Studying the Effects of Hydrogen Bonding in 1H-1,2,3-Triazole and Its Derivatives

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Abstract:

1,2,3-triazole is used as a building block in many pharmaceutical drugs. The molecule has several derivatives that are useful in other areas including treating fungal infections and in dealing with some environmental issues. One of its derivatives, benzotriazole, is commonly used as an inhibitor of corrosion through the formation of a copper-benzotriazole complex. One area of particular interest in studying triazoles is the ability of these molecules to tautomerize. The hydrogen atom can move from the 1H position to the 2H position and this transfer is thought to be affected by solvent interactions. Here, we study the effects of hydrogen bonding on triazoles by interacting 1H-1,2,3-triazole and benzotriazole with water. Techniques used to study the hydrogen bonding complexes include Raman and infrared spectroscopies and quantum chemistry calculations. Another area of interest is elucidating the liquid structure of 1H-1,2,3-Triazole and its long range structure. This is accomplished by comparing experimental spectroscopic results to quantum chemistry calculations.
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1 Introduction

1.1 Modern Day Medicine

The world of medicine is an ever changing, ever growing, field of study that is of obvious importance in our world. With modern day medicine, the goal is to make drugs as efficiently and cost effective as is possible. As stated in the Advanced Functional Materials journal, “Perhaps more than in any other field, the goal of material scientists, engineer, and manufacturers has been to achieve performance and a set of desired characteristics in the final material… in as simple and effective a manner as possible”.¹ Several methods have been experimented with in a means to find the most appropriate method for synthesizing drugs. One recently studied mechanism is drug extraction. However, this method is low yielding, materials are wasted, and a high amount of energy is wasted.² There are many studies that have been performed to try and enhance this method to make it more appealing for pharmaceutical companies.

Another method, and one that has been seemingly more effective, is the use of click chemistry. The invention of click chemistry has helped to do away with the slow, costly, labor-intensive process of previously described drug synthesis. In click chemistry, a few practical reactions are utilized. These reactions do not require “difficult separations or harsh conditions”, and have led to “the ability to form, modify, and control the
structure of materials on various scales”.¹ This method allows for a quicker synthesis of drug-like molecules. Click chemistry has helped to advance the process of synthesizing new drugs by creating a cheaper, more efficient way to do so. Due to this advancement in chemistry, there is a need and a search for molecules that are suitable reactants in click chemistry.

1.2 The Building Block of Drugs

1H-1,2,3-triazole is the building block of many drugs. Due to the invention of click-chemistry, this molecule has been of greater interest to scientists because of its many medicinal uses. 1H-1,2,3-triazole is a cyclic compound with the chemical formula of C₂N₃H₃. Triazoles belong in the chemical class of heterocyclic azoles, which are extremely common in click chemistry reactions.² The triazole ring is relatively rigid which prevents it from interacting with linked components, but allows it to be a useful linker for small molecules and polymers.³ Additionally, the structure of the molecule is what allows it to act as a functional building block. The presence of the three nitrogen atoms results in a polarization that puts a partial positive charge on the carbon atom.³ The presence of lone pairs of electrons on the nitrogen atoms also allows the triazole the ability to serve as a hydrogen bond acceptor.³

Triazoles, as mentioned previously, have extremely beneficial uses in modern day medicine. Every year, more and more experimental studies are being performed using triazole as the main molecule in the drug. One study, performed by researchers in Georgia and Texas, explored the use of triazole as a kinase inhibitor in the treatment of
Alzheimer’s disease. In this study, the scientists’ goal was to test inhibitors of the nitric oxide synthase and kinase activities as a way to treat Alzheimer’s disease. Alzheimer’s disease is one that presently has no cure. Fluorine atoms were introduced into the purine-triazole complex and the ability of this molecule to inhibit the NOS/kinase activity was observed and noted. Thus, Triazole has proven to be potentially effective in the treatment of Alzheimer’s.

![Triazole structure](image)

**Figure 1.** The structure of 1H-1,2,3-Triazole

Triazole derivatives have also been extremely helpful in aiding against fungal infections. They have relatively low toxicity and are able to be structurally modified. There have been several different studies to look at their ability to prevent this. One study, was led by A.J. Carillo and he looked at different triazole derivatives and their ability to treat the severe fungal infection by *Scedosporium*. This type of fungus has evolved into a fungus that leads to disseminated infections in mostly neutropenic patients. These types of infection are regularly unresponsive to antifungal medications. However, the results identified that many of the derivatives proved effective against the strain and one in particular, UR 9825, was extremely effective in treating the infection. Another triazole
based antifungal drug is Fluconazole. This drug is recommended by the World Health Organization and is the first choice treatment method for *Candida albicans*, yeast in gut flora, because it is safe, effective, and has favorable pharmacokinetic characteristics.

More recently, triazoles are being studied and experimented with as anticancer drugs. Heat shock protein 90 is a valuable target for the discovery of anticancer drugs because it expresses at manifest levels in tumor cells. There are inhibitors that have been previously established, like the inhibitor redicol. But, it was found that the incorporation of a triazole ring into these inhibitors could lead to an increased activity of these anticancer drugs. Specifically, the 1,2,3-triazole derivative of macrocyclic lactone of radical shows positive anticancer activity against leukemia cell line Kasumi-1. There are many other triazole based anticancer drugs, that are also proving to be effective means for treating cancer cells.

Triazoles also have use in areas that are not included in medicine, such as the environment. Triazole derivatives, like the one being studied in this thesis, have use aiding against corrosion and some even function as potential explosives. Anees Khadom conducted a study to test the ability of benzotriazole as a corrosion inhibitor. Benzotriazole is the derivative further looked at in this paper for its hydrogen bonding properties. Benzotriazole is important because it contains the ability to aid against the corrosion of copper. Copper is commonly used in heating and cooling systems because of its favorable thermal conductivity properties. But, when using hydrochloric acid a corrosion inhibitor must be added to prevent a negative reaction between the copper and HCl. In his experiment, Khadom explored the inhibition of copper corrosion by benzotriazole in a 5% HCl solution. Through data analysis, it was determined that
benzotriazole was a very effective inhibitor with inhibition ranging between 86% and 99.8%.  

One last area of interest is in the use of triazoles as explosives. Scientists have been working in recent years to achieve “an ideal combination of energetic properties”. These properties include stability and sensitivity. One way in achieving this is by replacing the conventional explosives with nitrogen rich compounds. The production of high energy density materials, known as HEDM, is an area that is being increasingly studied. The presence of nitrogen groups, as are seen in triazole, enhances the oxygen balance and the density of a material. A study found that triazole linked molecules give rise to compounds with high energetic properties. The addition of more nitro groups yields more energetic compounds. The numerous uses of triazole are still being discovered and studied today. Due to its many advantageous properties, it could be argued that triazole molecules are one of the most attractive in science at this time.

1.3 Chemical Bonding

Intramolecular forces are interactions that hold atoms together within a molecule. Without intramolecular interactions, there would be no molecules, but instead just individual atoms. An ionic bond, covalent bond, and metallic bonds are all examples of intramolecular interactions that occur in the world. These interactions are also classified in terms of strength. For intramolecular forces, the metallic bond is the strongest, and the covalent bonds are the weakest interactions that occur.

Intermolecular interactions in chemistry are the attractions or repulsions between a molecule and its neighboring molecules. In intermolecular interactions, the forces are
weaker than those of intramolecular forces. The types of intermolecular forces discussed in detail are dipole-dipole interaction, van der Waals forces, and hydrogen interactions.

The dipole-dipole interaction occurs between two molecules with permanent dipoles. These interactions occur between two molecules that are opposite in charge, a cation and an anion. On each molecule, there is a partial positive region and a partial negative region. The molecules will align themselves so that the positive and negative net charges will attract.

Van der Waals, or London dispersion forces are relatively weak non-covalent bonds. Van der Waals interactions are present in all molecules, due to their induced dipole moments. In van der Waals interactions, there are more electrons present in a certain area as opposed to the other. A molecular collision will occur between the two atoms, which will result in both molecules having a dipole moment.

The last type of intermolecular interaction, and the one studied here, is the hydrogen bond. Hydrogen bonds are a specific dipole-dipole interaction. Hydrogen bonds occur when a hydrogen atom bonds to a strong electronegative atom, such as a nitrogen atom. This interaction occurs with an electronegative atom that contains a lone pair of electrons. In this type of bond, the nitrogen or oxygen carries a partial negative charge whereas the hydrogen will carry a partial positive charge. The partial positive charge on the hydrogen will be attracted to the net charges on the other atom, which will allow a bond to form between the two. This bond is stronger than the London dispersion forces previously mentioned, but is weaker than covalent bonds. These bonds are the bonds that give water its distinct characteristics and cause its many shifts that can be seen in Raman spectrum.
The type of hydrogen bond that is present in a molecule is the intramolecular hydrogen bond. Intramolecular bonds occur in one single molecule that has multiple functional groups that can form hydrogen bonds with each other. In order for this type of bond to form it is essential that the molecule have a hydrogen bond acceptor and a hydrogen bond donor. The presence of these two things allows for the formation of the intramolecular bond, as long as the acceptor and donor are close enough to each other.

The hydrogen interactions that occur between two different molecules in a solution are intermolecular hydrogen bonds. Intermolecular bonds can occur between any type of like or unlike molecule as long as the same conditions listed in the previous paragraph are met. Thus, there must be a hydrogen bond donor and a hydrogen bond acceptor.

There are several factors that affect the ability of hydrogen bonding to occur. There are also ways though in which hydrogen bonds affect properties of the molecules they’re interacting with. The first factor that can prevent hydrogen bonding is electronegativity. As was stated in the previous paragraph, it is necessary for some electronegative atom to be present in order to pull the electron density created from the positive charge of the hydrogen atom. However, if there is not a large enough electronegative difference the hydrogen bond won’t form. This would mean there is no dipole moment, making this bonding impossible. An example of this is the PH₃ molecule. This molecule lacks an electronegativity difference needed to form hydrogen bonds, as both atoms have an electronegativity of 2.1. While it exhibits the same molecular geometry as NH₃ which is trigonal pyramidal, NH₃ is capable of forming hydrogen bonds. There is a significant difference between the nitrogen atom and the hydrogen atom electronegativity, which
allows for this bond formation. The nitrogen atom is attracted to the hydrogen atom whereas phosphorus lacks attraction.

The second factor is the size of the atom itself. If the hydrogen atom acceptor is too large it won’t allow for the formation of a hydrogen bond. If an interaction does occur, the interaction will be relatively weak. In this, there is a large electron cloud that surrounds and shields the positive charge of the nucleus from participating in the interaction. The electron radius of the accepting atom is too large, so the nucleus of the accepting won’t be able to reach close enough proximity to the hydrogen atom to generate a strong interaction. One example of this phenomenon would be the interaction between a chlorine atom and a hydrogen atom. The chlorine atom has a much larger radius and size compared to the hydrogen atom. This prevents the hydrogen atom from being able to be pulled close to the hydrogen atom. This size difference between the two atoms will result in a relatively weak interaction in comparison to hydrogen and another smaller atom.

The last quality hydrogen bonds have is that they can affect physical and chemical properties of molecules. As can be seen when examining the boiling point of many compounds, as the molar mass increases, typically, so does the boiling point. However, depending on the amount of hydrogen bonds that are present in a molecule, this trend can differ from the expected. Water, as an example, has a higher boiling point than many other compounds that are larger in mass. Water contains the highly electronegative oxygen atom and two positive hydrogen atoms. The presence of these net charges allows the atoms to stick together closer than molecules that lack these interactions. The other property affected is its viscosity. This trend is similar to that of the boiling point trend. The more hydrogen bonds that are present in a molecule, the higher the viscosity in relation to other
molecules in their group. If the molecule has the potential for more than one hydrogen bond this will increase the viscosity even more than if it only had one.9

1.4 Tautomerization of Triazole

One unique characteristic of Triazole is that it has the ability to tautomerize between its 1H-1,2,3-triazole form and the 2H-1,2,3-triazole form. Tautomers are two molecules that have the same chemical formula but they are connected in different ways. Generally this involves the transformation from one functional group into another functional group, usually the movement of a hydrogen atom. Tautomerization appears to be of similar definition to a structural isomer. However, tautomerization represents a dynamic equilibrium between two compounds. A stereoisomer has the same molecular formula, just different connections. “The most common form of tautomerization involves the migration of hydrogen atoms via chemical bond breaking and formation”.10 This concept has been studied increasingly more in the last few years because of the potential it has to act as a single molecule switch. The use of these molecules that have this ability to switch are a rather understudied field although they are being more commonly used. One group of researchers used the molecule porphycene, which is a molecule that has strong hydrogen bonds in it and has a fast tautomerization rate. They looked at this molecule for use in mechanochemistry, and the ability to induce tautomerization of a single molecule, which is important in many biological processes. They found that they could induce tautomerization with the tip-induced tautomerization method. There are several factors that affect tautomerization, such as the pH of a solution, the solvent, and the temperature
the solution is at. Additionally the phase of the sample, solid, liquid or gas, can affect the form that it exists in as well.

There are many different types of tautomerization reactions; the keto-enol tautomerization reaction is the most common. In this reaction, a keto is in rapid equilibrium with an enol. The keto form contains a double bonded oxygen and carbonyl. In the enol form, the double is broken and a single hydrogen atom is moved to the oxygen and the double bond forms between two carbons. In this form of tautomerization, the keto form tends to be the dominant form in equilibrium as it is lower in energy than the enol form. Another is the imine-enamine tautomerism, which is where imines are in equilibrium with enamines. The phenol-keto tautomerism exists between a phenol and a cyclic ketone. The ringtautomeri is a tautomerization reaction where the hydrogen atom can exist on different parts of the ring, as is seen in triazole.

1.5 Long range liquid structure studies

The identification of the structure of liquids is the least understood of three phases today. This is because in the liquid phase, a compound is in an intermediate state. The liquid will exhibit characteristics of both the solid and gas phases, which complicates determining the present phase. According to Bernal’s classic picture of liquids as homogeneous, coherent, and essentially irregular, this has strongly influenced the thinking in the scientific community of the liquid structure of compounds. It has been thought that liquid structure was similar to the solid phase, just more disorganized than the solid.

Scientists have used different techniques to attempt to elucidate structures of liquid compounds. A study done by the US food and drug administration discovered the
structure of liquid sildenafil through the use of liquid chromatography- mass spectroscopy. This drug is used to treat erectile dysfunction and has been of recent interest due to a concern that it contained a compound related to synthetic phosphodiesterase-5. The structure for the liquid compound however had yet to be elucidated. As with this thesis, the liquid state of sildenafil was of interest to researchers. The use of this instrumentation allowed researchers to determine the presence of the compound and its structure in order to identify it in drugs.

Many studies that dealt with liquid structure elucidation appeared to use liquid chromatography coupled with other instruments as the most common way to identify the liquid structure. Few studies have been done that use vibrational spectroscopy as a means for identification. Many proteins have been elucidated this way. Often, the use of this tool is coupled with another instrument like NMR or UV to give the NMR, UV, and mass spectra in order to correctly identify liquids. This has yielded the most success.

Studies have been performed that attempt to make the determination of the liquid structure of a molecule identifiable. In this study we attempt to determine the structure of liquid 1H-1,2,3-triazole through Raman Spectroscopy and computational chemistry. The elucidation of the liquid structure of 1H-1,2,3-triazole has long been debated and studied and has yet to be correctly identified. Both the gas and the solid phase states are identified for the molecule. In the gas phase, 1H-1,2,3-triazole exists primarily in the 2H form. The 2H form is known to be lower in energy than the 1H. As for the solid state, 1H-Triazole exists as a 1:1 ratio of both tautomers. Previously, Anna E. Craig attempted to identify the liquid structure with the help of Dr. Nathan Hammer and Dr. Gregory Tschumper. The experimental methods employed were Raman and NMR. These were
then compared with theoretical computations B3LYP/6-311++G(2df,2pd). The results yielded that it is likely only one tautomer was present in the liquid form.

## 1.6 Vibrational Spectroscopy

Spectroscopy is the study of the way in which light and matter interact as light can be scattered, absorbed or emitted. Vibrational spectroscopy is the collective form of spectroscopy that encompasses both Raman spectroscopy and infrared spectroscopy. These two tools are complementary to one another and are both non-invasive and non-destructive.¹⁸ The tools measure the vibrational energy levels that are associated with chemical bonds in the sample. Since each molecule has its own chemical “fingerprint” these two instruments can help to distinguish a molecule by giving information about its structure, interactions, and the composition of the molecule. The data that is generated by each molecule is presented in spectra form. The spectrum for each is different however. Raman spectrum shows the intensity of scattered light compared to the frequency, which is the energy difference. Infrared spectrum shows the amount of light absorbed or transmitted against the energy.¹⁸ One main difference between vibrational methods is that Raman requires a change in polarizability whereas infrared requires a change in dipole moment.

There are many applications for vibrational spectroscopy, which is what makes this method so essential. An example of where this has proved to be influential is in the molecular adsorption of CO on metallic surfaces. The use of vibrational spectroscopy has worked to explain the surface chemistry of carbon monoxide and its bonding to metal surfaces. In order to interpret its spectra, it relies mainly on the infrared spectrum of the
molecule to show this as it has related inorganic clusters and coordination complexes. This is only one of the many ways in which vibrational spectroscopy is utilized today and is thus utilized in this thesis.

Infrared spectrum and Raman spectrum can be used to identify the different stretches and bends in a molecule. There are more than two types of stretching but two of the most common are symmetric and asymmetric stretching. In symmetric stretching, two bonds are vibrating in opposite directions meaning that when one contracts the other will contract as well. Asymmetric stretching refers to the opposite of this, where when one bond stretches the other is contracting. In addition to these stretches, there are also four types of bends measured in infrared spectroscopy; rocking, wagging, twisting, and scissoring. Bending refers to a change in the angle between the two bonds. The way in which these bends and stretches occur depends on the molecule being studied.

1.7 Raman Spectroscopy

Raman spectroscopy is a reliable and a non-destructive technique that can be used for the qualitative and quantitative analysis of many molecules and many different drugs. Raman spectroscopy is able to analyze both solid and liquid samples relatively quickly. It explores that vibrational and rotational modes in the sample, and the spectrum can be used to determine the identity of unknown samples. Each molecule has its own unique fingerprint that is evident in Raman making it a principal instrument in chemistry.

When light is incident on a sample it can be absorbed, transmitted or scattered. Raman spectroscopy is a form of spectroscopy that looks at the scattering of light. There are two forms of scattered light; elastic scattering and inelastic scattering. Elastic
scattering, also known as Rayleigh scattering, is much more common and occurs when there is no difference in energy, or the frequency of incident radiation is equal to the frequency of scattered radiation.\textsuperscript{20} Energy is conserved throughout the process. Inelastic scattering refers to the excitement of a sample where there is a notable difference in energy after the light has hit the sample. Within inelastic scattering, the scattering can be further broken down into two more subcategories based on the way in which energy change occurs. When the frequency of incident light is greater than the frequency of scattered radiation, this will cause a Stokes line to appear on the spectrum. This method of scattering is called Stokes scattering. Conversely, when the frequency of incident light is less than the frequency of scattered light, this will cause an Anti-stokes shift on the spectrum.

![Figure 2. Raman Spectroscopy light scattering diagram](image)

Figure 2. Raman Spectroscopy light scattering diagram
As can be visualized in Figure 2, Stokes scattering involves the transition from lower to higher energy levels. Anti-stokes involves the transition from higher energy levels to lower energy levels. In spectra, “stokes bands are more intense than anti-Stokes bands”. In order for Raman to be effective and to work, a change in the polarizability of the molecule is necessary.

In this form of spectroscopy, light from a monochromatic laser interacts with the sample and creates scattered light. The reason a laser is used to induce this scattering as it has a strong light source. It is important that the light be monochromatic, which means of only one wavelength. The detector inside the Raman spectrometer measures the wavelengths of the scattered light giving spectra. In the spectra, the frequency difference between each peak corresponds to the vibrational frequency of a molecular bond, which also helps to indicate the structure.

Figure 3. Photograph of the Horiba Scientific LabRAM HR Evolution Raman Spectroscopy system (courtesy of Horiba Scientific).

One important feature of Raman, and the one that was extremely important for this thesis, is that it is relatively insensitive to water. This means that when saturating the triazole and its derivatives in water, there will be no peak on the spectrum belonging to the
water. This is one advantage to using Raman to analyze samples that use water as the main solvent. The use of water as a solvent is unfortunately the downside to the use of Infrared Spectroscopy. In Infrared Spectroscopy, water will inherently show on the spectrum that will make the results appear incorrectly.

### 1.7 Infrared Spectroscopy

Infrared spectroscopy is, as its name suggests, the study of the interaction of matter with infrared light. Infrared spectroscopy is used to determine different the functional groups that are present in a molecule. This is done through measurement of the vibrations of atoms. The infrared region ranges from 13000-10cm\(^{-1}\). This large region is further subdivided into the near IR region (13000-4000cm\(^{-1}\)), mid IR (4000-400cm\(^{-1}\)), and the far IR (400-10cm\(^{-1}\)). Traditionally, the mid IR region is the most commonly studied, and is the region explored in this study.

The way in which infrared spectroscopy works is by passing light through a sample and measuring the absorbance or transmission of light. There are two different types of IR spectrometers, the dispersive IR and the Fourier Transform IR. The method of IR used in this experiment was that of the Fourier Transform IR. Dispersive IR consists of a radiation source, a monochromator, and a detector.\(^{21}\) There are several potential light sources, but for mid IR traditionally a Nernst glower is used. A dispersive mechanism, like a prism or grating, is used to disperse the light. Once light passes through the sample, it reaches a splitter that disperses the light into its component wavelengths and then moves through a slit to the detector. The downside to dispersive IR though is that it is slow and has really low sensitivity.
Fourier Transform IR has in many cases replaced the dispersive IR. FTIR uses an interferometer instead of a prism or grating. In FTIR, the beam splitter that is in the interferometer splits the IR into two different beams. One beam will hit a fixed mirror, and the other will reflect off of a moving mirror. Once they are both reflected, they will come back to the middle, and join together to form an interferogram. The interferogram can be transformed through Fourier Transform into a spectrum of either absorbance or transmittance.

There are many different methods for sample preparation. The one studied here utilized the formation of a pellet with KBr. A KBr pellet is a sample that is combined with KBr and using a pellet press is pressed into a small pellet. The most important part in making a KBr pellet is the ratio of KBr to the sample. The sample should be roughly 0.2%–1% of the amount of KBr used.22 The reason KBr can be used is because it will present no peaks in the region and should not be visible when the sample is analyzed. The pellet should be translucent in color for best results.
2 Experimental Methods

2.1 Raman Spectroscopy

1H-1,2,3-triazole was examined under Raman spectroscopy in its pure form and in saturated form. Samples were prepared using different mol ratios of water to triazole. Deionized water was used to saturate the triazole. The ratios were 10% triazole, 31% triazole, and 93% triazole. The percent by mass calculations were 25% triazole, 50% triazole, 75% triazole, and 100% triazole. Samples were prepared the day they were analyzed. The laser used was the 532 nm frequency doubled YAG laser and a Horiba Scientific LabRAM HR Evolution Raman Spectroscopy system.

Benzotriazole was also analyzed using the same system as above. However, 1 g of solid benzotriazole was completely dissolved in 10 mL of deionized water to determine the effect of saturation. The laser used was again the 532 nm frequency doubled YAG laser and a Horiba Scientific LabRAM HR Evolution Raman Spectroscopy system.

All data was then analyzed using the software program Igor. Spectra were generated for all concentrations to determine the effect of water on the molecules being studied.

2.2 Infrared Spectroscopy

Infrared spectroscopy was used to analyze the liquid structure of 1H-1,2,3-triazole through two methods. The first was the attenuated total reflectance infrared spectroscopy.
This method meant that no sample preparation was necessary and the liquid sample could be analyzed straight.

The second method used was the KBr pellet method. The ratio used was a 5% ratio of triazole to KBr. The pellet was prepared by mixing Triazole with KBr in a mortar bowl and then the mixture was pressed into a pellet. A nice translucent pellet was obtained and then analyzed using the Bruker Tensor 27 FTIR. The data was then plotted in the software program Igor to generate the spectrum.

2.3 Computational Methods

Quantum mechanical computations to elucidate the structure of 1H-1,2,3-triazole was performed by Dr. Gregory Tschumper. Calculations were performed using Gaussian 98 software package. The M06L/6-311++G(2df,2pd) method and basis set combination were used. Theoretical spectra were created by combining Lorentzian type functions for each normal mode using a program written in National Instruments LabVIEW as shown previously. The software program Igor was then used to analyze the theoretical Raman spectra and compare them to experimental spectra. Images of the minimum energy molecular structures were created using the software program Molekel.
3. Results and Discussion

3.1 Low energy molecular structures of 1H-1,2,3-Triazole

The following Figures were all generated using the calculations performed by Dr. Gregory Tschumper using the M06L/6311++G(2df,2pd) methods and basis set. These are the most stable configurations of the molecule and the molecule bonding based on their low energy structure. The structures consist of varying chain lengths of triazoles including chain lengths of 2,4,6, and 8 triazoles. The triazole chain that consists of 8 triazoles is new to the research being done and the method used was also changed. The M06L method is able to account for weaker intermolecular forces, which should provide more accurate results from previous studies and experiments. Figures 4-26 show the optimal molecular structures at the M06L level of theory.

![Figure 4. 1 H monomer of Triazole](image)

![Figure 5. 2H monomer of Triazole](image)
Figure 6. Triazole 1H Dimer

Figure 7. Triazole 1H Dimer NH+CH

Figure 8. Triazole 1H+2H Dimer

Figure 9. Triazole 2H Dimer

Figure 10. Triazole 2H Dimer NH+CH

Figure 11. Triazole 1H Chain Opp Side
Figure 12. Triazole 1H Chain Same Side

Figure 13. 1H Triazole Cyclic

Figure 14. 4 Triazole 2H Cyclic

Figure 15. Triazole 1H Opp Side

Figure 16. Triazole 1H Same Side

Figure 17. 1H Triazole Cyclic
Figure 18. 2H Alt Chain Triazole  

Figure 19. 2H Triazole Cyclic  

Figure 20. 1H Chain Same Side  

Figure 21. 1H Chain Opp Side  

Figure 22. 1H Cyclic  

Figure 23. 2H Triazole Cyclic
Figure 24. 2H Alt Chain
3.2 Raman Analysis for Liquid Structure

Figure 25 shows the experimental Raman spectrum compared to the two triazole monomers quantum chemistry calculations.

![Graph showing experimental versus theoretical spectra](image)

Figure 25. Experimental versus the triazole monomers.

The experimental spectrum compared to the theoretical spectrum for the 1H monomer of triazole shows peaks in the 3300 region which are characteristic of the C-H and N-H stretches are present. Additionally, the same are visible in the 2H monomer as well. However, there are many peaks missing in these two as well, indicating this is likely not the best fit.
Figure 26 shows the results for triazole chains that have two triazole molecules. As can be seen, there is more agreement with the experimental and the theoretical data compared to Figure 25. However, there are still many peaks that are not seen that are not visible in the experimental that are shown in the quantum calculations. The closest match appears to be the 1H Dimer. There is only one peak present in the C-H and N-H stretching region of experimental that is puzzling. These results indicate that the more triazole molecules that are present in a chain, the more agreement there is to the experimental.
Figure 27. Experimental spectrum versus the 4-chain length triazole molecule.

Figure 27 shows that the trend is consistent with what has been seen in the previous two Figures, 25 and 26. As was seen in Figure 26, the addition of one more triazole molecule yielded slightly better agreement. In the above Figure 27, there are four triazole molecules linked which again increased the agreement. There are still many peaks present in the C-H stretching region of the quantum calculations, $3000 \text{ cm}^{-1}$, that are not visible in the experimental spectra.
Figure 28. Experimental versus calculated for a 6-chain triazole molecule.

Figure 28 illustrates that the six triazole chain has been the most agreeable so far. The region in the 3000’s shows various peaks that are again not seen in the experimental spectrum. The peaks in the 1200 cm$^{-1}$ region are more consistent and follow the trend that has been visible with the addition of more triazole molecules to the structure. Additionally, the 1H cyclic is also nicely matched with the experimental data. However, there are still peaks in this region that are not visible in the calculated spectra.
Following the general pattern seen in all previous spectra, the agreement for the experiment and theory is highest with the 8 triazole length chain shown in Figure 29. This was a new added spectra, since previous calculations were done for 6 length chains as the maximum. The C-H stretching region is again not matched. There is a good amount of agreement that allows for more confidence in the spectra in the 1200 cm$^{-1}$ region. However, there are still peaks missing and this is still not a perfect fit.

Figure 29. The experimental theoretical comparison for 8-chain linked triazole
Figure 30. Summation of the linear spectra.

Figure 31. Summation of the cyclic spectra.
As can be seen Figures 25-29, there is no specific best fit for the liquid structure, as all have different amounts of agreement. This would lead to the belief that there is a combination of different arrangements of these molecules in the liquid. To account for this, summation was taken for all of the 1H linear configurations for chain lengths 1,2,4,6, and 8 by equally weighting the contribution for each. The agreement for the single triazole molecule is the least agreeable, and the most agreement is found with the 8 triazole molecule chain. The trend appears to be as more triazole molecules are interacting with each other, the better the agreement with experiment. Once all of the linear were summed together, as is seen in Figure 30, there was more agreement than in any previous individual configurations. However, the cyclic structural motif is the architecture that should be lowest in energy and the expected configuration for triazoles. In Figure 31, the experimental spectrum is compared to the summation spectra of all cyclic configurations of the molecule. The results show more agreement, than the linear combination and better peak distinctions.

The puzzling region of this spectra is the C-H and N-H stretching region around 3000 cm\(^{-1}\). The experimental only produces one peak, compared to the calculated spectra. The lack of agreement has been confusing in the past, and remains confusing in the present. It is unclear why there are no peaks in this area. The calculations suggest a varying amount of peaks, not just one.
Figure 32. The saturation of 1H-1,2,3-triazole with varying % mass water.

Figure 33. Saturated 1H-1,2,3-triazole in the C-H region 1000cm$^{-1}$-1350cm$^{-1}$.
Figure 32 shows the results of the 1H-1,2,3-triazole saturation experiments that were done using distilled water. Three different mol ratios were used, which corresponded to percent by mass calculations of 25%, 50%, 75%, and 100% triazole. The saturation did not affect too much or change the spectrum in a very drastic way in the 3000 cm\(^{-1}\) region. However, when closely examined, a peak intensity difference can be noted in the 1000cm\(^{-1}\)-1350cm\(^{-1}\) region.

The most interesting aspect of the triazole saturation is the peak intensity switch around 1100 cm\(^{-1}\). As the % triazole increases, the right peak diminishes and the left peak intensifies. This is noticeable when looking at Figure 34 below. Once the experimental data was compared to the theoretical for the 1H monomer and 2H monomer, it appears that tautomerization has occurred. However, this would indicate that the 2H monomer is present in the liquid 1H triazole. Since this would not be expected, it is also possible that this intensity difference is instead due to the breaking of a hydrogen bond. This is still an area that needs to be further explored, but the assumption that tautomerization occurred is not realistic in this case.
3.3 Infrared Analysis of Triazole

In the past, the agreement between the theoretical infrared and the experimental infrared has been very weak. One of the goals of this thesis was to produce a more agreeable spectrum of experimental to theoretical. This thesis explored the agreement using the new basis set, M06L, that was promising in making the two more agreeable. As can be seen in the following Figures 35-38, the infrared of the molecule was obtained and compared with theoretical infrared and theoretical summation of infrared. As can be seen, there is more agreement than in previous studies.
Figure 35. The attenuated total reflectance of 1H-1,2,3-Triazole

Figure 36. The Fourier Transform Infrared Spectroscopy of 1H-1,2,3-Triazole
The FTIR of Triazole should have been at a ratio of 1%. However, this ratio produced a spectrum that was not reasonable. There was a lot of noise, which was cause for a very messy, unusable, spectrum. The 5% ratio produced a much neater spectrum that could be more critically analyzed. This is odd because normally the ratio works best when closer to 1%. In both infrared spectra, the C-H bends and stretches of the aromatic ring can be seen. The C-H stretch is visible around 3000 cm\(^{-1}\). The C=H stretch is located around 1400 cm\(^{-1}\), and is also present in both of the spectra. The N-H bend is visible after 1500 cm\(^{-1}\) very close to 1600 cm\(^{-1}\). Since all peaks are identifiable, the spectrum can be assumed to be fairly accurate. Additionally, since both spectra have the same big peaks this too allows for confidence in the generated spectra. There is a difference however in the intensities, as in ATR the right hand grouping is much weaker than the left side. In the FTIR analysis, the left peak area is much less intense than the right peak. Essentially, the two spectra switch. This change is odd, but could be due to a difference in the instrumentation and what it picks up. Infrared analysis cannot be used for saturation because the water would be visible in the spectrum. This is why no saturation was done using infrared analysis.
Figure 37. Summation of the theoretical IR of the linear chains compared with experiment.

Figure 38. Summation of the theoretical IR of cyclic chains compared with experiment.
In previous studies, there has been little agreement between the theoretical infrared spectrum and the experimental spectrum of 1H-1,2,3-Triazole. The addition of the two additional triazole molecules interacting in the chain, as well as the summation of all different chains, created nice and similar results in the lower region of the infrared spectrum. Summations were done for the infrared using the same method as was done with the Raman spectroscopy summation. The summation was done for both the linear molecules and the cyclic molecules. Again, all were weighted equally. Calculations were done using a harmonic method that needs to be corrected for. In order to do this, the theoretical calculations should be anharmonically shifted which would allow for the two to be correctly aligned. Harmonic approximations assume infinite life time, which is incorrect. The 1400 cm\(^{-1}\) area is characteristic of C=C stretch in an aromatic compounds. As can be seen there are peaks in this region. However, unfortunately the C-H stretching that would be noticeable in the 3000 cm\(^{-1}\) area does not agreeing with the experimental. It is thought that this could be due to protonation, which would affect the ability of these peaks to be sharp and noticeable. Although not all of the spectra matched up, there was still some agreement, which is a step in the right direction.
3.4 Raman Analysis of Benzotriazole

The final area of study in this thesis was examining the benzotriazole molecule and its saturation properties.

Figure 39. The structure of benzotriazole. 24

Figure 40. The saturation of benzotriazole with deionized water.
Figure 40 above shows the benzotriazole molecule saturated in 10mL of water. The benzotriazole was saturated in water of a specific amount due to it being a solid not liquid. The saturation of benzotriazole, like the saturation of triazole in Figure 33, shows the addition of more peaks in the saturated spectra. This is likely due to the water breaking the bonding interactions that are occurring. Otherwise, the spectra are very similar to one another and neither differs too much from the other.
4. Conclusions

The purpose of this thesis was to expand on what had already been studied and to work to make improvements on the data. The experimental Raman spectra exhibited a higher signal to noise ratio than the previous study was able to produce. First, this study attempted to elucidate the structure of liquid 1H-1,2,3-triazole. In the past, triazole chain lengths of six triazole molecules interacting together were the highest considered for this. In this thesis, the addition of the eight triazole molecule length chain was new and yielded better agreement between the experiment and theory. This held true for all spectra that were generated. The best fit was with the 1H cyclic modeled Figures as would be expected since the cyclic is lower in energy than the linear triazole models.

The second goal of this experiment dealt with the saturation of triazole. The results for saturating triazole and benzotriazole produced nice, clear data. The saturation of triazole was similar to what the previous thesis found the saturation to look like. It was thought that this might induce tautomerization, however, it is possible that instead of tautomerizing the molecule has interactions that are being broken. In the future, theoretical calculations should be performed in order to check the accuracy of the experimental for each molecule.

The last point of interest was trying to generate a clear image of the infrared spectrum that had more agreement with the experiment. The summation of the same molecules that were summed in the Raman analysis produced agreement in the 600-1600 range. However, agreement in the C-H stretching region of 3000 was not evident. It is thought that this could be due to protonation occurring in this region that keeps the spectra from being able to be clearly defined here.
All in all, progress was made in many of the areas and while results are still not perfect, they are better than they were. In the future, I would expect someone to be able to continue to improve upon the results found in this study and in previous studies. Hopefully results will become more accurate to what is expected and confidence can be found with all results.
Bibliography


