

# Review Article: Understanding Intermolecular and Intramolecular Hydrogen Bonds: Spectroscopic and Computational Approaches

Humphrey Sam Samuel<sup>1,\*</sup>, Ugo Nweke-Maraizu<sup>2</sup>, Emmanuel E. Etim<sup>1</sup>

<sup>1</sup>Department of Chemical Sciences, Federal University Wukari, Taraba State, Nigeria

<sup>2</sup>Department of Chemistry, Rivers State University, Nkpolu-Oroworukwo, Port Harcourt, Nigeria



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## ABSTRACT

Hydrogen bonds between and within molecules are essential interactions that control how molecules behave in various chemical and biological systems. To better understand the complex nature of hydrogen bonding events, spectroscopic and computational methodologies were integrated in this abstract. Direct probing of the vibrational and electronic fingerprints linked to hydrogen bonds has been made possible by spectroscopic techniques, such as infrared and nuclear magnetic resonance spectroscopy, providing crucial details regarding bond strength, length, and dynamics. Molecular dynamics simulations and advanced computational techniques like density functional theory (DFT) have simultaneously produced a theoretical foundation for comprehending the energetics and geometry of hydrogen bonds. A thorough understanding of hydrogen bonding interactions in a variety of settings, including biomolecular systems, liquids, and solids, has been made possible by the synergistic interaction between experimental data and theoretical discoveries. The combined efforts of spectroscopic and computational research have revealed the relevance of hydrogen bonds in molecular recognition, reaction processes, and material properties, even though difficulties still exist in adequately simulating solvent effects and long-range interactions. This multidisciplinary approach continues to lead to discoveries as technology develops, providing a deeper understanding of hydrogen bonding and its ramifications across other scientific disciplines.



**Samuel Humphrey Sam:** He is a Bachelor's degree holder in Industrial Chemistry from the Federal University Wukari, Taraba State, Nigeria. His research area focuses on Physical and Computational Chemistry.

\*Corresponding Author: Emmanuel E. Etim ([emmaetim@gmail.com](mailto:emmaetim@gmail.com))



**Ugo Nweke-Maraizu:** She received her Ph.D Degree in Analytical Chemistry from the Ignatius Ajuru University of Education, Rumuolumeni, Port Harcourt, Rivers State, Nigeria. She is currently a Lecturer with the Rivers State University, Nkpolu-Oroworukwor, Port Harcourt, Nigeria. Her research focus is on Analytical, Environmental and Physical Chemistry.



**Emmanuel E. Etim:** He received his PhD in Physical Chemistry from the prestigious Indian Institute of Science Bangalore, India; and did his Postdoctoral studies at the Max Planck's Institute for Extraterrestrial Physics in Munich, Germany. He a faculty member in the Department of Chemical Sciences at the Federal University Wukari in Taraba State, Nigeria. He currently chairs the IUPAC Task Group saddled with the responsibility of "Redefining Proton Affinity for Molecules with Asymmetric Proton Binding Sites". His research work focuses in the areas of Physical Chemistry, Computational Chemistry, Astrochemistry/Molecular Astrophysics, Molecular Spectroscopy, Thermochemistry, etc.

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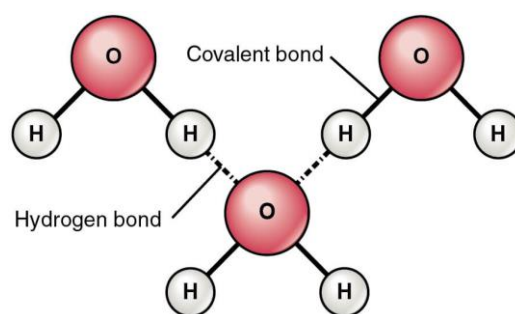
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## 1. Introduction

A wide range of chemical, physical, and biological processes depend heavily on non-covalent interactions, a class of intermolecular forces. Non-covalent interactions result from electrostatic, Van der Waals, and other weak forces, as opposed to covalent connections, which include the sharing of electrons between atoms. The stability of diverse molecular and supramolecular structures, molecular recognition, self-assembly, and protein folding depends on these interactions [1]. Many scientific fields, including chemistry, biochemistry, materials science, and medicine, depend on non-covalent interactions in one way or another. The basic forces that control molecular recognition, self-assembly, and stability in various systems are non-covalent interactions, we may say. The development and stability of molecular structures is made possible by a wide variety of their interactions, including electrostatic forces, Van der Waals forces, hydrophobic interactions, cation-interactions, halogen bonding, and hydrogen bonding [2]. When a hydrogen atom is bound to a strongly electronegative atom (such nitrogen, oxygen, or fluorine) and is drawn to another electronegative atom in a nearby molecule, this process is known as hydrogen bonding. Hydrogen bonds are essential for the structure and operation of biomolecules like DNA, proteins, and water, as shown in **Figure 1** because they are more powerful than conventional dipole-dipole interactions [3]. The stability of biomolecules like proteins and DNA,

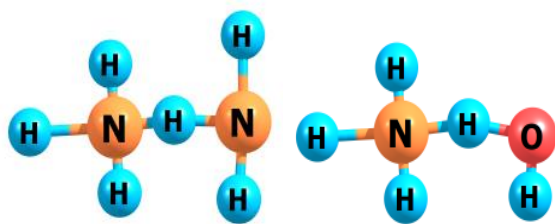
as well as the hydrogen bonding in water is displayed in **Figure 1** [4].

In a molecule, when a hydrogen atom is linked to a highly electronegative atom, it attracts the shared pair of electrons more, and so this end of the molecule becomes slightly negative while the other end becomes slightly positive. The negative end of one molecule attracts the positive end of the other, and as a result, a weak bond is formed between them. This bond is called the hydrogen bond [5]. As a result of hydrogen bonding, a hydrogen atom links the two electronegative atoms simultaneously, one by a covalent bond and the other by a hydrogen bond. The conditions for hydrogen bonding are as follows: the molecule should contain a highly electronegative atom linked to the hydrogen atom. With higher electronegativity, the polarization of the molecule increases and the size of the electronegative atom should be small. Indeed, the smaller the size, the greater the electrostatic attraction [6]. However, in many chemical, physical, and biological processes, hydrogen bonding is a particular



**Figure 1.** Hydrogen bond in water [4]

kind of non-covalent contact that is important. It happens when a hydrogen atom makes an electrostatic connection with another electronegative atom in a different molecule or within the same molecule after being covalently bound to an electronegative atom, such as nitrogen (N), oxygen (O), or fluorine (F) [7]. The strength of hydrogen bonds, which have a considerable impact on molecule structure, characteristics, and reactivity, is greater than that of conventional dipole-dipole interactions. Based on the chemical composition and configuration of the involved atoms, there are several forms of hydrogen bonding which include the intermolecular and intramolecular hydrogen bonding. Intermolecular and intramolecular hydrogen bonding are key phenomenon in chemistry and biology. It involves the attractive connection between a hydrogen atom and an electronegative atom (usually oxygen, nitrogen, or fluorine) in another molecule. It is essential to understand how various molecular systems, including liquids, solids, and biomolecules, are structured, stable, and reactive [8]. For disciplines like materials science, drug development, and catalysis to advance, an understanding of the nature and characteristics of intermolecular hydrogen bonding is crucial. In a material, different molecules form intermolecular hydrogen bonds. As long as hydrogen donors and acceptors are present and at places where they may interact with one another, they can happen between any numbers of similar or dissimilar molecules. For instance,  $\text{NH}_3$  molecules alone,  $\text{H}_2\text{O}$  molecules alone, or  $\text{NH}_3$  plus  $\text{H}_2\text{O}$  molecules can form intermolecular hydrogen bonds, as depicted in **Figure 2** [9].

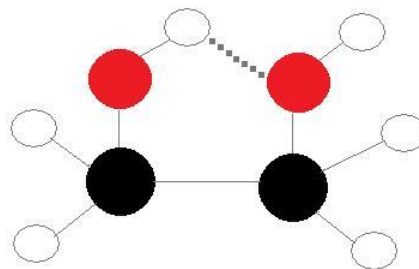


**Figure 2.** Intermolecular hydrogen bonding in  $\text{NH}_3$  and between  $\text{NH}_3$  and  $\text{H}_2\text{O}$  [9]

When a hydrogen atom concurrently establishes a hydrogen connection with one electronegative atom and another electronegative atom within the same molecule, it exhibits an interesting and significant phenomenon known as intramolecular hydrogen bonding [10]. The prevalence and importance of intramolecular hydrogen bonding are demonstrated by a number of instances. One example is the structure of 2,6-dihydroxybenzoic acid, where an intramolecular hydrogen bond is created as a result of intramolecular hydrogen bonding between the hydroxyl group and the carboxylic acid group. The stability and characteristics of the chemical are influenced by this hydrogen bonding. Another example of intramolecular hydrogen bonding occurs in ethylene glycol ( $\text{C}_2\text{H}_4(\text{OH})_2$ ) between its two hydroxyl groups due to the molecular geometry, as shown in **Figure 3** [11].

The creation of hydrogen bonds within a molecule, or intramolecular hydrogen bonding, is an intriguing phenomenon with important consequences for molecular structure, conformation, and characteristics. How intramolecular hydrogen bonding affects molecule behaviour and interactions requires a thorough comprehension of this phenomenon. The nature and dynamics of intramolecular hydrogen bonding have been studied and clarified with the use of experimental and computational methods [12].

Understanding the presence, strength, and shape of hydrogen bonding inside molecules is made possible through experimental methods. Hydrogen bonding interactions have frequently been studied using spectroscopic techniques including nuclear magnetic resonance (NMR) and infrared (IR) spectroscopy. The



**Figure 3.** Intramolecular hydrogen bonding in ethylene glycol molecule [11]

determination of bond strengths and lengths is made possible by the information about vibrational frequencies and intensities associated with hydrogen bonding that is provided by IR spectroscopy. On the other hand, NMR spectroscopy may provide light on chemical shifts and coupling constants, offering details on the dynamics and geometries of hydrogen bonds [13]. To understand intramolecular and intermolecular hydrogen bonding, computational methods have become essential tools. Details regarding the electronic structure, energetics, and kind of hydrogen bonding interactions are revealed by quantum mechanical simulations. In addition to the charge distribution and electron density related to these interactions, these simulations help clarify the strength, directionality, and stability of hydrogen bonds [14]. Another computer technique, molecular dynamics simulations, allow for the analysis of the dynamic behaviour and adaptability of intermolecular and intramolecular hydrogen bonding. Molecular dynamics simulations can shed light on the function of hydrogen bonding in conformational changes, molecular recognition, and solvent effects by modelling the mobility and interactions of atoms over time [15]. Furthermore, computational methods have the benefit of examining a variety of molecular systems and circumstances, offering a theoretical framework to explain and support experimental findings. A thorough knowledge of intermolecular and intramolecular hydrogen bonding is made possible by the combination of experimental data with computational models, which opens up new perspectives on the underlying ideas and behaviours of these interactions [16-17]. The aim of this article is to explore the experimental and computational methods in intermolecular and intramolecular hydrogen bonding. The objective is to examine key procedures and techniques utilized in experimental research, including NMR spectroscopy, and IR spectroscopy. We will also explore the computational approaches used to study the intermolecular and intramolecular hydrogen bonding, such as quantum

mechanical calculations and molecular dynamics simulations, demonstrating their capacity to offer insightful knowledge about the structure and dynamics of these interactions.

## 2. Intramolecular Hydrogen Bonding

### 2.1. Structural effects of intramolecular hydrogen bonding

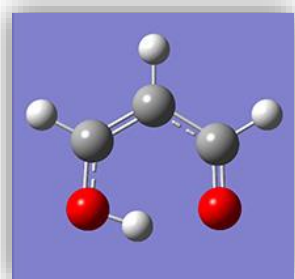
The structure, geometry, and preferred conformational states of the molecules are all significantly influenced by intramolecular hydrogen bonds [18]. The structural effects of intramolecular hydrogen bonding along with its impact on molecular shape and geometry and its function in maintaining molecular conformations are discussed as follow:

#### A. Influence on molecular shape and geometry

*i. Bent and linear intramolecular hydrogen bonds:* There are two basic geometries for intramolecular hydrogen bonds: bent and linear. The hydrogen atom, together with the other two atoms participating in the interaction, creates a non-linear configuration in a bent hydrogen bond. This frequently happens when the hydrogen bond giver and acceptor atoms in the molecule are close to one another, resulting in an angular or curved configuration [19]. For instance, the hydrogen link between the hydroxyl hydrogen and the carbonyl oxygen in malonaldehyde ( $C_3H_4O_2$ ) results in a twisted hydrogen bond [20].

The steric interactions between the two oxygen atoms are what cause this bent shape, as demonstrated in **Figure 4**. On the other hand, a linear hydrogen bond happens when the hydrogen atom and the two bonding atoms are all positioned in a straight line. When the atoms that form a hydrogen bond are arranged in a straight line, this geometry is visible. The hydroxyl group creates a hydrogen connection with the carbonyl oxygen in the -hydroxy carboxylic acids, resulting in a linear arrangement. This is an example of a linear intramolecular hydrogen bond [21].



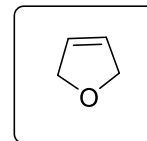


**Figure 4.** Hydrogen linkage in malonaldehyde [20]

ii. *Effects on torsional and bond angles:* Within a molecule, intramolecular hydrogen bonding can have a considerable impact on torsional and bond angles. Due to electrostatic repulsion or steric obstruction between the hydrogen atom and the surrounding atoms, the existence of a hydrogen bond might result in variations from the predicted bond angles [22]. For instance, in acetic acid, the hydroxyl hydrogen and carbonyl oxygen form intramolecular hydrogen bonds that result in a greater bond angle than would be predicted for a conventional  $sp^3$  hybridized carbon. Furthermore, torsional angles may be constrained by intramolecular hydrogen bonding, which restricts rotation around certain molecules links. This limitation is seen in situations when intramolecular hydrogen bonding affects the preferred conformation. For instance, in  $\beta$ -diketones, the presence of an intramolecular hydrogen bond can fix the torsional angle [23].

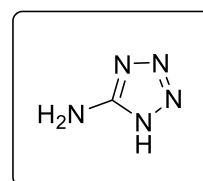
### B. Molecular conformation stabilization

i. *Role of intramolecular hydrogen bonding in ring creation:* The creation and stability of cyclic structures in organic compounds is greatly aided by intramolecular hydrogen bonding [24]. A molecule's hydrogen bonding can strengthen its cyclic structure and lessen ring strain. For example, in 2, 5-dihydrofuran, as shown in **Figure 5**, the hydroxyl hydrogen and the oxygen atom in the furan ring form an intramolecular hydrogen bond that aids in stabilizing the cyclic structure.



**Figure 5.** Structure of 2,5-dihydrofuran [24]

The preferred shape of cyclic compounds can also be determined by intramolecular hydrogen bonding. In essence, the hydrogen bonds "lock" the molecule into a certain conformation, causing stable rings with clearly defined geometries to develop [25-26]. This is shown in cyclic compounds like 5-aminotetrazole in **Figure 6**, where the cyclic structure is stabilized and the geometry is affected by intramolecular hydrogen bonding.



**Figure 6.** Structure of 5-aminotetrazole [27]

ii. *Impact on molecular stiffness and flexibility:* The stiffness and flexibility of a molecule can be dramatically influenced by intramolecular hydrogen bonding. Hydrogen bond formation can limit molecular mobility and lessen the flexibility of the molecule's conformation. This constraint becomes clear when inflexible cyclic structures or bulky groups are involved in intramolecular hydrogen bonding [28].

### 2.2. Experimental techniques for characterizing intramolecular hydrogen bonding

#### 2.3. Spectroscopic methods

##### 2.3.1. Infrared spectroscopy

Infrared spectroscopy is a potent experimental method that is frequently used to describe intramolecular hydrogen bonding [29]. It offers insightful information on the existence, potency, and shape of hydrogen bonds inside molecules. The fundamentals of IR spectroscopy will be covered in this part, along with how it may be used to examine intramolecular hydrogen bonds.

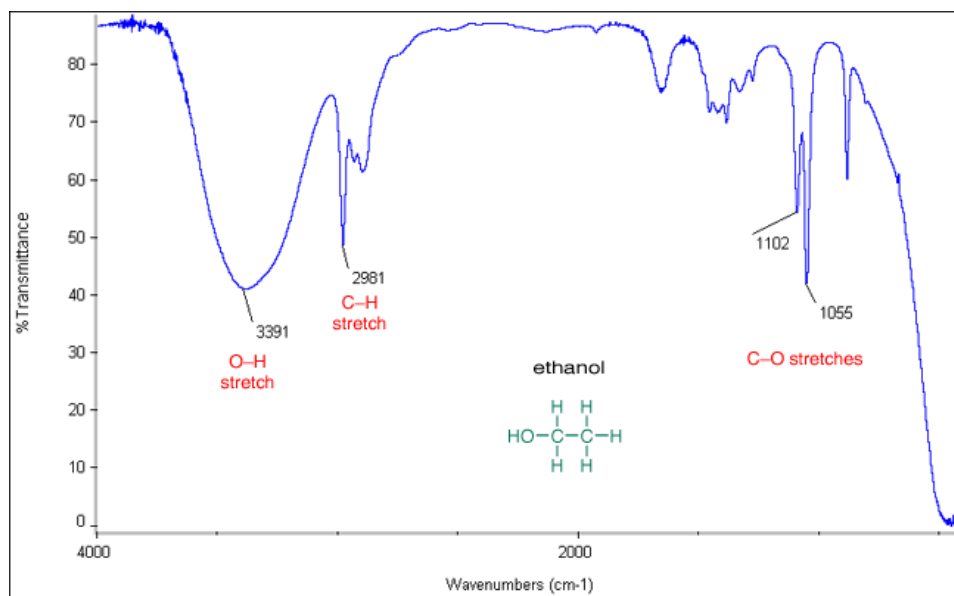


Figure 7. IR spectra of ethanol [32]

### Utilizing IR spectroscopy to analyse intramolecular hydrogen bonding

**1. Identification of hydrogen bonded functional groups:** The identification of functional groups involved in intramolecular hydrogen bonding is possible through the use of IR spectroscopy. The vibrational frequencies of the relevant functional groups can change when a hydrogen bond is present [30-31]. In general, the IR spectrum alters in a distinctive way as a result of hydrogen bonding involving the OH, NH, or CH groups. For instance, in alcohols, the O-H stretching band can expand and move to lower wave numbers due to intramolecular hydrogen bonding between the hydroxyl group and an electronegative atom, as illustrated in **Figure 7**. This change is a sign that a hydrogen bond is forming [32].

A similar shift in the amide I and amide II bands in the IR spectra can happen because of intramolecular hydrogen bonding involving the amide group in peptides and proteins [33-34].

**2. Hydrogen bond distance and strength determination:** IR spectroscopy may reveal details about the distance and strength of hydrogen bonds within a molecule. The strength of the bond may be determined by the intensity of the absorption band corresponding

to the hydrogen bond. Higher absorption intensities are seen for stronger hydrogen bonds [35]. Furthermore, information on the geometry and distance of the hydrogen bond may be gleaned from the position and shape of the absorption band. The bond strength may be connected to the wave number at which the absorption takes place, and the width of the absorption band can reveal details about the length and degree of hydrogen bond cooperativity [36].

**3. Examining the impact of environment and solvents:** IR spectroscopy is helpful in determining how solvents and other environmental elements affect intramolecular hydrogen bonding. By changing the polarity and hydrogen bond accepting capacity of the medium, the solvent can modify the strength and shape of the hydrogen bond [37]. It is feasible to spot variations in the hydrogen bonding behaviour by contrasting the IR spectra of a molecule in various solvents or environmental settings. By competing with the molecule to generate intermolecular hydrogen bonds, protic solvents, for example, can break intramolecular hydrogen bonds, shifting the IR absorption bands linked to the hydrogen bond [38].

**4. Intramolecular hydrogen bond structural analysis:** Infrared spectroscopy and isotopic

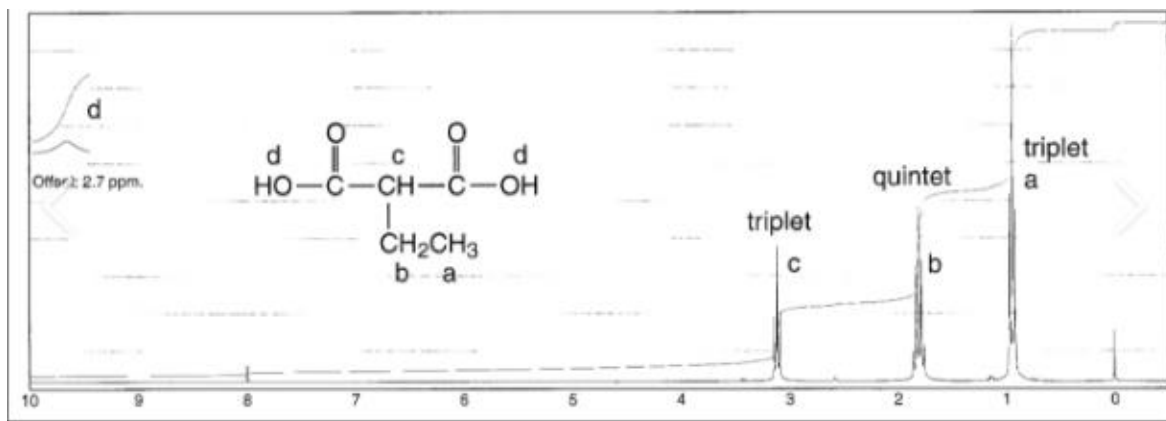
labelling can give precise structural details regarding intramolecular hydrogen bonds. It is possible to discriminate between the stretching and bending vibrations of the hydrogen bond and other vibrational modes by substituting one or both of the hydrogen atoms in the hydrogen bond with deuterium. Isotopic labelling can provide light on the particular atoms participating in the hydrogen bond and assist distinguish intramolecular hydrogen bonding from other weak interactions. The geometry, lengths, and angles related to the hydrogen bond inside the molecule may all be determined using this method [39]. Infrared spectroscopy is a flexible method for describing intramolecular hydrogen bonding. It makes it possible to recognize hydrogen-bonded functional groups, ascertain the geometry and strength of hydrogen bonds, investigate the effects of solvents and the environment, and perform structural analyses of intramolecular hydrogen bonds [40]. IR spectroscopy aids to a greater knowledge of the behaviour and characteristics of molecules with intramolecular hydrogen bonding by offering insightful information on these features [41].

### 2.3.2. NMR spectroscopy

The strong experimental method of Nuclear Magnetic Resonance (NMR) spectroscopy is utilized to describe intramolecular hydrogen bonding. The detection and characterisation of hydrogen bonding interactions are made possible by the useful information that NMR

spectroscopy offers about the chemical environment of hydrogen atoms within molecules. The use of proton chemical shift variations as markers of hydrogen bonding and the calculation of intramolecular hydrogen bond lengths and angles will be covered in this section's discussion of how NMR spectroscopy is used to research intramolecular hydrogen bonding [42-43].

i. *Proton chemical shift changes as hydrogen bonding indicators:* In NMR spectroscopy, protons' chemical shifts in a molecule provide details about their local electronic surroundings. The intensity and existence of intramolecular hydrogen bonding may be determined by changes in the chemical shifts of the protons participating in the hydrogen bond induced by hydrogen bonding interactions [44]. A downfield shift of the proton's resonance frequency is frequently caused by hydrogen bonding, which raises the chemical shift value. This downfield shift happens as a result of the hydrogen bond's de-shielding action, which lowers the electron density surrounding the hydrogen atom. The distance between the hydrogen bond donor and acceptor and the bond's strength are two variables that affect how much downfield shift occurs. For example, the hydrogen linked hydroxyl proton in carboxylic acids undergoes a downfield shift as a result of the de-shielding action produced by the nearby carbonyl oxygen atom, as shown in **Figure 8** [45].



**Figure 8.** NMR spectra of carboxylic acid [45]



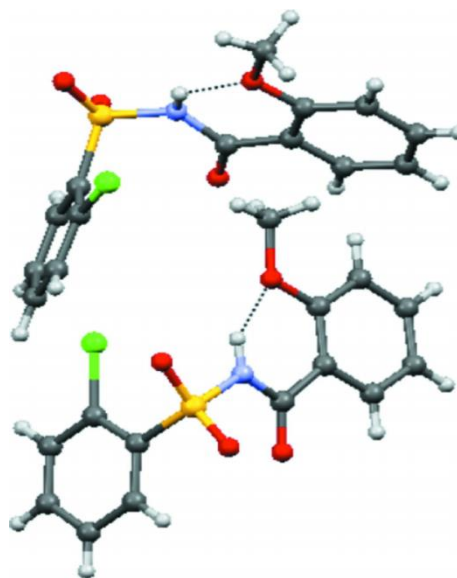
i. *Shielding effects on proton shifts*: In certain circumstances, intramolecular hydrogen bonding can have a shielding impact on the resonance frequency of the proton, resulting in a lower chemical shift value. When a hydrogen bond creates a closed ring or cyclic structure, it alters the electron distribution inside the molecule and causes the shielding effect. Cyclic chemicals like 5-aminotetrazole serve as an illustration of a shielding effect. The chemical shifts of the protons engaged in the hydrogen bond are protected by the existence of intramolecular hydrogen bonding in the cyclic structure [48].

ii. *Determination of intramolecular hydrogen bond distance and angle*: The lengths and angles related to intramolecular hydrogen bonding can also be determined by NMR spectroscopy [46]. It is possible to ascertain the spatial configurations and closeness of the hydrogen atoms engaged in the hydrogen bond by examining the J-coupling constants between them [47]. The spin-spin interactions between linked nuclei in a molecule give rise to scalar couplings, sometimes referred to as J-couplings. The dihedral angles between the linked nuclei have an impact on the magnitude of J-coupling, which may be calculated from the splitting patterns seen in the NMR spectra [48]. Scalar couplings can shed light on the torsional angles and conformations related to the hydrogen bond in the context of intramolecular hydrogen bonding. It is feasible to ascertain the relative orientations and separations between the hydrogen atoms engaged in the hydrogen bond by measuring the J-couplings between them [49].

iii. *NOE effects*: Another NMR phenomenon that may be used to examine intramolecular hydrogen bonding is the Nuclear Overhauser Effect (NOE). NOE is a phenomenon that results from dipolar interactions between nuclear spins and is characterized by an increase in the

signal strength of one nucleus (for example, the proton implicated in the hydrogen bond) when another nucleus (for example, the hydrogen bond acceptor) is present nearby. It is feasible to ascertain the separations and spatial configurations between the hydrogen atoms engaged in the hydrogen bond by monitoring the NOE effects between them [50].

Along with these approaches, 2D NMR techniques like Nuclear Overhauser Effect Spectroscopy (NOESY) and Rotating-frame Overhauser Effect Spectroscopy (ROESY) can provide more details regarding the connectivity and spatial closeness of hydrogen atoms engaged in  $N-H\cdots O$  in intramolecular hydrogen bonding, as demonstrated in **Figure 9**.



**Figure 9.** Formation of intramolecular  $N-H\cdots O$  hydrogen bonds [50]

#### 2.4. Computational approaches for characterizing intramolecular hydrogen bonding

To fully understand intramolecular hydrogen bonding, computational approaches are essential. They offer important new perspectives on the dynamics, energetics, and structural preferences of these interactions [51]. To simulate intramolecular hydrogen bond dynamics and forecast conformational preferences driven by hydrogen bonding, this section will address molecular dynamics

simulations as a computational tool for researching intramolecular hydrogen bonding.

#### 2.4.1. Molecular dynamics simulations

Computing techniques called molecular dynamics (MD) simulations are used to examine how atoms and molecules move and behave over time. MD simulations may offer precise information regarding the dynamic behaviour, energetics, and conformational preferences of molecules with intramolecular hydrogen bonding by solving the equations of motion for a system of interacting particles [52]. MD simulations are particularly useful for studying the dynamics of intramolecular hydrogen bonding. These simulations can shed light on how hydrogen bonds change, develop, and are broken inside molecules. MD simulations can capture the transient character of hydrogen bonding and highlight the kinetics and thermodynamics involved with hydrogen bond dynamics by following the locations and interactions of atoms across time [53]. With the use of MD simulations, it is possible to examine the impact of variables like temperature, solvent effects, and molecular flexibility on the longevity and stability of intramolecular hydrogen bonds. They can also provide insight into how hydrogen bonds play a part in conformational changes, such as shifts between various hydrogen-bonded conformations [54]. MD simulations may be used to study and predict the conformational preferences of molecules affected by intramolecular hydrogen bonding. MD simulations give information on the stable conformations taken by a molecule and the impact of hydrogen bonding on these conformations by modelling the mobility and interactions of atoms [55]. MD simulations can assist in identifying the preferred conformations connected to intramolecular hydrogen bonding by determining the relative populations and energy of various hydrogen-bonded conformations. These details help explain how hydrogen bonds affect molecule structure, stability, and reactivity [56]. In addition, to overcome energy barriers and more effectively explore the conformational space, additional sampling approaches including improved sampling methods (such

replica exchange molecular dynamics and meta-dynamics) can be used in MD simulations. A more complete picture of the conformational preferences driven by intramolecular hydrogen bonding may be obtained using these approaches, which allow the sampling of uncommon or high-energy conformations [57]. To acquire more precise and thorough information regarding the electronic structure, energetics, and nature of intramolecular hydrogen bonding, MD simulations can be further integrated with quantum mechanical calculations. These hybrid methods, referred to as quantum mechanics/molecular mechanics (QM/MM) simulations, provide a more precise description of the intramolecular hydrogen bond while taking the surrounding molecular environment into account [58].

#### 2.4.2. Quantum mechanical calculations

It is possible to examine intramolecular hydrogen bonding using quantum mechanical computations, which are computational techniques based on the ideas of quantum mechanics. In-depth knowledge regarding the electronic structure, energetics, and characteristics of molecules having hydrogen bonds is provided by these calculations [59].

*i. Assessment of intramolecular hydrogen bond energies and properties:* Quantum mechanical computations are incredibly helpful for determining the tensile strength and stability of intramolecular hydrogen bonds. These computations can identify the electronic energy associated with the hydrogen bond and reveal information about the kind and intensity of the interaction by solving the Schrödinger equation for the target molecule. The bond dissociation energy (BDE) and interaction energy of hydrogen bonds, for instance, may be determined by quantum mechanical calculations [60]. The interaction energy indicates the total intensity of the hydrogen bond interaction, whereas the BDE shows the energy needed to break the hydrogen bond.

*ii. Visualization of electron density distribution in intramolecular hydrogen bonding:* Electron density distribution in hydrogen bonds may be seen visually thanks to calculations made using

quantum mechanics, which is crucial for describing and comprehending the nature of these bonds. The distribution of electrons within a molecule is reflected in the electron density, which also sheds light on the geometry and strength of the hydrogen bond [61].

To observe the distribution of electron densities close to the hydrogen bond, electron density maps can be created through quantum mechanical computations. These maps make it possible to locate areas with high electron densities that are connected to the hydrogen bond. The kind of the hydrogen bond, such as whether it is covalent or electrostatic, may be identified by looking at the electron density distribution [62].

### 2.5. Advancements in characterizing intramolecular hydrogen bonding

Through various experimental and computational methodologies, intramolecular hydrogen bonding has become better understood. Some of the significant recent developments will be covered in this section.

i. *High-resolution structural methods*: The determination of high-resolution structures of molecules and materials with intramolecular hydrogen bonding has been made possible by improvements in X-ray crystallography and neutron diffraction methods. These methods offer thorough details on hydrogen bond lengths, angles, and the general configuration of molecules in the crystal lattice [63]. Understanding the function of intramolecular hydrogen bonds in crystal packing, polymorphism, and material characteristics is made easier by high-resolution structural data [64].

ii. *Ultrafast spectroscopy*: Ultrafast spectroscopic methods have become effective instruments for describing the dynamics of intramolecular hydrogen bonds. Examples include femtosecond transient absorption spectroscopy and 2D-IR spectroscopy. These methods shed light on the elapsed periods and routes for the production and rupture of

hydrogen bonds as well as the interactions between hydrogen bonding and other molecular movements [65]. A thorough knowledge of temporal characteristics of intramolecular hydrogen bonding is possible because to ultrafast spectroscopy, which enables the investigation of hydrogen bond dynamics in real-time [66].

iii. *Theoretical models and concepts*: New theoretical models and ideas have helped us grasp how intramolecular hydrogen bonds function. Refined ideas include the nature of hydrogen bonding, which includes its electrostatic and covalent components, and the function of cooperative effects in hydrogen bond networks [67]. Deeper understanding of the contributions of various interactions to intramolecular hydrogen bonding has come through the development of innovative theoretical models, such as energy decomposition analysis and electrostatic potential analysis [68-69].

iv. *Imaging Methods*: New imaging methods, including as atomic force microscopy (AFM) and scanning tunnelling microscopy (STM), have made it possible to see intramolecular hydrogen bonds in their natural state at the nanoscale. In self-assembled monolayer and supramolecular structures, these methods give spatially detailed information about the arrangement and organization of molecules [70]. Imaging methods provide insightful information on the structure-property relationships controlled by intramolecular hydrogen bonds [71].

High-resolution structural approaches, ultrafast spectroscopy, developments in NMR spectroscopy, computational methods, theoretical models, and imaging methods have all contributed to the improvement of intramolecular hydrogen bonding characterization [72-73]. These discoveries have deepened our understanding of the nature, dynamics, and characteristics of intramolecular hydrogen bonding, advancing our knowledge of its applications across a range of scientific disciplines and aiding the creation of useful molecules and materials [74].

### 3. Intermolecular Hydrogen Bonding

#### 3.1. Characteristics of intermolecular hydrogen bonding

When compared to other non-covalent interactions, intermolecular hydrogen bonding stands out due to a number of distinctive features. These traits are crucial in determining material qualities, regulating different biological and chemical processes, and sculpting molecular structures. Let's go through the features of intermolecular hydrogen bonding in detail:

##### 1. Strength and directionality

**Strength:** Compared to the other non-covalent interactions like dipole-dipole or Van der Waals forces, intermolecular hydrogen bonds are often more powerful. The electronegativity difference between the hydrogen-bond donor and acceptor, the separation between the interacting atoms, and the existence of extra stabilizing elements are few examples of the variables that affect the strength of a hydrogen bond. The strength of hydrogen bonding typically ranges from 5 to 30 kJ/mol [75].

Intermolecular hydrogen bonding has a high degree of directionality. The hydrogen atom serves as a link between the acceptor atom in one molecule and the electronegative atom it is connected to (hydrogen bond donor) [76]. As a result, the atoms participating in the hydrogen bond are arranged in a linear or nearly linear pattern. Electrostatic interactions and orbital alignment produce unique molecular configurations and geometries in condensed phases, which determine the directionality [77].

##### 2. Electrostatic nature

Hydrogen bonding is essentially an electrical connection, according to electrostatic attraction. The electronegative atom of another molecule (the hydrogen bond acceptor), which has a partial negative charge, and the hydrogen atom, which has a partial positive charge, join forces to create a weak link. Due to the acceptor's and hydrogen's different electronegativities, there is an electrostatic attraction. The hydrogen atom in an intermolecular hydrogen bond has a partial positive charge, whereas the acceptor atom has a partial negative charge. The dipole-dipole interaction caused by this charge separation

adds to the hydrogen bond's strength and directionality [78].

##### 3. Specificity and selectivity

The creation of intermolecular hydrogen bonds shows selectivity. Not all electronegative atoms can function as acceptors, and not all atoms with hydrogen atoms can form hydrogen bonds. The most frequent hydrogen bond acceptors are typically oxygen, nitrogen, and fluorine atoms, whereas hydrogen atoms attached to oxygen or nitrogen atoms act as donors [79]. The availability of suitable hydrogen bond donors and acceptors with adequate geometries and electrical characteristics determines the selectivity. The atom geometries and configurations engaged in hydrogen bonding are likewise particular. The formation and strength of hydrogen bonds are governed by the presence of certain functional groups and the relative orientations of hydrogen bond donors and acceptors. This specificity is essential for molecular recognition processes including DNA base pairing and protein-ligand binding.

##### 4. Molecular structure

Molecular structure is influenced by effects on conformation; hydrogen bonds have a substantial impact on the molecular structure and conformation of molecules. When hydrogen bonds are present, they can control how atoms and groups are arranged around the donor and acceptor, resulting in certain molecular conformations. For instance, in proteins, the secondary structural components (alpha helices and beta sheets) are determined by hydrogen bonding between amino acid residues [80].

Furthermore, by serving as internal structural pillars, hydrogen bonds provide molecular structures their stability. They support the general stability of the molecule by balancing the repelling forces between charged or polar groups. In substances like ice or certain crystals, hydrogen bonding networks offer stability and have an impact on their physical and chemical characteristics.

##### 5. Effects of solvents

Hydrogen bonding affects how molecules behave in solvents, which is known as solvent-solvent interactions. Extensive hydrogen



bonding networks that occur in protic solvents like water give rise to special features including high boiling temperatures, surface tension, and heat capacity. Compound solubility is further impacted by hydrogen bonding because interactions with solvent molecules and solvation depend on the strength and availability of hydrogen bonds.

### 6. Lifetime and dynamics

Hydrogen bonding between molecules is dynamic and fleeting in nature. They can quickly develop and break, having lifetimes between picoseconds to nanoseconds. Proton transfer processes and conformational changes are only two examples of how the dynamics of hydrogen bonds affect the general reactivity and behaviour of molecules. Hydrogen bonds are dynamic, which enables molecular structures to adjust and respond to environmental changes.

Temperature, pressure, solvent environment, and adjacent molecule interactions are only a few examples of the variables that affect the stability and longevity of hydrogen bonds. Longer lives and higher stability are associated with stronger and more favourable hydrogen bond interactions [81].

### 3.2. Experimental techniques for characterizing intermolecular hydrogen bonding

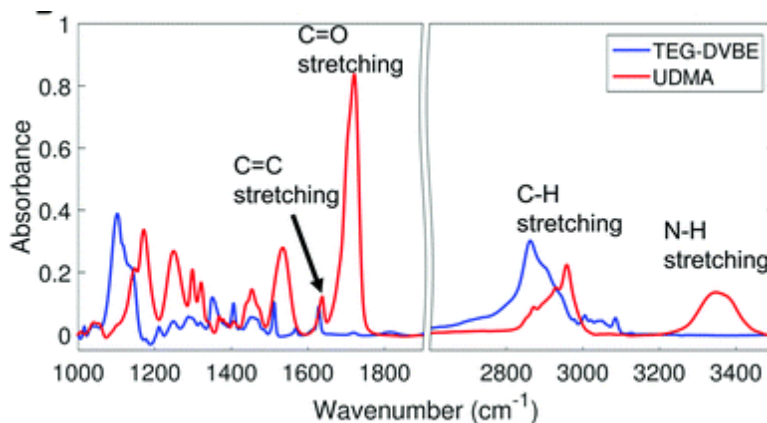
#### 3.3. Spectroscopic methods

##### 3.3.1. Infrared spectroscopy

A potent experimental method often employed to describe intermolecular hydrogen bonding is

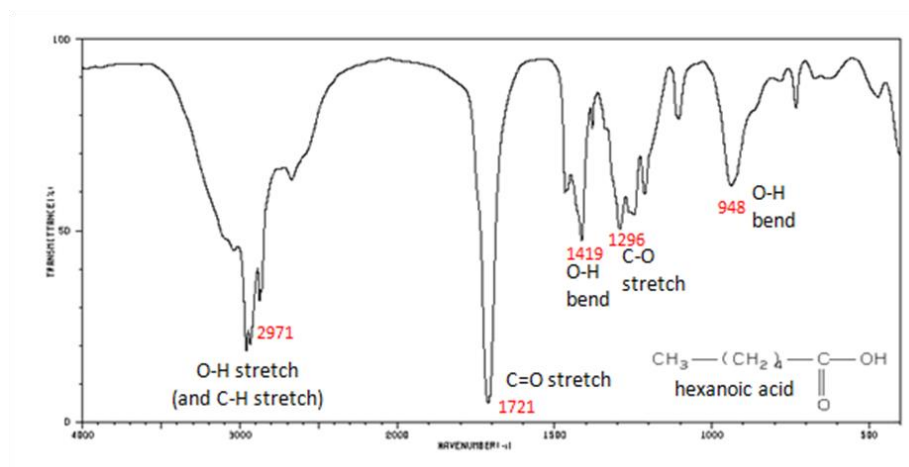
infrared (IR) spectroscopy. It offers important details regarding the presence, strength, and characteristics of hydrogen bonds in many systems. Based on how infrared radiation interacts with molecular vibrations, IR spectroscopy, the distinctive absorption bands seen in the IR spectrum may be linked to hydrogen bond stretching and bending vibrations. Here, accompanied by pertinent examples, we will go into great detail on how IR spectroscopy is used to characterize intermolecular hydrogen bonding:

*i. Identification of hydrogen bonding:* The presence of hydrogen bonds in a molecule or system may be determined via IR spectroscopy. In hydrogen bonds, the stretching vibrations of the hydrogen atoms take place at specified frequencies, usually between 1500 and 3500  $\text{cm}^{-1}$ . Hydrogen bonds are present in this area, as shown by the distinctive broad and strong absorption bands. For instance, the O-H stretching vibration of liquid water exhibits a large absorption band at around 3400  $\text{cm}^{-1}$  in the infrared spectrum, which is related to the creation of vast hydrogen bonding networks. Another example is analysing multiple hydrogen bonds in mixtures of two monomers: urethane dimethacrylate (UDMA) and triethylene glycol-divinylbenzyl ether (TEG-DVBE). The carbonyl stretching band in infrared (IR) absorption spectra is deconvoluted into free and hydrogen-bonded carbonyl group, as shown in **Figure 10** [82].



**Figure 10.** Infrared (IR) spectra of the two studied monomers [82]





**Figure 11.** Infrared spectrum of hexanoic acid [83]

*ii. Strength and length of hydrogen bonds:* IR spectroscopy can shed light on the strength and length of hydrogen bonds. According to the strength of the hydrogen bond and the length of the link between the hydrogen donor and acceptor atoms, the location and intensity of the absorption bands in the IR spectrum are connected. In the IR spectrum, stronger hydrogen bonds often have greater wavenumbers ( $\text{cm}^{-1}$ ) than weaker ones. The frequency shifts and intensity changes can be used to evaluate how the strength of the hydrogen bond will alter when the molecular environment or interactions change. For instance, changes in the O-H stretching band location in the IR spectra of various carboxylic acid samples correspond to variations in the hydrogen bond strength and the electrical environment of the hydroxyl group, as indicated in **Figure 11** [83].

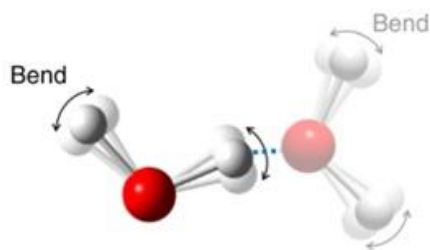
*iii. Dynamics and lifespan of hydrogen bonds:* IR spectroscopy in conjunction with time-resolved methods can provide light on the dynamics and lifespan of hydrogen bonds. One may examine the dynamics of bond creation and breakdown by observing the time-dependent changes in IR absorption bands linked to hydrogen bonds. For instance, time-resolved IR spectroscopy has been applied to study solvent dynamics, proton transfer, and hydrogen bond formation kinetics in acid-base processes [84].

*iv. Intermolecular interactions and solvent effects:* IR spectroscopy can examine how solvents and intermolecular interactions affect

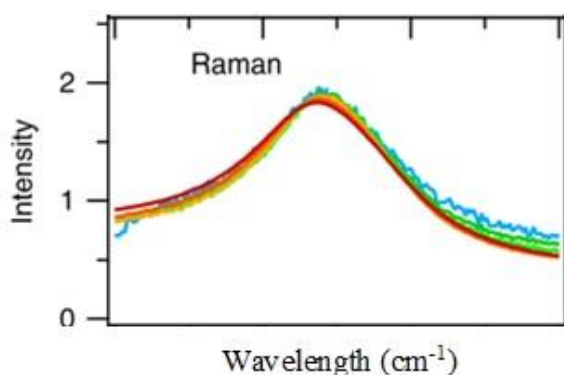
hydrogen bonding. Solvents can influence the strength and characteristics of hydrogen bonds, shifting or altering the intensities of absorption bands [85].

### 3.3.2. Raman spectroscopy

The characterisation of intermolecular hydrogen bonding can be greatly aided by the use of potent experimental method known as Raman spectroscopy. It is based on the Raman scattering, an inelastic scattering of light that happens when molecules go through vibrational transitions. Hydrogen bond strengths, geometries, dynamics, and the impact of hydrogen bonding on molecular structures may all be studied using Raman spectroscopy [86]. Here, using pertinent examples, we will go into great detail on how Raman spectroscopy is used to characterize intermolecular hydrogen bonding: Raman spectroscopy enables the investigation of the vibrational modes connected to hydrogen bonding. Because hydrogen atoms are involved in the production of intermolecular hydrogen bonds, distinctive shifts, and changes in the Raman spectrum can be seen. Hydrogen bond strength and existence may be determined by the unique Raman bands produced by the stretching and bending vibrations of hydrogen bonds. For instance, the O-H bending vibrational coupling shown in **Figures 12** and **Figures 13**, which are controlled by hydrogen bonding, are visible in the Raman spectrum of water and exhibit unique characteristics [87].



**Figure 12.** intermolecular O-H bend-bend coupling [87]



**Figure 13.** Raman spectra of H<sub>2</sub>O molecules [88]

Raman spectroscopy can provide light on the power of hydrogen bonds. It is possible to connect the hydrogen bond's strength with the intensity of the Raman bands linked to its vibrations. Raman bands are often more intense for stronger hydrogen bonds [89]. One may evaluate the relative strength of hydrogen bonding in various systems or environments by contrasting the intensity of hydrogen bond-related Raman peaks. Raman spectroscopy in conjunction with time-resolved methods allows for the investigation of hydrogen bonding kinetics. One may look at the kinetics of hydrogen bond formation and breaking by keeping an eye on the time-dependent changes in Raman spectra. Proton transfer and hydrogen bond rearrangements' dynamics have been studied using time-resolved Raman spectroscopy [90].

Raman spectroscopy sheds light on how solvents and intermolecular interactions affect hydrogen bonding. Solvent environments can vary or move the hydrogen bonding-related Raman bands by affecting the strength and other characteristics of hydrogen bonds [91]. To better understand the cooperative effects

and intermolecular interactions involved, Raman spectroscopy may also be used to investigate the interactions between hydrogen bonds and other functional groups in a molecule. Raman spectroscopy enables the quantitative study of hydrogen bond strengths by employing well-established calibration techniques. Hydrogen bond energies or strengths can be attributed to the intensity ratios of Raman peaks connected to hydrogen bonding [92-94].

Intermolecular hydrogen bonding may be studied using Raman spectroscopy. It enables the detection and measurement of hydrogen bonds by giving insights into vibrational modes related to hydrogen bonding [95]. Raman spectroscopy has the ability to measure the strength of hydrogen bonds, probe kinetics, and investigate the role of solvents and intermolecular interactions. Due to its adaptability and sensitivity, it may be used with various systems, including biological and nanoscale materials as well as liquids and solids. Raman spectroscopy can help scientists better comprehend intermolecular hydrogen bonds, advancing the study of many different scientific disciplines like biology, materials science, and chemistry [96].

### 3.3.3. X-ray crystallography

An effective experimental method frequently employed to describe intermolecular hydrogen bonds is X-ray crystallography. By examining the diffraction patterns of X-rays dispersed by a crystalline substance, it offers high-resolution structural data. The accurate measurement of molecular geometries and arrangements made possible by X-ray crystallography makes it possible to examine intermolecular interactions, particularly hydrogen bonds, in great detail [97]. Here, accompanied by pertinent examples, we will go into great detail on how X-ray crystallography is used to characterize intermolecular hydrogen bonding:

*i. Visualization of hydrogen bond geometries:* Hydrogen bond geometries may be directly seen via X-ray crystallography. Researchers can precisely calculate the angles and distances between the donor and acceptor atoms in a hydrogen bond by examining the crystal structure. This knowledge sheds light on the

direction and power of hydrogen bonding. For example, X-ray crystallography has shown that hydrogen bonds in DNA base pairs are extremely directed, with particular hydrogen bond geometries dictating the pairing of nucleotide bases [98].

*ii. Identification of hydrogen bond networks:* The identification of vast hydrogen bond networks within a crystal is made possible by X-ray crystallography. Researchers can determine the locations and connectivity of hydrogen bonds inside the crystal lattice by examining the crystal structure. The cooperative effects and long-range ordering of hydrogen bonding interactions are revealed by this data. In proteins, for instance, where hydrogen bonds are essential for maintaining protein structures, X-ray crystallography has proved helpful in revealing the complicated hydrogen bond networks.

*iii. Characterization of hydrogen bond strength:* By examining bond lengths and corresponding interatomic distances, X-ray crystallography can shed light on the strength of hydrogen bonds. Stronger hydrogen bonds are often correlated with shorter hydrogen bond lengths. Further enhancing hydrogen bonding is the existence of other stabilizing elements like charge delocalization or aromaticity. Based on structural factors, X-ray crystallography enables the quantitative evaluation of hydrogen bond strengths [99].

*iv. Hydrogen bonding in crystals and solvation effects:* X-ray crystallography helps clarify how solvation affects hydrogen bonding in crystals. Researchers can examine how changing solvent conditions impact the formation and strength of hydrogen bonds by comparing crystal structures produced under various solvent conditions. This knowledge sheds light on solvent-solute interactions and the function of solvation in regulating intermolecular interactions [100].

### 3.4. Computational Approaches for Characterizing Intermolecular Hydrogen Bonding

#### 3.4.1. Molecular dynamics simulations

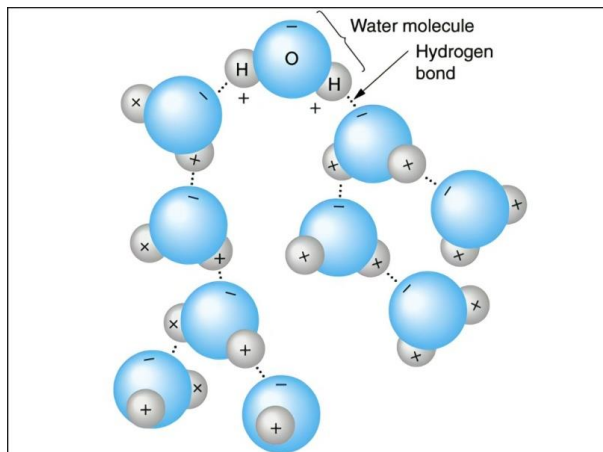
Intermolecular hydrogen bonding may now be studied computationally using molecular

dynamics (MD) simulations. To understand the dynamics, energetics, and characteristics of intermolecular interactions, particularly hydrogen bonding, researchers use MD simulations to model the mobility and behaviour of atoms and molecules across time [101]. The use of MD simulations to characterize intermolecular hydrogen bonding will be covered in-depth here, with examples that are pertinent.

*i. Exploration of Hydrogen Bond Dynamics:* By revealing atomistic details of bond formation, breaking, and fluctuations, MD simulations make it possible to explore hydrogen bond dynamics. Researchers can explore the lifetimes, frequency, and stability of hydrogen bonds using simulations. For instance, MD simulations have been used to study the dynamics of hydrogen bonds in water, showing how they form and break on a picoseconds time scale. Another example is dynamic intermolecular interactions through hydrogen bonding of water promote heat conduction [102].

*ii. Quantification of Hydrogen Bond Properties:* MD simulations can offer numerical insights into the characteristics of hydrogen bonds. Bond lengths, strengths, and orientations may be calculated by analysing the energy, angles, and distances involved in hydrogen bonding interactions. For example, MD simulations have been used to determine the hydrogen bond energies in protein-ligand complexes, revealing information on the stability and binding affinity of the structures [103].

*iii. Hydrogen Bond Network Analysis:* MD simulations make it possible to investigate intricate hydrogen bond networks in molecular systems. Researchers can recognize and examine the connectivity and cooperation of hydrogen bonding interactions by modelling huge ensembles of molecules. This knowledge may demonstrate how hydrogen bond networks affect the structural and dynamic characteristics of materials [39-40]. For instance, MD simulations have been used to examine the hydrogen bond network in ice and reveal how it affects the formation and stability of ice crystals, as shown in **Figure 14** [104].



**Figure 14.** Schematic diagram of hydrogen bond network in ice [104]

iv. *Hydrogen bond lifetime prediction:* By predicting the lifetimes of hydrogen bonds, MD simulations can shed light on the resilience and endurance of these interactions. Researchers can gather information on hydrogen bond durations and analyse their influence on environmental conditions by modelling chemical systems over extended timeframes [105]. Understanding the kinetics and thermodynamics of hydrogen bond creation and breaking benefits from knowing this fact. For instance, the hydrogen bond durations in liquid water under various situations have been predicted using MD simulations [106].

### 3.4.2. Quantum mechanical calculations

Intermolecular hydrogen bonding is frequently studied using quantum mechanical simulations, which offer important insights into the electronic structure, energetics, and characteristics of these interactions [107]. Quantum mechanical calculations may precisely predict and characterize the behaviour of molecules at the atomic and subatomic level by resolving the Schrödinger equation. Here, we will go into great detail on how quantum mechanical calculations may be used to describe intermolecular hydrogen bonding.

#### A. Electronic structures and energy

i. *Orbital interactions:* Calculations based on quantum mechanics make it possible to analyse the orbital interactions that are a part of intermolecular hydrogen bonding. These

computations investigate the overlap and energy matching of molecular orbitals to shed light on the creation and maintenance of hydrogen bonds. The interaction between the donor and acceptor molecular orbitals controls the hydrogen bond's type and strength [108].

ii. *Energy constituents:* The energy of a hydrogen bond may be broken down into several components using quantum mechanical techniques [109]. The many energy contributions, such as electrostatic interactions, polarization effects, dispersion forces, and charge transfer effects, may all be quantified using this methodology. It is possible to gain a thorough understanding of the stability and characteristics of hydrogen bonding interactions by understanding these energy components [110].

#### B. Geometric and binding energies

i. *Geometric parameters:* Bond lengths, angles, and orientations of hydrogen bonds are correctly predicted and optimized by quantum mechanical computations. To determine the strength and directionality of the contact, these computations offer exact information about the positioning and alignment of the atoms participating in the hydrogen bond [107].

ii. *Binding energies:* Quantum mechanical computations may determine the hydrogen bonds' binding energies, giving information about the force of the connection. The stability and thermodynamics of the hydrogen bond may be calculated using the energy difference between the bound and separated states. The relative potency of various hydrogen bonding interactions may be determined using this information [98].

#### C. Predictive capabilities and rational design:

Quantum mechanical computations are essential for the rational design of materials with appropriate hydrogen bonding characteristics. These computations support the selection and optimization of molecules for particular applications, such as catalysis, drug creation, and materials research, by assessing the electronic structure and energetic [97].



Quantum mechanical calculations have the capacity to forecast, which enables scientists to evaluate the stability, characteristics, and behaviour of hydrogen bonding in various chemical system [23]. These simulations shed light on the impacts of environmental variables, cooperative effects, and structural alterations on hydrogen bonding. Quantum mechanical calculations' predictive nature assists in the interpretation of experimental findings and directs the design of new experiments [24].

### *3.5. Advancements in characterizing intermolecular hydrogen bonding*

A fuller knowledge of the characteristics, dynamics, and practical uses of intermolecular hydrogen bonding has been made possible by recent developments in the field. Here are a few significant developments in this area: The study of intermolecular hydrogen bonding dynamics on extremely brief timescales has been transformed by ultrafast spectroscopy methods. Researchers may examine the ultrafast vibrational and structural dynamics of hydrogen bonds using time-resolved infrared spectroscopy and two-dimensional infrared spectroscopy. These methods have provided insights into the kinetics and mechanics of hydrogen bonding by exposing transient hydrogen bond creation and breaking events.

Direct observation and control of individual hydrogen bonds are now possible because to single-molecule manipulation techniques like atomic force microscopy (AFM) and scanning tunnelling microscopy (STM). These methods offer thorough information on the mechanical, stability, and strength characteristics of single hydrogen bonds. Hydrogen bonding plays an important part in molecular recognition, self-assembly, and mechanical characteristics of materials, according to single-molecule research [25].

The accuracy and predictive capability of researching intermolecular hydrogen bonding have improved thanks to developments in computer approaches, notably in quantum mechanics calculations and molecular dynamics simulations. Hydrogen bond energies, geometries, and spectroscopic characteristics may all be precisely predicted by high-level *ab initio* quantum mechanical computations [34].

The ability to simulate complicated systems, such as biomolecules and materials, is made possible by improved force fields and hybrid quantum mechanics/molecular mechanics (QM/MM) techniques.

Intermolecular hydrogen bonding has been investigated in the context of nanomaterials with the purpose of designing and building useful nanoscale structures. Researchers have shown how to manipulate hydrogen bonding interactions to provide desirable qualities including improved conductivity, mechanical strength, and selective adsorption in nanoparticle assemblies, nanowires, and supramolecular networks [27].

The significance of intermolecular hydrogen bonding in energy storage and conversion should be understood if energy storage and conversion technologies are to advance. Researchers have looked at how materials used in batteries, fuel cells, and hydrogen storage devices behave in relation to hydrogen bonding. In energy-related materials, modifying hydrogen bonding interactions can enhance stability, ionic conductivity, and charge transport characteristics [28].

## **4. Applications and Implications of Intermolecular and Intramolecular Hydrogen Bonding**

Intermolecular hydrogen bonding has numerous applications in different scientific fields. Intermolecular hydrogen bonding is essential for the creation of materials with certain features, according to materials science and engineering. Researchers can develop materials with improved mechanical strength, stability, and solubility by taking use of hydrogen bonding interactions [29]. For instance, in polymer science, the formation of hydrogen bonds between polymer chains can increase the tensile strength and endurance of materials. Hydrogen bonds may be used to govern the assembly, stability, and functioning of self-assembled materials such supramolecular structures and nanomaterials [22]. Hydrogen bonding is essential to the development of pharmaceutical molecules and the study of drug discovery. In drug-receptor interactions, hydrogen bonding is crucial because some hydrogen bond networks can



improve binding affinity and shape complementarity. Hydrogen bonding interactions are often modified throughout the rational drug design process to increase medicinal potency and minimize negative effects [18].

Intermolecular hydrogen bonding, which enables particular interactions between molecules, is the basis of molecular recognition processes, according to supramolecular chemistry. Hydrogen bonding is involved in the recognition and binding of molecules in biological and chemical systems, from host-guest interactions to enzyme-substrate binding. Hydrogen bonding is utilized in supramolecular chemistry to produce functional assemblies with regulated structure and reactivity. Hydrogen bonding ability to be selective and reversible makes it possible to create molecular receptors, sensors, and catalysts. Intermolecular hydrogen bonding has a critical role in both crystal engineering and solid-state chemistry. To produce crystals with the necessary qualities, hydrogen bond networks should be carefully planned and managed. Crystal packing, polymorphism, and the physical characteristics of materials are all influenced by hydrogen bonds [32]. Melting temperatures, boiling points, and phase transitions are only a few examples of the thermal characteristics influenced by hydrogen bonding in materials. The thermal stability and behaviour of liquids and solids can be dramatically impacted by the existence of dense hydrogen bonding networks [33]. The viscosity and surface tension of liquids are both influenced by hydrogen bonding. Processes like capillary action and wetting are impacted by the cohesive forces coming from hydrogen bonding interactions on the flow behaviour and sticky qualities of liquids. Intermolecular hydrogen bonding, which happens between molecules as opposed to within a single molecule, has several uses and ramifications in a variety of scientific disciplines. Some of the most significant uses and effects of intermolecular hydrogen bonding will be discussed as follow:

### *1. Solvent properties*

Intermolecular hydrogen bonding is a key factor in solvent characteristics. Due to the existence of intermolecular hydrogen bonds, hydrogen bonding solvents including water, alcohols, and amines display particular properties [34]. These solvents can withstand more heat, have higher boiling temperatures, and are better able to dissolve polar compounds. In disciplines including chemistry, biology, and material science, intermolecular hydrogen bonding capacity to promote solvation and boost solubility has significant ramifications [29].

### *2. Crystal properties*

One of the main processes in the development of crystal formations is intermolecular hydrogen bonding. In solid-state materials, it frequently determines how molecules are packed and arranged. Hydrogen bonds' directed character and strength enable the development of complex crystal structures with particular lattice configurations and intermolecular interactions. Understanding crystal packing, polymorphism, and the physical characteristics of materials requires a thorough understanding of the intermolecular hydrogen bonds that make up crystal structures [36].

### *3. Drug Design and Molecular Recognition*

Drug design and molecular recognition frequently take advantage of intermolecular hydrogen bonding. Many medications use interactions with intermolecular hydrogen bonds to affect their target molecules. Designing medications with high affinity and selectivity requires an understanding of the unique hydrogen bonding interactions between pharmaceuticals and their targets. Similar to how protein-ligand interactions and enzyme-substrate interactions include intermolecular hydrogen bonds; molecular recognition processes involve these bonds [94].

#### 4. Engineering and Material characteristics

Intermolecular hydrogen bonding has a significant impact on material characteristics. It has an impact on other physical attributes such as thermal stability and mechanical strength. Intermolecular hydrogen bonding, for instance, contributes to the special mechanical characteristics of natural fibres like silk and cellulose. The creation of innovative materials with enhanced capabilities for a variety of applications, including textiles, coatings, and biomaterials, can be facilitated by an understanding of and ability to manipulate intermolecular hydrogen bonding in materials [23, 24].

#### 5. Drug delivery

The knowledge of drug solubility and drug delivery mechanisms depends on intermolecular hydrogen bonding. The solubility and bioavailability of a medicine are influenced by the drug's molecule's capacity to create intermolecular hydrogen bonds with the solvent or carrier molecule [23-25]. Drug delivery systems' controlled release and drug stability can both be affected by intermolecular hydrogen bonds.

#### 5. Conclusion

Through spectroscopic and computational methods, the study of intermolecular and intramolecular hydrogen bonds has shed light on the complex nature of molecular interactions and given priceless insights into the behaviour of diverse substances in both gaseous and condensed phases. A deeper knowledge of hydrogen bonding events has been made possible by the interaction of advanced computational tools like density functional theory (DFT) and molecular dynamics simulations with experimental techniques like infrared and NMR spectroscopy. Through the use of spectroscopic techniques, scientists have been able to directly examine the vibrational and electronic signatures connected to hydrogen bonds, providing important details on the dynamics, length, and strength of the bonds. With the help of these methods, complex hydrogen bonding networks in biomolecules, liquids, and solids have been characterised,

shedding light on the significance of hydrogen bonds in influencing the characteristics and behaviours of molecules. The energetics and geometry of hydrogen bonding can now be understood theoretically thanks to quantum mechanical computations on the computing front. Researchers have been able to predict and rationalise hydrogen bonding interactions by DFT calculations and ab initio techniques, building a link between experimental results and theoretical understanding.

By capturing the dynamic nature of hydrogen bonds over time scales that are sometimes inaccessible to experiments, molecular dynamics simulations have furthered our understanding of this phenomenon. Combining spectroscopic and computational methods has produced a thorough understanding of hydrogen bonding that has aided in the development of new materials, the investigation of reaction mechanisms, and drug discovery. The representation of solvents, quantum effects, and long-range interactions, in particular, remains challenging. Future research projects promise to provide deeper insights into the nuances of hydrogen bonding and its numerous consequences in chemistry and biology as technology and methodology continue to advance.

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#### Orcid:

Humphrey Sam Samuel

<https://orcid.org/0009-0001-7480-4234>

Emmanuel E. Etim

<https://orcid.org/0000-0001-8304-9771>

#### References

- [1]. P. Vishwamittar, R. Batra, Chopra, *Molecular Communication*, **2023**, *28*, 33–53. [Crossref], [Publisher]
- [2]. A.E. Reed, L.A. Curtiss, F. Weinhold, Intermolecular interactions from a natural bond orbital, donor-acceptor viewpoint,

- Chemical Reviews*, **1988**, *88*, 899–926. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [3]. T. Clark, T. Brinck, The conversation on non-covalent interactions: an introduction, *Journal of Molecular Modeling*, **2022**, *28*, 272. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [4]. O. Yamauchi, Noncovalent interactions in biocomplexes, *Journal of Physical Sciences Reviews*, **2016**, *1*, 1-25. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [5]. G.A. Jeffrey, W. Saenger, The role of hydrogen bonding in the structure and function of the nucleic acids, *Hydrogen Bonding in Biological Structures*, Springer, **1994**, Berlin, Heidelberg, 394-422. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [6]. M.E. Khan, C.E. Elum, A.O. Ijeomah, P.J. Ameji, I.G. Osigbemhe, E.E. Etim, J.V. Anyam, A. Abel, C.T. Agber, Isolation, characterization, antimicrobial and theoretical investigation of some bioactive compounds obtained from the bulbs of calotropisprocera, *Journal of Nigerian Society of Physical Sciences*, **2023**, *5*, 1576. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [7]. R. Chang, General chemistry: The essential concepts. 3rd ed. New York: Mcgraw Hill, **2003**. [[Crossref](#)], [[Publisher](#)]
- [8]. E.E. Etim, Benchmark studies on the isomerization enthalpies for interstellar molecular species, *Journal of Nigerian Society of Physical Sciences*, **2023**, *5*, 527. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [9]. W.D. Kumler, The effect of the hydrogen bond on the dielectric constants and boiling points of organic liquids, *Journal of the American Chemical Society*, **1935**, *57*, 600-605. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [10]. S. Scheiner, Intramolecular hydrogen bonding 2017, *Molecules*, **2017**, *22*, 1521. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [11]. J.S. Murray, M.C. Concha, P. Lane, P. Hobza, P. Politzer, Blue shifts vs red shifts in sigma-hole bonding, *Journal of Molecular Modeling*, **2008**, *14*, 699-704. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [12]. a) J.S. Murray, P. Lane, T. Clark, K.E. Riley, P. Politzer,  $\Sigma$ -holes,  $\pi$ -holes and electrostatically-driven interactions, *Journal of Molecular Modeling*, **2012**, *18*, 541-548. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)] b) Shinggu, J., Etim, E. E., & Onen, A. (2023). Isotopic Effects on the Structure and Spectroscopy of Thioformaldehyde, Dihydrogen and Water. *Advanced Journal of Chemistry*, Section A, (*0*), 366-379.
- [13]. I.S. Ryu *et al.*, Stoichiometric analysis of competing intermolecular hydrogen bonds using infrared spectroscopy, *RSC Advances*, **2018**, *8*, 23481-23488. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [14]. B.N. Sunil *et al.*, Influence of inter- and intramolecular H-bonding on the mesomorphic and photoswitching behaviour of (*E*)-4-((4-(hexyloxy)phenyl)diazenyl)-*N*-phenyl benzamides. *RSC Advances*, **2020**, *10*, 20222-20230. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [15]. E. Oladimeji, E.E. Etim, M. Ojo, The thermodynamic properties of interstellar isomers with 3 atoms, *Advances in Space Research*, **2022**, *70*, 3745-3749. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [16]. C.C. Yu, K.Y. Chiang, M. Okuno *et al.*, Vibrational couplings and energy transfer pathways of water's bending mode, *Nature Communications*, **2020**, *11*, 5977. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [17]. C.B. Marble, X. Xu, G.I. Petrov, D. Wang, V.V. Yakovlev, New insights into a hydrogen bond: hyper-Raman spectroscopy of DMSO-water solution, *Physical Chemistry Chemical Physics*, **2021**, *23*, 23369-23376. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [18]. a) B.A. Kolesov, Hydrogen bonds: Raman spectroscopic study, *International Journal of Molecular Sciences*, **2021**, *22*, 5380. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)] b) A. Bozorgian, Investigation of Clathrate-like hydrates in the gas phase, *Journal of Engineering in Industrial Research*, **2021**, *2*, 90-94. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]

- [19]. T.W.N. Bieze, J.R.C. van derMaarel, J.C. Leyte, The intramolecular OH bond length of water in a concentrated poly(ethyleneoxide) solution. An NMR relaxation study, *Chemical Physics Letters*, **1993**, *216*, 56–62 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [20]. P. Larouche, J.-J. Max, C. Chapados, Isotope effects in liquid water by infrared spectroscopy. II. Factor analysis of the temperature effect on H<sub>2</sub>O and D<sub>2</sub>O, *The Journal of Chemical Physics*, **2008**, *129*, 064503. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [21]. Q. Hu, H. Zhao, S. Ouyang, Understanding water structure from Raman spectra of isotopic substitution H<sub>2</sub>O/D<sub>2</sub>O up to 573 K, *Physical Chemistry Chemical Physics*, **2017**, *19*, 21540–21547. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [22]. H. Ito, T. Hasegawa, Y. Tanimura, Effects of intermolecular charge transfer in liquid water on raman spectra, *The Journal of Physical Chemistry Letters*, **2016**, *7*, 4147-4151. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [23]. T. Begušić, G.A. Blake, Two-dimensional infrared-Raman spectroscopy as a probe of water's tetrahedrality, *Nature Communications*, **2023**, *14*, 1950. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [24]. T. Hasegawa, Y. Tanimura, A polarizable water model for intramolecular and intermolecular vibrational spectroscopies, *The Journal of Physical Chemistry B*, **2011**, *115*, 5545–5553. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [25]. H. Torii, R. Ukawa. Role of intermolecular charge fluxes in the hydrogen-bond-induced frequency shifts of the OH stretching mode of water, *The Journal of Physical Chemistry B*, **2021**, *125*, 1468-1475. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [26]. E.S. Feldblum, , I.T. Arkin, Strength of a bifurcated H bond, *Proceedings of the National Academy of Sciences of the United States of America*, **2014**, *111*, 4085-4090. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [27]. L.A. Malaspina, A. Genoni, D. Jayatilaka, M.J. Turner, K. Sugimoto, E. Nishibori, S. Grabowsky, The advanced treatment of hydrogen bonding in quantum crystallography, *Journal of Applied Crystallography*, **2021**, *54*, 1019-1034. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [28]. S. Aitipamula, V.R. Vangala, X-ray crystallography and its role in understanding the physicochemical properties of pharmaceutical cocrystals, *Journal of the Indian Institute of Science*, **2017**, *97*, 227-243. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [29]. M. Woińska, S. Grabowsky, P.M. Dominiak, K. Woźniak, D. Jayatilaka, Hydrogen atoms can be located accurately and precisely by x-ray crystallography, *Science Advances*, **2016**, *2*, e1600192. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [30]. J.-Y. Jo, H. Ito, Y. Tanimura, Full molecular dynamics simulations of liquid water and carbon tetrachloride for twodimensional Raman spectroscopy in the frequency domain, *Chemical Physics*, **2016**, *481*, 245-249. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [31]. B.A. Kolesov, Raman investigation of H<sub>2</sub>O molecule and hydroxyl groups in the channels of hemimorphite, *American Mineralogist*, **2006**, *91*, 1355-1362. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [32]. J. Zhou, S. Lin, H. Zeng, J. Liu, B. Li, Y. Xu, X. Zhao, G. Chen, Dynamic intermolecular interactions through hydrogen bonding of water promote heat conduction in hydrogels, *Materials Horizons*, **2020**, *7*, 2929-2936. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [33]. M. Wohler, T. Benselfelt, L. Wågberg, I. Furó, L.A. Berglund, J. Wohler, Cellulose and the role of hydrogen bonds: not in charge of everything, *Cellulose*, **2022**, *29*, 1-23. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]



- [34]. N. Kaur, N. Agnihotri, R. Agnihotri, R.K. Sharma, A treatise on spectrophotometric determination techniques of Palladium (II) ions, *Journal of Chemical Reviews*, **2022**, *4*, 81-99. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [35]. E.E. Etim, J.E. Asuquo, A.T. Atoshi, O.C. Ngana, Kinetic studies of biosorption of Cr<sup>2+</sup> and Cd<sup>2+</sup> ions using tea leaves (*Camellia Sinensis*) as adsorbent, *Journal of Chemical Society of Nigeria*, **2022**, *47*, 75-85. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [36]. J. Zhang *et al.*, Intermolecular hydrogen bonding strategy to fabricate mechanically strong hydrogels with high elasticity and fatigue resistance, *Soft Matter*, **2013**, *9*, 27, 6254-6261. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [37]. M.D. Mohammadi, H.Y. Abdullah, H. Louis, E.E. Etim, H.O. Edet, O.C. Godfrey, Hexachlorobenzene (HCB) adsorption onto the surfaces of C60, C59Si, and C59Ge: Insight from DFT, QTAIM, and NCI, *Chemical Physics Impact*, **2023**, *6*, 100234. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [38]. J.S. Murray, P. Lane, T. Clark, P. Politzer,  $\sigma$ -hole bonding: molecules containing group VI atoms, *Journal of molecular modeling*, **2007**, *13*, 1033-1038. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [39]. C. Trujillo, I. Alkorta, J. Elguero, G. Sánchez-Sanz, Cooperative effects in weak interactions: Enhancement of tetrel bonds by intramolecular hydrogen bonds, *Molecules*, **2019**, *24*, 308. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [40]. L. Mammìno, Intramolecular hydrogen bonding and conformational preferences of arzanol-An antioxidant acylphloroglucinol, *Molecules*, **2017**, *22*, 1294. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [41]. M.E. Khan, E.E. Etim, A.A. Anyam, I.G. Osigbemhe, C.J. Agber, Computational studies on Emodin (C<sub>15</sub>H<sub>10</sub>O<sub>5</sub>) from Methanolextract of *Pteridium aquilinum* leaves, *Journal of the Nigerian Society of Physical Sciences*, **2021**, *3*, 360-384. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [42]. M. Sil, P. Gorai, A. Das, B. Bhat, E.E. Etim, S.K. Chakrabarti, Chemical modeling for predicting the abundances of certain aldimines and amines in hot cores, *The Astrophysical Journal*, **2018**, *853*, 139. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [43]. S. Mejía, J.M. Hernández-Pérez, J. Sandoval-Lira, F. Sartillo-Piscil, Looking inside the intramolecular C-H...O hydrogen bond in lactams derived from  $\alpha$ -methylbenzylamine. *Molecules*, **2017**, *22*, 361. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [44]. P.A. Kollman, L.C. Allen, The theory of the hydrogen bond, *Chemical Reviews*, **1972**, *72*, 283-303. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [45]. P. Schuster, G. Zundel, C. Sandorfy, *The Hydrogen bond. recent developments in theory and experiments*; North-Holland Publishing Co.: Amsterdam, Netherlands, **1976**. [[Google Scholar](#)], [[Publisher](#)]
- [46]. S.J. Grabowski, Hydrogen bond and other Lewis Acid-Lewis Base interactions as preliminary stages of chemical reactions, *Molecules*, **2020**, *25*, 4668. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [47]. R. Wysokiński, W. Zierkiewicz, M. Michalczyk, T. Maris, S. Scheiner, The role of hydrogen bonds in interactions between [PdCl<sub>4</sub>]<sup>2-</sup>dianions in crystal, *Molecules*, **2022**, *27*, 2144. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [48]. G. Buemi, F.J. Zuccarello, Is the intramolecular hydrogen bond energy valuable from internal rotational barriers?, *Journal of Molecular Structure*, **2002**, *581*, 71-85. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [49]. V. Bertolasi, P. Gilli, V. Ferretti, G. Gilli, Evidence for resonance-assisted hydrogen bonding. 2. Intercorrelation between crystal structure and spectroscopic parameters in eight intramolecularly hydrogen bonded 1,3-diaryl-1,3-propanedione enols, *Journal of the American*



- Chemical Society*, **1991**, *113*, 4017–4925. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [50]. M.M. Nolasco, P.J.A. Ribeiro-Claro, C–H...O hydrogen bonds in cyclohexenone reveal the spectroscopic behavior of  $Csp^3$ -H and  $Csp^2$ -H donors, *ChemPhysChem*, **2005**, *6*, 496–502. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [51]. L. Sobczyk, S.J. Grabowski, T.M. Krygowski, Interrelation between H-bond and Pi-electron delocalization, *Chemical Reviews*, **2005**, *105*, 3513–3560. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [52]. E. Oksanen, J.-H. Chen, S.Z. Fisher, Neutron crystallography for the study of hydrogen bonds in macromolecules, *Molecules*, **2017**, *22*, 596. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [53]. X. Li, T. Haunold, S. Werkovits, L.D. Marks, P. Blaha, G. Rupprechter, CO adsorption and disproportionation on smooth and defect-rich Ir(111), *The Journal of Physical Chemistry*, **2022**, *126*, 6578–6589. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [54]. E.E. Etim, A. Magaji, G.O. Ogofotha, Pipeline corrosion and its preventions in the oil and gas sector: a review, *International Journal of Environment and Bioenergy*, **2022**, *17*, 1–11. [[Crossref](#)], [[Google Scholar](#)]
- [55]. C.A. Bauer, G. Schneider, A.H. Göller, Gaussian process regression models for the prediction of hydrogen bond acceptor strengths, *Molecular informatics*, **2019**, *38*, 1800115. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [56]. M. Albareda, J. Palacios, J. Imperial, L.F. Pacios, Computational study of the  $Fe(CN)_2CO$  cofactor and its binding to HypC protein, *The Journal of Physical Chemistry B*, **2013**, *117*, 13523–13533. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [57]. D. Pinotsi, L. Grisanti, P. Mahou, R. Gebauer, C.F. Kaminski, A. Hassanali, G.S. Kaminski Schierle, Proton transfer and structure-specific fluorescence in hydrogen bond-rich protein structures, *Journal of the American Chemical Society*, **2016**, *138*, 3046–3057. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [58]. J. Lohrman, E.A. Vázquez-Montelongo, S. Pramanik, V.W. Day, M.A. Hix, K. Bowman-James, G. Andrés Cisneros, Characterizing hydrogen-bond interactions in pyrazinetetracarboxamide complexes: Insights from experimental and quantum topological analyses, *Inorganic Chemistry*, **2018**, *57*, 9775–9778. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [59]. E.E. Etim, I.E. Mbakara, E.J. Inyang, O.A. Ushie, U. Lawal, C. Andrew, Spectroscopy of linear interstellar carbon chain isotopologues: Meeting experimental accuracy, *Tropical Journal of Applied Natural Sciences*, **2017**, *2*, 11–16. [[Crossref](#)], [[Google Scholar](#)]
- [60]. Q.G. Zhang, N.N. Wang, Z.W. Yu, The hydrogen bonding interactions between the ionic liquid 1-ethyl-3-methylimidazolium ethyl sulfate and water, *The Journal of Physical Chemistry B*, **2010**, *114*, 4747–4754. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [61]. F. Wu, C. Deraedt, Y. Cornaton, J. Contreras-Garcia, M. Boucher, L. Karmazin, C. Bailly, J.-Pierre Djukic, Making base-assisted C–H bond activation by  $Cp^*Co(III)$  effective: a noncovalent interaction-inclusive theoretical insight and experimental validation, *Organometallics*, **2020**, *39*, 2609–2629. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [62]. E.E. Etim, E. Arunan, Interstellar isomeric species: Energy, stability and abundance relationship, *The European Physical Journal Plus*, **2016**, *131*, 448. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [63]. E.E. Etim, B.S. Abah, I.E. Mbakara, E.J. Inyang, O.P. Ukafia, Quantum chemical calculations on silicon monoxide (SiO) and its protonated analogues, *Tropical Journal of Applied Natural Sciences*, **2017**, *2*, 61–68. [[Crossref](#)], [[Google Scholar](#)]
- [64]. C. Andrew, E.E. Etim, O.A. Ushie, G.P. Khanal. Vibrational-rotational spectra of normal acetylene and doubly deuterated acetylene: Experimental and computational studies, *Chemical Science Transactions*, **2018**, *7*, 77–82. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]

- [65]. E.E. Etim, J.E. Asuquo, O.C. Ngana, G.O. Ogofotha, Investigation on the thermochemistry, molecular spectroscopy and structural parameters of pyrrole and its isomers: a quantum chemistry approach, *Journal of Chemical Society of Nigeria*, **2022**, *47*, 129-138. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [66]. E.E. Etim, G.O. Emmanuel, I.F. Sambo, S.A. Olagboye, Quantum chemical studies on furan and its isomers, *International Journal of Modern Chemistry*, **2020**, *12*, 77-98. [[Crossref](#)], [[Google Scholar](#)]
- [67]. E.E. Etim, S.A. Olagboye, G.O. Emmanue, I.M. Atiatah, Quantum chemical studies on silicon tetrafluoride and its protonated analogues, *International Journal of Modern Chemistry*, **2020**, *12*, 26-45 [[Crossref](#)], [[Google Scholar](#)]
- [68]. I.G. Osigbemhe, H. Louis, E.M. Khan, E.E. Etim, D.O. Odey, A.P. Oviawe, H.O. Edet, F. Obuye, Synthesis, characterization, DFT studies, and molecular modeling of 2-(-(2-hydroxy-5-methoxyphenyl)-methylidene)-amino) nicotinic acid against some selected bacterial receptors, *Journal of the Iranian Chemical Society*, **2022**, *19*, 3561–3576. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [69]. I.G. Osigbemhe, H. Louis, E.M. Khan, E.E. Etim, E.E. Oyo-ita, A.P. Oviawe, H.O. Edet, F. Obuye, Antibacterial potential of 2-(-(2-Hydroxyphenyl)-methylidene)-amino) nicotinic Acid: Experimental, DFT Studies, and molecular docking approach, *Applied Biochemistry and Biotechnology*, **2022**, *194*, 5680–5701. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [70]. I.G. Osigbemhe, E.E. Oyoitab, H. Louis, E.M. Khan, E.E. Etim, H.O. Edet, O.J. Ikenyirimba, A.P. Oviawe, F. Obuye, Antibacterial potential of *N*-(2-furylmethylidene)-1, 3, 4-thiadiazole-2-amine: Experimental and theoretical investigations, *Journal of the Indian Chemical Society*, **2022**, *99*, 100597. [[Google Scholar](#)], [[Publisher](#)]
- [71]. I. Alkorta, J. Elguero, J.E. Del Bene, Perturbing the O–H···O hydrogen bond in 1-oxo-3-hydroxy-2-propene, *Molecules*, **2021**, *26*, 3086. [[Google Scholar](#)], [[Publisher](#)]
- [72]. L.E. Alkhimova, M.G. Babashkina, D.A. Safin, A family of ethyl *N*-salicylidene-glycinate dyes stabilized by intramolecular hydrogen bonding: Photophysical properties and computational study, *Molecules*, **2021**, *26*, 3112. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [73]. A.M. Lamsabhi, O. MÓ, M. Yáñez, Perturbating intramolecular hydrogen bonds through substituent effects or non-covalent interactions, *Molecules*, **2021**, *26*, 3556. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [74]. S. Zhou, Y. Liu, S. Wang, L. Wang, Chemical features and machine learning assisted predictions of protein-ligand short hydrogen bonds, *Research Square*, **2023**, 2895170. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [75]. I.G. Grosu, X. Filip, M.O. Miclăuş, C. Filip, Hydrogen-mediated noncovalent interactions in solids: What can NMR crystallography tell about?, *Molecules*, **2020**, *25*, 3757. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [76]. A. Gannouni, W. Tahri, T. Roisnel, S.I. Al-Resayes, M. Azam, R. Kefi, Single crystal investigations, hirshfeld surface analysis, DFT studies, molecular docking, physico-chemical characterization, and biological activity of a novel non-centrosymmetric compound with a copper transition metal precursor, *ACS Omega*, **2023**, *8*, 7738-7748. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [77]. E.E. Etim, E. Arunan, Partition Function and astronomical observation of interstellar isomers: Is there a link?, *Advances in Space Research*, **2017**, *59*, 1161-1171. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [78]. H.S. Samuel, U. Nweke-Mariazu, E.E. Etim Experimental and theoretical approaches in characterizing halogen bonding, *Journal of Applied Organometallic Chemistry*, **2023**, *3*, 169-183. [[Crossref](#)], [[Publisher](#)]
- [79]. X. Zhu, C. Zhang, H. Ma, F. Lu., Stereo-recognition of hydrogen bond and its implications for lignin biomimetic synthesis,

- Biomacromolecules*, **2022**, *23*, 4985-4994. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [80]. J.R. Lane, A.S. Hansen, K. Mackeprang, H.G. Kjaergaard, Kinetic energy density as a predictor of hydrogen-bonded OH-stretching frequencies, *The Journal of Physical Chemistry A*, **2017**, *121*, 3452-3460. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [81]. J. Contreras-García, W. Yang, E.R. Johnson, Analysis of hydrogen-bond interaction potentials from the electron density: integration of noncovalent interaction regions, *The Journal of Physical Chemistry A*, **2011**, *115*, 12983-12990. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [82]. N. Mandal, S.Md. Pratik, A. Datta, Exploring ultrashort hydrogen-hydrogen nonbonded contacts in constrained molecular cavities, *The Journal of Physical Chemistry B*, **2017**, *121*, 825-834. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [83]. A. Lakshmi Priya N. Suryaprakash. Two- and three-centered hydrogen bonds involving organic fluorine stabilize conformations of hydrazide halo derivatives: NMR, IR, QAIM, NCI, and theoretical evidence, *The Journal of Physical Chemistry A*, **2016**, *120*, 7810-7816. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [84]. E.M. Mas, R. Bukowski, K. Szalewicz, Ab initio three-body interactions for water. II. Effects on structure and energetics of liquid, *The Journal of Chemical Physics*, **2003**, *118*, 4404-4413. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [85]. R. Rey, K.B. Møller, J.T. Hynes, Hydrogen bond dynamics in water and ultrafast infrared spectroscopy, *Journal of Physical Chemistry A*, **2022**, *106*, 11993-11996. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [86]. Y. Tu, A. Laaksonen, The electronic properties of water molecules in water clusters and liquid water, *Chemical Physics Letters*, **2000**, *329*, 283-288. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [87]. A. Higuchi, T. Iijima, D.s.c. investigation of the states of water in poly(vinyl alcohol) membranes, *Polymer*, **1985**, *26*, 1207-1211. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [88]. A.V. Thoeny, I.S. Parrichini, T.M. Gasser, T. Loerting, Raman spectroscopy study of the slow order-order transformation of deuterium atoms: Ice XIX decay and ice XV formation, *The Journal of Chemical Physics*, **2022**, *156*, 154507. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [89]. E.E. Etim, E. Arunan, Accurate rotational constants for linear interstellar carbon chains: achieving experimental accuracy, *Astrophysics and Space Science*, **2017**, *362*, 4. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [90]. T. Hatakeyema, A. Yamauchi, H. Hatakeyema, Studies on bound water in poly(vinyl alcohol) hydrogel by DSC and FT-NMR, *European Polymer Journal*, **1984**, *20*, 61-64. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [91]. E.E. Etim, P. Gorai, A. Das *et al.*, C<sub>5</sub>H<sub>9</sub>N isomers: pointers to possible branched chain interstellar molecules, *The European Physical Journal D*, **2017**, *71*, 86. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [92]. D.J. Van der Waal, On the continuity of the gaseous and liquid states, Leiden: Universiteit Leiden; Ed J. S. Rowlinson, *Dover Publications, Inc.* **2004**. [[Google Scholar](#)], [[Publisher](#)]
- [93]. K. Kudo, J. Ishida, G. Syuu, Y. Sekine, T. Ikeda-Fukazawa, Structural changes of water in poly(vinyl alcohol) hydrogel during dehydration, *The Journal of Chemical Physics*, **2014**, *140*, 044909. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [94]. M. Bin, R. Yousif, S. Berkowicz, S. Das, D. Schlesinger, F. Perakis, Wide-angle X-ray scattering and molecular dynamics simulations of supercooled protein hydration water, *Physical Chemistry Chemical Physics*, **2021**, *23*, 18308-18313. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [95]. J. Schaefer, E.H.G. Backus, Y. Nagata, M. Bonn, Both inter- and intramolecular coupling of O-H groups determine the vibrational response of the water/air interface, *The Journal of Physical Chemistry Letters*, **2016**, *7*, 4591-4595. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]

- [96]. H.S. Samuel, U. Nweke-Mariazu, E.E. Etim Approaches for special characteristics of chalcogen bonding, *Journal of Applied Organometallic Chemistry*, **2023**, 3, 199-212. [Crossref], [Publisher]
- [97]. Z. Altun, E.A. Bleda, C. Trindle, Focal point evaluation of energies for tautomers and isomers for 3-hydroxy-2-butenamide: evaluation of competing internal hydrogen bonds of types -OH...O=, -OH... N, -NH...O=, and CH...X (X=O and N), *Molecules*, **2021**, 26, 2623. [Crossref], [Google Scholar], [Publisher]
- [98]. J.M. Guevara-Vela, M. Gallegos, M.A. Valentín-Rodríguez, A. Costales, T. Rocha-Rinza, A.M. Pendás, On the relationship between hydrogen bond strength and the formation energy in resonance-assisted hydrogen bonds, *Molecules*, **2021**, 26, 4196. [Crossref], [Google Scholar], [Publisher]
- [99]. G. Reddy, C.P. Lawrence, J.L. Skinner, A. Yethiraj, Liquid state theories for the structure of water, *The Journal of Chemical Physics*, **2003**, 119, 13012-13016. [Crossref], [Google Scholar], [Publisher]
- [100]. A.G. Kalinichev, Molecular simulations of liquid and supercritical water: Thermodynamics, structure, and hydrogen bonding, *Reviews of Mineralogy and Geochemistry*, **2001**, 42, 83-129. [Crossref], [Google Scholar], [Publisher]
- [101]. M. Jabłoński, A critical overview of current theoretical methods of estimating the energy of intramolecular interactions, *Molecules*, **2020**, 25, 5512. [Crossref], [Google Scholar], [Publisher]
- [102]. M.M. Deshmukh, S.R. Gadre, Molecular tailoring approach for the estimation of intramolecular hydrogen bond energy, *Molecules*, **2021**, 26, 2928. [Crossref], [Google Scholar], [Publisher]
- [103]. P.E. Hansen, A spectroscopic overview of intramolecular hydrogen bonds of NH... O, S, N type, *Molecules*, **2021**, 26, 2409. [Crossref], [Google Scholar], [Publisher]
- [104]. J. Jankowska, A.L. Sobolewski, Modern theoretical approaches to modeling the excited-state intramolecular proton transfer: An overview, *Molecules*, **2021**, 26, 5140. [Crossref], [Google Scholar], [Publisher]
- [105]. Ł. Hetmańczyk, P. Szklarz, A. Kwocz, M. Wierzejewska, M. Pagacz-Kostrzewa, M.Y. Melnikov, P.M. Tolstoy, A. Filarowski, Polymorphism and conformational equilibrium of nitro-acetophenone in solid state and under matrix conditions, *Molecules*, **2021**, 26, 3109. [Crossref], [Google Scholar], [Publisher]
- [106]. Ł. Hetmańczyk, E.A. Goremychkin, J. Waliszewski, M.V. Vener, P. Lipkowski, P.M. Tolstoy, A. Filarowski, Spectroscopic identification of hydrogen bond vibrations and quasi-isostructural polymorphism in *N*-salicylideneanilin, *Molecules*, **2021**, 26, 5043. [Crossref], [Google Scholar], [Publisher]
- [107]. J. Emsley, The composition, structure and hydrogen bonding of the  $\beta$ -diketones, Complex chemistry, structure and bonding, 57, Springer, Berlin, Heidelberg, **1984**. [Crossref], [Google Scholar], [Publisher]
- [108]. K. Kułacz, M. Pocheć, A. Jezierska, J.J. Panek, Naphthazarin derivatives in the light of intra- and intermolecular forces, *Molecules*, **2021**, 26, 5642. [Crossref], [Google Scholar], [Publisher]
- [109]. E.E. Etim, P. Gorai, A. Ankan Das, S.K. Chakrabarti, E. Arunan, Interstellar hydrogen bonding, *Advances in Space Research*, 61, 2870-2880. [Crossref], [Google Scholar], [Publisher]
- [110]. E.E. Etim, P. Gorai, A. Das, S.K. Chakrabarti, E. Arunan, Systematic theoretical study on the interstellar carbon chain molecules, *Astrophysical Journal*, **2016**, 832, 144. [Crossref], [Google Scholar], [Publisher]