View metadata, citation and similar papers at core.ac.uk
brought to you by CORE
provided by The University of Mississippi

RAMAN SPECTROSCOPIC AND COMPUTATIONAL ANALYSIS OF THE EFFECTS OF NONCOVALENT INTERACTIONS ON DMSO

Ashton T. Nicholson

A thesis submitted to the faculty of The University of Mississippi in partial fulfillment of the requirements of the Sally McDonnell Barksdale Honors College

University of Mississippi

August 2014

Approved by

_____

Advisor: Professor Nathan Hammer

_____

Reader: Professor Gregory Tschumper

_____

Reader: Professor Jason Ritchie

Copyright © 2014 Ashton T. Nicholson

All rights reserved

ABSTRACT

Dimethyl sulfoxide (DMSO) is a widely used chemical in synthetic chemistry and also has unique and important biological applications. In the pure liquid, DMSO forms chain like structures of alternating sulfur and oxygen atoms due to its high self-association. However, it is known that DMSO/water mixtures form solutions with unique physical characteristics depending on the mole ratio. For instance, at a 1:2 ratio of DMSO/water a eutectic mixture forms with a freezing point of-70 C. Vibrational spectroscopy allows us to study the effects of noncovalent interactions when water and DMSO interact in solution. Spectral shifts can be analyzed in order to give a clearer picture of the structure of DMSO in DMSO/water mixtures and also in solutions with other hydrogen bond donors that cannot form as extensive hydrogen bonded networks. The anomalous properties of DMSO/water mixtures have been the subject of a large number of studies. It has been previously established that the reason for the unique properties of such solutions lies in the formation of strong hydrogen bonds between water and DMSO. Despite the many studies there is still no clear picture of the structure of DMSO in the water mixture. When

a DMSO/water mixture is formed there is great increase in temperature of the solution. This suggests a significant perturbation of water's hydrogen bond network due to interactions with DMSO. Here, the hydrogen bonding geometries of DMSO/water mixtures are studied using Raman spectroscopy and computational chemistry.

ACKNOWLEDGEMENTS

This work has been supported, in part, by the National Science Foundation (EPS-0903787 and CHE-0955550).

TABLE OF CONTENTS

ABSTRACT **ii**

ACKNOWLEDGEMENTS **iv**

LIST OF FIGURES **vii**

CHAPTER 1 **1**

NONCOVALENT INTERACTIONS **1**

CHAPTER 2 SPECTROSCOPIC AND COMPUTATIONAL METHODS **4**

2.1 FUNDAMENTALS OF SPECTROSCOPY 4

2.2 RAMAN SPECTROSCOPY 5

2.3 EXPERIMENTAL METHODS 7

2.4 COMPUTATIONAL METHODS 9

CHAPTER 4 DIMETHYL SULFOXIDE (DMSO) **10**

4.1 WHAT IS DMSO? 10

4.2 HISTORY AND APPLICATIONS OF DMSO 11

4.3 PREVIOUS STUDIES 11

CHAPTER 5 RAMAN SPECTROSCOPIC AND COMPUTATIONAL ANALYSIS OF THE EFFECTS OF NONCOVALENT INTERACTIONS ON DMSO **14**

5.1 INTRODUCTION 14

5.2 EXPERIMENTAL AND COMPUTATIONAL PROCEDURES 14

5.3 RESULTS 15

5.4 DISCUSSION 21

5.5 CONCLUSIONS 22

CHAPTER 5 BIBLIOGRAPHY **24**

LIST OF FIGURES

1Figure 1.1 Pyrimidine/water cluster(Ashley M. Wright, 2013) 2

2Figure 1.2 Lewis Structure of DMSO 3

3Figure 2.1. Types of Raman scattering. 6

4Figure 2.2 Raman spectrometer setup 7

5Figure 2.3 Raman spectrometer in use 8

6 Figure 4.1. Molecular structure of DMSO. 10

7Figure 5.1 Experimental Raman spectra at different mole fractions (χ) 15

8Figure 5.2 Experimental Raman spectra of select normal modes 16

9 Figure 5.3 DMSO optimized molecular structure (CS symmetry) 16

10Figure 5.4 DMSO 1W-A molecule optimized molecular structure (CS symmetry) 17

11Figure 5.5 DMSO 1W-B molecule optimized molecular structure (CS symmetry) 17

12Figure 5.6 DMSO 2W-A optimized molecular structure (CS symmetry) 18

13Figure 5.7 Theoretical Raman spectra of optimized molecular structures 19

14Figure 5.8 Theoretical Raman spectra of selected normal modes 20

15Figure 5.9 Comparison of the experimental and theoretical raman spectra of dmso/water mixtures 20

CHAPTER 1

NONCOVALENT INTERACTIONS

Noncovalent interactions, unlike covalent bonds, do not involve the sharing of electrons. Instead, they rely on interactions within a molecule or between them. The energy released in the formation of a non-covalent bond is considerably less than that of a covalent bond. Many molecules at room temperature possess enough energy to break these bonds. Non-covalent interactions can be both intermolecular forces and intra molecular forces. The non-covalent interaction that will be most important to this research is the hydrogen bond. Hydrogen bonding is a special type of dipole-dipole interaction. Figure 1.1 shows an optimized molecular cluster with a number of hydrogen bonds of varying strength. The uppermost methanol is donating an OH⋯N hydrogen bond to a nitrogen atom in pyrimidine but is also accepting an OH⋯O hydrogen bond from a second methanol molecule below it. Pyrimidine is also donating a weak CH⋯O hydrogen bond to a third methanol molecule. This type of hydrogen bond is called weak because carbon and hydrogen have similar electronegativities and therefore the interaction with the adjacent oxygen atom is weaker than in the case of OH⋯O hydrogen bonds.

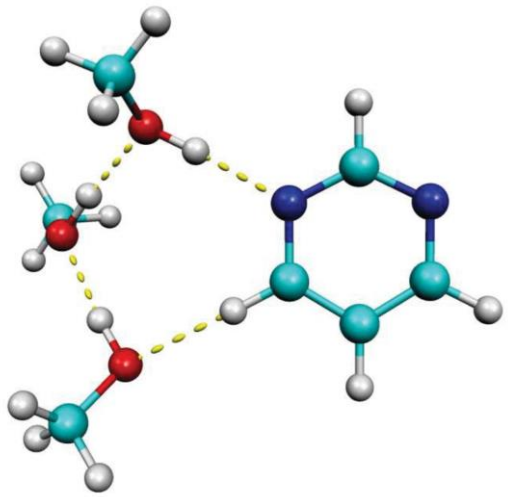

Figure 1.1 Pyrimidine/water cluster[1]

The Lewis structure of DMSO is shown in Figure 1.2. In DMSO/water interactions, DMSO can accept OH⋯O and OH⋯S hydrogen bonds from water and donate CH⋯O hydrogen bonds to water. Hydrogen is able to form one bond with just one other atom. However, if bonded to an electronegative donor atom, hydrogen can form another weak association with an acceptor group. This additional weak association is a hydrogen bond. The hydrogen bonding between water molecules is responsible for the aqueous environment in which all life on earth depends. Water molecules are a prime example of hydrogen bonding. The hydrogen of one water molecule forms a hydrogen bond to another through attraction to the valence electrons of oxygen. Water molecules can also form hydrogen bonds with other molecules, especially those that possess a hydroxyl group, which are also soluble in water. Hydrogen bonds are weaker than covalent bonds because there is no direct sharing of electrons between atoms. Due to this fact hydrogen bonds are longer than covalent bonds. The strongest hydrogen bonds possess the donor, the hydrogen atom, and the acceptor in a bond angle closest to 180°. The strength of a hydrogen bond is related to directionality. Though weaker than linear

hydrogen bonds, non-linear hydrogen bonds still help stabilize 3-dimensional structures like proteins.

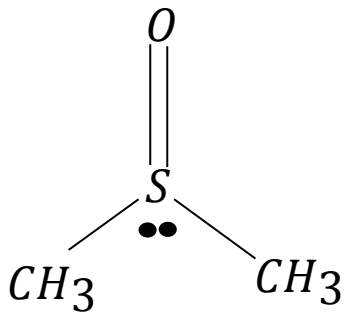

Figure 1.2 Lewis Structure of DMSO

CHAPTER 2

SPECTROSCOPIC AND COMPUTATIONAL METHODS

2.1 FUNDAMENTALS OF SPECTROSCOPY

Spectroscopy is the study of the interactions between light and matter. The nature of matter and light had been a source of debate in the pages of sciences history for centuries since Christiaan Huygens and Issac Newton had differing views in describing the nature of light in the 17th century. Huygens described light as waves while Newton, on the other hand, described light as particles. Einstein put the debate to rest when he concluded that both theories were needed to fully describe light and that separately they could not fully explain light, but together they could. Planck further revolutionized 20th century science through his work on quantum theory. All of this work led to advances in spectroscopy and opened up a new door for research and exploration. When describing light, it is sometimes easier to think of light as a stream of particles. These particles are known as photons. The following equation, developed by Planck, describes the energy of a photon (E).

$$E = hv = \frac{hc}{\lambda} \tag{2.1}$$

h is Planck's constant, and v is the frequency in hertz.[2]

This research focused on the use of vibrational spectroscopy which detect transitions between vibrational states, but they can occur between other states as well. A transition occurs when there is a change in the energy of a molecule. A change in energy can occur from any

change in motion or electron energy. There are multiple possibilities of transitions between energy levels in molecules such as vibrational, rotational, and electronic. The energy of these transitions is increasing in this order rotational < vibrational < electronic. Transitions in rotational states lead to spectra in the microwave region. Transitions involving vibrational states produce spectra in the infrared region. Transitions can also occur in electronic states of molecules which can produce spectra in the visible and ultraviolet regions. There are other types of transitions as well as types of spectroscopy to study them. However, this research is only concerned with using Raman spectroscopy. At room temperature most molecules exist in their ground state, the lowest energy state. When light, an excitation source, hits a sample of matter, the light can take several paths. Light can be absorbed, transmitted, reflected, or scattered by the sample. An excitation source can excite a molecule at ground state to an elevated state.

2.2 RAMAN SPECTROSCOPY

In this project vibrational spectroscopy was used in order to study how water and DMSO interacted with one another. Raman spectroscopy was used in order to generate vibrational spectra to study the shifts in energy levels that occur with differing concentrations of DMSO in water. Raman spectroscopy was first developed in 1928 by C. V. Raman and is hence named in his honor. Raman spectroscopy is referred to as the compliment of IR spectroscopy because the selection rules differ between the two methods. While infrared spectroscopy requires a change in the dipole moment of the molecule, Raman spectroscopy depends on the molecular polarizability of the molecule. Polarizability is the tendency of a molecule to take on an electric dipole when in

the presence of an electric field.[3] In other words this is the ability of the molecule to distort its electron cloud.

In Raman spectroscopy when the molecule is hit with radiation the photons are absorbed at one frequency which is followed by the emission of photons with a change in frequency. The difference between the photon energy is either absorbed or scattered. The scattered radiation is observed and measured at right angles to the beams direction. The three types of Raman scattering; Rayleigh, Stokes, and Anti-Stokes are depicted in the figure below.

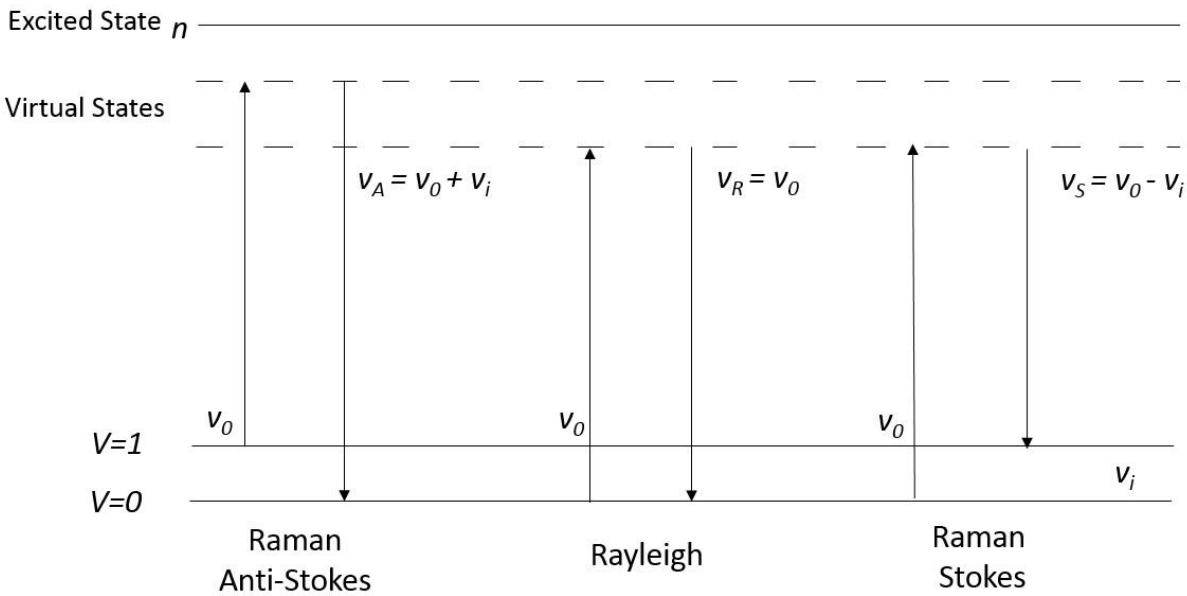

Figure 2.1. Types of Raman scattering.

Rayleigh scattering, also known as elastic scattering, is the most common and indicates that the scattered radiation has the same frequency as the source radiation. A laser is typically used as the source of radiation. Stokes and anti-Stokes are examples of inelastic scattering. The change in energy between the scattered and the incident beam indicates vibrational transition in the molecule.

2.3 EXPERIMENTAL METHODS

Raman spectra were obtained for this project using a Jobin-Yvon Ramanor HG2-S scanning Raman spectrometer. Molecules were excited using a SpectraPhysics Kr+/Ar+ laser using the 514.5 nm line.

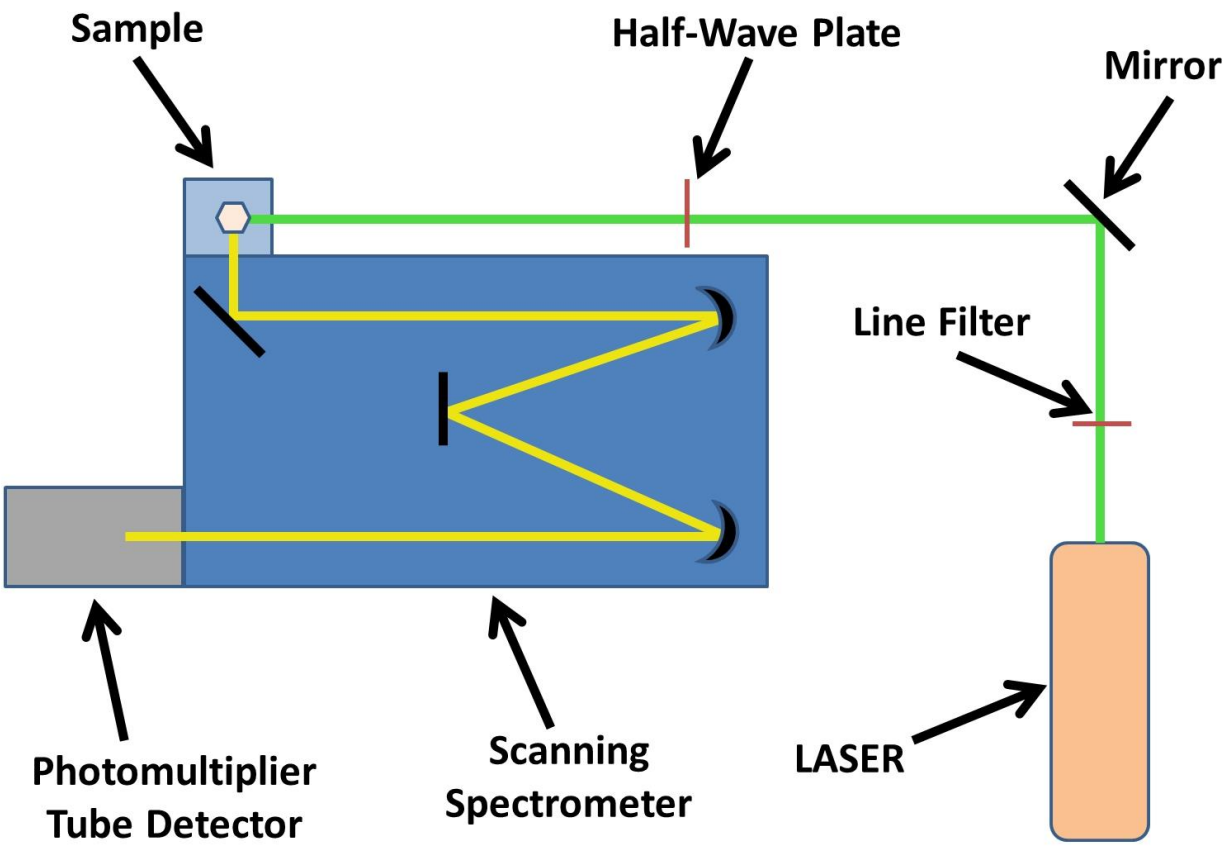

Figure 2.2 Raman spectrometer setup

As depicted in figure 2.2 the light from the laser follows a path through the line filter which narrows the light to exclusively the 514.5 nm line. The light is then reflected off a mirror towards the sample but first passes through the half-wave plate which rotates the light to the correct polarization. Finally the light hits the sample and is scattered into the spectrometer at a right angle. Within the spectrometer the light is reflected off a mirror into a grating which separates

the light back to another mirror and through another grating before individual lines of light are focused into the photomultiplier tube detector. A photomultiplier tube detector is used to amplify the signal that occurs from Raman scattering due to the fact that Raman Stokes scattering only occurs in about 1 in a million photons. Although the photomultiplier tube, PMT, is capable of amplifying these signals it requires a maintained cool temperature to do so. This cool environment reduces the possibility of stray electrons hitting the detector. Figure 2.3 shows the spectrometer while in use during this research.

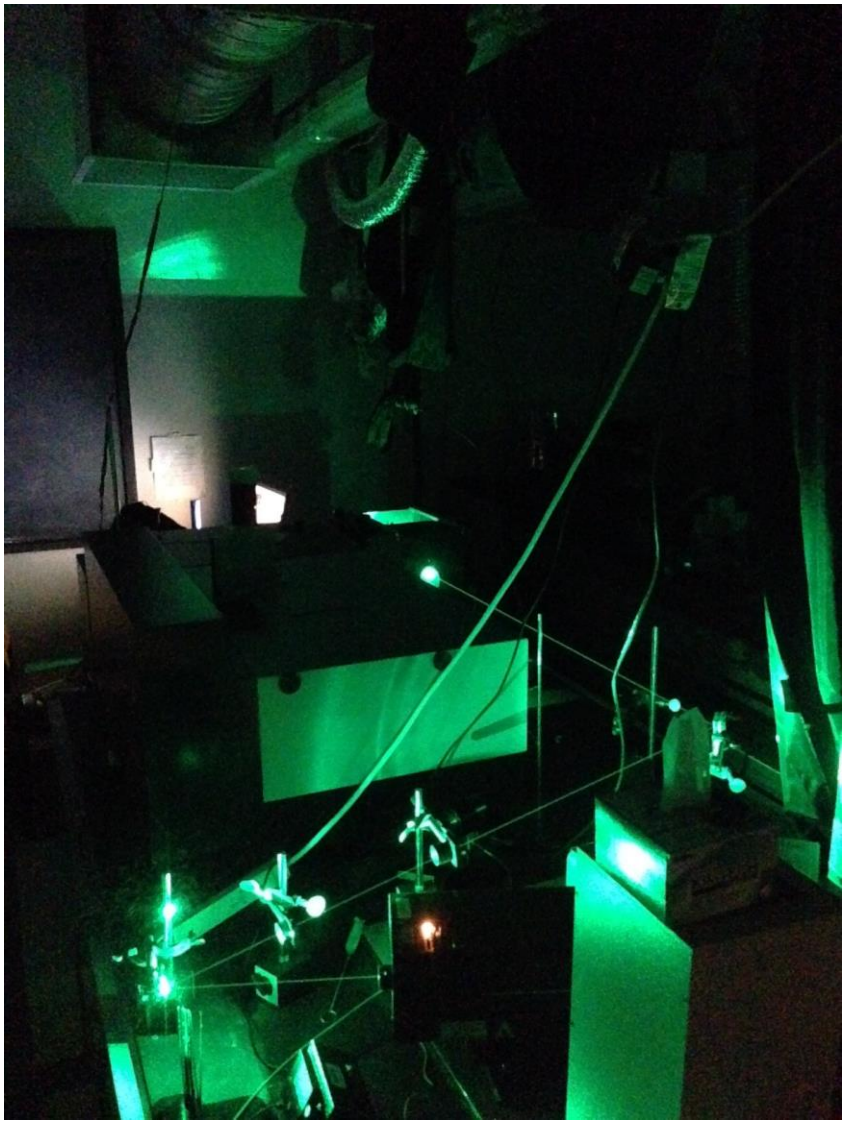

Figure 2.3 Raman spectrometer in use

2.4 COMPUTATIONAL METHODS

Computational chemistry was used in this study to model the micro-hydrated hydrogen bonded network of DMSO and to explain the experimental observables. Density Functional Theory, DFT, calculations were used to simulate Raman vibrational spectra of DMSO/water mixtures. The calculations used in this research were done through Gaussian 09 software using the B3LYP method with a 6-311++g(2*df*,2*pd*) basis set.[4] These calculations approximate to solve for the time-independent Schrodinger equation for multiple electron systems. The Schrodinger equation cannot be completely solved for in systems containing more than one electron due to electron-electron interactions.[3]

CHAPTER 4

DIMETHYL SULFOXIDE (DMSO)

4.1 WHAT IS DMSO?

Dimethyl Sulfoxide, DMSO, is the byproduct of the wood industry which has been discovered to have many applications including those in medicine. DMSO has the formula $(CH_3)_2SO$ and its structure is depicted below in Figure 4.1.

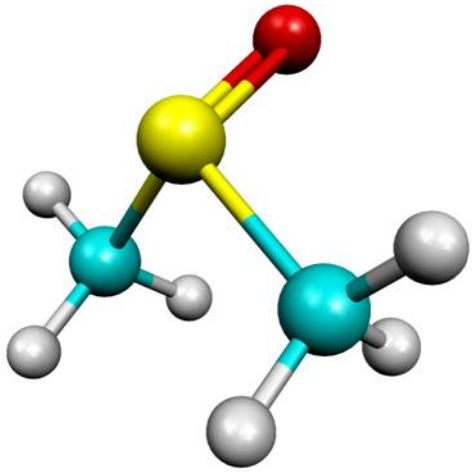

Figure 4.1. Molecular structure of DMSO.

DMSO has been used as a solvent since 1953.[5] However, despite the more than 40,000 articles about this organosulfur compound it is still not fully understood. DMSO has a tendency to form intermolecular associations with itself, in the dimer form, and other molecules. This is what has sparked so much interest around the non-ideal physicochemical behaviors that DMSO exhibits.[6]

4.2 HISTORY AND APPLICATIONS OF DMSO

Along with being used as a solvent DMSO also has many other uses in both industry and medicine. In the United States DMSO only has a limited approval for medical use by the FDA. However, in Canada, Great Britain, Germany and Japan it is commonly prescribed by doctors for many uses including pain, inflammation and arthritis.[5] What makes DMSO so useful in the medical field is its ability to permeate membranes. DMSO can even pass through skin at higher concentrations. This gives it the unique ability of transporting other drugs such as a pain relievants across membranes. DMSO/water mixtures also have a variety of uses. At 1:2 mixtures DMSO/water mixtures form a eutectic mixture, a chemical composition that solidifies at a lower temperature than either compound in the mixture would regularly form. At low concentrations DMSO also forms a cryoprotectant which is important due to its ability to protect biological tissue from freezing damage. This is commonly used in sperm preservation.

4.3 PREVIOUS STUDIES

DMSO has been at the center of thousands of papers for multiple applications and studies. Due to its early use as a pharmaceutical the first vibrational spectroscopic study involving hydrogen bonding took place in 1958.[7] This research is focused on DMSO/water mixtures. Previous studies have revealed that DMSO forms intermolecular associations with other DMSO molecules to form dimers as well as other molecules such as water.[8] These dimeric formations were also confirmed using dielectric relaxation techniques.[6] DMSO/water mixtures themselves have a variety of uses including being used to study the biochemical properties of some alpha-amino acids.[9] Infrared spectroscopy spectra revealed both DMSO/water hydrogen

bonding and water/water hydrogen bonding within DMSO/water mixtures. The reorientation time of water was identified to be coupled to the reorientation time of DMSO.[10] DFT calculations using M06-2X theory have also been carried out to reveal that DMSO and water form stable structures due to hydrogen bonding between the two molecules. The hydrogen bonding between DMSO and water was found to be stronger than the hydrogen bonding between water molecules. Polarizabilities were also found to increase with cluster size.[11] Raman spectroscopy studies have been carried out with 1:1 DMSO/water mixtures and identified that decreasing temperatures enhance the hydrogen bonding between DMSO and water.[12] Configurations of DMSO/water mixtures have also been studied before with some success. In a previous study involving infrared spectroscopy, NMR spectroscopy, and ab initio calculations two configurations of DMSO/water clusters were identified. In half of the water monomers both OH groups formed hydrogen bonds with DMSO. While in the other half of the water monomers only one OH group formed a hydrogen bond with DMSO.[13]

Within DMSO/water mixtures some unique properties arise at varying concentrations of DMSO. This unique property is due to the fact that while water is both a hydrogen bond donor and accepter DMSO is only an acceptor. However, DMSO does possess the potential to donate weak hydrogen bonds. The unique properties of these mixtures have resulted in multiple studies. At 1:2 ratio of DMSO and water a eutectic mixture is formed. However at lower concentrations of DMSO a cryoprotectant is formed. The DMSO/water cryoprotectant has a depressed freezing point of 203K.[14] There are also strong deviations from ideality, resulting from an increase in viscosity in mole fractions from 0.3-0.4 of DMSO in the DMSO/water mix.[15] Most recently Raman scattering experiments and DFT calculations were used to analyze structural features of DMSO and water mixtures focusing on the S=O stretching region at ~1045cm^{-1}. Upon dilution,

the smaller the DMSO mole fraction, an additional peak was observed at ~1017cm^{-1} due to the hydrogen bonding of DMSO to water. Due to the stretching of the dimeric S=O mode at 0.1 DMSO mole fraction it was determined that even at low concentrations DMSO still exists as a dimer. The blue shifting of the C-H shifting region was also attributed to the hydrogen bonding.[16]

CHAPTER 5

RAMAN SPECTROSCOPIC AND COMPUTATIONAL ANALYSIS OF THE EFFECTS OF NONCOVALENT INTERACTIONS ON DMSO

5.1 INTRODUCTION

The anomalous properties of DMSO/water mixtures have been the subject of a large number of studies. It has been previously established that the reason for the unique properties of such solutions lies in the formation of strong hydrogen bonds between water and DMSO. Despite the many studies there is still no clear picture of the structure of DMSO in the water mixture. When a DMSO/water mixture is formed there is great increase in temperature of the solution. This suggests a significant perturbation of water's hydrogen bond network due to interactions with DMSO. While the S=O and the C-H stretching regions have been analyzed this research will look at the spectra from 200 cm^{-1} to 1800 cm^{-1}.

5.2 EXPERIMENTAL AND COMPUTATIONAL PROCEDURES

Purified Dried DMSO and purified water obtained from a NANOpure Diamond machine were used to create the DMSO/water mixtures. The spectra were obtained using a Jobin-Yvon Ramanor HG2-S Raman spectrometer with a scan speed of 1 cm^{-1}/s. Molecules were excited via a SpectraPhysics Kr+/Ar+ laser using the 514.5 nm line. DMSO/water mixtures were formed at 7 different mole fractions of DMSO (χ=0.9,0.66,0.5,0.4,0.2,0.1).

5.3 RESULTS

Figure 5.1 depicts the experimental Raman spectra of DMSO at χ=0.1, 0.2, 0.4, 0.5, 0.66, 0.9, DMSO, and water. Spectra was obtained from 200 cm^{-1} – 1800 cm^{-1}. As can be seen in the figure there are several red and blue shifts present. Figure 5.2 shows an enhanced visual of the spectra obtained. As the concentration of DMSO is decreased the magnitudes of the spectral shifts increase.

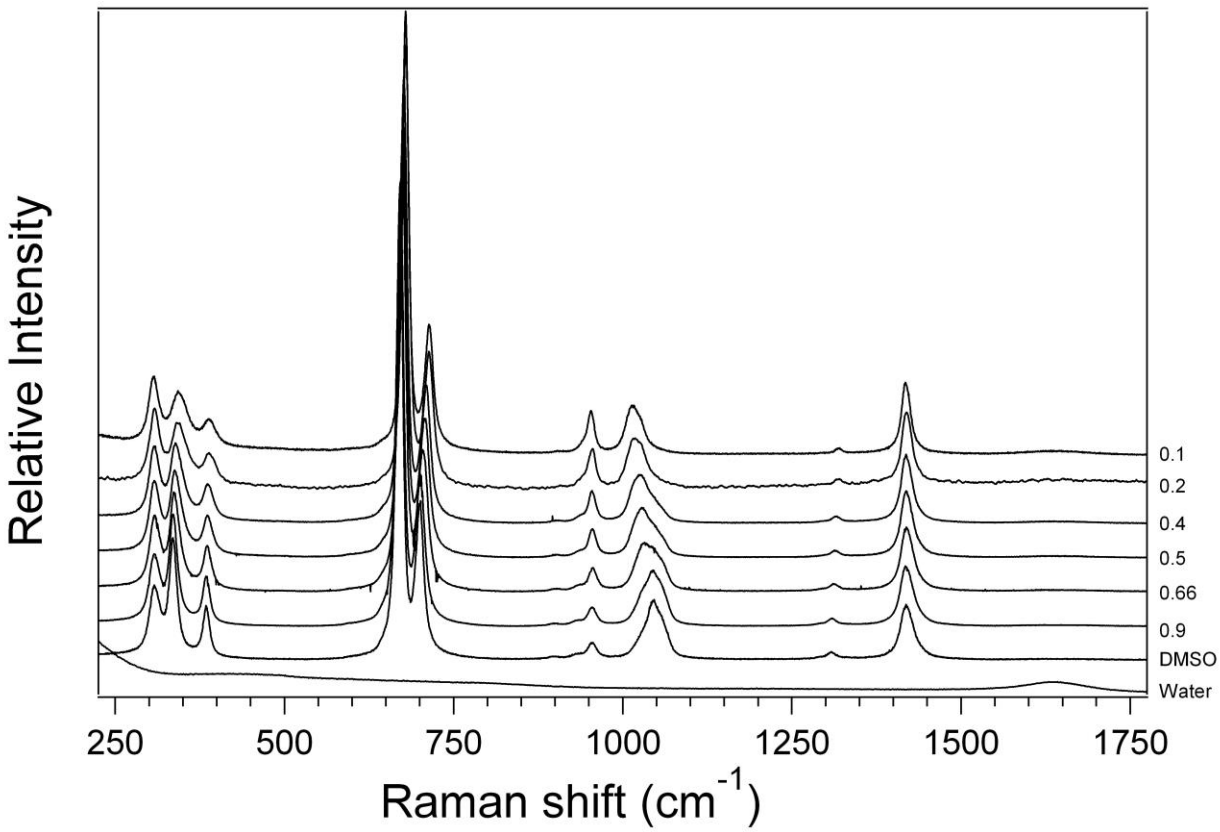

Figure 5.1 Experimental Raman spectra at different mole fractions (χ)

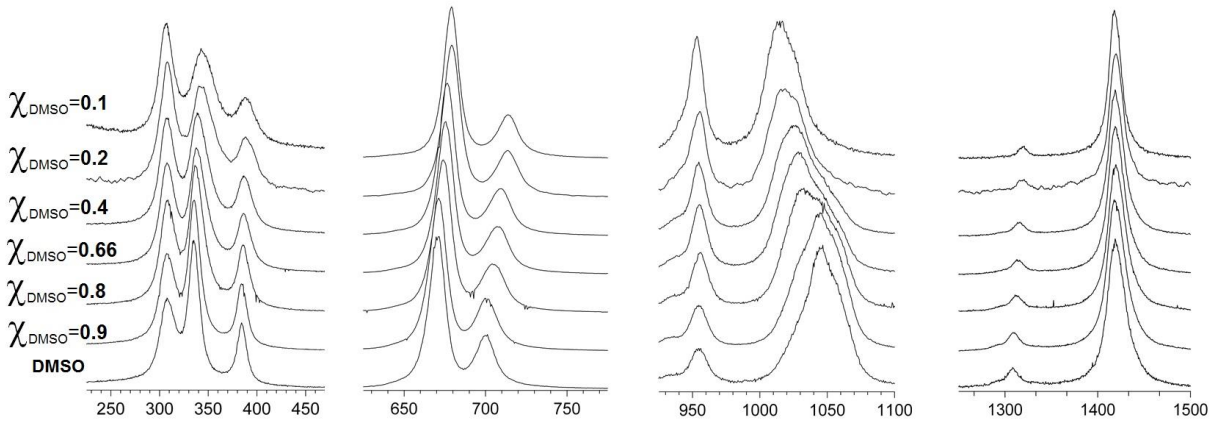

Figure 5.2 Experimental Raman spectra of select normal modes

Figures 5.3-5.6 show optimized molecular geometries for a monomer of DMSO hydrogen bonding to water molecules. As can be seen in Figure 5.6, DMSO is an acceptor to both water molecules in the formation of the hydrogen bonds.

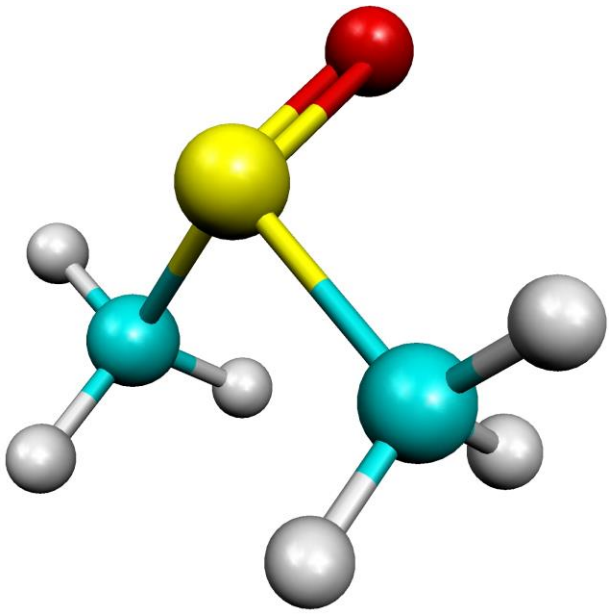

Figure 5.3 DMSO optimized molecular structure (C_S symmetry)

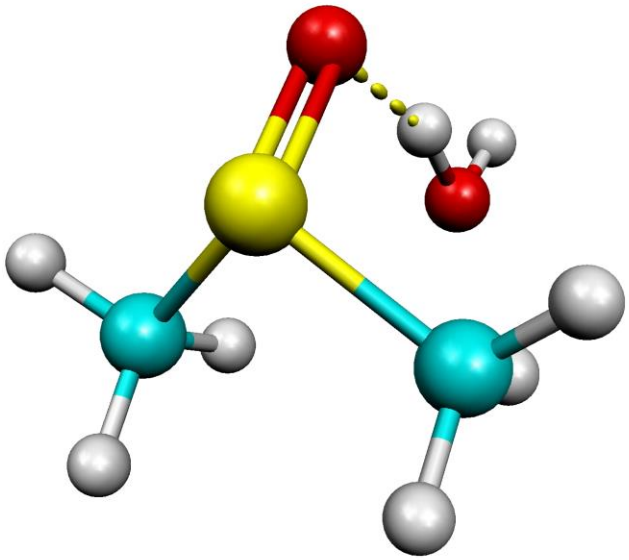

Figure 5.4 DMSO 1W-A molecule optimized molecular structure (C_S symmetry)

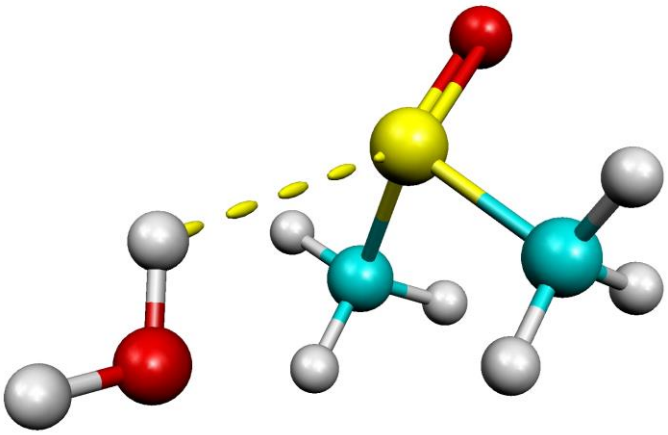

Figure 5.5 DMSO 1W-B molecule optimized molecular structure (C_S symmetry)

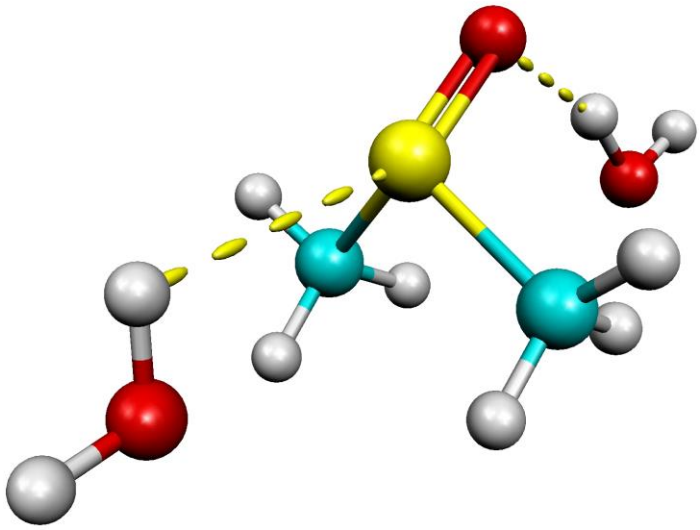

Figure 5.6 DMSO 2W-A optimized molecular structure (C_S symmetry)

Structure	Energy (hartrees)	E_{int} (kcal/mole)	Zero Point Energy (hartrees)	ZPE Corrected (hartrees)	E_{int}^{o} (kcal/mole)	Relative Energy (kcal/mole)
DMSO	-553.301445	-	0.079017	-553.222428	-	-
Water	-76.463541	-	0.021350	-76.442191	-	-
1W-A	-629.778317	8.4	0.103742	-629.674575	6.2	0.0
1W-B	-629.769330	2.7	0.102226	-629.667104	1.6	4.7
2W-A	-706.245928	10.9	0.126621	-706.119307	7.8	-

Table 5.1 Computed Energies, Interaction Energies (E_{int}), Zero Point Energies (ZPE), ZPE Corrected Energies, ZPE Corrected Interaction Energies (E_{int}^{o}), and Relative Energetics of DMSO/Water Molecular Clusters.

Figures 5.7 and 5.8 show the theoretical Raman spectra of DMSO/water mixtures for the optimized geometries considered here. As shown in the figures, the same shifts that occur

experimentally also reproduced theoretically. This can be more clearly seen in Figure 5.9 which suggests that the experiment can be described by the theoretical models considered here.

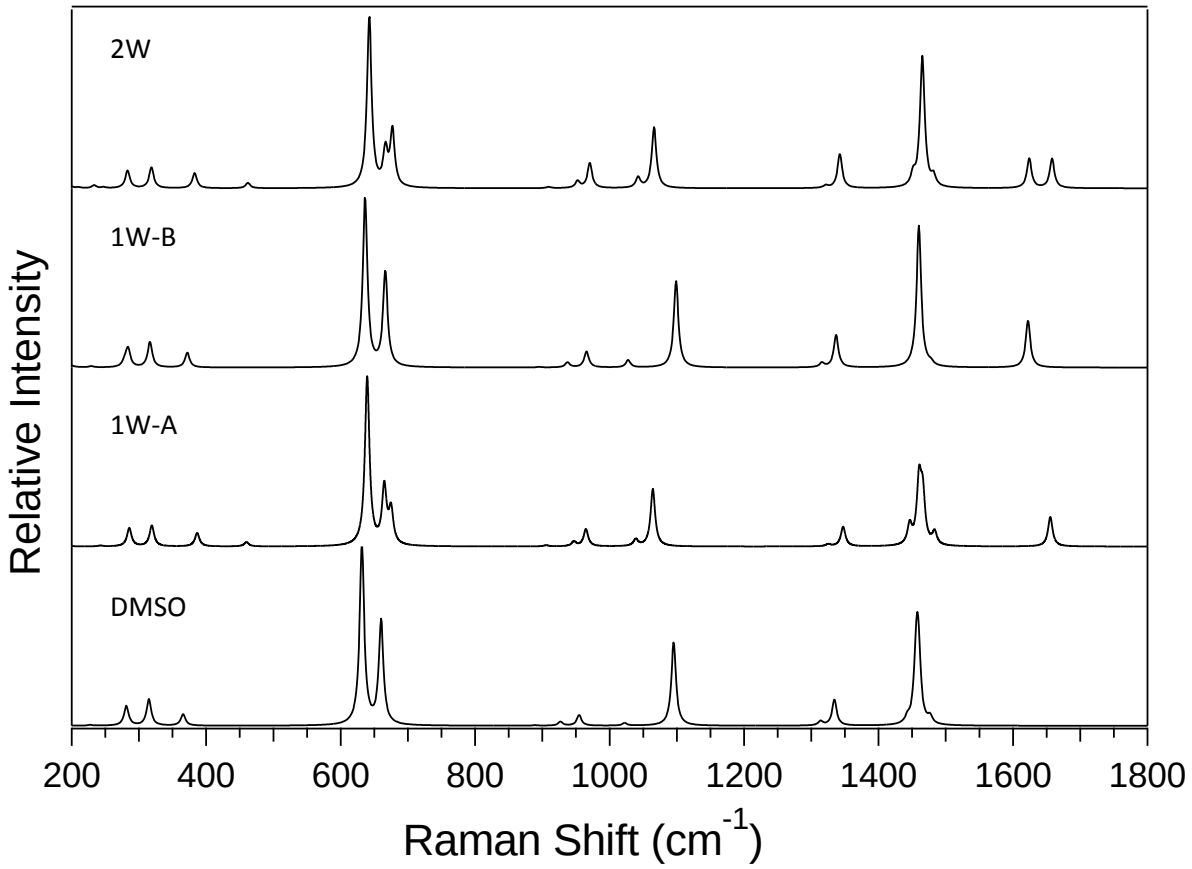

Figure 5.7 Theoretical Raman spectra of optimized molecular structures

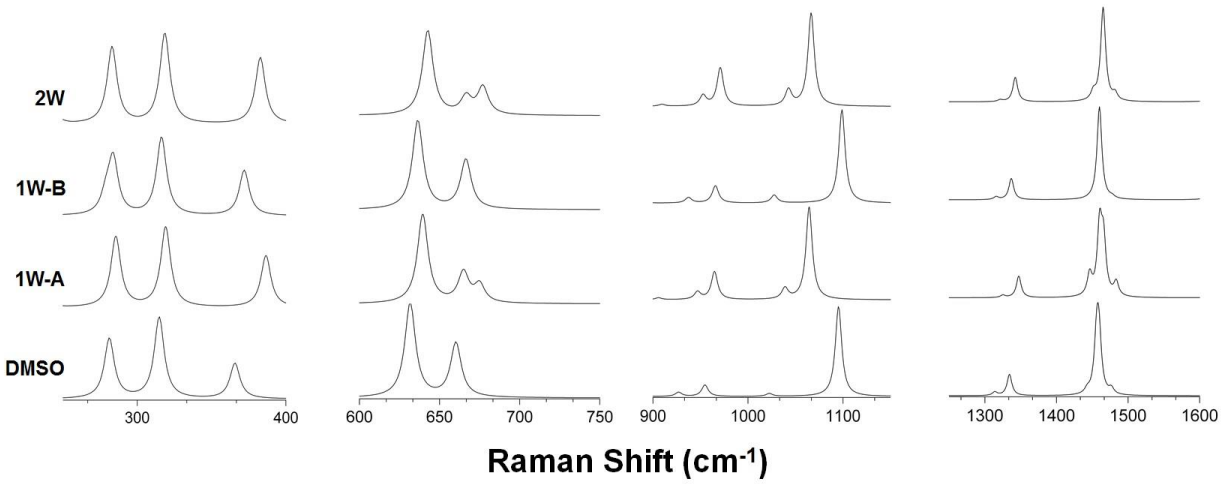

Figure 5.8 Theoretical Raman spectra of selected normal modes

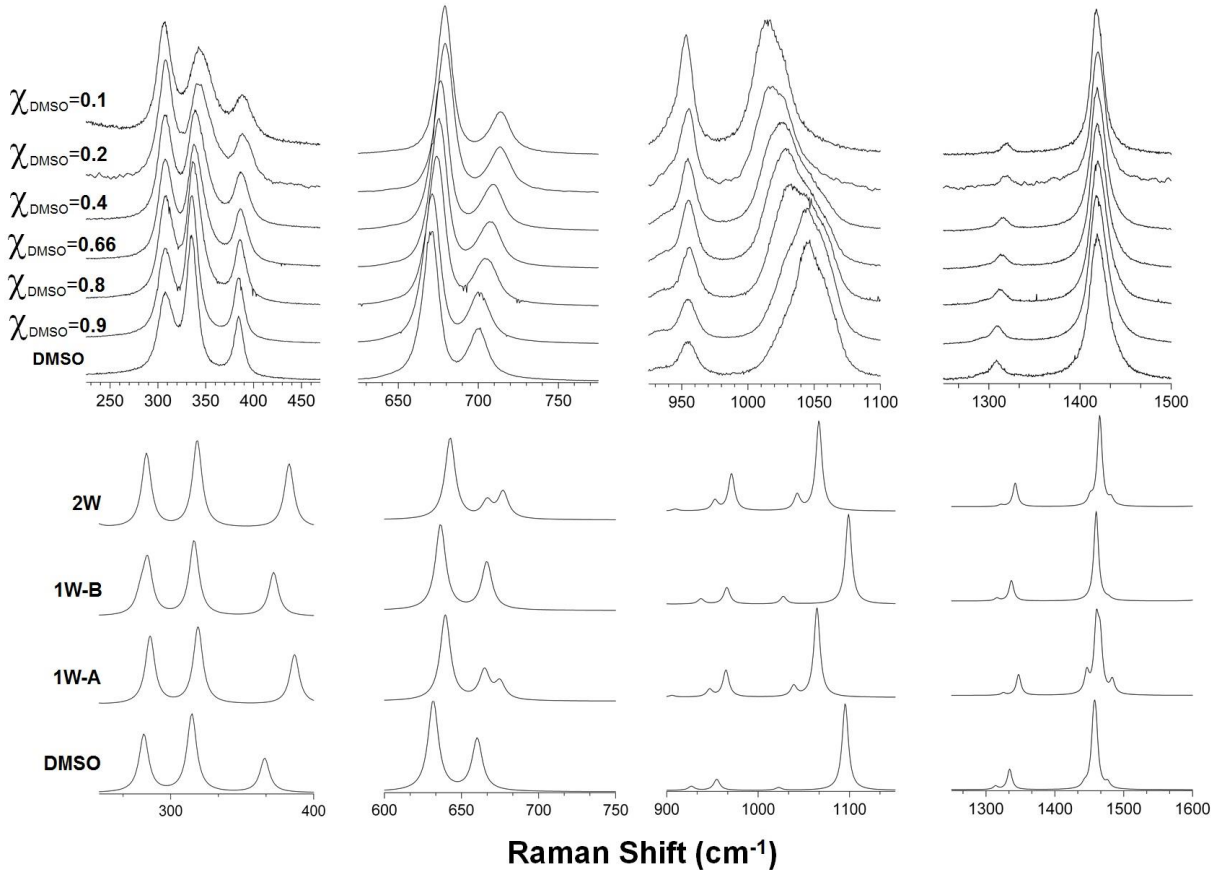

Figure 5.9 Comparison of the experimental and theoretical Raman spectra of DMSO/water mixtures

5.4 DISCUSSION

Overall, theory and experiment agree very well, suggesting that the hydrogen bonding of just one water molecule to DMSO's oxygen atom is sufficient to describe the important electronic and structural interactions at play. Table 5.2 summarizes the experimental and theoretical shifts observed here. Poor absolute agreement in DMSO's S-C stretching modes is likely due to DMSO - DMSO interactions, which are not considered here. Red and blue are terms commonly used in literature to explain a shift to lower wavenumbers (red) or to higher wavenumbers (blue). There are a number of noticeable red and blue shifts apparent in DMSO's Raman spectrum. The largest shift is a red shift of -30 cm^{-1} in DMSO's S=O stretching mode (ν_{20}) centered at 1045 cm^{-1}. This agrees well with earlier studies of this mode and predictions from theory.[10, 16] Earlier investigations attributed this peak to several complex DMSO/water structures. Here, the 30 cm^{-1} shift is recovered very well by the 1W-A structure, which predicts a shift of 31 cm^{-1}.

Mode[17]	**Original location(cm^{-1})**	**Max shift (cm^{-1})**	**1W-A shift (cm^{-1})**
ν_{12}	308	-1	+5
ν_{23}	335	+5	+4
ν_{11}	384	+10	+20
ν_{10}	670	+9	+7
ν_{22}	700	+14	+15
ν_{9}	955	-2	+10
ν_{20}	1045	-30	-31
ν_{6}	1308	+10	+13
ν_{17} & ν_{5}	1419	-1	+4

Table 5.2 Maximum Experimental Shifts of Selected Normal Modes of DMSO in Aqueous Solution Compared to Shift Observed in the 1W-A Structure

DMSO also exhibits several blue shifts. The largest blue shift is +14 cm^{-1} in DMSO's S-C asymmetric stretching mode (ν_{22}) centered at 700 cm^{-1}. This blue shift is also recovered very well by the 1W-A structure, which predicts a shift of 15 cm^{-1}. A blue shift of +5 cm^{-1} is apparent in DMSO's C-S-O bending mode (ν_{23}) centered at 335 cm^{-1}. Theory predicts this shift to be 4 cm^{-1}. A blue shift of +10 cm^{-1} in DMSO's deformation mode (ν_{11}) centered at 384 cm^{-1} compared to a predicted shift of 20 cm^{-1}. The poor agreement in the case of this mode is likely due to not considering effects of DMSO dimer interactions. A blue shift of +9 cm^{-1} in DMSO's symmetric S-C stretching mode (ν_{10}) centered at 670 cm^{-1} agrees well with the predicted shift of +7 cm^{-1}. A blue shift of +10 cm^{-1} in DMSO's CH_3 wagging mode (ν_6) centered at 1308 cm^{-1} also agrees well with the predicted shift of +13 cm^{-1}. Interestingly, only very small shifts were observed in DMSO's CSC bending mode (ν_{12}) at 308 cm^{-1} and the overlapped CH bending modes (ν_{17} & ν_5) centered at 1419 cm^{-1}. When forming the 1W-A complex, the S=O bond length in DMSO changed from 1.49576 to 1.50936 Angstroms. This lengthening is believed to be due to an electron density transfer due to the hydrogen bonding of the water molecule to DMSO. The large blue shifts, however, also have an additional origin. The large +14 cm^{-1} shift in ν_{22} is likely due to the fact that this mode in the 1W-A complex is strongly coupled to a water wagging motion of the hydrogen bound proton.

5.5 CONCLUSIONS

The effects of hydrogen bonding by water on DMSO's normal modes can be adequately reproduced by the addition of just one water molecule. This includes the large red shift of -30 cm^{-1} in DMSO's S=O stretching mode (ν_{20}) and the large blue shift of +14 cm^{-1} in DMSO's S-C

asymmetric stretching mode (ν_{22}). In both cases, a theoretical structure of DMSO and one hydrogen bound water molecule reproduces experimental results to within 1 cm^{-1}. The reasons for these two shifts, however, have different origins. In the case of the large red shift, electron density reorganization lengthens the S=O bond, which leads to the red shift. In the case of ν_{22}, strong coupling of a large amplitude motion of the water molecule to the mode leads to the large blue shift.

CHAPTER 5

BIBLIOGRAPHY

REFERENCES

1. Ashley M. Wright, A. A. H., J.Coleman Howard, Gregory S. Tschumper, and Nathan I. Hammer, Charge Transfer and Blue Shifting of Vibrational Frequencies in a Hydrogen Bond Acceptor. *J. Phys. Chem. A* **2013**.
2. James W. Robinson, E. M. S. F., George M. Frame II, *Undergraduate Instrumental Analysis*. 6th ed.; Marcel Decker: New York, NY, 2005.
3. Mortimer, R. G., *Physical Chemistry*. 2nd ed.; Academic Press: San Diego, CA, 2000; p 751-806.
4. (a) Becke, A. D., Density-functional thermochemistry. III. The role of exact exchange. *J. Chem. Phys.* **1993,** *98* (7), 5648-52; (b) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J., Gaussian 09, Revision B.01. In *Gaussian 09, Revision B.01, Gaussian, Inc., Wallingford CT*, Wallingford CT, 2009; (c) Lee, C.; Yang, W.; Parr, R. G., Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. *Phys. Rev. B: Condens. Matter* **1988,** *37* (2), 785-9.
5. Muir, M. DMSO: Many Uses, Much Controversy. (accessed June 11th).
6. Shikata, T.; Sugimoto, N., Dimeric molecular association of dimethyl sulfoxide in solutions of nonpolar liquids. *Journal of Physical Chemistry A* **2012,** *116* (3), 990-999.
7. Tamres, M.; Searles Jr, S., Hydrogen bonding abilities of cyclic sulfoxides and cyclic ketones. *Journal of the American Chemical Society* **1959,** *81* (9), 2100-2104.
8. Shikata, T.; Sugimoto, N., Reconsideration of the anomalous dielectric behavior of dimethyl sulfoxide in the pure liquid state. *Physical Chemistry Chemical Physics* **2011,** *13* (37), 16542-16547.
9. El-Sherif, A. A.; Shoukry, M. M.; Abd-Elgawad, M. M. A., Protonation equilibria of some selected α-amino acids in DMSO-water mixture and their Cu(II)-complexes. *Journal of Solution Chemistry* **2013,** *42* (2), 412-427.

10. Wong, D. B.; Sokolowsky, K. P.; El-Barghouthi, M. I.; Fenn, E. E.; Giammanco, C. H.; Sturlaugson, A. L.; Fayer, M. D., Water dynamics in water/DMSO binary mixtures. *Journal of Physical Chemistry B* **2012,** *116* (18), 5479-5490.
11. Venkataramanan, N. S., Microsolvation of DMSO: Density functional study on the structure and polaraizabilities. *International Journal of Quantum Chemistry* **2012,** *112* (13), 2599-2606.
12. Ouyang, S. L.; Li, Z. Q.; Wu, N. N.; Li, Z. W.; Sun, C. L.; Fan, L. M., Temperature effect on the hydrogen bonding behavior between DMSO and water in aqueous DMSO solutions studied by Raman spectroscopy. *Guang Pu Xue Yu Guang Pu Fen Xi/Spectroscopy and Spectral Analysis* **2013,** *33* (9), 2425-2428.
13. Wulf, A.; Ludwig, R., Structure and dynamics of water confined in dimethyl sulfoxide. *ChemPhysChem* **2006,** *7* (1), 266-272.
14. Lovelock, J. E.; Bishop, M. W. H., *Prevention of freezing damage to living cells by dimethyl sulphoxide*.
15. Cowie, J. M. G.; Toporowski, P. M., *Association in the binary liquid system dimethyl sulfoxide-water*.
16. Singh, S.; Srivastava, S. K.; Singh, D. K., Raman scattering and DFT calculations used for analyzing the structural features of DMSO in water and methanol. *RSC Advances* **2013,** *3* (13), 4381-4390.
17. Skripkin, M. Y.; Lindqvist-Reis, P.; Abbasi, A.; Mink, J.; Perssone, I.; Sandstrom, M., Vibrational spectroscopic force field studies of dimethyl sulfoxide and hexakis(dimethyl sulfoxide)scandium(III) iodide, and crystal and solution structure of the hexakis(dimethyl sulfoxide)scandium(III) ion. *Dalton Transactions* **2004,** *2004*, 4 0 3 8 – 4 0 4 9.

Ashley M. Wright, A. A. H., J.Coleman Howard, Gregory S. Tschumper, and Nathan I. Hammer. (2013). Charge Transfer and Blue Shifting of Vibrational Frequencies in a Hydrogen Bond Acceptor. *J. Phys. Chem. A.* doi: DOI: 10.102/jp401642b

Becke, A. D. (1993). Density-functional thermochemistry. III. The role of exact exchange. *J. Chem. Phys., 98*(7), 5648-5652. doi: DOI: 10.1063/1.464913

Cowie, J. M. G., & Toporowski, P. M. *Association in the binary liquid system dimethyl sulfoxide-water*.

El-Sherif, A. A., Shoukry, M. M., & Abd-Elgawad, M. M. A. (2013). Protonation equilibria of some selected α-amino acids in DMSO-water mixture and their Cu(II)-complexes. *Journal of Solution Chemistry, 42*(2), 412-427. doi: DOI: 10.1007/s10953-013-9966-0

Frisch, M. J., Trucks, G. W., Schlegel, H. B., Scuseria, G. E., Robb, M. A., Cheeseman, J. R., . . . Fox, D. J. (2009). Gaussian 09, Revision B.01 *Gaussian 09, Revision B.01, Gaussian, Inc., Wallingford CT*. Wallingford CT.

James W. Robinson, E. M. S. F., George M. Frame II. (2005). *Undergraduate Instrumental Analysis* (6th ed.). New York, NY: Marcel Decker.

Lee, C., Yang, W., & Parr, R. G. (1988). Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. *Phys. Rev. B: Condens. Matter, 37*(2), 785-789.

Lovelock, J. E., & Bishop, M. W. H. *Prevention of freezing damage to living cells by dimethyl sulphoxide*.

Mortimer, R. G. (2000). *Physical Chemistry* (2nd ed.). San Diego, CA: Academic Press.

Muir, M. (1996, August 1996). DMSO: Many Uses, Much Controversy. Retrieved June 11th 2014

Ouyang, S. L., Li, Z. Q., Wu, N. N., Li, Z. W., Sun, C. L., & Fan, L. M. (2013). Temperature effect on the hydrogen bonding behavior between DMSO and water in aqueous DMSO solutions studied by Raman spectroscopy. *Guang Pu Xue Yu Guang Pu Fen Xi/Spectroscopy and Spectral Analysis, 33*(9), 2425-2428. doi: 10DOI: .3964/j.issn.1000-0593(2013)09-2425-04

Shikata, T., & Sugimoto, N. (2011). Reconsideration of the anomalous dielectric behavior of dimethyl sulfoxide in the pure liquid state. *Physical Chemistry Chemical Physics, 13*(37), 16542-16547. doi: DOI: 10.1039/c1cp21479a

Shikata, T., & Sugimoto, N. (2012). Dimeric molecular association of dimethyl sulfoxide in solutions of nonpolar liquids. *Journal of Physical Chemistry A, 116*(3), 990-999. doi: DOI: 10.1021/jp210122y

Singh, S., Srivastava, S. K., & Singh, D. K. (2013). Raman scattering and DFT calculations used for analyzing the structural features of DMSO in water and methanol. *RSC Advances, 3*(13), 4381-4390. doi: DOI: 10.1039/c3ra22730h

Skripkin, M. Y., Lindqvist-Reis, P., Abbasi, A., Mink, J., Perssone, I., & Sandstrom, M. (2004). Vibrational spectroscopic force field studies of dimethyl sulfoxide and hexakis(dimethyl sulfoxide)scandium(III) iodide, and crystal and solution structure of the hexakis(dimethyl sulfoxide)scandium(III) ion. *Dalton Transactions, 2004*, 4 0 3 8 – 4 0 4 9.

Tamres, M., & Searles Jr, S. (1959). Hydrogen bonding abilities of cyclic sulfoxides and cyclic ketones. *Journal of the American Chemical Society, 81*(9), 2100-2104.

Venkataramanan, N. S. (2012). Microsolvation of DMSO: Density functional study on the structure and polaraizabilities. *International Journal of Quantum Chemistry, 112*(13), 2599-2606. doi: DOI: 10.1002/qua.23289

Wong, D. B., Sokolowsky, K. P., El-Barghouthi, M. I., Fenn, E. E., Giammanco, C. H., Sturlaugson, A. L., & Fayer, M. D. (2012). Water dynamics in water/DMSO binary mixtures. *Journal of Physical Chemistry B, 116*(18), 5479-5490. doi: DOI: 10.1021/jp301967e

Wulf, A., & Ludwig, R. (2006). Structure and dynamics of water confined in dimethyl sulfoxide. *ChemPhysChem, 7*(1), 266-272. doi: DOI: 10.1002/cphc.200500425

1. Ashley M. Wright, A. A. H., J.Coleman Howard, Gregory S. Tschumper, and Nathan I. Hammer, Charge Transfer and Blue Shifting of Vibrational Frequencies in a Hydrogen Bond Acceptor. *J. Phys. Chem. A* **2013**.

2. James W. Robinson, E. M. S. F., George M. Frame II, *Undergraduate Instrumental Analysis*. 6th ed.; Marcel Decker: New York, NY, 2005.

3. Mortimer, R. G., *Physical Chemistry*. 2nd ed.; Academic Press: San Diego, CA, 2000; p 751-806.

4. (a) Becke, A. D., Density-functional thermochemistry. III. The role of exact exchange. *J. Chem. Phys.* **1993,** *98* (7), 5648-52; (b) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.;

Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J., Gaussian 09, Revision B.01. In *Gaussian 09, Revision B.01, Gaussian, Inc., Wallingford CT*, Wallingford CT, 2009; (c) Lee, C.; Yang, W.; Parr, R. G., Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. *Phys. Rev. B: Condens. Matter* **1988,** *37* (2), 785-9.

5. Muir, M. DMSO: Many Uses, Much Controversy. (accessed June 11th).
6. Shikata, T.; Sugimoto, N., Dimeric molecular association of dimethyl sulfoxide in solutions of nonpolar liquids. *Journal of Physical Chemistry A* **2012,** *116* (3), 990-999.
7. Tamres, M.; Searles Jr, S., Hydrogen bonding abilities of cyclic sulfoxides and cyclic ketones. *Journal of the American Chemical Society* **1959,** *81* (9), 2100-2104.
8. Shikata, T.; Sugimoto, N., Reconsideration of the anomalous dielectric behavior of dimethyl sulfoxide in the pure liquid state. *Physical Chemistry Chemical Physics* **2011,** *13* (37), 16542-16547.
9. El-Sherif, A. A.; Shoukry, M. M.; Abd-Elgawad, M. M. A., Protonation equilibria of some selected α-amino acids in DMSO-water mixture and their Cu(II)-complexes. *Journal of Solution Chemistry* **2013,** *42* (2), 412-427.
10. Wong, D. B.; Sokolowsky, K. P.; El-Barghouthi, M. I.; Fenn, E. E.; Giammanco, C. H.; Sturlaugson, A. L.; Fayer, M. D., Water dynamics in water/DMSO binary mixtures. *Journal of Physical Chemistry B* **2012,** *116* (18), 5479-5490.
11. Venkataramanan, N. S., Microsolvation of DMSO: Density functional study on the structure and polaraizabilities. *International Journal of Quantum Chemistry* **2012,** *112* (13), 2599-2606.
12. Ouyang, S. L.; Li, Z. Q.; Wu, N. N.; Li, Z. W.; Sun, C. L.; Fan, L. M., Temperature effect on the hydrogen bonding behavior between DMSO and water in aqueous DMSO solutions studied by Raman spectroscopy. *Guang Pu Xue Yu Guang Pu Fen Xi/Spectroscopy and Spectral Analysis* **2013,** *33* (9), 2425-2428.
13. Wulf, A.; Ludwig, R., Structure and dynamics of water confined in dimethyl sulfoxide. *ChemPhysChem* **2006,** *7* (1), 266-272.
14. Lovelock, J. E.; Bishop, M. W. H., *Prevention of freezing damage to living cells by dimethyl sulphoxide*.
15. Cowie, J. M. G.; Toporowski, P. M., *Association in the binary liquid system dimethyl sulfoxide-water*.
16. Singh, S.; Srivastava, S. K.; Singh, D. K., Raman scattering and DFT calculations used for analyzing the structural features of DMSO in water and methanol. *RSC Advances* **2013,** *3* (13), 4381-4390.
17. Skripkin, M. Y.; Lindqvist-Reis, P.; Abbasi, A.; Mink, J.; Perssone, I.; Sandstrom, M., Vibrational spectroscopic force field studies of dimethyl sulfoxide and hexakis(dimethyl sulfoxide)scandium(III) iodide, and crystal and solution structure of the hexakis(dimethyl sulfoxide)scandium(III) ion. *Dalton Transactions* **2004,** *2004*, 4 0 3 8 – 4 0 4 9.

1. Ashley M. Wright, A. A. H., J.Coleman Howard, Gregory S. Tschumper, and Nathan I. Hammer, Charge Transfer and Blue Shifting of Vibrational Frequencies in a Hydrogen Bond Acceptor. *J. Phys. Chem. A* **2013**. DOI: 10.102/jp401642b
2. James W. Robinson, E. M. S. F., George M. Frame II, *Undergraduate Instrumental Analysis*. 6th ed.; Marcel Decker: New York, NY, 2005.

3. Mortimer, R. G., *Physical Chemistry*. 2nd ed.; Academic Press: San Diego, CA, 2000; p 751-806.
4. (a) Becke, A. D., Density-functional thermochemistry. III. The role of exact exchange. *J. Chem. Phys.* **1993,** *98*, 5648-52. DOI: 10.1063/1.464913; (b) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J., Gaussian 09, Revision B.01. In *Gaussian 09, Revision B.01, Gaussian, Inc., Wallingford CT*, Wallingford CT, 2009; (c) Lee, C.; Yang, W.; Parr, R. G., Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. *Phys. Rev. B: Condens. Matter* **1988,** *37*, 785-9.
5. Muir, M. DMSO: Many Uses, Much Controversy. (accessed June 11th).
6. Shikata, T.; Sugimoto, N., Dimeric molecular association of dimethyl sulfoxide in solutions of nonpolar liquids. *Journal of Physical Chemistry A* **2012,** *116*, 990-999. DOI: 10.1021/jp210122y
7. Tamres, M.; Searles Jr, S., Hydrogen bonding abilities of cyclic sulfoxides and cyclic ketones. *Journal of the American Chemical Society* **1959,** *81*, 2100-2104.
8. Shikata, T.; Sugimoto, N., Reconsideration of the anomalous dielectric behavior of dimethyl sulfoxide in the pure liquid state. *Physical Chemistry Chemical Physics* **2011,** *13*, 16542-16547. DOI: 10.1039/c1cp21479a
9. El-Sherif, A. A.; Shoukry, M. M.; Abd-Elgawad, M. M. A., Protonation equilibria of some selected α-amino acids in DMSO-water mixture and their Cu(II)-complexes. *Journal of Solution Chemistry* **2013,** *42*, 412-427. DOI: 10.1007/s10953-013-9966-0
10. Wong, D. B.; Sokolowsky, K. P.; El-Barghouthi, M. I.; Fenn, E. E.; Giammanco, C. H.; Sturlaugson, A. L.; Fayer, M. D., Water dynamics in water/DMSO binary mixtures. *Journal of Physical Chemistry B* **2012,** *116*, 5479-5490. DOI: 10.1021/jp301967e
11. Venkataramanan, N. S., Microsolvation of DMSO: Density functional study on the structure and polaraizabilities. *International Journal of Quantum Chemistry* **2012,** *112*, 2599-2606. DOI: 10.1002/qua.23289
12. Ouyang, S. L.; Li, Z. Q.; Wu, N. N.; Li, Z. W.; Sun, C. L.; Fan, L. M., Temperature effect on the hydrogen bonding behavior between DMSO and water in aqueous DMSO solutions studied by Raman spectroscopy. *Guang Pu Xue Yu Guang Pu Fen Xi/Spectroscopy and Spectral Analysis* **2013,** *33*, 2425-2428. 10DOI: .3964/j.issn.1000-0593(2013)09-2425-04
13. Wulf, A.; Ludwig, R., Structure and dynamics of water confined in dimethyl sulfoxide. *ChemPhysChem* **2006,** *7*, 266-272. DOI: 10.1002/cphc.200500425
14. Lovelock, J. E.; Bishop, M. W. H., *Prevention of freezing damage to living cells by dimethyl sulphoxide*.

15. Cowie, J. M. G.; Toporowski, P. M., *Association in the binary liquid system dimethyl sulfoxide-water*.
16. Singh, S.; Srivastava, S. K.; Singh, D. K., Raman scattering and DFT calculations used for analyzing the structural features of DMSO in water and methanol. *RSC Adv.* **2013,** *3*, 4381-4390. DOI: 10.1039/c3ra22730h
17. Skripkin, M. Y.; Lindqvist-Reis, P.; Abbasi, A.; Mink, J.; Perssone, I.; Sandstrom, M., Vibrational spectroscopic force field studies of dimethyl sulfoxide and hexakis(dimethyl sulfoxide)scandium(III) iodide, and crystal and solution structure of the hexakis(dimethyl sulfoxide)scandium(III) ion. *Dalton Transactions* **2004,** *2004*, 4 0 3 8 – 4 0 4 9.