbital) are determined by solving the 1-particle equations under the constraint to reproduce the density of the real interacting system and termed as "Kohn-sham (KS) equations".

$$\left[-\frac{1}{2}\nabla^2 + V_{eff}(f)\right]\Psi_i = E_i\Psi_i \tag{3.25}$$

Where the effective potential $V_{eff}(r)$ contains external potential $V_{ext}(r)$, the classical coulombic potential due to electron-electron repulsion V_H and the exchange correlation potential $V_{xc}(r)$,

$$V_{eff}(r) = V_{ext}(r) + \iint \frac{\rho(1)\rho(2)}{r_{12}} dr_1 dr_2 + V_{XC}(r) \tag{3.26}$$

The density $\rho(r)$ of the real system can be given in terms of Kohn-Sham orbitals ψ_i,

$$\rho(r) = \sum_{i=1}^{N} |\Psi_i(r)|^2 \tag{3.27}$$

and the exchange-correlation potential $V_{xc}(r)$ is given by the derivative of the $E_{xc}[P]$ with respect to the density,

$$V_{xc}(r) = \frac{\delta E_{xc}[\rho(r)]}{\delta\rho(r)} \tag{3.28}$$

If $E_{xc}[\rho]$ is known, $V_{xc}[r]$ is obtained.

The Kohn –Sham equation has the same structure as HF equations. Hence, the effective potential V_{eff}depends on the density itself, the equation have to be solved by self-consistent method. By using some approximations for the functional dependence of E_{xc} on ρ, compute V_{xc} as a function of r. The set of K-S equation is then solved to obtain an initial set of K-S orbitals (ψ_i). This set is used to compute an improved ρ by using equation (3.27). The

process is repeated until the ρ and the E_{xc} converge to within certain tolerance. The electronic energy is then calculated from the equations (3.16) and (3.23).

The equations are non-linear, the K-S orbitals are computed numerically. Within this formalism the kinetic energy of the non- interacting system is determined indirectly by using N one-electron wave functions, but still exact. Only the exchange correlation functional $E_{xc}[\rho]$ remains unknown. Finding good approximations of $E_{xc}[\rho]$ is one of the greatest challenges in modern DFT.

3.4.3 LOCAL DENSITY APPROXIMATION (LDA)

The simplest and the most widely used method is "local density approximation (LDA)." This approximation is based on the assumption that a system of electrons in molecules or atoms is like an electron gas. In the homogeneous electron gas model, the electron move in an infinite region of space with uniform positive charge background to preserve charge neutrality. For an inhomogeneous system, assume exchange-correlation energy and are obtained by approximating the density of the inhomogeneous system locally by the density of the homogeneous system of electron gas. Although the LDA is a crude approximation, it has been used widely and gives good results **[6].**

3.5 ADVANTAGES OF DFT WHEN COMPARED TO AB INITIO

- DFT is computationally very efficient.
- DFT is conceptually simple.
- DFT can be easily combined with molecular dynamics of the nuclei.**[5]**

3.6 SEMI EMPIRICAL METHOD

Semi empirical molecular quantum mechanical methods use a simpler Hamiltonian and use parameters whose values are adjusted to fit experimental data or the results of ab initio calculations**(4).**Semi empirical methods are very important in computational chemistry for treating large molecules. It speeds up computational time, but in general it is not very accurate.

The use of empirical parameters appears to allow some inclusions of correlation effects into the methods **(1).** The central assumption of semi-empirical methods is the zero differential overlap (ZDO) approximation, which neglects all products of basis functions

depending on the same electron coordinate, when located on different atoms.

3.7 BASIS SETS

A basis set is a set of plane wave functions used to create the molecular orbitals, which are expanded as a linear combination with coefficient to be determined, that describe the shape of atomic orbitals. The molecular orbitals are computed using the selected theoretical model by linearly combining atomic orbitals. The level of approximation of calculations is directly related to the basis set used. It makes the computational cost low. The choice to make is a trade-off between accuracy of results and CPU time. Additionally, basis set composed of sets of plane waves are often especially in calculations involving systems with periodic boundary conditions. If the finite basis is expanded towards an infinite complete set of functions, calculations using such a basis set are said to approach the basis set limit.

In quantum chemistry, the "basis set" usually refers to the set of (nonorthogonal) one-particle functions used to build molecular orbitals. Sometime, theorists might also refer to N-electron basis sets, which are something else entirely- sets of slater determinants.

3.7.1 CLASSIFICATION OF BASIS SET

The basis sets can be broadly classified in to the following types.

MINIMAL BASIS SET (STO-NG)

In minimal basis set each AO is represented by an STO which in turn is a linear combination of N GTF'S (Gaussian type function). Once the coefficients of expansion and the Gaussian orbital exponents are determined and are fixed throughout the calculations. The most commonly used minimal basis sets is STO-3G. A gaussian basis set is often denoted by the notation (A) [B} or (A/B, where A is a listing of the primitive gaussians and B is a listing of the contracted gaussians. The second notation is more convenient to use.
STO-3G basis set for H and Li are (3s) [1s] or (3s/1s) and (6s3p) [2s1p] or (6s3p/2s1p) respectively. The integers should not be confused with the principal quantum number.

EXTENDED BASIS SETS

a) Split valance double zeta(SVDZ) basis set

SVDZ basis set results when each AO in the minimal basis set is replaced by two AO's with different zetas (exponents). The example of (SVDZ) basis set is 4-31G. The numbers 4, 3 and 1 in the notation 4 - 31G identify the contraction lengths. Since there are p- type orbitals (p_x, p_y and p_z) the two p CGTF's included six p orbitals.

b) Split valance double zeta plus polarization (SVDZP) basis set

An SVDZP basis set results when a set of polarization functions are added to the SVDZ basis set. When a set of polarization functions are added on all the atoms in the molecule the resulting basis set is denoted by 4-31G*

c) Split valance double zeta polarization plus diffuse (SVDZPD) basis set

This basis set result when an s-type diffuse GTF's are included in the SVDZP basis set. The basis set 4-31+G*, 4-31+G** and 4-31++G** are of this type. On hydrogen only an s-type diffuse function is added.

d) Split valance triple zeta polarization plus diffuse (SVTZPD) basis set

The 6-311+G*, 6-311+G** and 6-311++G** basis set belongs to this type **[3].**

3.8 BOND LENGTH

The distance between two atomic nuclei in a covalent molecule is called the bond distance or bond length. The bond lengths are characteristic properties of a molecule and give information about its structure, properties etc., bond length and bond angle are determined by X-ray diffraction, electron diffraction or spectroscopic methods. The bond lengths are measured in Angstrom (Å) unit which is equal to 10^{-8} cmor 10^{-10}m. The bond distances are generally affected by hybridization, electronegativity, steric condition or delocalization.

3.9 BOND ENERGY

The energy required to break a bond into constituents is referred to as bond energy and is a measure of bond strength. The greater the energy required to break a bond, the

greater will be the strength. Thus bond energies provide a useful picture of the various bonds. They are expressed in Kcal\mole.

3.10 BOND ANGLE

Bond angle is the internal angle between the orbitals having bonded pair of electrons in the valency shell of the central atom in a molecule. It depends upon the type of hybridization, presence of lone pair of electrons electronegativity of the atom.

3.11 CHEMICAL PARAMETERS

3.11.1 CHEMICAL POTENTIAL

Chemical potential (μ) is a measure of how much the free energy of a system changes (dG_i) by adding or removing a number of particles (dn_i).

$$dG_i = (\partial G/\partial n_i) \bullet dn_i \tag{3.29}$$

The definition of μ

$$\mu = (- I + A) / 2 \tag{3.30}$$

Where, I is the ionization potential ($-E_{HOMO}$) and A is the electron affinity ($-E_{LUMO}$). According to koopman's theorem the ionisation potential is simply the orbital energy of the (HOMO), with the change in sign. For spin paired molecules, the electron affinity is the negative of the orbital energy of the LUMO.

$I = (-E_{HOMO})$ Highest occupied molecular orbital,

$A = (-E_{LUMO})$ Lowest occupied molecular orbital

.

3.11.2 CHEMICAL HARDNESS AND CHEMICAL SOFTNESS

Hardness is defined as the second order derivative of energy with respect to the number of electron and it has the meaning of resistance to change in number of electron. The chemical hardness of molecules is exactly the screened interaction energy of the electron in the frontier (HOMO, LUMO) orbitals, whereas the derivative of the Kohn-sham potential relative to the electron number is a screened local hardness measuring the local reactivity of molecules and solids. **[8]**

$$\eta = (E_{LUMO} - E_{HOMO})/2 \tag{3.31}$$

Chemical softness is the inverse of chemical hardness. The total softness is defined as

$$S = (1/2\eta) \quad (3.32)$$

Where S is the softness and η is the absolute hardness.

3.12 DIPOLE MOVEMENT

Dipole moment (μ) is the measure of net molecular polarity, which is the magnitude of the charge Q at either end of the molecular dipole times the distance r between the charge.

$$\mu = Q\ X\ r \quad (3.33)$$

A molecule has a dipole, when there is a charge separation. The strength of the dipole depends upon the difference in electronegativity of the atoms in the molecule. The larger the difference in electronegativity of bonded atoms, the larger the dipole moment. A partial negative charge is sometime given the symbol δ^- and the positive charge given the symbol δ^+. Example, Nacl has the highest dipole moment because it has an ionic bond (i.e. highest charge separation). The unit of dipole moment is debye (D) **[9].**

3.13 COMPUTATIONAL DETAILS OF PRESENT STUDY

- In the present work,Cysteine amino acid in normal, zwittrionic, cationic and anionic forms has been optimized by using HF/6-311+G (2d,2p) of abinitio and B3LYP/6-311++G** of Density Functional Theory.
- The bond length, bond angle, bond energy, dipole moment (μ_D), chemical hardness (η), chemical potential (μ), chemical softness (S) have been calculated by using the above levels of theory.
- All the calculations have been performed using Gaussian 09 package.
- The spectroscopic values have been computed with the IR and Raman spectra.

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RESULTS AND DISCUSSION

CHAPTRE IV

RESULT AND DISCUSSION

4.1 INTRODUCTION

In recent years, there has been considerable interest in radicals derived from biomolecules in the gas phase due to their structure and relativities of radicals is necessary to understand the role of transient species involved in protein radical catalysis and in oxidative damage of proteins **[1].** Amino acids play a key role in protein folding while also taking part in lypophilic interactions and secondary structure properties. Understanding the structures and conformational presences of zwitteronic forms is important to gain insight into protein folding by hydrophilic interactions that determine the H- bonding scheme **[3-8];** it is an attractive target for computational chemists because they contain a variety of intermolecular interactions and a tractable size for high level abinitio calculations. Theoretical studies provide important information to the experimentalist to identify gaseous amino acids by their microwave or IR spectrum. Naturally occurring amino acids have a large conformational flexibility and the computational studies can determine conformers and statistical populations that found in experimental data. Not all of the 20 α- amino acids are of equal interest. For model studies one frequently focuses the attention exclusively on cysteine i.e one of the smallest amino acids. The principle structure NH_2-CH(R)-COOH is equal for all amino acids and contains a carbon backbone with a carboxyl group (COOH), an amino group (NH_2) and a varying organic side group (R) linked to the same tetrahedral carbon atom $C_{\alpha.}$ In solution these acidic and basic groups may react with each other forming a zwitterions, which also builds up the crystalline phase. The chemical and physical properties of the gas phase species, which are considered in this study, vary considerably with side group, for cysteine (R = CH_2 - SH)**[2**].Moreover, the presence of sulfur in cysteine, which is known to bind covalently to metallic surface **[9],** opens up also the possibility for well-characterized stable molecule – electrode contacts. A cysteine molecule can have large number of conformations owing to the existence of many possible Intramolecular hydrogen bonds and single bond rotamers **[11].**

The present study is about the computational investigation of the optimization and vibrational spectral analysis of an amino acid cysteine (HO_2 CCH (NH2) SH, 2-Amino - 3-sulfhydryl Propanoic acid) at different protonation states such as normal, zwitterionic, cationic (protonated) and anionic (deprotonated) forms at HF of ab-initio method through 6-311+G (2d, 2p) basis set and B3LYP of density functional theory using 6-311++G** basis set. The values that obtained in above forms are compared with each other.

4.2 GEOMETRICAL STRUCTURE OPTIMIZATION

Cysteine is best known for its unique ability to form cross-links via disulfide bonds and has considerable interest in biochemistry and a number of human diseases, it is the most effective amino acids at scavenging radicals in solution that forms a radical at the sulfur atom**[10].** An extensive computational investigation of such cysteine have been performed in its normal, zwitteronic (CysZW), anionic (CysAN) and cationic (CysCAT) form by implementing HF/6-311+G (2d, 2p) of ab initio and B3LYP/6-311++G** of density functional theory using Gaussian 09 package. The geometrical parameters such as bond length, bond angle, chemical hardness, chemical softness, chemical potential, energy, dipole moment and vibrational spectra were determined. The optimized structures of normal cysteine, CysZW, CysCAT, CysAN are shown in **fig .4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7 and fig 4.8** respectively.

4.3 HYDROGEN BONDING

The hydrogen bond is a weak attraction between a hydrogen atom bonded to an electronegative element and an electron lone pair on another atom. The optimized structure is confirmed by the presence of Intramolecular hydrogen bond. The intramolecular hydrogen bond exists in cysteine radicals stabilize their structure.

- **Normal Cysteine**

N – H … O and O – H...O Intramolecular hydrogen bond were obtained on both HF/6-31`1+ G(2d, 2p) and B3LYP/6-311++G** with a length of 2.32423 Å and 2.2606Å in HF/6-311+G (2d, 2p) and 2.26942Å ad 2.29445Å in B3LYP/6-311++G**.

- **Zwitteronic Cysteine**

Cys ZW has N – H … O Intramolecular bond formation having a length of 2.2342Å in HF/6-311+G (2d, 2p) of ab initio and 2.2440Å in B3LYP/6-311++G** of DFT.

- **Cationic Cysteine**

Cys CAT formed an Intramolecular N – H … O and O – H...O hydrogen bond in HF/6-311+G (2d, 2p) with a bond length of 2.20557Å and 2.3424Å and N – H … O bond formation was observed at B3LYP/6-311++G** that has a bond length of 2.0990Å, it found to be weak when compared with HF/6-311+ G *(2d, 2p).

- **Anionic Cysteine**

Similarly on CysAN radical, N – H … O Intramolecular hydrogen bond with a length of 2.1527Å and 2.0788Å at HF/6-311+G (2d, 2p) and B3LYP/6-311++G**were observed. Normal cysteine is found to be highly strong, since it forms an N – H … O and O – H...O Intramolecular hydrogen bond with high bond length compared with other radicals.

4.4 GEOMETRICAL PARAMETER

A selection of geometric parameters have been made to clearly visualize how the geometric structures are similar regarding both conformations and geometric data when they are optimized by using HF/6-311+G (2d, 2p) of ab initio and B3LYP/6-311++G** of density functional theory.

4.4.1 NORMAL CYSTEINE

a) BOND LENGTH AND BOND ANGLE

The bond length of sulfhydryl group S – H, carbonyl C - C and C – S are found to be 1.3236Å, 1.5259 Å and 1.8222Å at HF/6-311+G (2d, 2p) of ab initio method and the bond lengths obtained at B3LYP/6-311++G** of DFT is 1.3479Å, 1.5310Å and 1.8500Å. The bond angle for C – C = O H – S – C and S – C - C in HF/6-311+G (2d, 2p) and B3LYP/6-311++G** are 124.224(degree), 97.444(degree), 116.434(degree) and

124.118(degree), 95.561(degree), 111.335(degree). The bond length and bond angle for normal cysteine optimized at HF/6-311+G (2d, 2p) and B3LYP/6-311++G** are shown in **table 4.1.**

b) ENERGY AND DIPOLE MOMENT

The energy and dipole moment of the normal cysteine calculated at HF/6-311+G (2d, 2p) and B3LYP/6-311++G** are listed in **table 4.9**. The energy value of normal cysteine is found to be -719.513 (a.u) at HF/6-311+G (2d, 2p), and at B3LYP/6-311++G** the value is -722.061 (a.u). The dipole moment is the first derivative of energy with respect to the applied field. The value of dipole moment for normal cysteine is 3.3644(Debye) at HF/6-311+G (2d, 2p), and 2.6521(Debye) at B3LYP/ 6-311++G**. Thus the value of energy and dipole moment of normal cysteine at HF/6-311+G (2d, 2p) is observed to be high when compared to B3LYP/6-311++G**.

c) CHEMICAL POTENTIAL AND CHEMICAL HARDNESS

The chemical hardness signifies the resistance towards the deformation of electron cloud of chemical system under small perturbation encountered during the chemical process. The values of chemical potential calculated at HF/6-311+G (2d, 2p) and B3LYP/6-311++G** level of theories are -0.2052eV and -0.1050eV. It is noted that the chemical potential of normal cysteine is found to be high at B3LYP/6-311++G** when compared to HF/6-311+G (2d, 2p). Similarly the chemical hardness is found to be 0.2054eV in HF/6-311+G (2d, 2p) and 0.1050eV in B3LYP/6-311++G**. The chemical hardness of normal Cysteine is high at HF/6-311+G (2d, 2p) when compared to B3LYP/6-311++G** level of theory. The chemical hardness and chemical potential of normal cysteine calculated at both HF/6-311+G (2d, 2p) and B3LYP/6-311++G** levels are tabulated in **table 4.9**.

d) CHEMICAL SOFTNESS

Chemical hardness and softness are the important factors of the charge transfer resistance and these are inversely proportional to each other. The chemical softness of normal Cysteine optimized at HF/6-311+G (2d, 2p) level is found to be 2.43350eV and at B3LYP/6-311++G** level is found to be 4.7580eV. The chemical softness of normal

Cysteine is lower at B3LYP/6-311++G** when compared to HF/6-311+G (2d, 2p). At both the levels of theory the chemical softness of normal cysteine is found to large when compared to hardness, thus the normal form of cysteine is highly polarizable. The calculated chemical softness of normal cysteine at HF/6-311+G (2d, 2p) and B3LYP/6-311++G** levels are given in **table 4.9**.

4.4.2 ZWITTERONIC CYSTEINE

a) BOND LENGTH AND BOND ANGLE

For optimized structure of CysZW, the bond lengths of sulfhydryl group S – H, carbonyl C = C and C – S are found to be 1.3245 Å, 1.5330Å and 1.8346Å respectively at HF/6-311+G (2d, 2p). At B3LYP/6-311+G (2d, 2p) level of theory the sulfhydryl group S – H, carbonyl C = C and C – S bond lengths of the CysZW are found to be 1.3512Å, 1.5478Å and 1.8346Å respectively. For CysZW, the bond angles of O – C = O, H – S – C and H – N - C are found to be 124.969(degree), 97.640(degree), 112.0(degree) respectively in HF/6-311+G(2d,p) and 116.071(degree), 97.035(degree), 112.780(degree) in B3LYP/6-311+G**. The other values of bond length and bond angle for CysZW optimized at HF/6-311+G (2d, 2p) and B3LYP/6-311+G** are shown in **table 4.2**.

b) ENERGY AND DIPOLEMOMENT

The energy and dipole moment of the CysZW calculated at HF/6-311+G (2d, 2p) and B3LYP/6-311++G** are listed in **table 4.9**. The energy value of CysZW at HF/6-311+G (2d, 2p) is found to be -719.227 (a.u) and at B3LYP/6-311++G** the energy value is found to be -721.726 (a.u). The energy value of CysZW at HF/6-311+G (2d, 2p) level is found to be higher than the energy observed at B3LYP/6-311++G**.The dipole moment of normal cysteine is 3.3644(Debye) at HF/6-311+G (2d, 2p), and 2.6521(Debye) at B3LYP/ 6-311++G** respectively. Thus dipole moment of CysZW at B3LYP/6-311++G** is observed to be high when compared to HF/6-311+G (2d, 2p).

c) CHEMICAL POTENTIAL AND CHEMICAL HARDNESS:

The chemical potential of CysZW is -0.2235eV in HF/6-311+G (2d, 2p) and -0.1127eV in B3LYP/6-311+G**. From the observed value it is found that the chemical potential of CysZW at B3LYP/6-311+G (2d,2p) level is high when compared to HF/6-311+G (2d, 2p) . The chemical hardness of the optimized structure in HF/6-311+G (2d, 2p) and B3LYP/6-311+G (2d, 2p) is found to be 0.2235eV and 0.1127eV. The chemical hardness of CysZW is found to be high at HF/6-311+G (2d, 2p) when compared to B3LYP/6-311+G**. The chemical hardness and chemical potential of CysZW calculated at HF/6-311+G (2d, 2p) and B3LYP/6-311++G** levels are tabulated in **table 4.9**.

d) CHEMICAL SOFTNESS

The chemical softness of CysZW is found to be 2.2433eV in HF/6-311+G (2d, 2p) and 4.7580eV in B3LYP/6-311+G (2d, 2p), by the comparison of these values the chemical softness of CysZW at B3LYP/6-311+G (2d, 2p) are found to be higher than the chemical softness of HF/6-311+G (2d, 2p). Thus the chemical softness of CysZW is found to be large when compared to chemical hardness at both HF/6-311+G (2d, 2p) and B3LYP/6-311++G**, so the zwitterionic form of cysteine is highly polarisable. The calculated chemical softness of CysZW at HF/6-311+G (2d, 2p) and B3LYP/6-311++G** levels are listed in **table 4.9**.

4.4.3 ANIONIC CYSTEINE

a) BOND LENGTH AND BOND ANGLE

In HF/6-311+G (2d, 2p) the bond lengths of N – H and S – H are observed as 1.001Å and 1.3243Å and at B3LYP/6-311++G** the values of N – H and S - H are 1.8528Å and 2.3527Å respectively. The bond length of carbonyl group of C = O in HF/6-311+G (2d, 2p) is 1.2286Å and in B3LYP/6-311G++** the carbonyl group has C – O formation with a length of 1.2554Å. The observed bond angles of C – C = O and H – S – C at HF/6-311+G (2d, 2p) is 114.582 (degree) and 97.25 (degree). In B3LYP/6-311++G** the bond angle of C – C – O and H – S – C are 114.879 (degree) and 93.097 (degree).The bond length and bond angle of CysAN observed in the optimized structure are shown in **table 4.4**.

b) ENERGY AND DIPOLEMOMENT

The energy and dipole moment of CysAN at both the levels of theory are given in **table 4.9.** The energy value of CysAN is found to be -718.961(a.u) at HF/6-311+G (2d, 2p) and at B3LYP/6-311++G** the energy value is found to be -721.528 (a.u). The determined energy value of CysAN high at HF/6-311+G (2d, 2p) when compared to the energy value of B3LYP/6-311++G**. The dipole moment of CysAN at HF/6-311+G (2d, 2p) is 6.5447(Debye) and at B3LYP/6-311++G** level the value of dipole moment is found to be 5.9558 (Debye). By comparison of these two values of dipole moment, CysAN at HF/6-311+G (2d, 2p) is higher than CysAN at B3LYP/6-311++G**.

c) CHEMICAL POTENTIAL AND CHEMICAL HARDNESS

The chemical hardness and chemical potential of CysAN calculated at HF/6-311+G (2d, 2p) and B3LYP/6-311++G** levels are tabulated in **table 4.9**. The chemical potential of CysAN is observed to be -0.1840eV in HF/6-311+G (2d, 2p) and -0.0804eV in B3LYP/6-311++G**. The chemical potential of CysAN at B3LYP/6-311++G** level is found to be high when compared to CysAN at HF/6-311+G (2d, 2p). Similarly the calculated chemical hardness is 0.1840eV in HF/6-311+G (2d, 2p) and 0.0804eV in B3LYP/6-311++G**, the chemical hardness of CysAN at HF/6-311+G (2d, 2p) is high when compared to the hardness of CysAN at B3LYP/6-311++G** level.

d) CHEMICAL SOFTNESS

Thus the optimized structure of CysAN has a chemical softness of 2.7164eV at HF/6-311+G (2d, 2p) and at B3LYP/6-311++G** the softness is found to be 6.2169eV. It is noted that, CysAN is highly polarizable because the chemical softness is high when compared to the chemical hardness at both HF/6-311+G (2d, 2p) and B3LYP/6-311++G** levels. The calculated chemical softness of CysAN at HF/6-311+G (2d, 2p) and B3LYP/6-311++G** levels are given in **table 4.9**.

4.4.4 CATIONIC CYSTEINE

a) BOND LENGTH AND BOND ANGLE

The bond length of 1.3250Å, 1.5274 Å and 1.8302Å are obtained for S – H, carbonyl C = C and C – S in HF/6-311+G (2d, 2p) and in B3LYP /6-311++G** the noted values of S – H, carbonyl C = C and C – S are 1.3483Å, 1.5396Å and 1.8500 Å respectively. The variation observed in bond angle at both HF/6-311+G (2d, 2p) and B3LYP /6-311++G** level of theories are listed in the table **table 4.3**.

b) ENERGY AND DIPOLE MOMENT

The energy value of CysCAT at HF/6-311+G (2d, 2p) is found to be -719.872 (a.u) and at B3LYP /6-311++G** is -722.418 (a.u) respectively. From the observed energy values the most stable structure is found is found to be CysCAT of B3LYP /6-311++G** when compared to the structure of CysAN at B3LYP /6-311++G** level, since the energy value of CysCAT is high at HF/6-311+G (2d, 2p) when compared to B3LYP /6-311++G**. The dipole moment of CysCAT at HF/6-311++G (2d, 2p) is 8.0438 (Debye) and at B3LYP/6-311++G** is 7.2016 (Debye). The dipole moment is high at HF/6-311+G (2d, 2p) of CysCAT when compared to B3LYP/6-311++G**. The energy and dipole moment of CysCAT at both the levels of theory are given in **table 4.9.**

c) CHEMICAL POTENTIAL AND CHEMICAL HARDNESS

The chemical hardness and chemical potential of CysCAT calculated at HF/6-311+G (2d, 2p) and B3LYP/6-311++G** levels are given in **table 4.9.** In HF/6-311+G (2d, 2p) the chemical potential is observed to be -0.2159eV and at B3LYP/6-311++G** the chemical potential is found to be -0.1108eV. By comparing the chemical potential, the value of CysCAT at B3LYP/6-311++G** is high when compared to HF/6-311+G (2d, 2p). Similarly the chemical hardness of CysCAT at HF/6-311+G (2d, 2p) is 0.2159eV and 0.1108eV at B3LYP/6-311++G**. The chemical hardness of HF/6-311+G (2d, 2p) is higher than the hardness of B3LYP/6-311++G**.

d) CHEMICAL SOFTNESS

The calculated values of chemical softness of CysCAT is 2.3155eV at HF/6-311+G (2d, 2p) and 4.5126eV B3LYP /6-311++G**. The chemical softness of HF/6-311+G (2d, 2p) is higher than the value of B3LYP/6-311++G**. At both the level of theories, softness is found to high when compared to chemical hardness, so the CysAn is highly polarizable. The calculated chemical softness of CysAN at HF/6-311+G (2d, 2p) and B3LYP/6-311++G** levels are given in **table 4.9**.

By comparing all the values of geometrical parameters and chemical reactivity parameters for normal cysteine, CysZW, CysAN, and CysCAT, the minimum energy level is obtained at CysCAT at both HF/6-311+ G (2d, 2p) and B3LYP/6-311++G** levels, so the structure of CysCAT is found to be more stable. Then the dipole moment of CysCAT is also high at both HF/6-311+ G (2d, 2p) and B3LYP/6-311++G**. The hardness signifies the resistance towards the deformation of electron cloud of chemical systems under small perturbation encountered during the chemical process. The chemical hardness observed at CysAN is high when compared to all other conformers at both HF/6-311+ G (2d, 2p) and B3LYP/6-311++G**. At both the level of theories softness found to large when compared to hardness in anionic form. So the CysAN is highly plarizable.

The chemical potential of CysAN is high when compared to all optimized structures of CysCAT,CYSZW and normal cysteine at both the level of HF/6-311+ G (2d, 2p) and B3LYP/6-311++G** theories. It is seen that the chemical potentials of normal cysteine, CysZW, CysAN and CysCAT are negative and means that these structures are stable. These structures do not decompose spontaneously into the elements they are made up of.

4.5 MOLECULAR VIBRATIONS

Molecular vibrations occur when atoms in a molecule are in periodic motion, while the molecule as a whole has constant translational and rotational motion. The frequency of molecular vibrations ranges from less than 10^{12} to approximately 10^{14}Hz. It depends upon the interatomic binding energy which determines the force needed to stretch or a compress a bond. In general, a molecule with N atoms has 3N-6 normal modes of vibration, but linear molecule has 3N-5 modes, as rotation about its molecular axis cannot

be observed. Molecular vibration is excited when the molecule absorbs a quantum of energy (E), corresponding to the vibration's frequency (v) according to the relation E = hv (where h is planck's constant). A fundamental vibration is excited when one such quantum of energy is absorbed by the molecule in its ground state.The common molecular vibrations that are excited by IR radiations are stretching or bonding vibrations and bending or deformation vibrations. These are called modes of vibrations. Stretching involves a change in bond lengths resulting in a change in interatomic distance. Bending involves a change in bond angle or a change in the position of a group of atoms, with respect to the rest of molecule. The two stretching modes are: symmetric stretching and asymmetric stretching. The two H atoms in CH_2 group, move away from the C atom - a symmetrical stretch and one H atom moves away from the C atom and one moves toward the C atom - an symmetric stretching.

Bending or deformational modes are of four types Scissoring and Rocking are in plane bending modes, the H atoms remain in the same plane as the C atom (i.e in the plane of the page). Wagging and Twisting are out-of-plane (oop) bending modes, which the H atoms are moving out of the plane containing the C atom [12].

4.6 SPECTROSCOPIC ANALYSIS OF PRESENT STUDY

The variation in the frequency significantly alters the intensity of the spectrum. The IR and Raman spectra obtained for cysteine in its normal, zwitterionic, anionic and cationic forms, optimized at HF/6-311+G (2d, 2p) and B3LYP/6-311++G** levels of theory are plotted in graph with frequency in the X- axis and intensity in Y-axis.

a) NORMAL CYSTEINE

The IR spectra of normal Cysteine at both HF/6-311+G (2d, 2p) and B3LYP/6-311++G** are shown **in fig.4.9 and 4.11.** The vibrational spectra of normal cysteine have 36 modes of vibrations on both the levels of theory. The strongest peak in the IR spectrum at HF/6-311+G (2d, 2p) and and B3LYP/6-311++G** functions are 1151.58 $cm^{-1}$and 1983.9179 cm^{-1}having a vibrational mode of 20 and 29 that attributed to the stretching of hydroxyl (OH) group and rocking of (amide) NH_2 group in HF/6-311+G (2d, 2p) and C = O stretching at and B3LYP/6-311++G** respectively. The other vibrational modes observed for normal cysteine at both HF/6-31+ G (2d, 2p) and

B3LYP/6-311++G** levels are given in **table 4.10.** The second strongest peak is 1814.75 with a mode of 20 providing C = O stretching in HF/6-311+ G (2d, 2p) and129l.5152cm^{-1} of mode 29 provide OH stretching and NH_2 twisting in DFT.

In Raman spectrum, the first strongest peak is 2912.0985 cm^{-1} and 3082.2596cm^{-1} with a vibrational mode of 31 corresponds to the $C_1 - H_3$ stretching obtained for both HF/6-311+G(2d, 2p) and B3LYP/6-311++G** respectively. The other vibrational modes observed for normal cysteine at HF/6-31+ G (2d, 2p) and B3LYP/6-311++G** levels are given in **table 4.10.** The second strongest peak is 2672.0985cm^{-1} of mode 30 with SH stretching and 3762.9047 cm^{-1} with a mode 34 indicates a symmetric stretching of amide group are found in HF/6-311+G (2d, 2p) and B3LYP/6-311++G** levels of theory. The Raman spectra of normal Cysteine at both HF/6-311+G (2d, 2p) and B3LYP/6-311++G** are shown **in fig.4.10 and 4.12.**

b) ZWITTERONIC CYSTEINE

The total number of modes observed in CysZW is 36 on both HF/6-311+G (2d, 2p) and B3LYP/6-311++G**. The IR spectra of CysZW at both HF/6-311+G (2d, 2p) and B3LYP/6-311++G** are shown **in fig.4.13 and 4.15** respectively. In IR spectrum, the first strongest peak is 1985.28cm^{-1} having a mode of vibration 29 that corresponds to C = O stretching in HF/6-311+G (2d, 2p) and 3135.4008 cm^{-1} having NH stretching of vibrational mode 31in B3LYP/6-311++G**. In HF/6-311+G (2d, 2p) the second strongest peak has a vibrational mode of 26 with amino (NH_3) in plane bending of scissoring with a frequency of 1652.4033cm^{-1} and frequency of 1483.883cm^{-1} is found for NH_3 in plane bending of scissoring at B3LYP/6-311++G**. The other vibrational modes observed for CysZW at both HF/6-31+ G (2d, 2p) and B3LYP/6-311++G** levels are given in **table 4.11.**

The strongest peak of Raman spectrum is found to be 2852.5382 cm^{-1}in HF/6-311+G (2d, 2p) with a vibrational mode of 30, that attributed to the SH stretching and at B3LYP/^-311++G**. The other vibrational modes observed for CysZW at both HF/6-31+ G (2d, 2p) and B3LYP/6-311++G** levels are given in **table 4.11.** The first strongest peak is observed at 1216.6265 $cm^{-1}$with a vibrational mode of 20, corresponds

to $H_3 - C_3 - H_4$ out of plane bending twisting. Second strongest peak with vibrational mode 31 having frequency 3234.15 cm^{-1}attributed to $H_4 - C_2 - H_5$ symmetric stretching and $C_1 - H_1$ stretching in HF/6-311+G (2d,2p) and frequency of 3135.4008 cm^{-1} having vibrational mode 33 possess N_1H_5 stretching in B3LYP/6-311++G**. The Raman spectra of CysZW at both HF/6-311+G (2d, 2p) and B3LYP/6-311++G** are shown **in fig.4.14 and 4.156** respectively.

c) ANIONIC CYSTEINE

The vibrational spectra of anionic cysteine have 33 modes of vibrations on both the levels of theory. The strongest peak in the IR spectrum at HF/6-311+G(2d,2p) and B3LYP?6-311++G**functions are 1802.708 cm^{-1} and 1681.10cm^{-1} having a vibrational mode of 26 and 27 that attributed to the in plane bending Scissoring of amide (NH_2) group in HF/6-311+G(2d,2p) and COO^- asymmetric stretching with Scissoring of amide group at B3LYP/6-311++G** respectively. The other vibrational modes observed for CysAN at both HF/6-31+G (2d,2p) and B3LYP/6-311++G** levels are given in **table 4.12.** The second strongest peak is 1503.515cm^{-1} with a mode 23 that providing $C_1 = C_3$ stretching at HF/6-311+G(2d,2p) and at B3LYP/6-311++G** in plane bending scissoring of $H_5 - C_2 - H_4$ is observed at a frequency range of 1652.658cm^{-1} with a vibrational mode 26. The IR spectra of CysAN at both HF/6-311+G (2d, 2p) and B3LYP/6-311++G** are shown **in fig.4.17 and 4.19**

In Raman spectrum the first strongest peak is 3206.96 cm^{-1} in HF/6-311+G(2d,2p) of mode 29 corresponds to the $C_1 - H_1$ and $C_1 - H_3$ stretching and in B3LYP/6-311++G**, frequency of 2620.518 cm^{-1} with a vibrational mode of 29 attributed to S_1- H_6stertching. The other vibrational modes observed for CysAN at both HF/6-31+G(2d,2p) and B3LYP/6-311++G** levels are given in **table 4.12.**The second strongest peak is 2851.274cm^{-1} with a mode 28 SH stretching is observed at HF/6-311+G9(2d,2p) and at B3LYP/6-311++G** CH symmetric stretching is noted with a frequency 3041.41 cm^{-1} which has a mode of 29. The Raman spectra of CysAN at both HF/6-311+G (2d, 2p) and B3LYP/6-311++G** are shown **in fig.4.18 and 4.20.**

d) **CATIONIC CYSTEINE**

The vibrational spectrum of cysteine in cationic form has 39 modes of vibrations at both HF/6-311+G (2d, 2p) and B3LYP/6-311++G** level. The IR spectra of CysCAT at both HF/6-311+G (2d, 2p) and B3LYP/6-311++G** are shown **in fig.4.21 and 4.23** respectively. The first strongest peak observed in IR spectrum is at 2054.164 cm^{-1} with the mode 31 is attributed to carbonyl C=O stretch in HF/6-311+G (2d, 2p) and frequency at 3134.663 cm^{-1} stretching at amino(NH_3) group is seen at B3LYP/6-311++G**. The second strongest peak observed at IR spectrum is at 4059.811 cm^{-1}, associated with O_2-H_7 stretching with a mode 39 in HF/6-311+G (2d, 2p). At B3LYP/6-311++G** the frequency 1872.08 cm^{-1} with mode 31 corresponds to C=O stretching. The other vibrational modes observed for CysCAT at both HF/6-31+ G (2d, 2p) and B3LYP/6-311++G** levels are given in **table 4.13.**

The Raman spectra of CysCAT at both HF/6-311+G (2d, 2p) and B3LYP/6-311++G** are shown **in fig.4.22 and 4.24** In Raman spectrum, the first strongest peak at 3251.95 cm^{-1} and second strongest peak at 3097.575 cm^{-1} is attributed to H-C-H symmetric stretching, sulfhydryl stretching with same mode 34 at both HF/6-311+G (2d, 2p) and B3LYP/6-311++G** respectively. Similarly, the first strongest peak at 2675.027 cm^{-1} and second strongest peak at 2846.287 cm^{-1} are both attributed to SH stretching with same mode 34 at HF/6-311+G (2d, 2p) and B3LYP/6-311++G** respectively. The other vibrational modes observed for CysCAT at both HF/6-31+G (2d,2p) and B3LYP/6-311++G** levels are given in **table 4.13.**

From the observed result it is concluded that the maximum spectral values are obtained in the cationic form of cysteine (CysCAT) at both HF and B3LYP levels.

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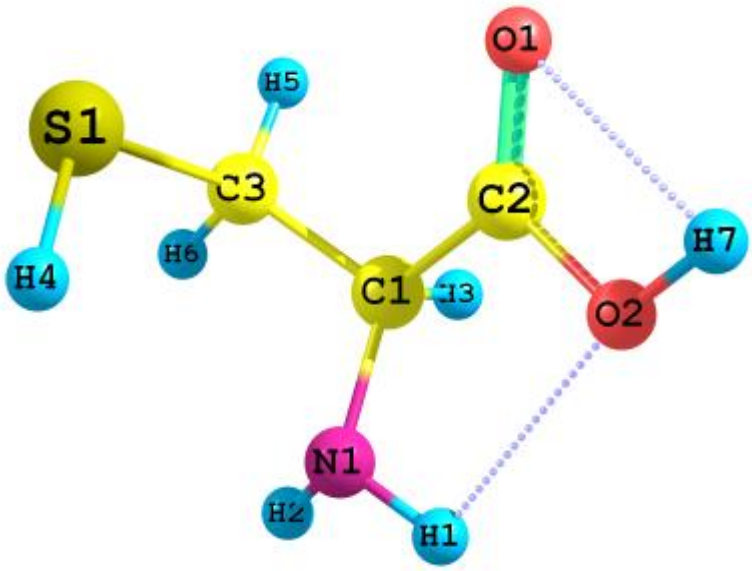
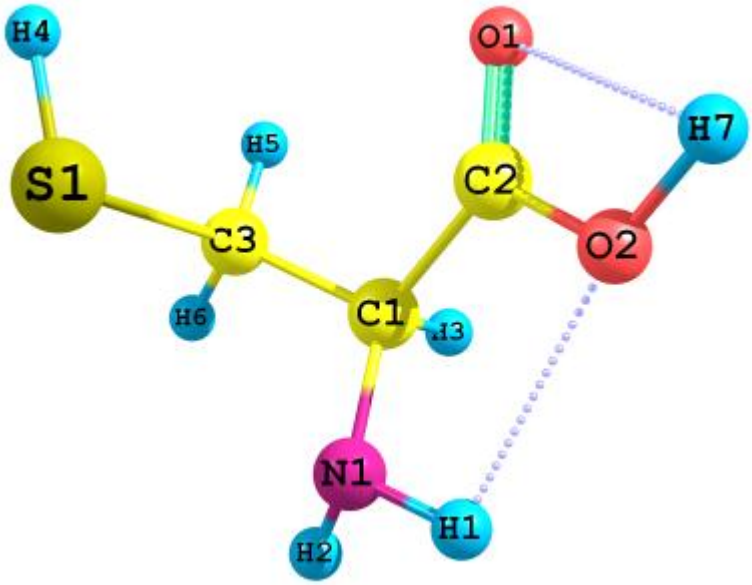


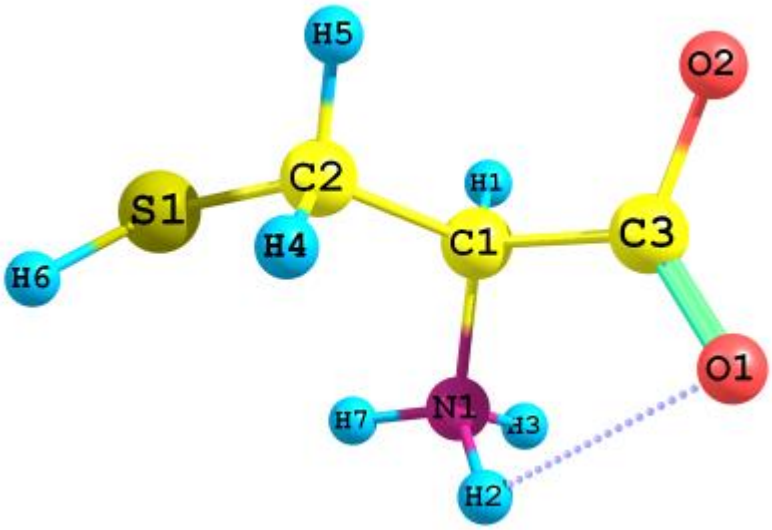
The optimized structure of Normal Cysteine at HF/6-311+G (2d, 2p)

Fig. 4.1



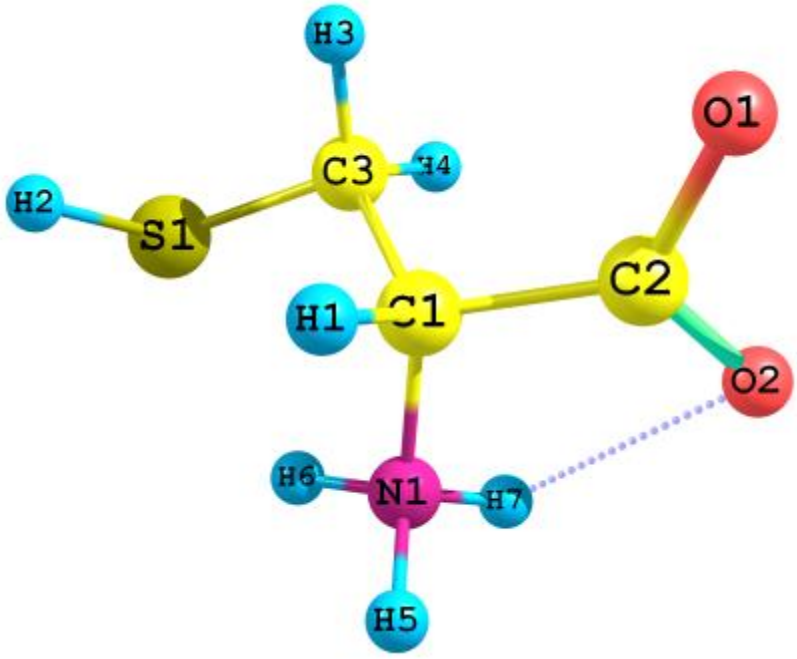
The optimized structure of Normal Cysteine at B3LYP/6-311++G**

Fig. 4.2



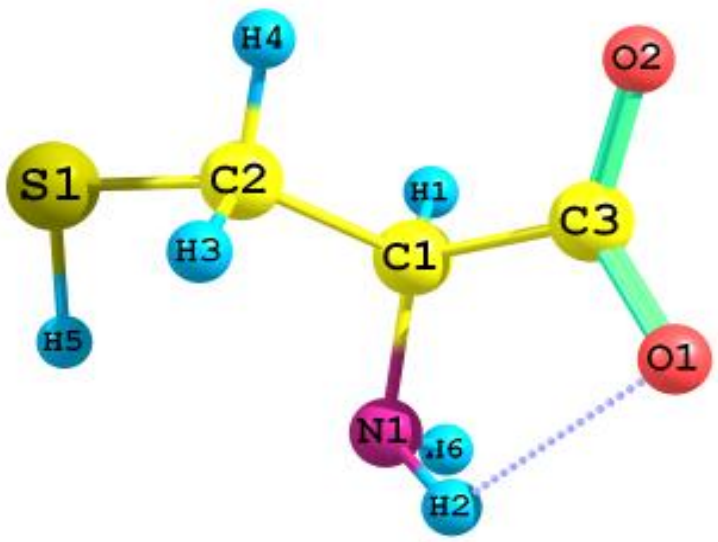
The optimized structure of CysZW at HF/6-311+G (2d, 2p)

Fig. 4.3



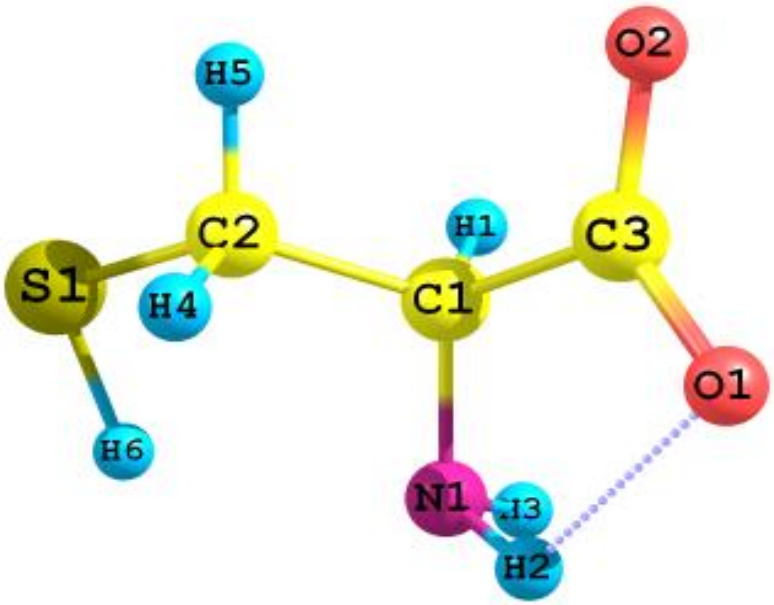
The optimized structure of CysZW at B3LYP/6-311++G**

Fig. 4.4



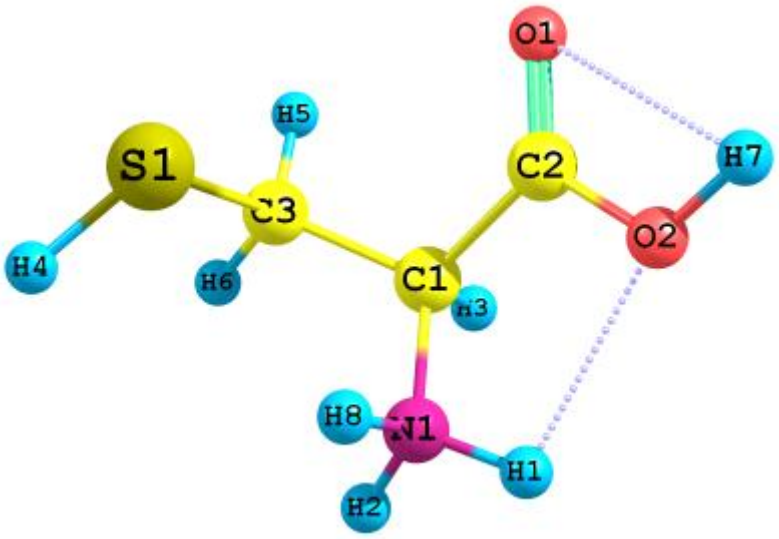
The optimized structure of CysAN at HF/6-311+G (2d, 2p)

Fig. 4.5



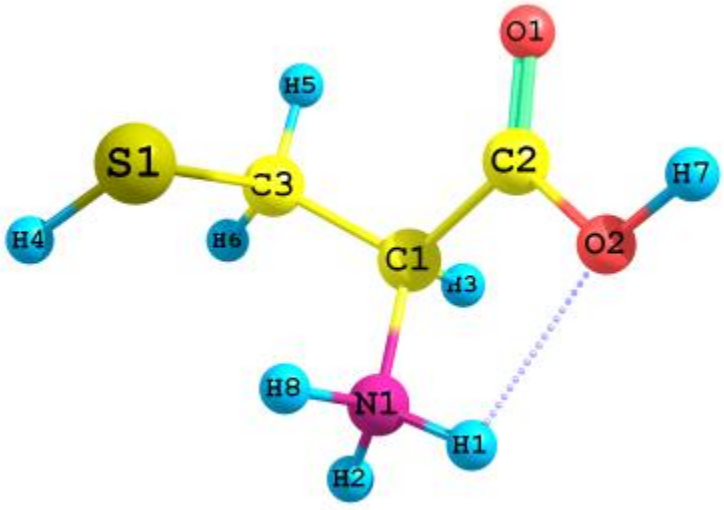
The optimized structure of CysAN at B3LYP/6-311++G**

Fig. 4.6



The optimized structure of CysCAT at HF/6-311+G (2d, 2p)

Fig. 4.7



The optimized structure of CysCAT at B3LYP/6-311++G**

Fig. 4.8

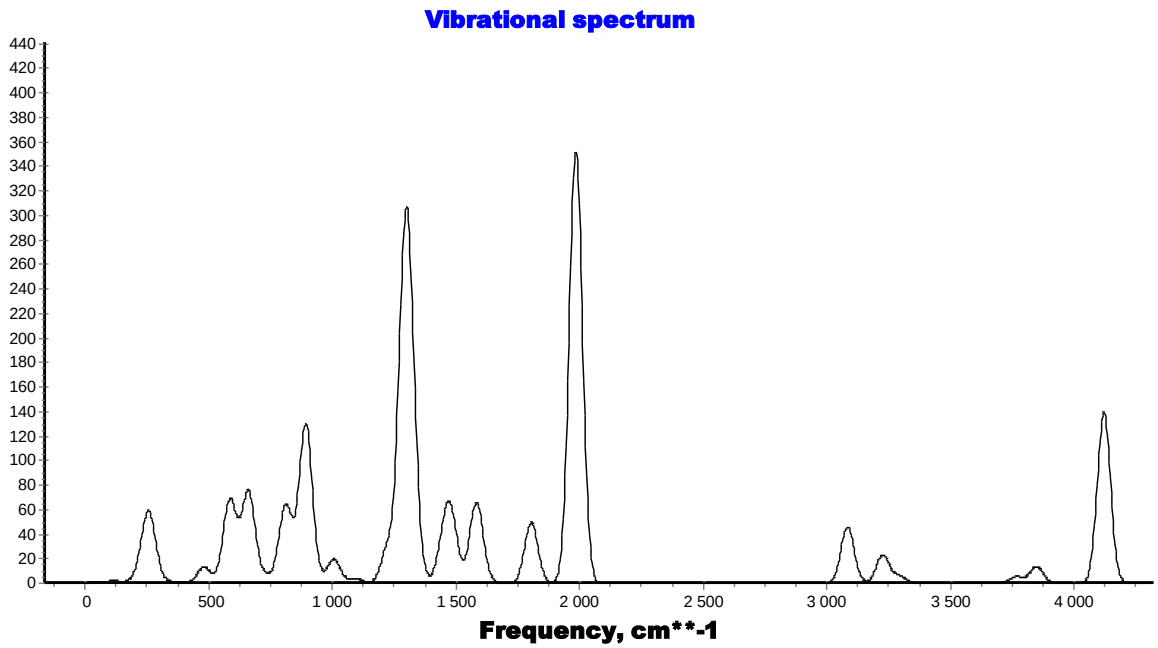


Fig. 4.9 A graph between wave number (vs) IR intensity for normal Cysteine at HF/6-311+G (2d, 2p)

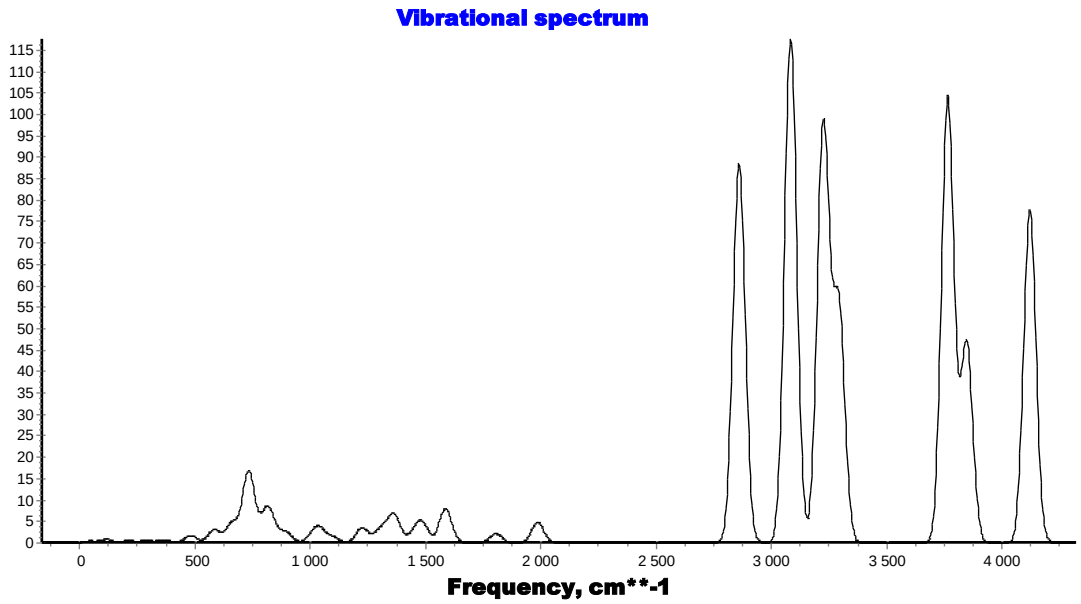


Fig. 4.10 A graph between wave number (vs) Raman intensity for normal Cysteine at HF/6-311+G (2d, 2p)

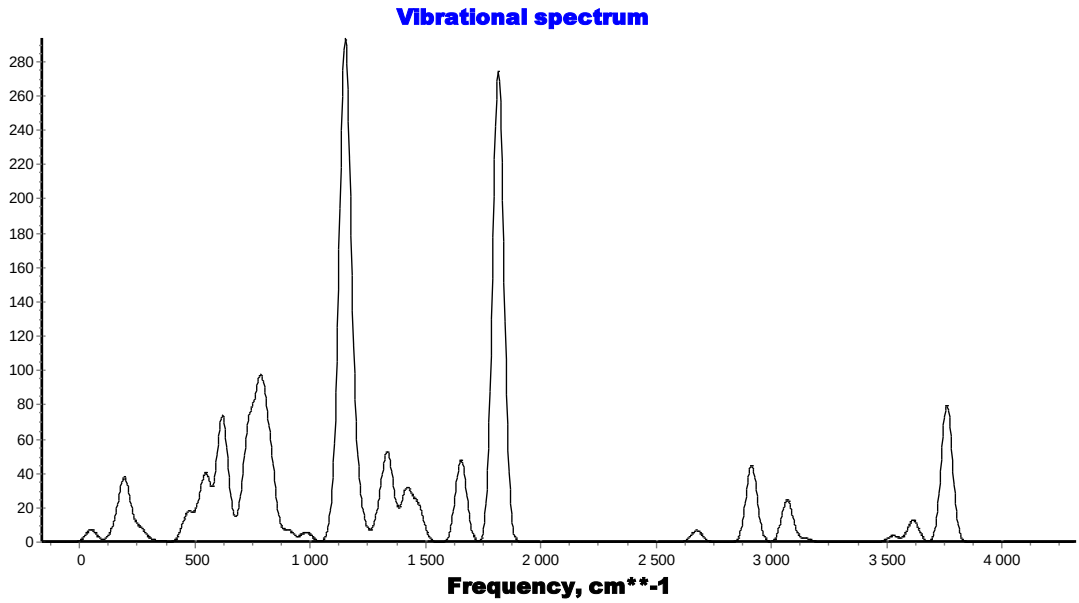


Fig. 4.11 A graph between wave number (vs) IR intensity for normal Cysteine at B3LYP/6-311++G**

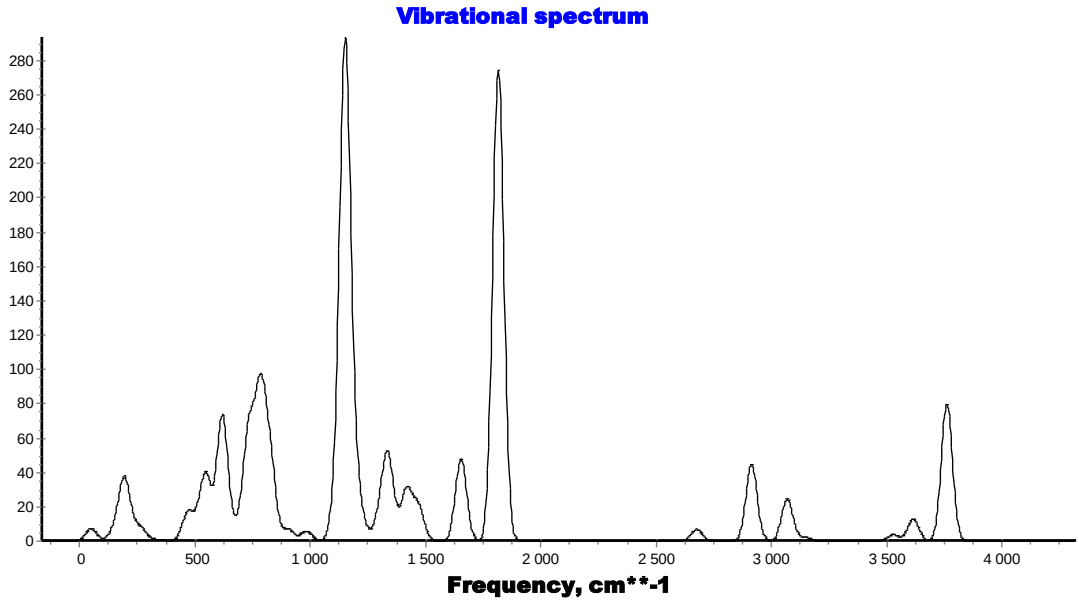


Fig. 4.12 A graph between wave number (vs) Raman intensity for normal Cysteine at B3LYP/6-311++G**

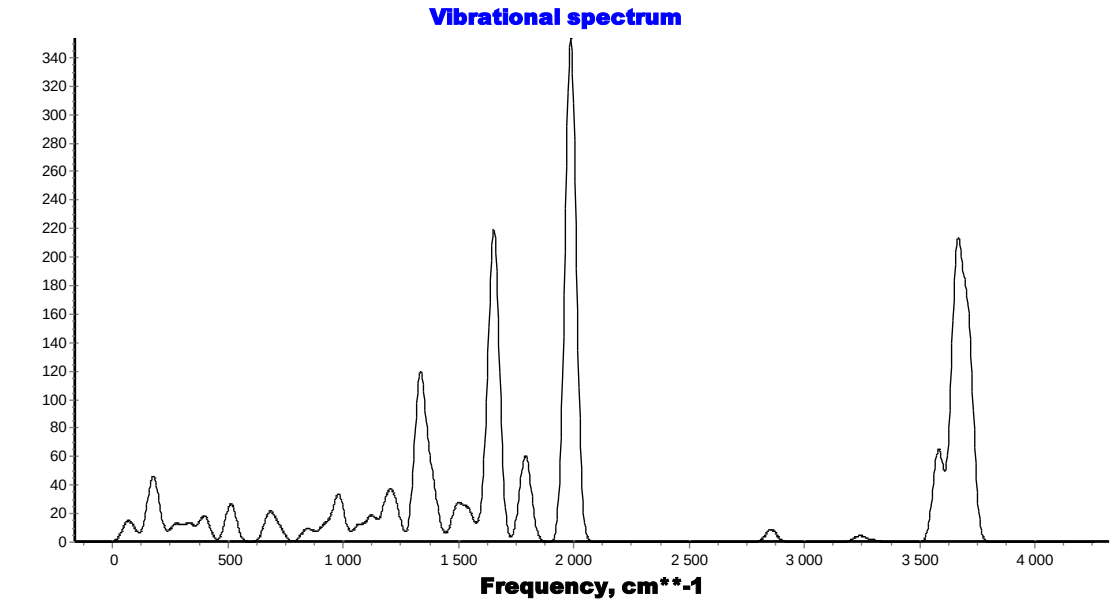


Fig. 1.13 A graph between wave number (vs) IR intensity for CysZW at HF/6-311+G (2d, 2p).

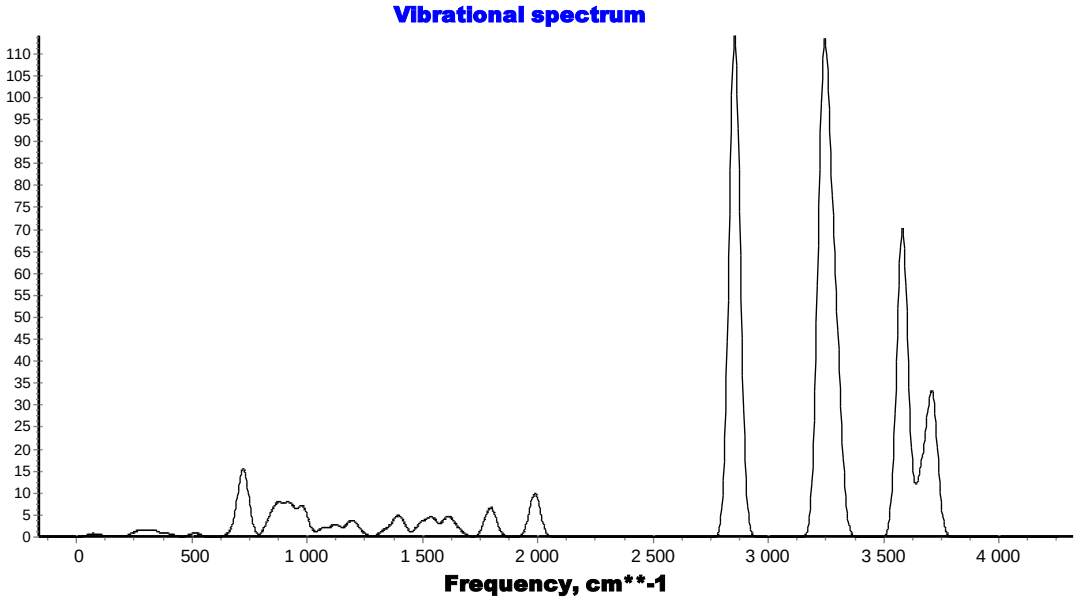


Fig. 1.14 A graph between wave number (vs) Raman intensity for CysZW at HF/6-311+G (2d, 2p)

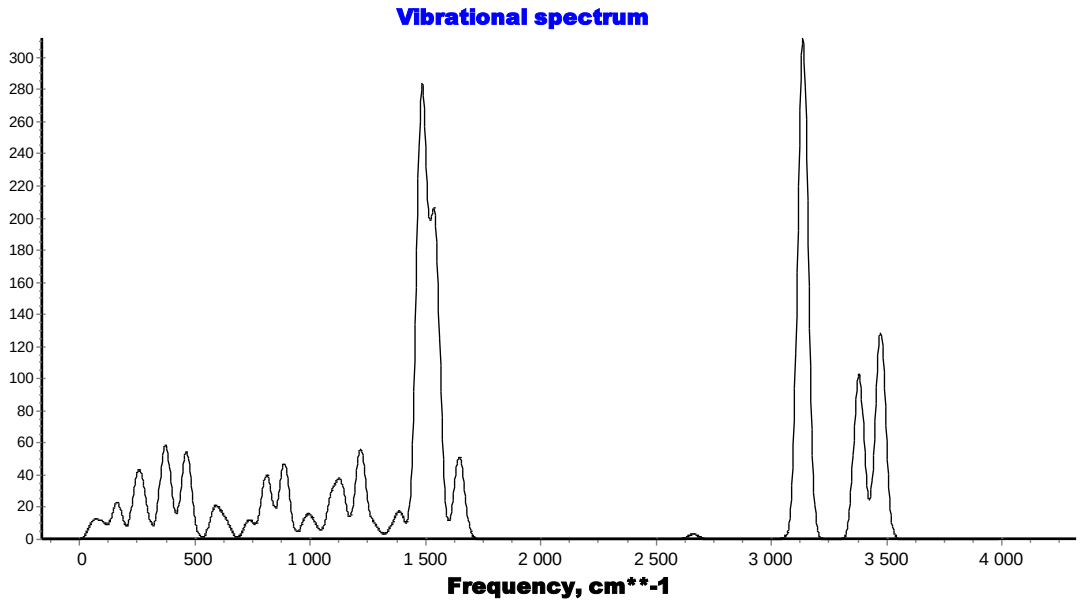


Fig.4.15. A graph between wave number (vs) IR intensity for CysZW at B3LYP/6-311++G.**

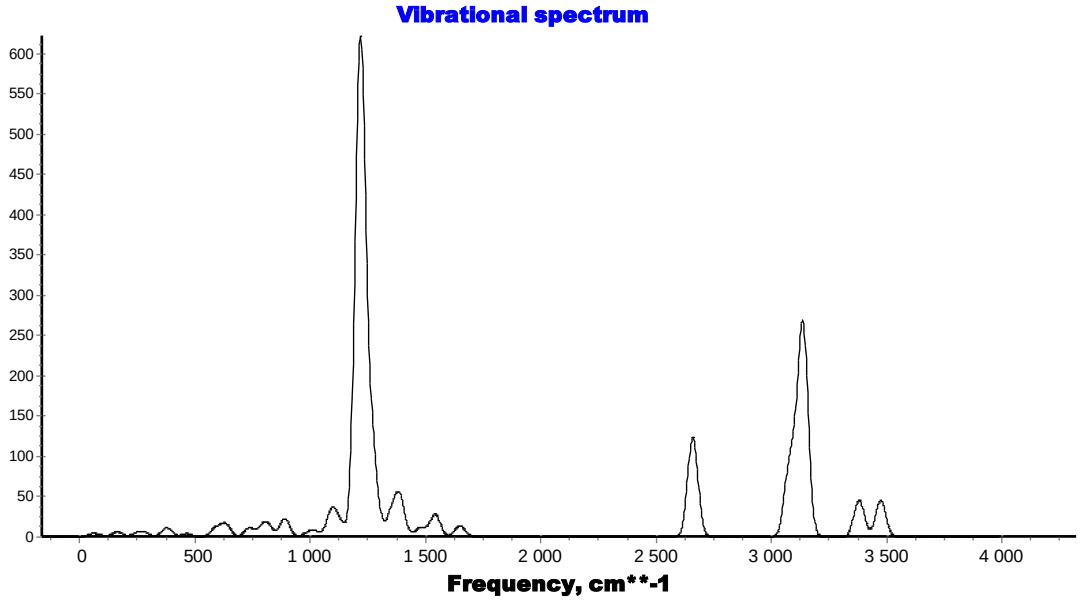


Fig.4.16 A graph between wavenumber (vs) Raman intensity for CysZW at B3LYP/6-311++G.**

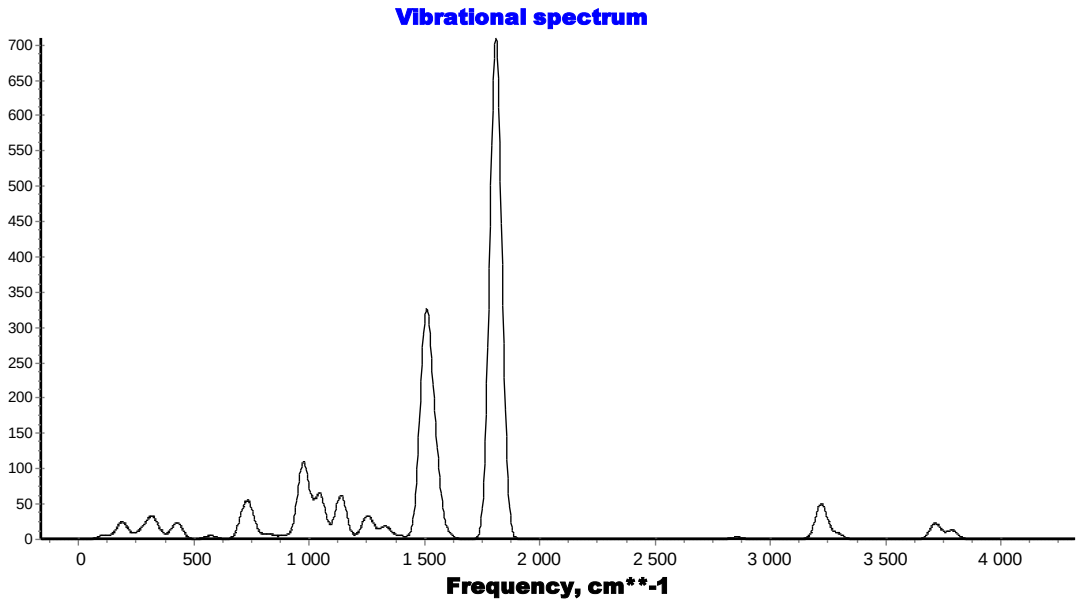


Fig 4.17 A graph between wavenumber (vs) IR intensity for CysAN

at HF/6-311+G (2d, 2p)

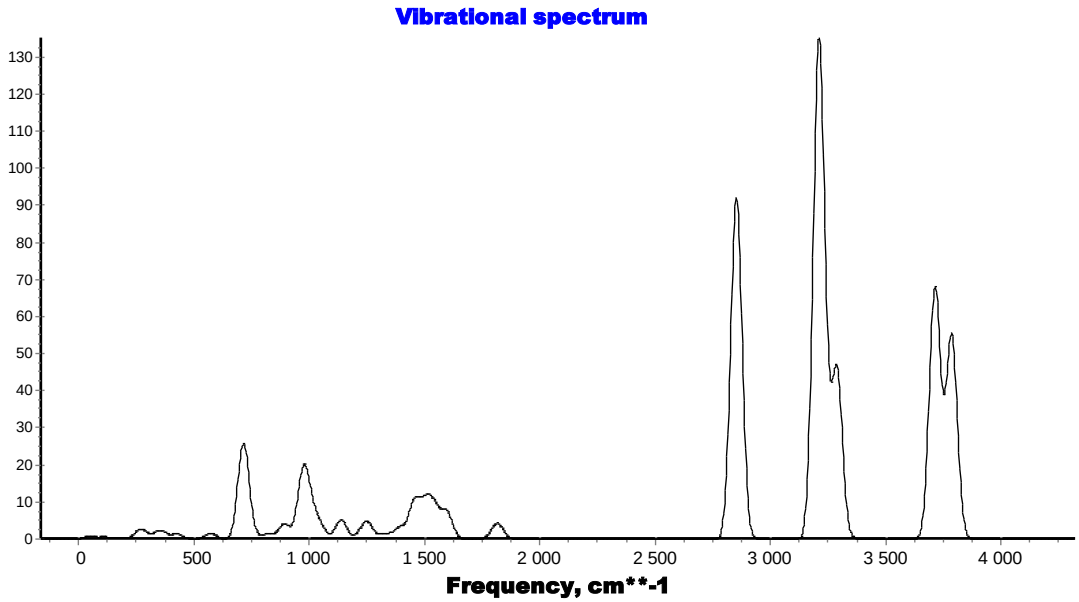


Fig4. 18 A graph between wavenumber (vs) Raman intensity for CysAN

at HF/6-311+G (2d, 2p)

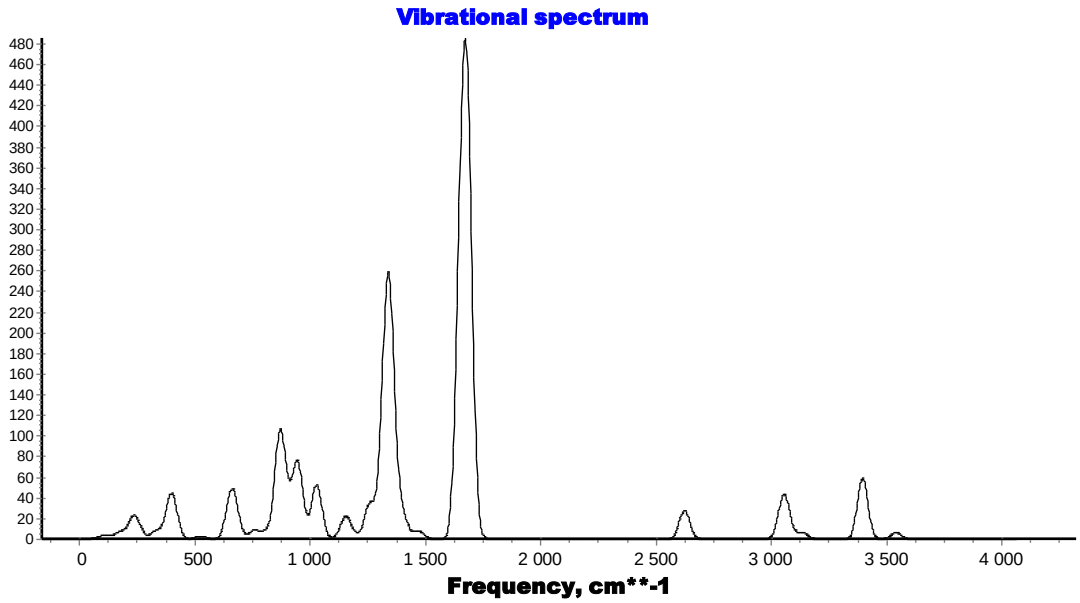


Fig 4.19 A graph between wave number (vs) IR intensity for CysAN

at B3LYP/6-311++G**

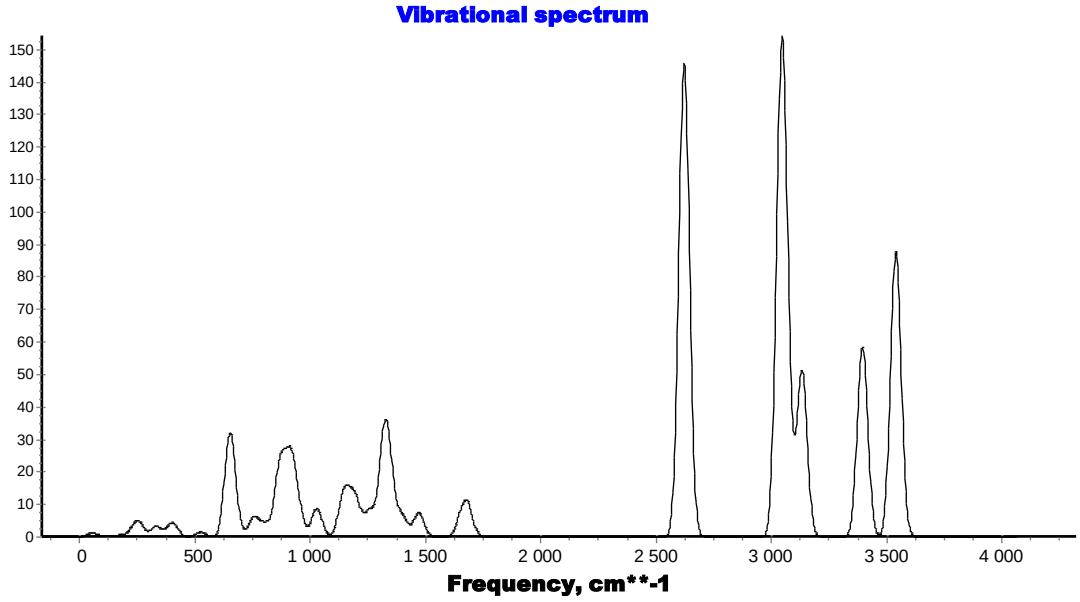


Fig 4.20 A graph between wave number (vs) Raman intensity for CysAN

at B3LYP/6-311++G**

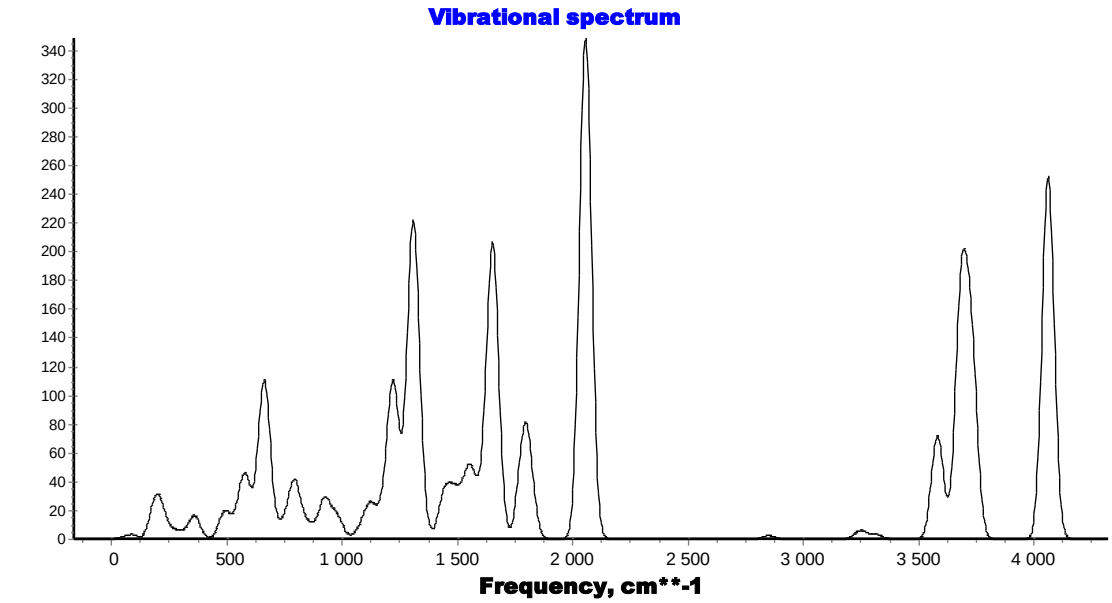


Fig 4.21A graph between wave number (vs) IR intensity for CysCAT

at HF/6-311+G (2d, 2p)

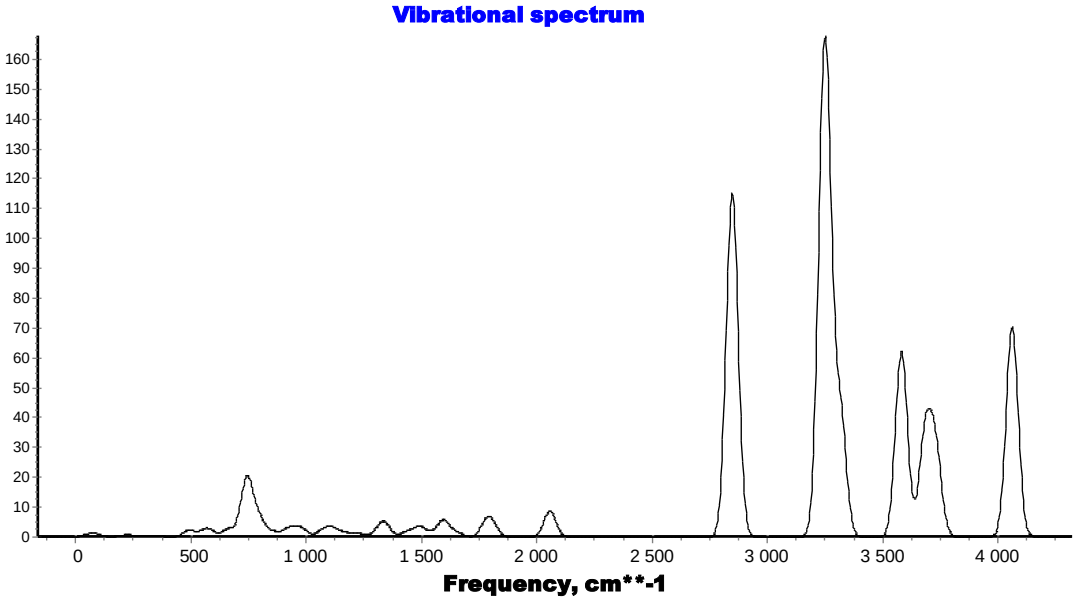


Fig 4.22 A graph between wave number (vs) Raman intensity for CysCAT

at HF/6-311+G (2d, 2p).

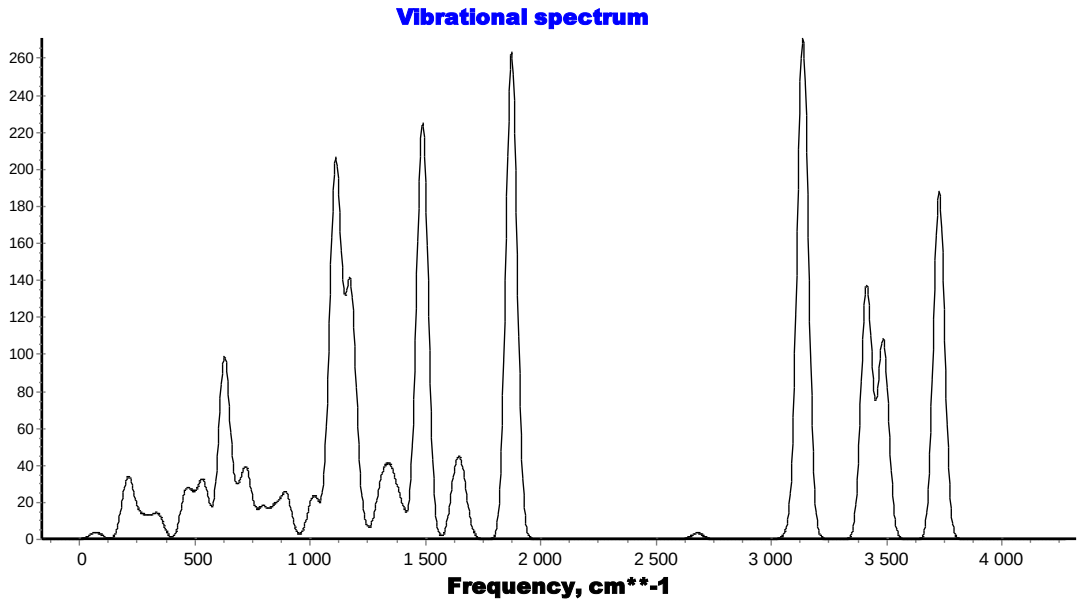


Fig. 4.23A graph between wave number (vs) IR intensity for CysCAT

at B3LYP/6-311++G**

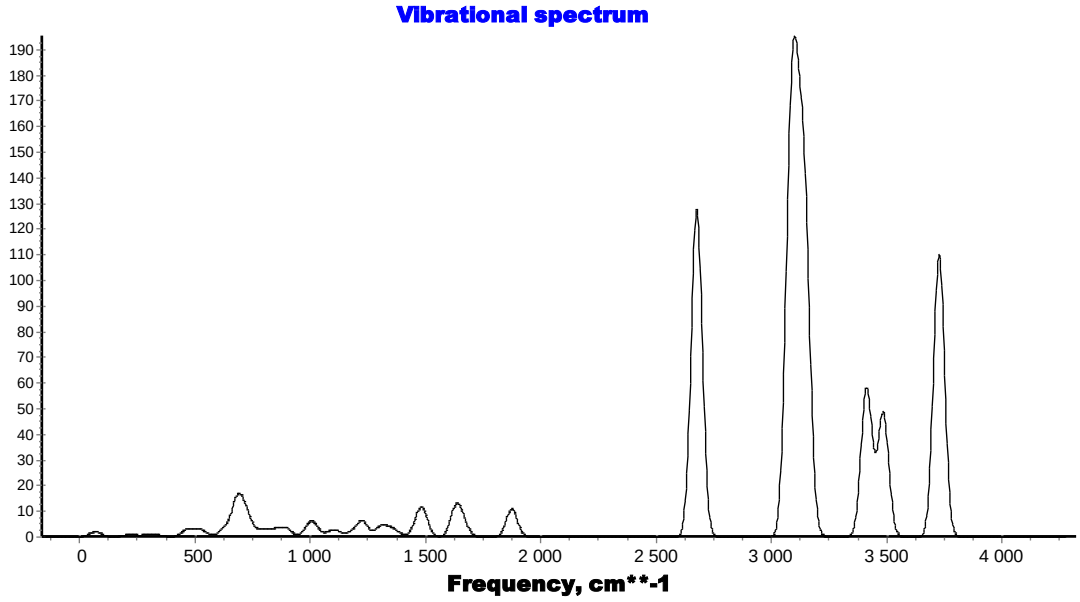


Fig. 4.24 A graph between wave number (vs) Raman intensity fo CysCAT

at B3LYP/6-311++G**

Table 4.1

Bond lengths (Å) for normal cysteine optimized at HF/6-311+G (2d, 2p) and B3LYP/6-311++G levels of theory.**

PARAMETERS	Ab Initio HF/6-311+G (2d, 2p)	PARAMETERS	DFT B3LYP/6-311++G**
$C_2 = O_1$	1.1824	$C_2 = O_1$	1.2040
$C_2 – O_2$	1.3238	$C_2 – O_2$	1.3521
$O_2 – H_7$	0.9447	$O_2 – H_7$	0.9692
O_1... H_7	2.2605	O_1 ... H_7	2.2944
O_2.. H_1	2.3242	O_2 … H_1	2.2694
$C_2 – C_1$	1.5159	$C_2 – C_1$	1.5261
$C_1 – H_3$	1.0931	$C_1 – H_3$	1.1059
$C_1 – N_1$	1.4456	$C_1 – N_1$	1.4584
$N_1 – H_1$	0.9955	$N_1 – H_1$	1.0124
$N_1 – H_2$	0.9965	$N_1 – H_2$	1.0135
$C_1 – C_3$	1.5259	$C_1 – C_3$	1.5310
$C_3 – H_5$	1.0764	$C_3 – H_5$	1.0878
$C_3 – H_6$	1.0807	$C_3 – H_6$	1.0914
$C_3 – S_1$	1.8222	$C_3 – S_1$	1.8500
$S_1 – H_4$	1.3236	$S_1 – H_4$	1.3479

Table 4.2

Bond lengths (Å) for CysZW optimized at HF/6-311+G (2d, 2p) and B3LYP/6-311++G levels of theory.**

PARAMETERS	Ab Initio HF/6-311+G (2d, 2p)	PARAMETERS	DFT B3LYP/6-311++G**
$C_3 – O_2$	1.3079	$C_2 – O_1$	1.2704
$C_3 = O_1$	1.1748	$C_2 = O_2$	1.2323
$C_3 – C_1$	1.5273	$C_1 – C_2$	1.5237
O_1… H_2	2.2342	O_2… H_7	2.2640
$C_1 – N_1$	1.4937	$C_1 – N_1$	1.5105
$C_1 – H_1$	1.0795	$C_1 – H_1$	1.0913
$N_1 – H_2$	1.0101	$N_1 – H_5$	1.0237
$N_1 – H_3$	1.0066	$N_1 – H_7$	1.0293
N_1 - H_7	1.0116	N_1 - H_6	1.0425
$C_1 – C_2$	1.5330	$C_1 – C_3$	1.5478
$C_2 – H_4$	1.0745	$C_3 – H_4$	1.0924
$C_2 – H_5$	1.0778	$C_3 – H_3$	1.0891
$C_2 – S_1$	1.8281	$C_3 – S_1$	1.8346
$S_1 – H_6$	1.3245	$S_1 – H_2$	1.3512

Table 4.3

Bond lengths (Å) of CysAN optimized at HF/6-311+G (2d, 2p) and B3LYP/6-311++G levels of theory.**

PARAMETERS	Ab Initio HF/6-311+G (2d, 2p)	PARAMETERS	DFT B3LYP/6-311++G**
$C_3 = O_2$	1.2286	$C_3 - O_2$	1.2495
$C_3 = O_1$	1.2307	$C_3 - O_1$	1.2554
$C_3 – C_1$	1.5605	$C_3 – C_1$	1.5851
$C_1 – H_1$	1.0813	$C_1 – H_1$	1.0938
$C_1 – N_1$	1.4606	$C_1 – N_1$	1.4747
$N_1 – H_2$	1.0013	$N_1 – H_2$	1.0243
$N_1 – H_6$	0.9974	$N_1 – H_3$	1.0147
$H_2 \ldots O_1$	2.1552	$H_2 \ldots O_1$	2.0785
$C_1 – C_2$	1.5252	$C_1 – C_2$	1.5314
$C_2 – H_3$	1.0800	$C_2 – H_4$	1.0921
$C_2 - H_4$	1.0777	$C_2 - H_5$	1.0892
$C_2 – S_1$	1.8327	$C_2 – S_1$	1.8528
$S_1 – H_5$	1.3243	$S_1 – H_5$	2.3527

Table 4.4

Bond lengths (Å) of CysCAT optimized at HF/6-311+G (2d, 2p) and B3LYP/6-311++G levels of theory.**

PARAMETERS	Ab Initio HF/6-311+G (2d, 2p)	PARAMETERS	DFT B3LYP/6-311++G**
$C_2 = O_1$	1.1683	$C_2 = O_1$	1.1912
$C_2 – O_2$	1.3197	$C_2 – O_2$	1.3486
$O_2 –H_7$	0.9489	$O_2 –H_7$	0.9725
$O_1 \ldots H_7$	2.3424	$O_1 – H_7$	2.3886
$C_2 – C_1$	1.5274	$C_2 – C_1$	1.5396
$C_1 – H_3$	1.0817	$C_1 – H_3$	1.0936
$C_1 – N_1$	1.5012	$C_1 – N_1$	1.5148
$N_1 – H_1$	1.0069	$N_1 – H_1$	1.0262
$N_1 – H_2$	1.0058	$N_1 – H_2$	1.0230
$N_1 – H_8$	1.0124	$N_1 – H_8$	1.0428
$H_1 \ldots O_2$	2.2055	$H_1 \ldots O_2$	2.0990
$C_1 – C_3$	1.5255	$C_1 – C_3$	1.5355
$C_3 – H_5$	1.0760	$C_3 – H_5$	1.0887
$C_3 – H_6$	1.0783	$C_3 – H_6$	1.0891
$C_3 – S_1$	1.8302	$C_3 – S_1$	1.8500
$S_1 – H_4$	1.3250	$S_1 – H_4$	1.3483

Table 4.5

Bond angle of (Å) normal cysteine optimized at HF/6-311+G (2d, 2p) and B3LYP/6-311++G levels of theory.**

PARAMETERS	Ab Initio HF/6-311+G (2d, 2p)	PARAMETERS	DFT B3LYP/6-311++G**
$O_1 = C_2 – O_2$	122.398	$O_1 = C_2 – O_2$	122.812
$C_1 – C_2 = O_1$	124.224	$C_1 – C_2 = O_1$	124.118
$C_1 – C_2 – O_2$	113.246	$C_1 – C_2 – O_2$	112.949
$C_2 – O_2 – H_7$	108.558	$C_2 – O_2 – H_7$	107.286
$H_3 – C_1 – C_2$	103.119	$H_3 – C_1 – C_2$	103.225
$H_3 – C_1 – N_1$	112.310	$H_3 – C_1 – N_1$	112.974
$C_3 – C_1 – H_3$	106.066	$C_3 – C_1 – H_3$	106.539
$C_3 – C_1 – N_1$	111.690	$C_3 – C_1 – N_1$	110.520
$C_3 – C_1 – C_2$	111.366	$C_3 – C_1 – C_2$	110.360
$H_2 – N_1 – H_1$	108.370	$H_2 – N_1 – H_1$	108.833
$H_2 – N_1 – C_1$	110.757	$H_2 – N_1 – C_1$	111.033
$N_1 – C_1 – H_3$	112.310	$N_1 – C_1 – H_3$	112.974
$H_1 –N_1 – C_1$	111.949	$H_1 –N_1 – C_1$	112.178
$N_1 – C_1 – C_2$	111.847	$N_1 – C_1 – C_2$	112.837
$H_5 – C_3 – H_6$	107.574	$H_5 – C_3 – H_6$	108.854
$H_5 – C_3 – C_1$	110.103	$H_5 – C_3 – C_1$	109.738
$H_6 – C_3 – C_1$	108.352	$H_6 – C_3 – C_1$	109.122
$S_1 – C_3 – C_1$	116.434	$S_1 – C_3 – C_1$	111.335
$H_4 – S_1 – C_3$	97.444	$H_4 – S_1 – C_3$	95.561
$S_1 – C_3 – H_5$	108.566	$S_1 – C_3 – H_5$	108.984
$S_1 – C_3 – H_6$	105.393	$S_1 – C_3 – H_6$	108.765
$O_2 – H_7...O_1$	74.041	$O_2 – H_7...O_1$	74.863
$N_1 – H_1...O_2$	99.102	$N_1 – H_1...O_2$	101.355

Table 4.6

Bond angles (degree) of CysZW optimized at HF/6-311+ G (2d, 2p) and B3LYP/6-311++G levels of theory.**

PARAMETERS	Ab Initio HF/6-311+G (2d, 2p)	PARAMETERS	DFT B3LYP/6-311++G**
$O_2 – C_3 = O_1$	124.969	$O_2 = C_2 – O_1$	116.071
$C_1 – C_3 – O_2$	112.549	$C_1 – C_2 = O_2$	122.932
$C_1 – C_3 = O_1$	122.471	$C_1 – C_2 – O_1$	120.946
$H_1 – C_1 – N_1$	107.516	$H_1 – C_1 – N_1$	107.484
$N_1 – C_1 – C_3$	105.407	$N_1 – C_1 – C_2$	106.795
$H_1 – C_1 – C_3$	110.668	$H_1 – C_1 – C_2$	110.410
$C_2 – C_1 – C_3$	111.558	$C_3 – C_1 – C_2$	111.658
$C_2 – C_1 – N_1$	110.811	$C_3 – C_1 – N_1$	109.866
$H_7 – N_1 – H_3$	108.900	$H_7 – N_1 – H_5$	107.330
$H_2 – N_1 – H_3$	106.730	$H_6 – N_1 – H_5$	109.502
$H_7 – N_1 – C_1$	109.066	$H_7 – N_1 – C_1$	110.633
$H_3 – N_1 – C_1$	112.000	$H_5 – N_1 – C_1$	112.780
$H_2 – N_1 – C_1$	110.030	$H_6 – N_1 – C_1$	106.528
$H_4 – C_2 – H_5$	108.147	$H_4 – C_3 – H_3$	107.573
$H_5 – C_2 - C_1$	108.184	$H_4 – C_3 – C_1$	110.591
$H_4 – C_2 - C_1$	110.460	$H_3 – C_3 - C_1$	109.029
$H_6 – S_1 – C_2$	97.640	$H_2 – S_1 – C_3$	97.035
$S_1 – C_2 – H_5$	109.794	$S_1 – C_2 – H_3$	110.918
$S_1 – C_2 – H_4$	109.620	$S_1 – C_3 – H_4$	105.489
$S_1 – C_2 – C_1$	110.587	$S_1 – C_3 – C_1$	113.070
$C_2 – C_1 – H_1$	110.684	$C_3 – C_1 – H_1$	110.475
$H_7 – N_1 – H_2$	110.084	$H_6 – N_1 – H_7$	110.076
$C_3 – C_1 – N_1$	105.407	$C_2 – C_1 – N_1$	106.795
$N_2 – H_7..O_2$	102.289	$N_1 – H_2..O_1$	100.384

Table 4.7

Bond angles (degree) of CysAN optimized at HF/6-311+G (2d, 2p) and B3LYP/6-311++G levels of theory.**

PARAMETERS	Ab Initio HF/6-311+G (2d, 2p)	PARAMETERS	DFT B3LYP/6-311++G**
$C_1 – C_3 = O_2$	114.582	$C_1 – C_3 – O_2$	114.879
$C_1 – C_3 = O_1$	116.059	$C_1 – C_3 – O_1$	115.364
$H_1 – C_1 – N_1$	109.506	$H_1 – C_1 – N_1$	109.986
$H_1 – C_1 – C_3$	107.369	$H_1 – C_1 – C_3$	107.590
$C_1 – N_1 – H_2$	105.644	$C_1 – N_1 – H_2$	104.097
$C_1 – N_1 – H_6$	109.144	$C_1 – N_1 – H_3$	109.223
$H_6 – N_1 – H_2$	105.225	$H_3 – N_1 – H_2$	105.399
$C_2 – C_1 – C_3$	107.741	$C_2 – C_1 – C_3$	107.898
$C_2 – C_1 – N_1$	110.670	$C_2 – C_1 – N_1$	110.632
$C_3 – C_1 – N_1$	113.523	$C_3 – C_1 – N_1$	112.619
$C_2 – C_1 – H_1$	107.826	$C_2 – C_1 – H_1$	107.590
$H_3 – C_2 – C_1$	110.311	$H_4 – C_2 – C_1$	110.154
$H_4 – C_2 – C_1$	109.650	$H_5 – C_2 – C_1$	109.656
$H_4 – C_2 – H_3$	108.570	$H_4 – C_2 – H_5$	108.778
$S_1 – C_2 – C_1$	114.562	$S_1 – C_2 – C_1$	113.526
$S_1 – C_2 – H_4$	105.442	$S_1 – C_2 – H_5$	106.751
$S_1 – C_2 – H_3$	108.060	$S_1 – C_2 – H_4$	107.823
$H_5 - S_1 – C_2$	97.257	$H_6 - S_1 – C_2$	93.097
$C_1 – C_2 – H_3$	110.311	$C_1 – C_2 – H_4$	110.154
$C_1 – C_2 – H_4$	109.650	$C_1 – C_2 – H_5$	109.656
$O_2 = C_3 = O_1$	129.346	$O_1 - C_3 – O_2$	129.747
$N_1 – H_2..O_1$	113.035	$N_1 – H_2..O_1$	117.340

Table 4.8

Bond angles (degree) of CysCAT form optimized at HF/6-311+G (2d, 2p) and B3LYP/6-311++G levels of theory.**

PARAMETERS	Ab Initio HF/6-311+G (2d, 2p)	PARAMETERS	DFT B3LYP/6-311++G**
$O_1 = C_2 – O_2$	125.948	$O_1 = C_2 – O_2$	126.251
$C_1 – C_2 = O_1$	122.119	$C_1 – C_2 = O_1$	122.721
$C_1 – C_2 – O_2$	111.892	$C_1 – C_2 – O_2$	110.977
$C_2 – O_2 – H_7$	110.740	$C_2 – O_2 – H_7$	110.154
$H_3 – C_1 – N_1$	106.674	$H_3 – C_1 – N_1$	107.395
$C_3 – C_1 – C_2$	112.519	$C_3 – C_1 – C_2$	112.317
$C_1 – N_1 – H_1$	111.398	$C_1 – N_1 – H_1$	110.894
$C_1 – N_1 – H_2$	111.309	$C_1 – N_1 – H_2$	112.405
$C_1 – N_1 – H_8$	108.825	$C_1 – N_1 – H_8$	106.108
$H_1 – N_1 – H_2$	108.762	$H_1 – N_1 – H_2$	109.482
$H_1 – N_1 – H_8$	108.429	$H_1 – N_1 – H_8$	109.161
$H_2 – N_1 – H_8$	108.017	$H_2 – N_1 – H_8$	108.676
$H_5 – C_3 – H_6$	108.226	$H_5 – C_3 – H_6$	108.490
$H_5 – C_3 – C_1$	107.637	$H_5 – C_3 – C_1$	107.713
$H_6 – C_3 – C_1$	110.431	$H_6 – C_3 – C_1$	110.771
$S_1 – C_3 – H_5$	108.853	$S_1 – C_3 – H_5$	108.937
$S_1 – C_3 – H_6$	109.453	$S_1 – C_3 – H_6$	109.592
$S_1 – C_3 – C_1$	112.137	$S_1 – C_3 – C_1$	111.261
$H_4 – S_1 – C_3$	97.729	$H_4 – S_1 – C_3$	96.767
$C_3 – C_1 – H_3$	110.117	$C_3 – C_1 – H_3$	110.062
$H_3 – C_1 – C_2$	106.570	$H_3 – C_1 – C_2$	110.020
$N_1 – C_1 – C_2$	109.895	$N_1 – C_1 – C_2$	110.020
$N_1 – C_1 – H_3$	106.674	$N_1 – C_1 – H_3$	107.395
$C_3 – C_1 – N_1$	110.816	$C_3 – C_1 – N_1$	110.393
$N_1 – H_1 \ldots O_2$	100.958	$N_1 – H_1 \ldots O_2$	107.146
$O_2 – H_7 \ldots O_1$	70.988	$O_2 – H_7 \ldots O_1$	70.687

Table 4.9

Geometrical parameters of normal cysteine, CysZW, CysAN, CysCAT optimized at HF/6-311+G (2d, 2p) and B3LYP/6-311++G levels of theory.**

conformers	PARAMETERS AT Ab Initio HF/6-311+G (2d, 2p)					PARAMETERS AT DFT B3LYP/6-311++G**				
	Dipole moment (μ_D) (debye)	Energy (a.u)	Chemical potential (μ) (eV)	Chemical hardness (η) (eV)	Chemical softness (s) (eV)	Dipole moment (μ_D) (debye)	Energy (a.u)	Chemical potential (μ) (eV)	Chemical hardness (η) (eV)	Chemical softness (s) (eV)
Cysteine Normal	3.3644	-719.513	-0.2052	0.2054	2.2433	2.6521	-722.061	-0.1050	0.1050	4.7580
CysZW	4.5953	-719.227	-0.2235	0.2235	2.2363	5.3243	-721.726	-0.1127	0.1127	4.4357
CysAN	6.5447	-718.961	-0.1840	0.1840	2.7164	5.9558	-721.528	-0.0804	0.0804	6.2161
CysCAT	8.0438	-719.872	-0.2159	0.2159	2.3155	7.2016	-722.418	-0.1108	0.1108	4.5126

Table 4.10

Frequency mode of vibration of normal cysteine optimized at HF/6-311+G (2d, 2p) and B3LYP/6-311++G levels of theory.**

Ab Initio HF/6-311+G (2d, 2p)			DFT B3LYP/6-311++G**		
Frequency Cm^{-1}	**Parameters**	**Vibrations**	**Frequency Cm^{-1}**	**Parameters**	**Vibrations**
1361.57	$H_5 - C_3 - H_6$	twisting	825.41	$H_5 - C_3 - H_6$	rocking
1803.20	NH_2	scissoring	1486.20	$H_5 - C_3 - H_6$	scissoring
1983.92	$C = O_1$	stretching	1652.90	NH_2	scissoring
1983.92	$H_7 - O_2 - C_2$	scissoring	2672.52	$S_1 - H_4$	stretching
2858.66	$S_1 - H_4$	stretching	2912.10	$C_1 - H_3$	stretching
3082.26	$C_1 - H_3$	stretching	3066.68	$H_5 - C_3 - H_6$	symmetric stretching
3223.54	$H_6 - C_3 - H_5$	symmetric stretching	3142.89	$H_5 - C_3 - H_6$	asymmetric stretching
3762.90	NH_2	symmetric stretching	3525.82	NH_2	symmetric stretching
3844.88	NH_2	asymmetric stretching	3612.29	NH_2	asymmetric stretching
4118.95	$O_2 - H_7$	stretching	3759.21	$O_2 - H_7$	stretching

Table 4.11

Frequency mode of vibration of CysZW optimized at HF/6-311+G (2d, 2p) and B3LYP/6-311++G levels of theory.**

Ab Initio HF/6-311+G (2d, 2p)			DFT B3LYP/6-311++G**		
Frequency Cm^{-1}	**Parameters**	**Vibrations**	**Frequency Cm^{-1}**	**Parameters**	**Vibrations**
1379.94	$H_5 - C_2 - H_4$	twisting	732.67	$C_3 - S_1$	stretching
1652.40	NH_3	bending	1013.35	$N_1 - C_1$	stretching
1985.28	$C_3 = O_1$	stretching	1091.72	NH_3	scissoring
2852.24	$S_1 - H_6$	stretching	1216.62	$H_3 - C_3 - H_4$	twisting
3234.15	$H_5 - C_2 - H_4$	symmetric stretching	1483.88	NH_3	scissoring
3234.15	$C_1 - H_1$	stretching	1539.64	$C_1 - C_2$, $C_2 = O_2$	stretching
3294.11	$H_5 - C_2 - H_4$	asymmetric stretching	2657.57	$S_1 - H_2$	stretching
3579.36	NH_3	Symmetricstretching	3377.72	H_7 - $N_1 - H_5$	asymmetric stretching
3699.80	$H_3 - N_1 - H_2$, $H_2 - N_1 - H_7$	asymmetric, symmetric	3471.58	$N_1 - H_5$	asymmetric stretching

Table 4.12

Frequency mode of vibration of CysAN optimized at HF/6-311+G (2d, 2p) and B3LYP/6-311++G levels of theory.**

Ab Initio HF/6-311+G (2d, 2p)			DFT B3LYP/6-311++G**		
Frequency Cm^{-1}	**Parameters**	**Vibrations**	**Frequency Cm^{-1}**	**Parameters**	**Vibrations**
972.71	$C_1 – C_3$	stretching	805.35	$C_3 – C_1 – C_2$	stretching
1254.64	$H_4 – C_2 – H_3$	twisting	1255.57	$H_4 – C_2 – H_5$	wagging
1389.51	$H_6 – N_1 – H_2$	twisting	1317.72	$H_3 – N_1$ - H_2	rocking
1802.71	$H_6 – N_1 – H_2$	scissoring	1468.48	$H_5 – C_2 – H_4$	scissoring
2851.27	$S_1 – H_5$	stretching	1681.10	$O_2 – C_3 – O_1$, $H_3 – N_1$ - H_2	asymmetric, scissoring
3206.96	$C_1 – H_1$, $C_2 – H_3$	stretching	2620.52	S_1 - H_6	stretching
3221.30	$H_4 – C_2 – H_5$, $C_1 – H_1$	symmetric, stretching	3041.41	$H_4 – C_2 – H_5$	symmetric stretching
3286.04	$H_4 – C_2 – H_3$	asymmetric stretching	3131.04	$H_4 – C_2 – H_5$	asymmetric stretching
3712.18	$H_6 – N_1 – H_2$	symmetric stretching	3393.56	$H_3 – N_1$ - H_2	symmetric stretching
3784.90	$H_6 – N_1 – H_2$	asymmetric stretching	3538.53	$H_3 – N_1$ - H_2	asymmetric stretching

Table 4.13

Frequency mode of vibration of CysCAT optimized at HF/6-311+G (2d, 2p) and B3LYP/6-311++G levels of theory.**

Ab Initio HF/6-311+G (2d, 2p)			DFT B3LYP/6-311++G**		
Frequency Cm^{-1}	**Parameters**	**Vibrations**	**Frequency Cm^{-1}**	**Parameters**	**Vibrations**
852.39	$H_5 – C_3 – H_6$	rocking	790.00	$H_5 – C_3 – H_6$	rocking
1335.39	$H_5 – C_3 – H_6$	scissoring	1222.52	$H_5 – C_3 – H_6$	twisting
1651.65	NH_3	scissoring	1347.81	NH_3	wagging
2054.16	$C_2 = O_1$	stretching	1872.08	$C_2 = O_1$	stretching
2846.29	$S_1 – H_4$	stretching	2675.03	$S_1 – H_4$	stretching
3251.95	$H_5 – C_3 – H_6$	symmetric, stretching	3097.57	$H_5 – C_3 – H_6$	asymmetric stretching
3579.80	NH_3	symmetric, stretching	3134.66	$N_1 – H_8$	stretching
3682.82	NH_3	asymmetric stretching	3411.09	$H_1 – N_1 – H_2$	stretching
3727.88	$N_1 – H_2$	asymmetric stretching	3483.47	$H_1 – N_1 – H_2$	asymmetric stretching
4059.81	$O_2 – H_7$	stretching	3725.44	$H_7 – O_2$	stretching

SUMMARY AND CONCLUSION

CHAPTER V

SUMMARY AND CONCLUSION

The cysteine amino acid in normal, CysZW, CysAN and CysCAT forms were optimized at HF/6-311+G (2d, 2p) level of ab initio and B3LYP/6-311+G** level of Density functional theory level. The geometrical parameters such as bond length, bond angle, chemical hardness, chemical potential, chemical softness, energy, dipole moment and vibrational spectra of the optimized structures were calculated and compared with each other. By comparing all the values of geometrical parameters and chemical reactivity parameters of normal cysteine, CysZW, CysAN, and CysCAT, the minimum energy is obtained for CysCAT at both HF/6-311+ G (2d, 2p) and B3LYP/6-311++G** levels, so the structure of CysCAT is found to be more stable than others . Then the dipole moment of CysCAT is also high both at HF/6-311+ G (2d, 2p) and B3LYP/6-311++G**. The hardness signifies the resistance towards the deformation of electron cloud of chemical systems under small perturbation encountered during the chemical process. The chemical hardness observed at CysAN is high when compared to all other conformers both at HF/6-311+ G (2d, 2p) and B3LYP/6-311++G**. At both the level of theories, softness is found to be large when compared to hardness in anionic form. So the CysAN is highly plarizable. It is seen that the chemical potentials of normal cysteine, CysZW, CysAN and CysCAT at both HF/6-311+ G (2d, 2p) and B3LYP/6-311++G** levels of theory are negative and means that these structures are stable. These structures do not decompose spontaneously into the elements they are made up of. The chemical potential of CysAN is high when compared to all optimized structures of CysCAT,CYSZW and normal cysteine at both the level of HF/6-311+ G (2d, 2p) and B3LYP/6-311++G** theories. Then the calculated vibrational frequency shows that the optimized structures are in local minima without the imaginary frequencies.