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Coordination Directed Self Assembly of Pt/Pd Mono-and Multinuclear Complexes

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Coordination-Directed Self-Assembly of

Palladium/Platinum Square Complexes

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THESIS

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The completion of this journey would have been impossible without the help and encouragement of a cast of seemingly hundreds over the past years. It is said that no man is an island and that could not be more true than now. I could not have achieved any of my current successes without the support of my family, from a pair of supportive patience with infinite amounts of patience to a younger sister who was always ready to take a backseat when it seemed I needed the lion's share of attention and resources. Grandparents with us and not, all of whom provided inspiration and desire for success, and while not all of them are here to celebrate this and other achievements I know they are with me always, watching and protecting long after I think I no longer need it. There are also members of my family who have sought higher education as well, traveling the path ahead of me, giving me a roadmap of what to expect, giving guidance and advice that is rooted in personal experiences, which is more valuable that one can imagine during this time of my life. Lastly the introduction of the newest member of my family has given me a renewed desire to strive to succeed and achieve. He is my reason for looking to the future and chasing success. As I was blessed in my own life to be surrounded with positive role models and examples of achievement, I will work all my life to exhibit that same drive and help him develop tools to go even further than I ever will.

The help and support do not end once I leave home. There is an incredible support network on campus that cannot be overlooked. My undergrad research career was started in Dr. Beth Gardner's lab, a woman who gave me a start when I had no experience and took countless hours to train me and involve me with all of her ongoing projects, as well as allow me to explore my own curiosities. Upon her departure from the university I was taken in by Dr. Juan Noveron, a man who made me feel at home in his group from the first day. He has provided me with the guidance and knowledge to take my project to this level. During my stay as a graduate student I was blessed enough to receive a fellow position in the NSF GK-12 program (DGE 0538623). While the stellar finical assistance this fellowship provided cannot be overlooked, the greatest part of this experience was the unconditional support and encouragement the faculty and staff offered during, and long after the project had ended, for that I am grateful. I also spent a year under the supervision of Dr. Bonnie Gunn. As her TA I learned a whole new system of classroom management and more so an enthusiasm for teaching chemistry. She took me in and gave me the opportunity to prove myself when it seemed others were not eager to do the same. Having spent countless hours working with me one on one analyzing my compounds and giving feedback is one of the many ways she went above and beyond her position. For that I am thankful.

Finally, I owe a debt of thanks to all my friends both in and out of the department who have made my life exciting, enjoyable and at times unpredictable. No sane person could have made it through this process without laughter and good times. While the support I received from all areas of my life made my achievements possible, the kinship I received from my social circle made the journey enjoyable.

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ABSTRACT

This research focuses on the development of mononuclear platinum complexes; multinuclear platinum complexes, both of which self assemble into micelles in the presence of water. This work also involved the synthesis of a reverse micelle that allows for detection of water nanocrystals within a defined size molecular envelope. The novel synthesis of these compounds allows for ligand substitution and the creation of a library of compounds.

CHAPTER 1:

INTRODUCTION AND LITERATURE REVIEW

Mononuclear platinum complexes, multinuclear platinum complexes, and inverse micelle synthesis are the main focus of this research. When speaking about platinum complexes, one cannot leave out the amazing discovery of cisplatin.

As illustrated by Howell in his paper (1991), "Cis-Platin, discovered by B. Rosenberg, et. al. in 1969 is nowadays one of the best and widely used antitumor agents in cancer chemotherapy…Various attempts have been made to prepare future generation antitumor Pt complexes, ameliorating severe toxicities" (pp. 127). Cisplatin has been renowned for years as having been a leading anti-cancer drug. Here, some of the remarkable advances in cancer research will be thoroughly discussed, with the advent of platinum-based drugs having had a wondrous impact on science and coordination chemistry in general.

Cisplatin is favored by many in the biomedical sciences as the wonder drug that has actively helped several people overcome cancer. Cisplatin is not just a miraculous drug in the sense that it is currently being used against many forms of breast cancer, while it does kill tumors, it does not cure people. Cisplatin is also miraculous in the sense that it has gone above and beyond what was expected of it as a drug. Cisplatin has shattered the perceptions of what could possibly be done in coordination chemistry.

Modern inorganic chemistry has faced the boondoggle of developing effective cancer therapy drugs for years. However, it was not until cisplatin was discovered that scientists finally got the idea to begin testing more platinum drugs. Other Pt complexes have begun to be clinically tested and distributed over time. Not only that, but there are more and more coordinated compounds that continue to be developed that have platinum bases, in order to combat cancer and its ill effects.

Certainly, the properties evidenced in cisplatin are germane to other sciences. Not as stated by Gispert (2008), "Polynuclear transition metal chemistry is an area of modern science whose interfaces with many disciplines have provided invaluable opportunities for crossing boundaries both within and between the sciences of chemistry, physics, and biology. Indeed, molecular multimetallic compounds have unusual and useful catalytic, optical, photochemical, electronic, and magnetic properties" (pp. 129).

Other sciences are now realizing the value that this research has unearthed, particularly with polynuclear compounds such as multinuclear platinum complexes. This will be discussed later, second, along with mononuclear platinum complexes, first, and inverse micelle synthesis, third.

Cisplatin is now considered one of the leading anti-cancer drugs currently being studied. The value of this drug cannot go unnoticed. Without a doubt, chemists will be analyzing the molecular make-up of this drug in order to replicate similar drugs. Physicians and bio-chemists will want to know the make-up of cisplatin as well. They will want to be able to explain the physics and the hard science of how cisplatin works. Biologists will want to know how cisplatin affects the living organism and its cells. Biologists especially will need this information in order to help other scientists excel in cancer research.

Ligands play a large role in how mononuclear platinum complexes are structured. Singh (2002), "In coordination compounds, metals are surrounded by groups that are called ligands", they play a major role in the chemistry of metal complexes. The…groups that may surround a metal atom or ion are …varied, but they may be broadly considered to be of two types: ligands that bond to metal atoms or ions through carbon atoms, and ligands that do not" (pp. 88). A ligand, in a mononuclear platinum complex—to illustrate the point—is much like the core of a

mango. The middle of the structure has one single core (the ligand), while the rest of the structure surrounds it (the molecules of Pt, platinum). The ligand, by definition, is basically the glue that holds together the entire structure. Ligands are important because, without them, the structure would not be able to be held together properly in place.

Sometimes ligand substitutions can occur. According to Choy (2003), "Platinum complexes are characterized by slow rates of ligand substitution reactions compared with other metal complexes. Evidence from Peter Stang's research supports this. Because of the slew reactions involved in platinum drugs binding to DNA, other intracellular nucleophiles…may compete with DNA for reaction" (pp. 47), this documented behavior gave cause for further study of metal-ligand complex interactions as related to biological activities.

What this is saying is that, basically, when there are slow reactions when ligand substitution happens, there are other parts between cells which may try to react faster. This could be problematic, especially if one ligand is particularly slow in reacting in contrast with another metal complex or other metal complexes. Ligands are a necessity. Without them there would be much difficulty in trying to facilitate the structure of the mononuclear platinum complex.

Many things can affect the platinum atom. In the works of Marusak, Doan, and Cummings (2007), "Force fields for *cis*-platin binding to DNA have been aggressively developed over the past 15 years.

Parameter refinements include the deviation of…bond[s] from the plane of the coordinated purine, planarity of the platinum moiety…and charges of the Pt atom, [among other things]" (pp. 151). Cisplatin is remarkable for many reasons, as well as other platinum-based drugs. The benefits of these drugs will be discussed more in detail later on, as well as what

cancer patients have to gain from this valuable research. A review of the literature includes sections about mononuclear platinum square complexes, multinuclear platinum complexes, and inverse micelle synthesis, as well as a discussion and conclusion.

Cisplatin is a very popular complex which is widely and used in current cancer treatment. Mackay, Mackay, and Henderson (2002), "The most widely used drug in the Western world and Japan for the treatment of cancer is a simple inorganic coordination complex…commonly known as *cisplatin*. This drug is particularly effective in the treatment of solid tumors…Like a number of other important scientific discoveries, [this was discovered by accident]" (pp. 559).

Cisplatin has proven to be very useful in treating cancer. This is why it has been labeled as a "wonder" drug. The development of cisplatin as an anti-cancer drug has been enormous. It has been widely researched across cultures and has been found to have excellent success in treating cancer, as aforementioned. Some researchers are so biased in favor of cisplatin that they do not want to test any new drugs. However, the bulk of the research goes against the idea that one should not look for new therapies approaching miraculous results. The way that cancer is treated deals with how the body reacts to chemicals. According to Kelland and Farrell (2000), "Accumulation of a drug is the net effect of drug influx and efflux.

Since the first reports of accumulation defects in cells with acquired resistance to cisplatin, much effort has been directed toward defining the mechanisms that cisplatin enters and leaves cells. "These mechanisms have been difficult to pinpoint" (pp. 89).

The way cisplatin is absorbed by the body has much to do with how the body reacts to having it in one's system. Basically, cisplatin in one's body changes the body chemistry. Therefore, some patients experience sickness. Once one has cisplatin in the system, it can tend to have an effect of build-up in the system. This could be helpful but it usually turns out to be

harmful in some way. Cancer patients are famous for feeling nauseous as well as vomiting. This is in part caused by the effects platinum-based drugs have on the body. Platinum is a naturally-occurring element in the body, but too much of it being introduced into the body can make a cancer patient sick. Because of the success of several types of drugs, this is fomenting new research.

In the works of Lippert (1999), "The success of cisplatin and carboplatin in treating cancer, combined with the intrinsic and acquired resistance of many tumors to traditional platinum chemotherapy, has generated considerable interest in developing next-generation platinum drugs. Since the discovery of the antitumor activity of cisplatin, researchers have reported…thousands of platinum compounds (pp. 523).

The possibility that there are more platinum compounds available make this facet of cancer research very exciting. The fact that there "could be" more potentially life-saving drugs which just remain undiscovered is a possibility that scientists are continually considering. Since there is no cure for cancer, cisplatin has proved close to being a cure. But researchers are still not there yet.

While everyone would like to acknowledge that some kind of a cure has been found, still this is not the case. Since Farrell's discovery of platinum-based drugs' effects in the '90s, many researchers in this field of cancer research have begun rethinking they way they saw anti-cancer drug therapy. Platinum complexes fight tumors effectively, which will be discussed in-depth in the next two sections. According to Gielen and Tiekink (2005), "The mode of action of platinum agents can also be considerably affected by means other than changing of chemical structure…originally inactive compounds can be activated…after [being] delivered to the target tumor cells or to their intracellular components, Platinum (IV) complexes represent one example

of this expanding class of anti-tumor agents" (pp. 499). The way that the chemical structure of platinum complexes is set up, they make perfect foils for targeting cancerous cells.

Knowing about different platinum complexes could be the breakthrough in solving the mystery of the cure for cancer. Written in Gielen, Willem, and Wrackmeyer (2004), "It is widely believed that the principal target of platinum anticancer agents in cells is DNA and the resulting DNA lesions are responsible for their biological activities…some…evidences have indicated that the attack of platinum complexes on other non-DNA cellular targets could… play roles in the antitumor activity of platinum drugs" (pp. 169).

CHAPTER 2:

MONONUCLEAR PLATINUM SQUARE COMPLEXES

2.1 Summary

The synthesis of a novel class of mononuclear cis-Pt/Pd phospine complexes with long chain lipids was accomplished. These compounds exhibit amphillic properties that allow them to self-assemble in water as micelles and have remarkable physical properties such as high stability in water. Figure 2.1 shows the molecular structure of the compounds presented in this chapter.

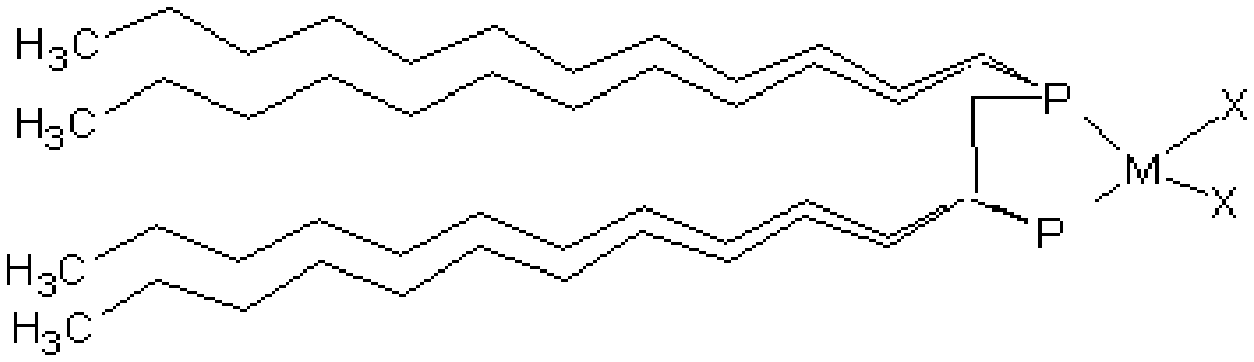

Figure 2.1. Structure of cis-Pt/Pd complex where M=Pt or Pd and X=Lewis Base

Introduction

Mononuclear platinum square complexes have three distinct aspects about them: usually they are square-planar; they effectively change the DNA of cells around them; and they are distinctively different from polynuclear or multinuclear platinum complexes. Mononuclear platinum square complexes are square-planar. This means that they basically have four atoms of platinum surrounding one atom of a particular ligand. In research conducted by Wiberg, Wiberg, and Holleman (2001), "Square planar complexes are formed especially readily by metal centers with [a certain] electron configuration…[usually] low-spin and therefore diamagnetic… Tetrahedral…complexes are paramagnetic with no unpaired electrons…only diamagnetic complexes are allowed with square coordination" (pp. 1187). A ligand is some type of element

that basically is made up of the atom in the center of the complex. There are a few different types of elements that could make up the central connecting ligand. The ligand is basically the part of the complex that connects the whole complex together. Without the ligand, there would be no bonding. Within the bonding of inorganic compounds, this is called coordination chemistry. It is a branch of inorganic chemistry.

Metallopharmaceuticals is the branch of medicine that deals with inorganic metals being placed into prescription drugs. What is important about the square-planar aspect follows shortly. Basically, the firm structure of the square-planar model makes for an excellent example of what is right with cancer research. This cannot go unnoticed. The square-planar model is a structurally efficient model. Only four atoms of platinum are needed for every one atom of ligand—whatever the element of that ligand might be.

As stated in Sykes (1994), "Deviations of each metal atom from the coordination plane defined by the four donor atoms are taken as a plus value when the metal atoms deviate from the coordination plane toward each other. It directly correlates with the difference between…distances only when the complexes have an eclipsed configuration" (pp. 194). Mononuclear platinum square complexes ultimately change the DNA of the cells around them. This is what makes them so effective at combating cancer and this is why they should be studied more.

Mononuclear platinum square complexes definitely are different from multinuclear platinum complexes. Although researchers are not entirely sure, they have many good hunches that multinuclear platinum complexes react differently than do their mononuclear counterparts. In fact, in some parts of the research world in cancer research, the jury is out as to which platinum complex is more effective. Right now, it seems as though there is still much interest in

the mononuclear platinum square complex. Because of the fact that it only has one ligand, this makes the mononuclear structure particularly desirable. Although small, a solid structure such as the square-planar platinum complex is being studied in-depth to determine if it is indeed more desirable than the multinuclear platinum complex.

Mononuclear platinum complexes are mainly distinctive from their multinuclear counterparts exactly because of that they have different counts of atoms in their centers. While mononuclear platinum square complexes have four atoms of platinum surrounding one atom of a ligand, multinuclear platinum complexes may have several atoms of a ligand in the nucleus.

In Demeunynck, Bailly, and Wilson (2003), "[There is a] fundamental difference between mononuclear and dinuclear platinum chemistry and biology—in the mononuclear case cisplatin is active, while its' direct isomer transplatin is antitumour-inactive…provid[ing] the impetus for the studies of molecular mechanisms underlying these differences" (pp. 205). Another distinct difference between mononuclear and multinuclear platinum complexes is the fact that they each have varying rates of effectiveness at curing cancer. One is favored more over the other in terms of its rate of efficiency in being able to eradicate cancer.

What happens is that, usually, the complex's ability to bind with DNA is a key factor in deciding whether it will bind to cancerous cells and then destroy them. The complex may have a substitutionary ligand that may react quicker than another ligand. So, in taking all of these matters into consideration, basically it depends upon the complex itself. If one ligand is reacting to the DNA faster than another ligand, it is more important that that particular complex is used (whichever one that is).

Substitutionary ligands become important to the project when one realizes that the faster-acting ligand will take place of the slower one. This can prove a major finding when conducting

an experiment. Basically, the way DNA is affected by the mononuclear platinum complex depends on a variety of factors. The quality of the platinum being used in the experiment could definitely affect how fast an element would bond to its metal ion ligand. According to Van Leeuwen (2004), "[R]ecent findings support a mononuclear platinum complex as the resting state and active state of the platinum…catalyst" (pp. 377). Usually, platinum complexes tend to be square-planar, as demonstrated in the research of Macintyre and Macintyre (1995), "Pt(II) complexes are predominantly square planar…"

"Most platinum complexes are air- and moisture-stable, and can be handled conventionally at ordinary temperatures" (pp. 2997). Crosslinking agents aid in the abetment of cancer. Thus, tetrahedron complexes such as this one are very helpful in the destruction of cancer cells. Written in Sigel and Sigel (2004), "Tetrafunctional complexes are also very effective ternary DNA-protein crosslinking agents…" (pp. 274).

These complexes also change themselves relevant to their surroundings. According to Dupont (2008), "Mononuclear…platinum complexes were mesomorphic…" (pp. 262). Reactions within the mononuclear square platinum complexes are a highly sought-after research topic. As documented in Screttas and Steele (2002), "[There is] a longstanding interest in the kinetics and reaction of mechanisms of four-coordinate coordination and organometallic square-planar complexes, especially those of platinum(II)" (pp. 208).

Sometimes tetrahedral complexes can become larger. In studies conducted by Gispert (2008), "Very large ligands tend not to yield this geometry, and neither do very small ligands favor it as they tend to increase the coordination number, giving rise to octahedral coordination" (pp. 64). The research among platinum compounds is exploding. Written in Farrell (1999), "During the last ten years,…a number of novel dinuclear Pt compounds [have been prepared],

where two platinum-amine coordination units are linked by a variable length diamine linker, as potential antitumor drugs… Extensively studied…new classes of platinum compounds [helped one] understand the patterns of DNA modification [with respect to] cytotoxicity…" (pp. 125).

2.3 Goals and Objectives

The goal is to synthesize a novel class of cis-Pt/Pd phospine complexes with long chain lipids. These compounds will exhibit amphiphillic properties that would allow them to self assemble in water as a micelle.

2.4 Multi-step Synthesis

The synthesis of the mononuclear compounds presented here in was carried out according to the following protocol:

Starting with palladium (II) chloride was reacted with 1.3 equivalents of cyclooctadiene in the presence of dichloromethane at room temperature for 24 hours. The solution was then filtered using gravity filtration. A bright yellow chalky solid was collected. The remaining solution was then roto-evaporated to extract any remaining product still in solution. The total yield was 82%. This gave a cis-Pd complex with chlorine on one end and cyclooctadiene on the opposite. (figure. 2.2).

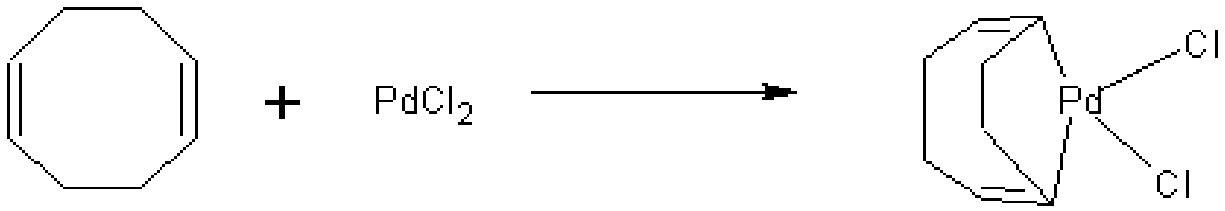

Figure 2.2 Synthesis of cid-Pd compound with cyclooctadiene

In the second step, the cis-Pd complex was reacted with a phospine ligand that had four dodecyl groups ($C_{12}H_{25}$) lipid chains attached. Because the phospine ligand was highly hygroscopic and in the presence of air would oxidize, the synthesis had to be carried out under anaerobic conditions using argon gas. The reaction vessel was prepared by using an acetone bath followed by one hour in the drying oven at a constant temperature. The hot round bottom flask was then removed and set up immediately before allowing it to cool and accumulate micro condensation. A septum was placed over the flask and one syringe needle was inserted to act as ventilation, argon gas was then allowed to flow in via a second syringe needle, since argon is heavier than oxygen, allowing it to flow freely into the reaction vessel for about thirty minutes replaced a sufficient amount of oxygen in order to nearly eliminate the possibility for premature oxidation. The cis-Pd /cyclooctadiene compound was reacted with the phospine ligand in a 1:21 ratio in the presence of chloroform and argon at room temperature for a 24 hour period. The resulting solution was filtered under gravity filtration. A crystalline white solid was collected. The filtrate was then rotoevaporated to obtain any product remaining in solution. The yield was 74%. The resulting cis-Pd compound now has the phospine ligand with lipid chains opposite the two chlorines

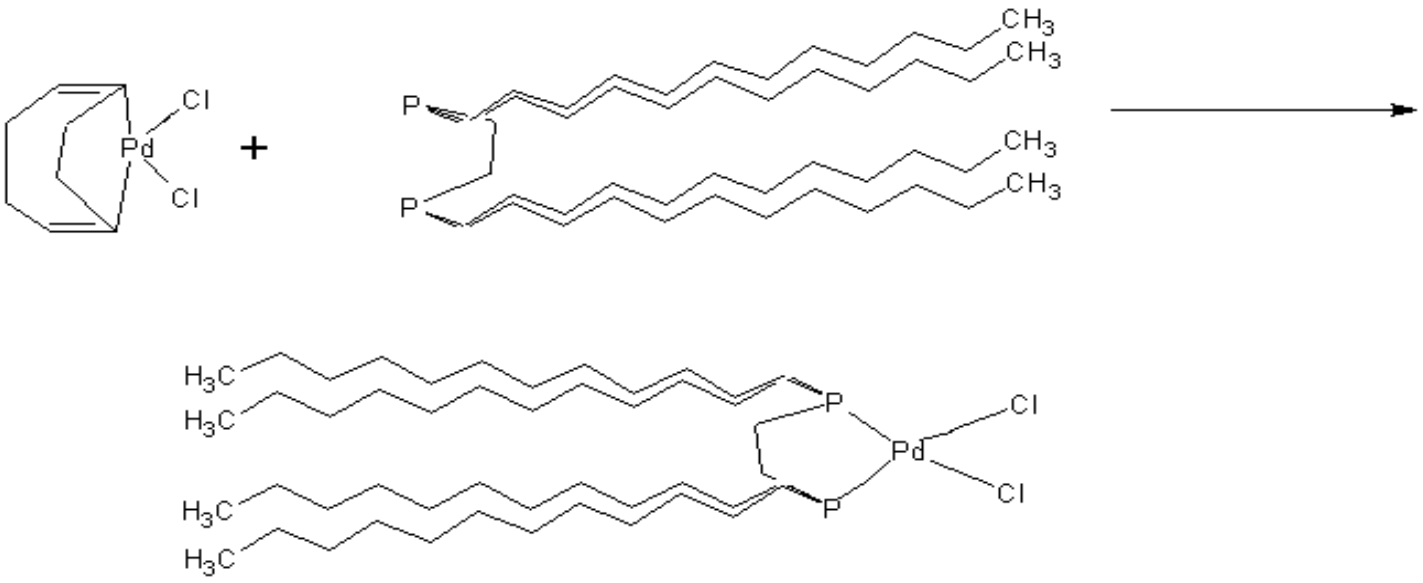

Fig 2.3 Synthesis of cis-Pd complex with Phosphine ligand.

The compound is then reacted with 2.4 equivalents of silver triflouromethane sulfonate in the presence of chloroform for 24 hours to replace the chlorides for the triflates, which can be easily cleaved in subsequent experiments. This reaction was done in a covered vessel to prevent light from photoreacting the protecting group, as silver is photosensitive. The resulting product is filtered in small scale increments under gravity filtration using glass fiber filters to collect the side product of silver chloride which is a fine black powder. This process had to be repeated several times in order to ensure no remaining silver chloride was in the solution. The resulting product remained in chloroform solution, the silver chloride was discarded. The resulting compound is similar to the aforementioned figure with the chlorine atoms replaced by a larger and easily cleavable protecting group.

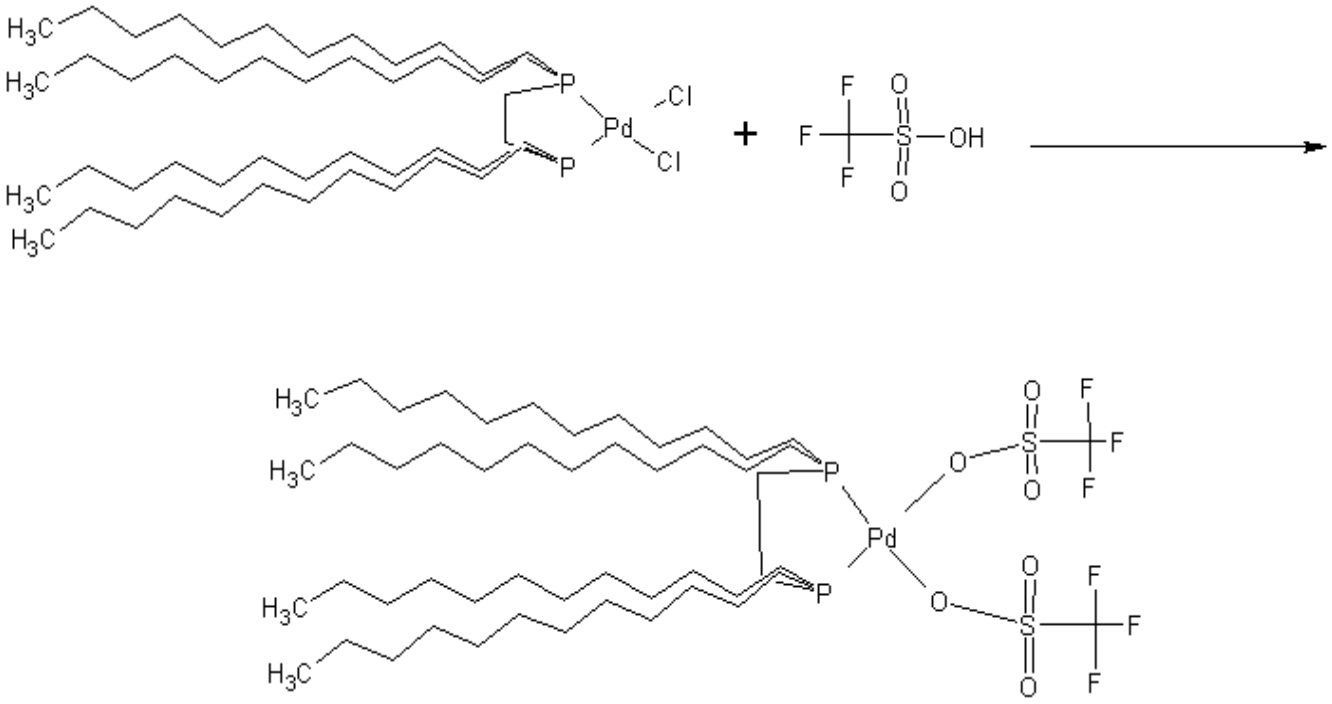

Figure 2.4 Synthesis of cid-Pd complex with triflouromethane sulfonate ligands

A mononuclear ligand was then substituted onto the complex after cleaving of the leaving group. This reaction took place in the presence of chloroform at room temperature for a 48 hour period with constant agitation. The ligand was added in a 2.3:1 ratio with the PD complex, as each individual

molecule required two ligands. The resultant product was then filtered under gravity filtration to remove the triflouromethane sulfonate that was replaced.

The remaining product was rotovaped and stored in a controlled molarity solution in deuterated methanol. This allowed for ease of characterization later on as well as optimal storage

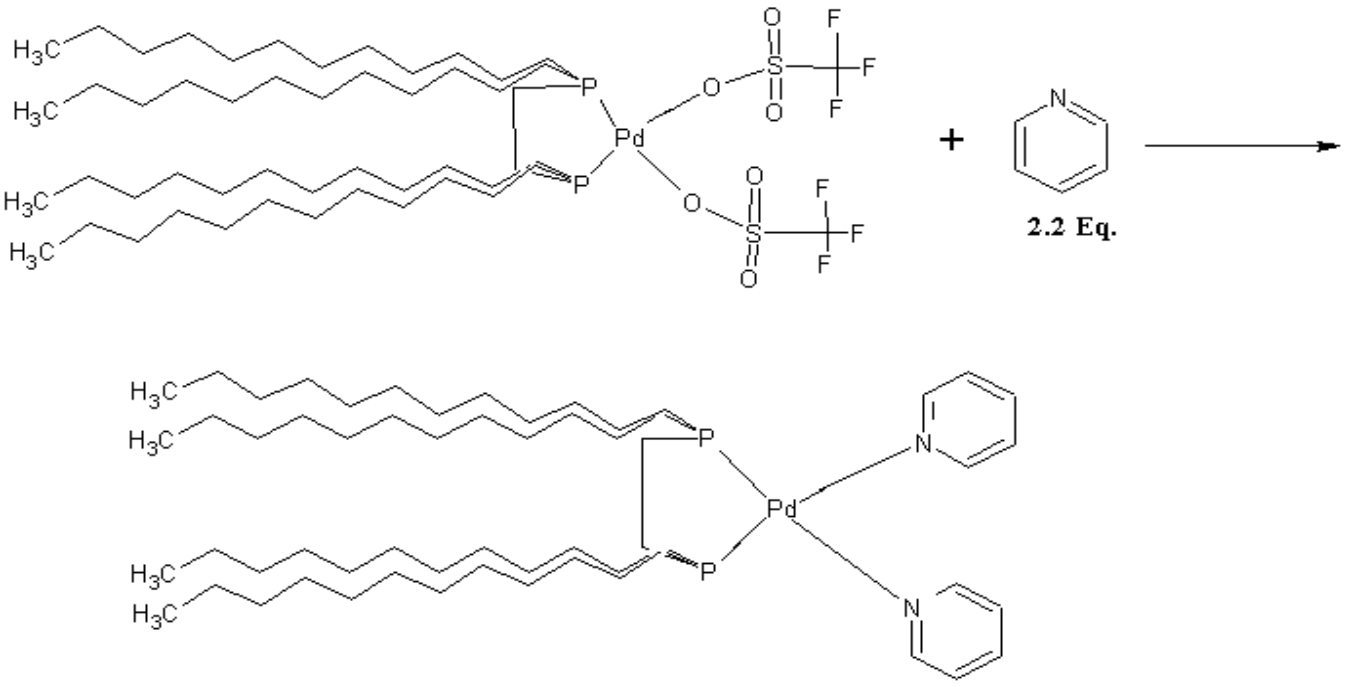

Figure 2.5 Synthesis of cis-Pd complex with mononuclear ligand

The compound was characterized using a JEOL 600MHz NMR instrument. As illustrated in the NMR data that confirms that the synthesis was a success. An initial ^{31}P scan of the compound with the triflouromethane sulfonate protecting groups shows a single intense peak, this is expected as the phospine ligands are symmetrical on the compound that would give rise to the single reading (figure 1). When a subsequent ^{31}P NMR experiment was run on the compound post substitution the same single intense peak appears and had also shifted, which as illustrated in the literature is consistent with pyridine ligands that were added (figure 2). Proton and carbon spectra respectively, were also used to assist in the characterization of the compound (figures 3 & 4).

The dynamic light scattering (DLS) data illustrates a single population distribution size of approximately 4600 nm (figure 5). This is consistent with the predicted structure of the compound. It also demonstrates a successful synthesis with little to no starting material present. These experiments were carried out in deuterated methanol.

CHAPTER 3:

MULTINUCLEAR PLATINUM COMPLEXES

3.1 Summary

The synthesis of a multi-nuclear cis-Pt/Pd phospine complex with long chain lipids was accomplished. These compounds exhibit amphiphillic properties that allow them to self-assemble in water as micelles and have remarkable physical properties such as high stability in water. Figure 2.1 shows the molecular structure of the compounds presented in this chapter.

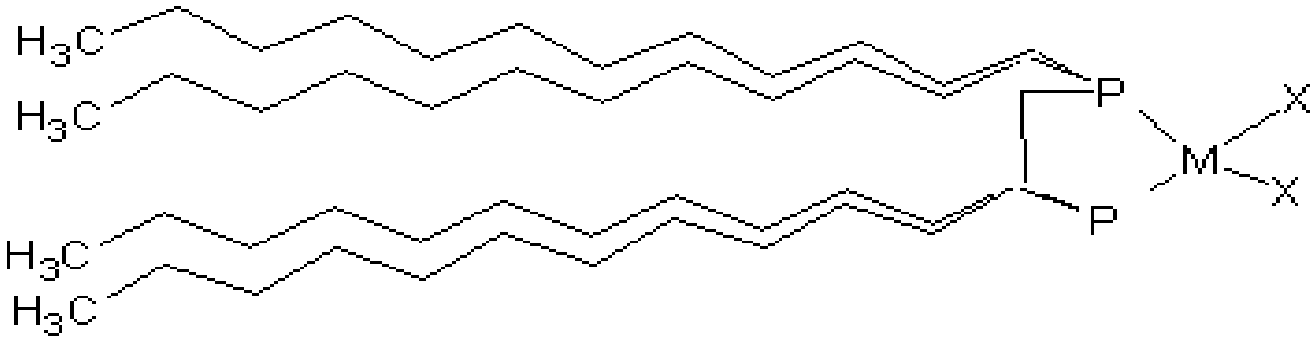

Figure 3.1 Molecular Structure of multinuclear Pt/Pd-complex where M=Pt/Pd and X=multinuclear ligand

In Moldave (2002), "The dinuclear platinum complexes, similar to cisplatin or carboplatin, bind to DNA and inhibit DNA replication and transcription, which indicates that DNA modification by dinuclear platinum complexes plays an important role in the mechanism of their biological action" (pp. 44). DNA modification seems to be a major plus of multinuclear platinum complexes which researchers like.

In work conducted by Hud (2009), "[There is] support [for] the original hypothesis that polynuclear platinum compounds coordinating and modifying DNA in a different way than the mononuclear complex represent a novel class of platinum anticancer drugs acting by a different mechanism than cisplatin and its analogues" (pp. 375).

The cytotoxicity of the multinuclear platinum complex (or its ability to kill cancer) is very high. According to Clarke, Sadler, and Alessio (1999), "A further determinant of cytotoxicity is the amount of platinum actually bound to intracellular DNA, which reflects both the inherent affinity of the drug for DNA as well as the effect of competing metabolic processes such as binding to plasma proteins and intracellular thiols…" (pp. 112). Thanks to polynuclear platinum complex research, there is more awareness about the drug cisplatin and its effectiveness.

Demonstrated in Diederich (2009), "Nowadays there is a marked interest toward designing cisplatin-dissimilar complexes, which are anticipated to interact with DNA in a fundamentally different manner and hence to bypass the resistance to the classical platinum drugs…[one of the most intriguing of which is based] on the development of dinuclear and multinuclear coordination compounds" (pp. 650). As mentioned before, there is increasing evidence that multinuclear platinum complexes have greater cytotoxicity than mononuclear ones. Research conducted in Hong and Chen (2009), "Multinuclear platinum complexes have shown great potential for cancer chemotherapy. These complexes contain two, three, or four platinum centers, with both *cis* and/or *trans* configurations, and bind to DNA in a manner different from that of cisplatin…multinuclear complexes [have enhanced cytotoxicity]" (pp. 393).

Several different kinds of complexes exist, but only a few are very effective. As published by Ram and Bhethanabotla (2008), "Thus, sterically hindered complexes, *trans* complexes, multinuclear platinum complexes, complexes with biologically active carrier ligands, and water-soluble complexes have been studied. In general, platinum (II)- based drugs possess high affinity for nucleotides" (pp. 271).

Varying ligands are favored for the multinuclear platinum complex, but there are several

that can be considered effective. According to Abel et. al. (2002), “Many ligand-substitution reactions of divalent platinum are proposed to involve pentacoordinate intermediates, and there has been continuing interest in detectable and isolable examples of this class complex. One [advance] in this area has featured monoalkene complexes of platinum(II), mainly with a variety of bidentate nitrogen-donor ligands as ancillary ligands” (pp. 542).

What is most important is the understanding of the multinuclear platinum complex’s contribution to the miracle of modern inorganic coordination chemistry regarding organometallic pharmaceuticals.

3.2 Goals and Objectives

The goal was to synthesize a multinuclear cis-Pt/Pd phospine complexes with long chain lipids. These compounds will exhibit amphiphillic properties that would allow them to self assemble in water as a micelle and in organic solvents as a reverse micelle.

3.3 Synthesis and Design

The synthesis of this compound was carried out in a multi step process. Palladium (II) dichloride was reacted with 1.3 equivalents of cyclooctadiene in the presence of dichloromethane at room temperature for 24 hours. The solution was then filtered using gravity filtration. A bright yellow chalky solid was collected. The remaining solution was then rotovaped to extract any remaining product still in solution. The total yield was 82%. This gave a cis-Pd complex with Chlorine on one end and cyclooctadiene on the opposite.

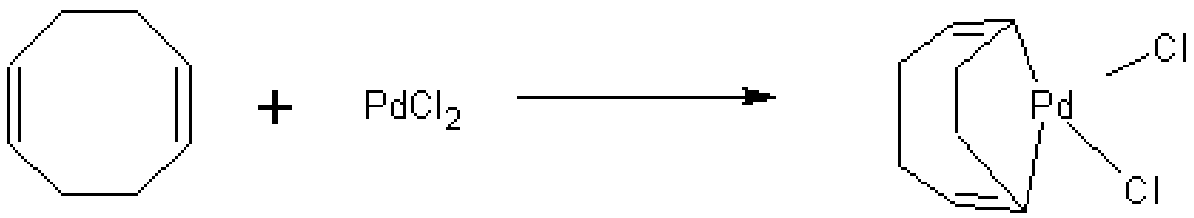

Figure 3.2 synthesis of cis-Pd/Pt complex with cyclooctadiene

In the second phase, the cis-Pd complex was reacted with a phospine ligand which had four C12 lipid chains attached. Because the phospine ligand was highly hygroscopic and in the presence of air would oxidize, the synthesis had to be carried out under argon conditions. The reaction vessel was prepared by using an acetone bath followed by one hour in the drying oven at a constant temperature. The hot round bottom flask was then removed and set up immediately before allowing it to cool and accumulate micro condensation. A septum was placed over the flask and one syringe needle was inserted as ventilation, argon gas was then allowed to flow in via a second syringe needle, since argon is heavier than oxygen, it was allowed flow freely into the reaction vessel for about thirty minutes, this replaced a sufficient amount of oxygen, which significantly reduced the possibility for premature oxidation. The cis-Pd /cyclooctadiene compound was reacted with the phospine ligand in a 1:2.1 ratio in the presence of chloroform and argon at room temperature for 24 hours. The resulting solution was filtered under gravity filtration. A crystalline white solid was collected. The filtrate was then rotovaped to obtain any product remaining in solution. The yield was 74%. The resulting cis-Pd compound now has the phospine ligand with lipid chains opposite the two Chlorines.

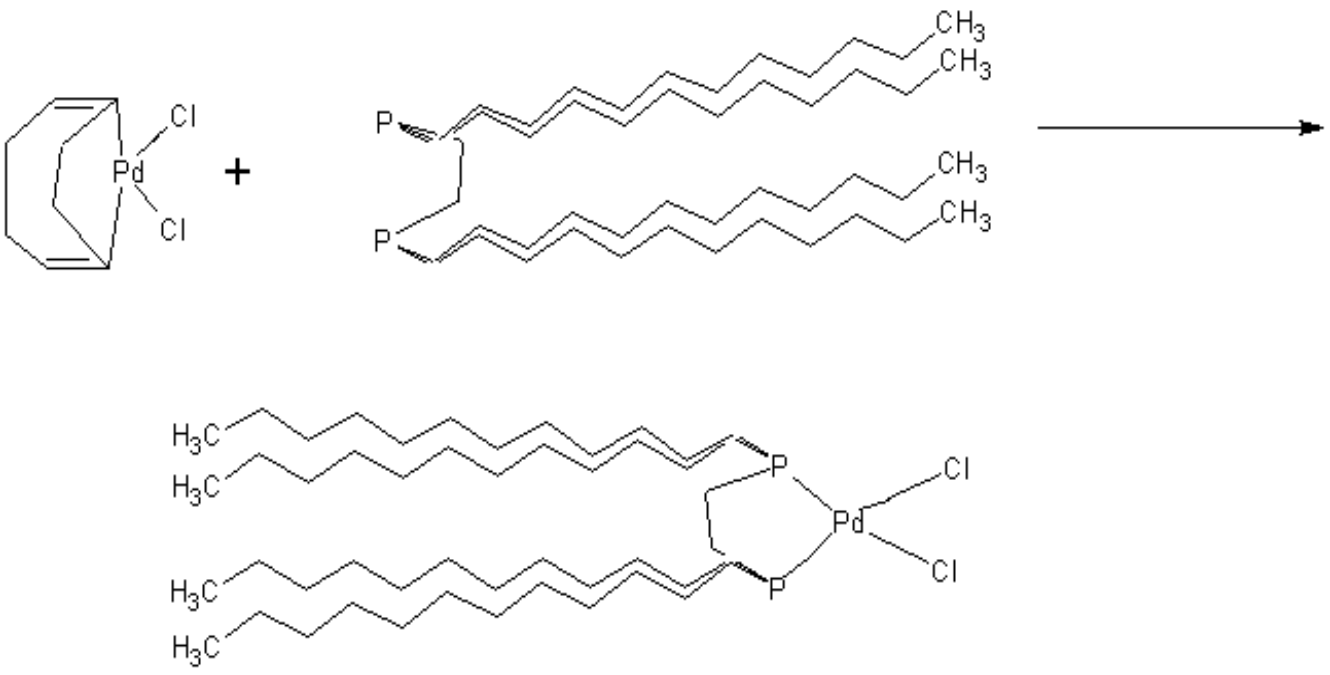

Figure 3.3 Synthesis of cis-Pt/Pd complex with chlorine ligand

The compound is then reacted with 2.4 equivalents of silver triflouromethane sulfonate in the presence of chloroform for 24 hours to replace the cis-chlorines with a protecting group, which can easily be cleaved for later experiments. Because silver is photosensitive this reaction has to be done in a covered vessel to prevent light from photoreacting the protecting group. The resulting product is filtered in small scale increments under gravity filtration using glass fiber filters to collect the side product of silver chloride which is a fine black powder. This process had to be repeated several times in order to ensure no remaining silver chloride was in the solution. The resulting product remained in chloroform solution, the silver chloride was discarded. The resulting compound is similar to the aforementioned figure with the chlorine atoms replaced by a larger and easily cleavable protecting group.

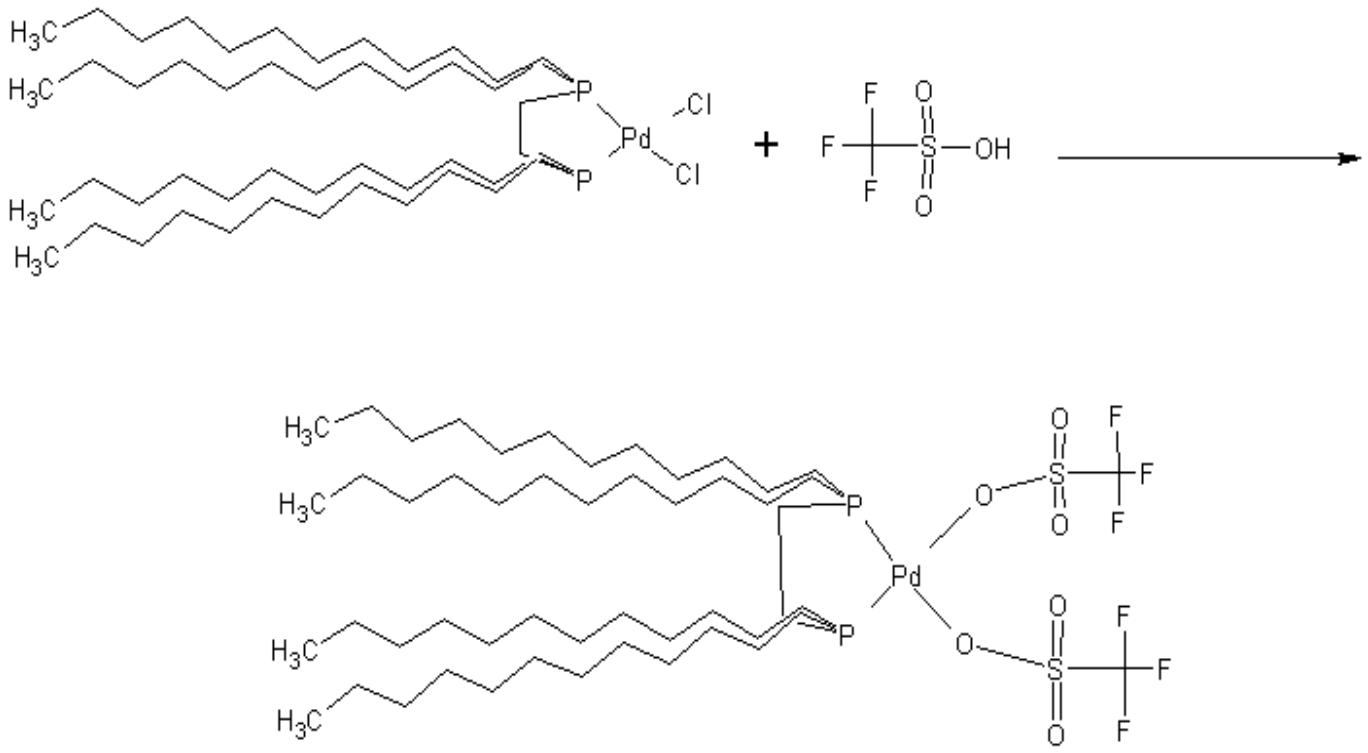

Figure 3.4 Substitution of Cl ligands with triflouromethane sulfonate

A multinuclear ligand was then substituted onto the complex after cleaving of the leaving group. This reaction took place in the presence of chloroform at room temperature for a 48 hour period with constant agitation. The ligand was added in a 2.5:1 ratio with the palladium complex, as each individual molecule required two ligands. The resultant product was then filtered under gravity filtration to remove the triflouromethane sulfonate that was replaced. The remaining product was rotovaped and stored in a controlled molarity of deuterated methanol solution. This allowed for characterization ease later on as well as optimal storage conditions.

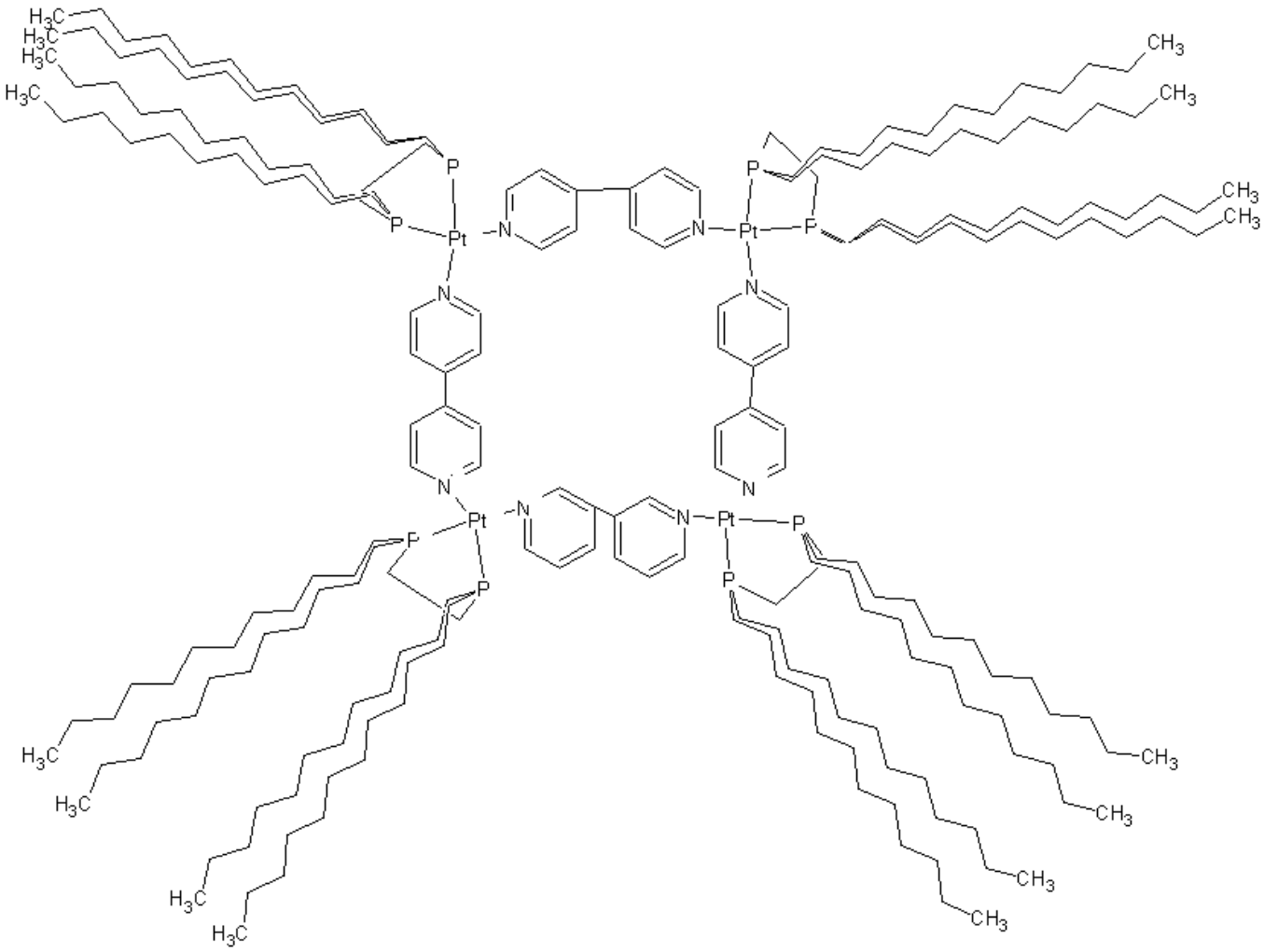

Figure 3.5 cis Pd/Pt complex with multinuclear ligand

As illustrated in the NMR data there is a confirmation of the synthesis was a success. An initial 31P scan of the compound with the triflouromethane sulfonate protecting groups shows a single intense peak, this is expected as the phospine ligands are symmetrical on the compound resulting a the single peak for both (figure 1). When a subsequent 31P NMR experiment was run on the compound post substitution the same single intense peak appears however it had shifted, which is illustrated in the literature is consistent with multinuclear ligands that had been added. Proton and carbon NMR (respectively) were also collected that were used to assist in characterization of the compounds. (figure 6 & 7).

The dynamic light scattering (DLS) data illustrates a population distribution size of 5200 nm average (figure 8). This dual population distribution can be attributed to the synthesis not going completion. It is evident that some of the Pd complex did not completely react leaving some unsubstantiated Pd complex as well as some fully substituted complexes with the intended multinuclear ligands. The average size however, is consistent with the predicted size not only of the multinuclear compound but also with that of the unreacted triflouromethane protected starting material.

CHAPTER 4:

INVERSE MICELLE

4.1 Summary of Chapter:

This chapter discusses the novel synthesis of a Platinum centered inverse micelle in tetrahedral conformation. This compound is designed to self assemble in the presence of an organic solvent and will have a hollow cavity in the center of defined size. This cavity uptakes a finite amount of water for low temperature NMR studies. These studies will create and confirm the presence of water nanorystals in their solid form with a uniform size population.

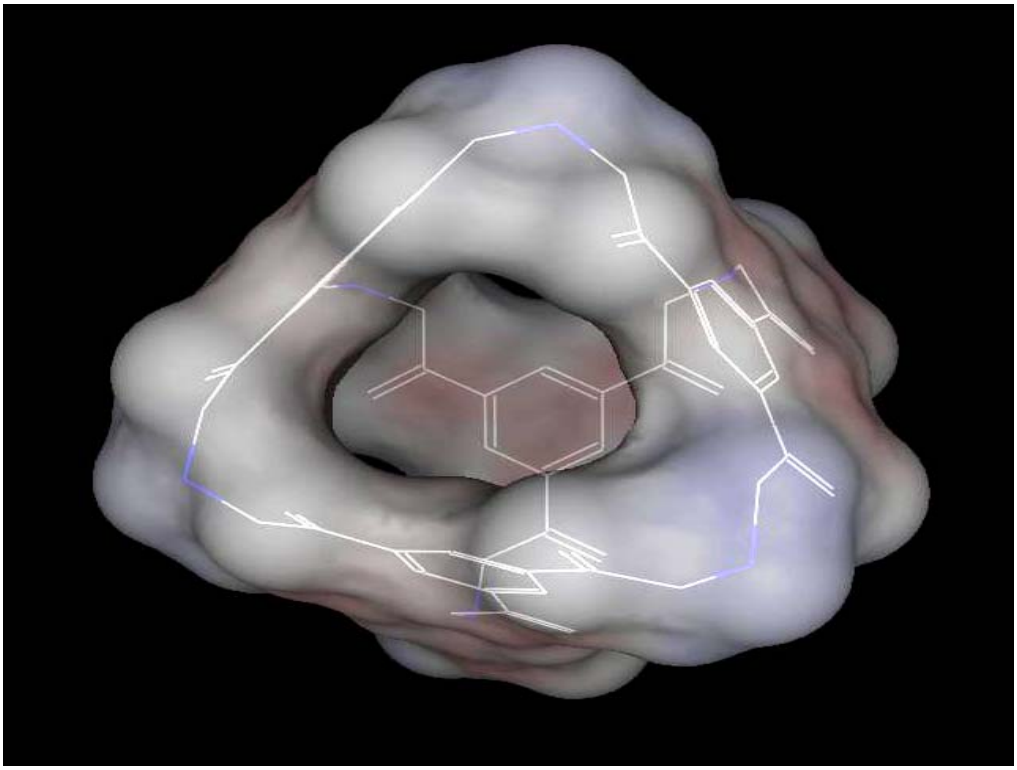

Figure 3.1 3-D rendering of inverse micelle

The formulation of nanocrystals is important in several areas of scientific research. According to Vo-Dinh (2007), "The current intense interest in the use of semiconductor nanocrystals…and related applications can be traced to the 1998 publications by Bruchez et. al. and Chan and Nie…" (pp. 4-1). One may wonder what inverse micelles are. Simply, as written by Klabunde (2001), "Reverse micelles are water-in-oil droplets" (pp. 62).

The formulation of crystals is important to finding a precipitate. According to Zheng et. al. (2010), "[F]unctionalization of the dendrons and/or the supramolecular core should allow access to 3-D hollow supramolecular functional systems with potential applications such as guest encapsulation, nano-reactor, and drug delivery." (pp. 4749) One aspect of the inverse micelle is that the experimenter actually has great control in deciding how large to make the particle that will be distilled. According to Spencer and Moore (2001), "Inverse micelle environments allow for a great deal of control not only over particle size [and] particle shape…Perhaps the most severe limitation of the inverse micelle approach is that it can only form nanocrystals whose precursors are stable and solvated by water…alternative reactions which proceed in dry, organic solvents are necessary" (pp. 2592).

As stated in Giacomelli (2010): "The micellization process leads to the formation of ordered structures in which the contact between the insoluble block and the solvent is minimized" (pp. B). There are various symbols used in helping to follow the chemical reactions since they large and cumbersome to draw. Physically speaking, according to Feldheim and Foss (2002), "M is [the symbol for] the metal ion precursor to the nanocrystal material" (pp. 208). Inverse micelle synthesis basically involves water, oil, and a surfactant. These are combined in perfect harmony in order to produce a distillation of water nanocrystals.

As stated by Schwarz, Contescu, and Putyera (2004), "The inverse micelle synthesis [requires the presence of an] ionic metal salt precursor metal salt concentration of 0.01-0.1 M and surfactant concentrations of ~5-10 wt.% (~0.2 M)[;] there are only about 1-4 precursor ions/micelle. [Growth] of N=10-10000 atoms must occur via micellar diffusion, micelle collision, temporary interface fusion, and atomic interchange" (pp. 3179). This is a very common experiment, which is performed in order to bring about nanocrystals.

In research of Robinson (2003), “Reverse micelles can be used as nanoreactors to produce nanoparticles. In most cases, a spherical template produces nanospheres. …hydration of the water pool, procedure mode and size of the template control the nanocrystal growth” (pp. 27). Microemulsion only occurs when there is larger particles.

However, according to Klimov (2004), which states that, “In general, the reverse-micelle approach entails preparation of a surfactant-polar solvent-nonpolar solvent microemulsion, where the content of the spontaneously generated spherical micelles is the polar-solvent fraction and that of the external matrix is the non-polar solvent” (pp. 13). It is important to regulate the amount of water placed in the mixture.

According to Mattoussi and Cheon (2009), who indicated that “One can vary the water content of the mixture to control the size of the water droplets…suspended in the oil phase” (pp. 5). Additional evidence states, in Rotello (2004), “[S]ize control represented a major advance in the field, due to the critically size-dependent properties of nanoparticles” (pp. 33).

Even more evidence attesting to this fact follows. In the works of Knauth and Schoonman (2002), “Colloidal solutions are good candidates for controlling the shape of nanocrystals. For a given surfactant-water-oil system, it is well known that a large variety of self-organizations of the surfactant can be produced” (pp. ii). The way the nanocrystals are produced depends largely upon the template that is used in forming the crystals.

As stated by Somasundaran (2006), “The obtained results demonstrate that the water phase of microemulsions at least partially controls the shape of the produced nanoparticles, i.e., a template-directed growth exists…[t]he templating effect of elongated water droplets in the…nanocrystal growth has been…confirmed by…induced formation of silver nanorods and nonfibers in AOT reverse micelles” (pp. 6194).

The surfactant that is usually used in such an experiment of inverse micelle synthesis is AOT. According to Vij (2004), "AOT (sodium dialkylsulphosuccinate)…is especially suitable for this application as it can solubilize up to 50 moles of water per mole of surfactant. Reverse micelles of AOT in water have also been used to template the synthesis of CdTe nanocrystals. [Synthesis happens in] in colloidal solutions containing stabilizers" (pp. 177).

Precipitation or distillation of the nanocrystals is usually the end result of the experiment. According to Rao, Thomas, and Kulkarni (2007), "Reverse or inverted micelles formed by the dispersion of water in oil, stabilized by surfactants are useful templates to synthesize nanoscale particles of metals, semiconductors, and oxides…In order to synthesize nanocrystals, one mixes micelles made of aqueous metal ions with micelles consisting of an appropriate reagent that can bring about…precipitation" (pp. 54). The idea of the experiment is to capture the nanocrystals in a calcified state.

Based on data from Lalena and Cleary (2010), "[Within using inverse micelles, t]he challenge is to capture the desired size and shape of the particle such that it is preserved once the template is removed, usually by calcination. In the early 1990s, researchers at Mobil…showed…mesoporous silicates could be synthesized…using lycrotropic liquid crystalline phases as the template" (pp. 522).

4.2 Objectives:

An inverse micelle was designed and a novel synthesis created to create a compound with a definable size hollow center that will readily uptake water when added. This will allow the study of a defined size water drop in low temperature environments. When taken to a freezing range the water inside will crystallize and form defined size water nanocrystals.

4.3 Design and Synthesis:

In a one pot synthesis 9 mg of $(L_3P)_2Pt(OTF)_2$ were reacted with 1 mg of 1,3,5-tricarboxyclic benzene and 1.5 microliters of tri-isopropylamine. This reaction took place in the presence of deuterated acetonitrile and allowed to agitate at room temperature for 24 hours.

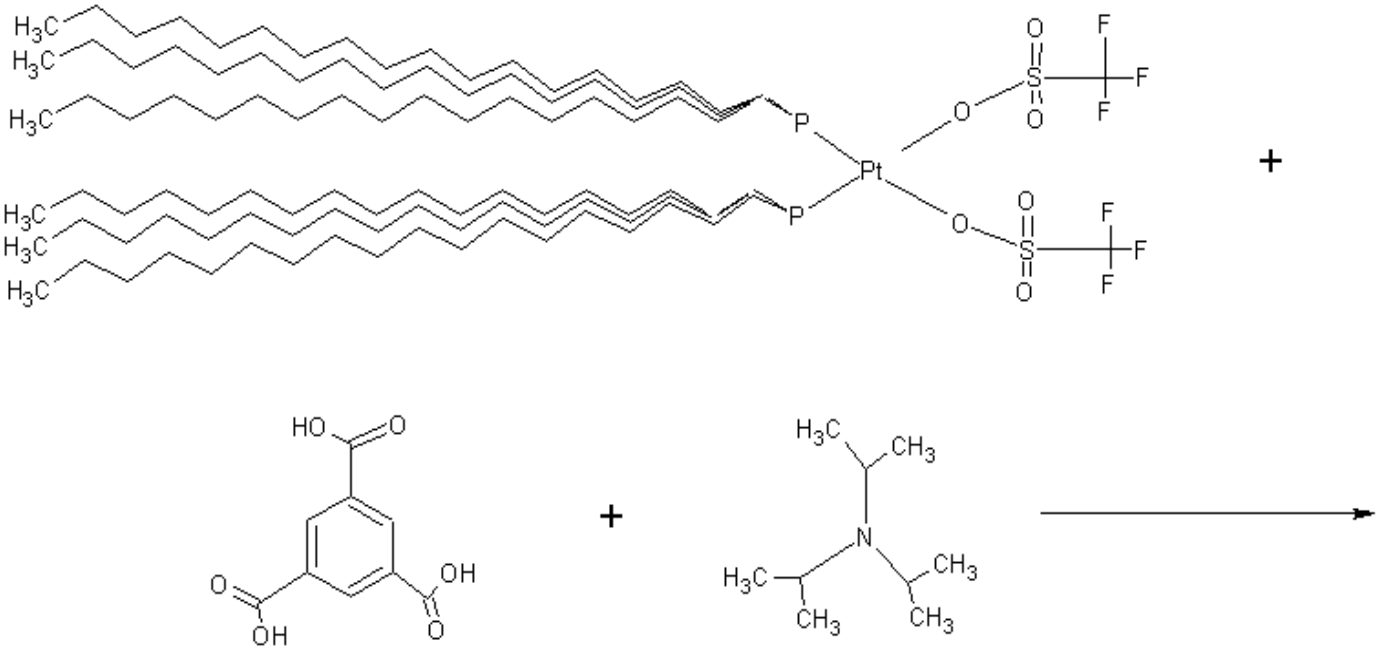

Figure 4.1 One pot synthesis of inverse micelle inverse micelle as product omitted from scheme ,refer to figure 16 in appendix for illustration.

As illustrated in the above figure 4.1 the resultant product is an inverse micelle in tetrahedral conformation with $C_{18}H_{37}$ lipid chains extending from each platinum anchor. This compound has a defined size region in the center that is measurable through DLS analysis.

A controlled amount of water (4 microliters) was added to the compound in solution. When water was added to the solution an instant emulsion was formed, illustrating the uptake of water into the micelles hollow center. As illustrated in (figure 9) there is a single population

distribution in reference to size of the water uptake. This gives inference to the amount of water present in the micelle.

The NMR studies were the most revealing part of the characterization process. These were all run on a 600MHz instrument under cryo conditions. A series of proton NMR studies were conducted at decreasing temperature intervals of 10˚C until a low mark of -40˚C.

The figures illustrating these studies (figure 10-12) are three per page with the original room temperature run at the top of each for comparison basis. In the presence of chloroform, the solvent used in these experiments, the water peak appears at approximately 1.5 ppm. It is the behavior of this peak at the varying temperatures that we are most interested in. Secondly at approximately 0.5 ppm there is a peak showing bound water that is water which is in solvent. It is evident that as temperature is decreased the peak increase, this is common behavior at lower temperatures. As we track the compounds behavior in the freezing environment several changes of interest occur. It was noted that the intensity of the bound water peak (~4.8 ppm) decreases significantly over the course of the experiment, while the free water intensity (~2.5 ppm) increases, over the same temperature range. This demonstrates a shift of water present in the system out of solution with chloroform and congregating into the single hollow area provided within the synthesized compound. This trend begins at the -10˚C interval and continues through the end of the experimental run. With the freezing temperature of chloroform being approximately -60˚C we were able to go well into the freezing temperature of water while not freezing the solvent which the compound was present in. This allowed for a focus on only the behavior of the water and no other liquids in the system. It is also important to note the rise of a peak that begins to show itself at -10˚C and continues to increase in intensity as the temperature

decreases. This same peak disappears again as the temperature is increases by the same 10˚C increments it was decreased (figure 13-15). It is an occurrence that warrants further study.

The compilation of these experiments demonstrates strong evidence for the formation of water nanocrystals in a controlled and defined size population, after a thorough literature review this type of characterization has not yet been published in any journal.

CHAPTER 5:

DISCUSSION

The mononuclear compound was well characterized via NMR studies. Once characterization was accomplished a study into the proposed behavior was conducted. First, DLS (dynamic light scattering) studies were conducted to determine the population size and distribution of the compound in emulsion (1% by weight). As predicted there was a uniform single size population with an average micelle diameter of 4600nm. Under optical microscopy the micelles were observed in emulsion. This was visual evidence of the mononuclear compound self assembling in the presence of water via hydrophobic interactions to form said micelles. Conversely as water was removed from the emulsion to create dehydrated conditions, the micelles began to dysmorph and break apart into their individual component compounds. This demonstrated not only confirmation of a discrete supramolecular structure via defined size, but also confirmation of predicted behavior in emulsion.

The multinuclear compound was characterized in the same fashion as the mononuclear compound. Again once this was complete a DLS study of the compound in emulsion was conducted to determine the size and distribution of the micelle population. According the studies there were two average size populations in the emulsion. While this did not correlate to the earlier studies of the mononuclear studies, it did not mean the experiment was unsuccessful. Since the multinuclear compound formed square planar Pt-ligand complexes, the ring stacking interactions allowed for extended multinuclear structure, meaning they would self assemble into infinite size supramoleular structures. This was confirmed when the emulsion was viewed under optical microscopy. It was evident that not only was the emulsion more densely populated with micelles, it was clear that there was a wide range of size, from those mirroring the mononuclear complex to some almost 5micrometers in diameter. Again when the emulsion was dehydrated the supramolecular complex began to dysmorph and break apart into its individual component

compounds. This confirmed the predicted synthesis and behavior of a extended supramolecular structure via square planar Pt complexes.

The novel synthesis of the reverse micelle began with a similar compound to the aforementioned complexes. Pt centered with lipid chains this complex would self assemble in the presence of organic solvent, this would cause a reverse of the hydrophobic effect, where the lipid chains would orient outwards as opposed to inwards. This behavior would create a hollow center cavity of defined size vis a vi the tetrahedral conformation of the structure. Once characterized the compound was then put in emulsion with a defined amount of water (4 microliters).

The DLS studies showed a single size population distribution of approximately 65nm, much smaller than the low echelon of visible light, therefore very difficult to observe even with optical microscopy. The most telling behavior was observed in low temperature NMR studies, conducted on the JEOL 600 MHz instrument. These studies showed well defined water peaks, one showing free water, that is water in solvent comprised of individual molecules, and bound water, that is water hydrogen bonding to other water molecules to form a suprastruture. As temperatures decreased beyond freezing, the free water peak began to disappear completely from the spectra as the bound water peak began to sharpen up and increase in intensity. The behavior of this peak was the inverse of not only the free water peak, but of all other peaks present in the spectra.

The overall impact of this research is far reaching and widely applicable in supramolecular chemistry. The novel synthesis of a new class of metal-ligand complexes with lipid chains brings a new dimension of potential to the current work being conducted in the field. Furthermore, the ability to easily substitute mononuclear ligands for the synthesis of discreet

supramolecualr structures as well as multinuclear ligands for extended supramolecular structures further extends the potential of said complexes. This will allow us to follow the protocol and create a library of compounds.

This work also highlights the novel synthesis of a Pt centered complex that allows for the creation of a reverse micelle with a defined size hallow cavity for the creation and study of water nanocrystals in a confined environment via low temperature NMR studies. The ability to study water nanocrystals in these conditions has not yet been published in any works to date.

Chapter 6:

A PERSONAL PERSPECTIVE OF THE

STATE OF CURRENT CANCER TREATMENT

The benefits of platinum-based anti-cancer drugs cannot go unnoticed. From its very inception, especially, the drug cisplatin stands out as one of the most major discoveries in cancer research.

Cisplatin and other platinum-based drugs give people: hope for the present; help for the present; the promise of a future; and a necessary focus on having a person-centered approach in curing cancer with regards to palliative care, or end-of-life care and inter-agency working.

When someone comes into the doctor's office, the last thing he or she wants to hear is the dreaded "C" word: cancer. Cancer, years ago, was a death sentence. However, today—due to the advancement of anti-cancer drug therapy and research, including various therapies that can be employed in the eradication of cancer—cancer is no longer a death sentence. Cancer has become a treatable illness that people can live with, and, yes, even beat—if they follow a healthy regimen and continue with all of their necessary doctor-prescribed treatments.

Drugs like cisplatin and other platinum-based drugs give cancer patients, as well as their families, hope that a cure is possible. And, in fact, studies have shown that people with a variety of types of cancers have been cured through usage of cisplatin.

Cisplatin has been found to be very effective in the treatment of various types of tumors. It is not surprising, then, that these various types of cancers can now be cured with the usage of cisplatin and other platinum-based drugs.

It has been shown in research that cisplatin and other platinum-based drugs retard the growth of cancer cells. It is of premier importance that this knowledge be taken into account when doctors are considering which drug(s) to prescribe his or her patient in the treatment of any kind of cancer.

These kinds of drugs give cancer patients and their families hope. New research means that clinical trials can be begun on even newer and better platinum drug therapies which hold the key to the future. Hope is a valuable resource for the cancer patient, as sometimes the cancer patient does not have much else. Their time, their money, their resources—all of it is dedicated to the eradication of cancer.

Families are stressed out by many aspects of having to deal with the patient's cancer. In this respect, many families have difficulties with health insurance and providing the right type of care for their sick family member(s) without even having to deal with the aspect of what kind of drug or drugs the patient will be taking. Hope is a valuable tool. It can be used to combat stress in the midst of difficult times during drug therapy. Many times, cancer patients have to struggle with the fact that they are facing death. Additionally, what makes the experience worse is the fact that, oftentimes, platinum-based drugs usually cause side effects in the patient.

These drugs do give patients help for the present as well. This, however, can be overshadowed by the fact that, as aforementioned, the platinum-based drugs can have nasty side effects that completely turn the patient's life upside-down. Side effects from platinum-based drugs vary. The side effects of platinum-based drugs include diarrhea, upset stomach, inability to eat and drink, and general nausea—among other things. Although the advancement of science in platinum-based drugs is welcome, one of the areas in which scientists must do a better job is figuring out how to develop drugs with few or no side effects. This is because, what happens is that the platinum-based drugs—along with killing cancer cells—kill normal cells as well.

This precludes a major rejection of the drugs from the body's system. This "rejection" is preempted by several side effects, one of which is the feeling of nausea. Usually this nausea is

so extreme that patients will not want to eat, get out of bed, or basically do anything for long stretches of time—sometimes days. Generally, cancer patients who are on these platinum-based drugs also experience weakness all over.

Patients on platinum-based drug therapy will generally not want to do much. They are so greatly weakened by the therapy that they will have to forego other activities they might have liked to do. Cancer patients must undergo some temporary pain on these platinum-based drugs in order to receive help for their situation. Although it is not very palatable, they must undergo this difficult process in order to live a normal, healthy, productive life. Help for the present has come in the form of these platinum-based anti-cancer drug therapies. Although cancer patients may have to endure much suffering, basically it is to their credit that they can pull through these trying times in order to live a better life.

Platinum-based drugs like cisplatin are definitely allies in the race to find a cure for cancer. Physicists, chemists, and biologists should all take note of the fact that there is already a cure out there—it just has to be perfected in order to help the patient more. Platinum-based drugs can be perfected in order so that there are not as many, or no, side effects. However, scientists must figure out how to make the drugs target only abnormal, unhealthy, and/or cancerous cells. Scientists must figure out how to stop these platinum-based drugs from targeting healthy cells while killing cancerous cells. If they can do that, they will revolutionize cancer research. As it stands today, the drugs that are being developed in order to combat cancer have horrible side effects. For the most part, this is the worst part about being a cancer patient.

Every cancer patient most likely dreads some aspect of their therapy that will eventually make him or her sick—so sick that illness will impede him or her from doing things they would do in everyday life. Whether it is chemotherapy, radiation therapy, or platinum-based drug

theory (in combination with a variety of other drugs)—the bottom line is that the cancer patient is going to have to go through some suffering in order to be healthy again.

That is the bare reality of cancer treatment today. It is a very hard road to hoe on the way to being cancer-free. However, those drugs are what represent, in a very tangible form, the key to a cancer patient's survival. Therefore, other such drugs that are platinum-based should be researched until there is a definitive cure for cancer that is found. Help for the present is available in the form of these platinum-based drugs. Although it is frustrating that these drugs have visible side effects, everything that is in scientists' power should be done in order to search for the cure for cancer.

Obviously, cancer research needs funding. Help for cancer patients may be found in continuing to raise awareness about the illness, as well as having annual funds, drives, and walks in the hopes of raising money for research, which can be life-saving. This type of research should be supported all across the United States and elsewhere in the world, as cancer is one of the leading killers worldwide. The morbidity rate for different cancers varies depending on what type of cancer one has.

Still, researchers should continue being dogged about the way they approach research. They could possibly save their grandchildren from ever having to worry about dying from the awful fate of cancer. What will help cancer patients the most are the fundraisers and the researchers who are doing everything in their power to contribute to the fight against cancer. They are, respectively, raising money for research and probing deeper into the causes and cures of the illness itself.

Hopefully, the help for the present, in the form of cisplatin and other platinum-based drugs, can assist in deterring and curing cancer on a short-term basis. On a long-term basis,

however, one must look ahead toward the promise of a brighter future with therapy that heals completely. The promise of a new tomorrow awaits. Steadily, researchers are making progress in the arena of cancer research. For some people, finding the cure will come too late.

For others, however, this could be the major key to their overall health and well-being. It is important to realize that no one should ideally ever have to face cancer. They should ideally not have to worry about knowing if they are going to ever get well again or not (by going into remission). Dealing with cancer is difficult, but the hope is that research will continue making new advances. Scientific discoveries will only continue to ameliorate the problems cancer causes.

Ultimately it is hoped that a cure for cancer will be found. Since cancer is one of the top ten killers in the United States, it is hoped that cancer will someday be largely a thing of the past and will be eradicated. The promise of the future is that cancer will one day, indeed, be an illness which no one needs to worry about contracting because it will be curable.

However, as things currently are, there remains no single effective cure for cancer. As such, fundraisers and researchers must remain dogged in the pursuit to eliminate this illness from the face of the earth. It can be done, if people just focus on trying to make breakthroughs in both the raising of money for research and the actual research needed to rid the body of the disease.

On the part of fundraisers, this means being vigorous in assuming that almost anyone can contribute to the fight to end cancer. People should be made aware of how important it is to fight cancer, and how this can affect all of us in terms of hurting people we know and love. Fundraisers must realize that every dollar that goes towards cancer research is a dollar towards ending the grips that cancer has on peoples' physical bodies.

Researchers should also realize how precious time is, and that so many people do not have much time left, due to the fact that there was not good research in place when they got cancer. The promise of the future is that no man, woman, or child will have to live with cancer. It will be a happy day when that happens. Researchers also play roles, too. Researchers should dedicate themselves wholeheartedly to the cause of finding a cure for cancer.

Researchers should find employment in sectors where cancer research is funded. Researchers should be encouraged to find jobs where they are, in turn, pushed and prodded to do research that will save lives. This does not necessarily have to be about finding the research for cancer only. They can also look for cures for other diseases in the process. However, cancer is such a common illness that this should be the main focus of the push to end cancer. In order to do this, researchers should be encouraged to dedicate themselves to eliminating a major disease throughout their lifetime.

Two decades ago, it was the practitioners who had been dominating the health and social care environment with the patients/service users being placed at the lower end of the spectrum as passive takers of such services. This has been gradually shifting, thanks to the approach of the Government, whose rhetoric now promotes the principles of choice and control for service users within a seamless service. This has brought in a paradigm shift in the delivery of health care services, wherein, the earlier 'professional directed approach' is being replaced by a 'person-centered approach' which demands practitioners to tune their thinking and implement practicing to the needs, desires and the rights of the users of health care services.

A major challenge this writer poses need to be highlighted. It relates to 'jargons and terminologies.' For instance, from a practitioner's point of view, the term 'patient' has been used in a generic fashion, which does not gel with the way midwives or social workers may use it.

To midwives, there has been an extended meaning to such terms as women- or child-catered care to include their families. In the same manner, social workers more often use the term ‘service users/careers’ whereas the occupational therapists treat them as their 'clients.’ For the purposes of this paper, the definition of Overetveit et al. (1997) produced herein under is taken:

‘If one of the purposes of interprofessional working is the combining of different perspectives then the patients or service users are interprofessional workers par excellence [since] they...unify and combine the different advice and perspectives integrating them into daily living and making health choices as they do so” (p.117). This approach centers around five theoretical concepts, as identified by Leventhal and Cameron (1987) that are considered to be relevant to this paper, which are: (1) bio-medical; (2) behavioral; (3) communication; (4) cognitive; and (5) self-regulatory.

In the bio-medical theory as elsewhere pointed out in this paper, the patients are taken to be passive recipients of doctors' instructions; the absence of good health or presence of disease is traced to bio-medical causes and the treatment is based on the patient’s body. The solutions are mechanical reflected in a prescriptive regime, and the non-adherence to treatment is traced to the physical characteristics of the patient. A major limitation of this theory is that it takes into account only the patient characteristics that may impact their health behavior. The behavioral theory places emphasis on the learning perspectives and focuses on the environment and the teaching of skills to manage adherence.

It treats behavior as a product of antecedents which could be arising out of internal or external factors, as thoughts and environments respectively and the consequences of them could be reflected either in the form of punishments or rewards. The limiting factor of this theory is

the lack of an individualized approach and also the tendency in not taking into account the factors that consciously influence the behavior that is not linked to immediate rewards. Communication theory places the emphasis on patient-practitioner relationship and is based on patient education and good health care worker communications skills. It further relies on three factors: treatment, instruction and comprehension.

In this context, the academicians and researchers have started to emphasize the concept of 'narrative-based medicine' to promote the physician-patient based communication that is found to promote the physician-patient based communication and enable a better outcome on the health of those undergoing treatment. The principle behind this concept is the emphasis that is laid down on the information-sharing between the two during the medical interview, and such a perspective—though the research has supported to have positive outcomes…—has been found in reality to be lost.

Major criticisms of this theory centre on its not taking into account attitudinal, motivational and interpersonal factors that may interfere with the reception of the message and the translation of knowledge into behavioral changes. Nevertheless, among all the approaches, this is considered to be the cornerstone of every patient-practitioner relationship and most relevant to this paper and of late more and more reviews are being undertaken to determine the effects communication elements. The cognitive model bases its arguments on a number of sub-elements, the chief among which are health-belief, socio-cognitive factors, reasoned-action, planned-behavior and protection-motivation.

The health-related behavior is based on certain attitudes, beliefs, the outcomes of the expectations based on a futuristic perspective. The basis of these approaches suffer from the weaknesses of not accounting for non-voluntary factors that could affect behavior, sub-optimal

outcomes from a cost-benefit analysis, power relationship and social reputation. According to health belief theory, health behavior is based on the outcome of a rational appraisal that is arrived at through a balancing of barriers to and benefits of action. It relies on the demographic and socio-psychological variables to construct the barriers and benefits. The threats to health and benefits out of the outcomes of the treatment are the major factors that influence the behavior.

This theory is criticized, firstly, for the lack of empirical evidence of the relationship between the variables and secondly, for the non-inclusion of social influence. Self-regulatory theory focuses itself on the patient, advances that it is imperative to examine the individual's subjective experience of health threats to understand the manner in which they adapt to these threats and they form the cognitive representatives of health threats by committing new information with past experience. Its central theme is that people, by engaging themselves into active and self-regulating behavior, are the problem-solvers of their illness. The main criticism relating to this theory is that it is more intuitive rather than evidence- based.

These theories can broadly be reduced into two philosophies which currently drive the interprofessional practitioner-patient models, which are the medical and social models. The medical model relies on the belief of medical experts in that they know what is the best for their patients whereas the social model lays emphasis on issues of power in the professional role and though curiously looks at as to how the 'helping' relationship can also prove to be disempowering and produce a level of dependency on the professional.

Inter-agency working (IAW), put in another way, is nothing but collaborative working which has the support of those who have seen for themselves the advantages of working with a diverse disciplines in a person-centered care. At the same time, interprofessional working also

calls for a significant reorientation of professional working practices. If this be the case, one has to focus at finding out what are those factors that govern the interprofessional working. Awareness at work, both at organizational and interpersonal levels—which falls under the academic psychology—includes the structural issues that weave around various elements of the players.

Both practitioners and users involved in the health sector have to face the cultural issues including anti-divinatory practices, whether based on religion, sex and or age, which are some of those important factors. The plays of such factors also imply a shift from patient-to-person entered care. However, with regard to palliative care, there are two theories which may be appropriate for being mentioned here. The "Praxis Theory of Suffering" focuses on the Behavioral-experiential nature of suffering.

Here, suffering is perceived as comprising of two behavioral states, enduring and suffering. Enduring is characterized by suppression of emotion whereas in the other case, it is manifested in a state of distress in which the emotions are released. The complexity theory compares the palliative care to the physical, biological and social systems. As they have been found to have relevance in those areas as broad as meteorology, biology, organizational theory, etc., the same is also being applied and evaluated in order to find its relevance to the field of palliative care.

If this is the development that has been taking place in the health sector, which places emphasis on social care, it is imperative to consider its implications from a theoretical and practical perspective and that is the central objective here. It would critically explore the values and concepts of Inter-Agency (IAW) approaches with specific reference to palliative care. *Ethike* is a Greek word from which the word ethics is derived. Ethos is a value which one has

and consistently applies to one's life. Within the palliative care setting, there are three aspects of patient care that need special attention: the realms of the palliative care patient; the realm of the palliative care nurse; and the realm of the palliative care team.

The realm of the palliative care patient is mainly concerned with the patients' well-being even though he or she is in the end stages of terminal illness. The patient is still given treatment, in most instances, for what ails him or her, but the patient is prepared to die at any moment. Thus, palliative care focuses on maintaining a sense of homeostasis within the patient even tough; unfortunately, the patient is ultimately most likely going to die of his or her disease in most cases instead of being discharged from palliative care.

It is important to remember when dealing with a palliative care patient is that there are many things that a supportive caregiver or family member should, as well as should not do. Therefore, people must be sensitive to these areas of the palliative care patient's psyche which could be easily damaged. First of all, the palliative care patient does not want to be lectured; especially, it is important not to blame a patient for his or her illness. For example, saying things like, "Well, if you hadn't smoked all your life, you wouldn't have gotten lung cancer."

Or, someone might be thoughtless enough to say something like, "If you had eaten healthier earlier in life, you wouldn't have had…" fill-in-the-blank—chronic health problem X, Y, or Z such as heart failure, diabetes, cancer, etc. Additionally, if a palliative care patient has cancer, it is tempting to want to demonstrate Lance Armstrong Syndrome. The idea that if a person has a strong mind and a positive mental attitude (PMA), one will overcome cancer—is an illogical fallacy. Although there is indeed much debate about "mind over matter" in medicine, the bald truth is that cancer is a very tangible problem which cannot simply be overcome by someone just willing it to be so with the power of one's mind.

Truly, a positive attitude is not the only thing that one must have in order to beat cancer. One also must have the biological predisposition to overcome the cancer. In other words…if the underlying pathology of the patient suggests that he or she will continue to be ill, that is exactly what will happen, and he or she will not be able to overcome the illness by simply willing it away—no matter how strong their psychic faculties be. One fundamental flaw about people with Lance Armstrong Syndrome is that they assume that someone must be weak-willed or having lack of fortitude of mind if they cannot overcome cancer by simply having a positive attitude. This is, again, an illogical fallacy.

Now, clearly, there are people who are of the philosophical bent which ascribe to the theory that one can overcome illness by simply having enough faith. Again, this is also an illogical fallacy which may be difficult for some to overcome. However, it is a must that people heed the fact that not everyone is going to be a cancer survivor. Realizing this fact is facing reality.

Sometimes people are not realistic in their assessments, i.e., dealing with their relatives who are in palliative care. For example, they may think mistakenly, or perhaps, were led astray to believe, that their loved one, if cared for enough, would somehow miraculously recover. Many family members of patients who are in palliative care mistakenly assume, many times wrongly, that their loved one will indeed get better. However, sadly, this is usually not the case.

What is common is that the patient's condition deteriorates, and the family is suddenly caught in arrears because, unfortunately, they have a difficult time accepting the inevitable—the fact that their loved one is dying. This is the phase of the dying process called denial. They slowly then come to acceptance after having just been in disbelief. They then move to denial and then acceptance.

Unfortunately, the family may have a more difficult time than the patient. The family has a difficult time basically because they are the ones who are left behind to contemplate the meaning of life without their loved one. In essence, funerals are then, not for the dead but for the living. Truly, it is possible for someone who is dying of cancer to overcome his or her illness. But, for a family to hold on hope that their loved one will definitely get better is a false hope in palliative care practice settings. Understandably so, palliative care nurses must be continually assessing and evaluating the needs of the palliative care patient. Are the patients' medications at the correct dosages? Do they need to be adjusted?

The duty of the palliative care nurse is to continuously be monitoring a patient's relative progress or the lack thereof. A palliative care nurse, if there is any significant change in the patient's status (positive or negative) should make notes of this in his or her care plans and make contingency plans to provide for any changes in temperament in the patient. The duty of the palliative care team is to reassure that all the patient's needs are coordinated.

Usually a palliative care team consists of: the nurses that are working on all of the palliative care patients; the main doctors which oversee the palliative care setting; the social worker; the chaplain; and perhaps most obviously, the family and/or caregivers. It is the duty of the palliative care team on the end of the hospital or other organization taking care of the patient—not now speaking of the family and/or caregivers—that they establish a sense of trust and reliability with the patient. Since the palliative care nurse is the person who will have the most contact with the patient, it is of maximum importance that the nurse be professional, respectable, and affable.

It is the duty of the other nurses to patiently listen as each individual nurse expresses his or her reflections on the progress of the patients. Similarly, it is the doctors' duty to reflect on

how the status of the patients is. The social worker is available in order to address any issues that might come up regarding the patient's living conditions, environment, etc. The chaplain is available in order to help out with a patient's spiritual needs.

In any case, the palliative care team is very important, and of course, one cannot forget the importance of the role of the family and/or caregivers, which must work with the hospitals or organizations palliative care team members. The palliative care team works together to provide the service of helping the patient through this troubling and complex time in his or her life. Hopefully the team can make that patient's journey an easier and perhaps less stressful one.

The skills needed for interagency working in palliative care are as follows. The demand for palliative care education for generalists would grow along with the spread of such a care. Provisions hence would have to be made for the practitioners, irruptive of their fields of specializations, to have easy access to courses and short term clinical attachments. Within the general education, there has to be more emphasis on 'modular education,' especially for the nursing professionals.

With the advent of the Internet and technological developments, more reliance could be placed on distance-learning which can further be accelerated by especially providing such facilities by catering to the needs of those working in residential homes. At a higher level, institutions of higher learning could augment the facilities by creating professional chairs in medical, nursing and social work.

As pointed out elsewhere in this paper, the current paucity in research could be made good if funding bodies and pharmaceutical industries recognize the relevance and need for palliative care.

A vast magnitude of the population in the UK, for example (over 2,300,000) is reported

to be afflicted with cancer. Patients and their families face shocks, uncertainties and need support at all stages. Though such a support was available, it was revealed that there were still a considerable number of such patients who stated that they did not receive the information and support they needed. All the more showed considerable variations in the quality of care delivered across countries. One of the reasons for this was attributed to the poor interprofessional communication and coordination.

Several different agencies have been directed to and engaging themselves in and developing standards, having realized that effective face-to-face communication between health and social care professionals is important, on the one hand. Patients and caregivers, on the other hand, are fundamental to the provision of high-quality health care. In practice it was found that much of the professional support furnished to the patients afflicted with advanced cancer was delivered by non-specialist social and health care professionals in palliative care, which has been an area of concern. In this regard, it is indicated that there is also a paucity of literature and in order to fulfill this gap, it is widely perceived that budgetary provisions should be enhanced.

The disparities in the provisions of the palliative care around the world have given rise to a new genre of rhetoric in that it is seen as a human right belonging to the arms of international law. So much of rhetoric dominates the literature about the entitlement of people needing palliative care in the name of human rights, but, when removed from such rhetoric, the realities which remain are totally different. This is explained with reference to one sensitive topic, i.e., assisted suicide.

Compassion and the right of the patient to die are two commonly-presented reasons in favor of the concept of assisted suicide. Emotions are wrought by the usage of compassion because of its universal appeal. But when divorced from emotions, it would become clear that

compassion can be distorted and harmful. In this particular case, the human beings would be deprived of their dignity, and in effect it would mean their being killed.

It may be a moral reason for relieving the humans from the sufferings that terminal illness brings on them, but, not a moral justification for ending a human life. In effect, while handling terminally ill patients needing palliative care, the leaders of governance, policy-makers and the practitioners all should remove themselves from such rhetoric. People should engage themselves in efforts that would make such a life as comfortable as possible without injecting further sadness into them. These are the effects of good palliative care and interagency working with people who have cancer.

Multi-professional working is looked at as a driver of social inclusion, but, the problem is the policy directives are considered to be running ahead of conceptualization. This is especially so in as minimal attention has been considered to be paid to conceptualizing the forms of professional learning that is required to expand the interagency practice and there does not seem to be any theoretical backing in the practical implementation of inter-agency work. This paper deals with some of the concerns that have come into focus in this regard.

Many governments since at least the turn of the 21st century have been giving priority to tackling social exclusions, which are defined as the loss of access to life chances that connect the individuals to the mainstream of social participation. Interagency collaboration is seen as a vehicle to achieve such social inclusion which is seen in the initiatives taken by various governments. While at policy level multi-professional working is seen as a 'self-evident good,' problems have cropped up in both strategy and operation.

The inter-agency model of working rests upon ‘non-conflictual’ models of collaboration, but, in reality it denies the tensions that exist between different agencies both at vertical and

horizontal levels. Moreover, the problems have been identified and discussed by confining them to managerial or technological issues ignoring the human factors. The conceptual framework obtaining at present places minimum emphasis upon the need for agencies to learn the working something as a 'learning process' in which there are as much tensions and difficulties as insights and motivations.

Of particular concern in this regard is the tendency to use partnership and participation in an interchangeable manner. It is indeed considered, a pitfall, if one were constrained to use that term, that to pursue post-bureaucratic analyses of professional practices. This is more than reflected in the current practices followed to prevent 'social exclusion'. For instance, a single child in the current scheme of things may have to encounter multiple agencies spanning the education, health, social services and similar but multifarious agencies that have the effect of only exacerbating an already existing contentious relationship.

Effectiveness is equated with the containment of distribution to a moderate form and diminution of conflict. Thus, nothing is resolved, in effect. There is perceived to be an organizational ambivalence in the inter-agency working both at the vertical and horizontal forms. They are considered to impede the development of inter-agency working as the practitioners working at operational level regard barriers to develop in inter-agency approaches within small, short-term projects as irresolvable in a situation where the mainstream service remained divided at the top level.

In a setting of this type, the senior level commitment to the multi-professional agency is considered to remain only at a rhetorical level on account of the fact that overarching departmental structures remain insulated from one another.

The effect of this is that there is a wedge between micro and macro levels of

collaborations. While at the micro level, there could be innovations that remain truncated as they are isolated in the macro level. The working practices did not sustain in the case of short term projects as there was no mechanism for offering the expertise of the multi-agency professionals to subsequent inter-agency projects. The inter-agency working is also considered to promote the emergence of new hybrid professional types which has resulted in the creation of 'fluidity of roles' in which the practitioners have wade through a number of boundary issues.

These may either be internal or external or a combination of both of them. It also poses problems of cultural change. The areas of concerns could then be summarized as the ones that relate to the conceptualization of inter-agency working, which places multiple demands upon the practitioners and clients (patients/careers). In this context, interagency working cannot be construed as a virtuous solution and or an ideal model of service delivery. It is also equated with 'partnership' tools and considered suitable for analyses of collaboration.

The origins of Integrated Care Pathways (ICPs) or the Clinical Care Pathways as it is known in the recent literature could be traced to the USA. It is developed by a multi-professional team involved in the caring process, has to be based on evidence and should follow prescribed guidelines. It deals with the process of care that is delivered in a given clinical situation. This has proven to have major success within palliative care practice. It sets the role of each health care professional in the care of the patient and the caregivers and the details of the expected outcomes which are recorded on the ICP.

As and when the expected outcome is not achieved, then the reasons for such an outcome are documented and such deviations are termed as 'variance'. It is through a review of such variances future educational needs would be identified which in turn would help in the improvement of health deliveries in the future. ICPs thus in effect are a dynamic in nature and in

being done over and over one document may replace another which process may continue until a central coordinating document emerges.

The applicability of ICP in palliative care rests on the principle of holistic care in which the patient and careers are involved. While it does not prevent the delivery of individualized care, it simultaneously allow for the clinical freedom to furnish care within an evidence-based setting. In a palliative care environment, it has the effect of acting as a multi-professional document which the professionals can use to coordinate and record the care of the patient. This includes EMRs (electronic medical records). Its ascendancy to prominence everywhere is of recent origin. The current emphasis in this regard focuses on interprofessional education which departs from the earlier multi-disciplinary approach to education. The critical pathway in this is collaborative practice.

This implies that the Inter Professional Education (IPE) aims at involving the patients/service users and careers as experts. In essence, caretakers must be experts in order to know what kind of care to give to their clients/patients. The implementation of the various frameworks and their expansion into covering more diseases has heightened the need for collaborative working between health and social services that would ultimately bring in a holistic approach to patient care. Primary care in this connection has been identified as the key driver in the implementation of the frameworks.

In regard to the development of the critical pathway, this again is seen as involving the whole workforce in the provision of first-level care. In other words this is described as an 'interprofessional framework' or tool. This implies for the critical pathway further to develop interagency working would bring in innovations in patient care. This would be obvious.

While the importance of an education program in an ICP is over-recognized, yet in

practice, it is underachieved. One common reason for this is the excessive workload of the professionals and exposure to theories in them do not bring in any change in the practices. This is because implementing an ICP demands a major commitment in terms of time because of the need to comply with a lengthy procedural requirement.

Nevertheless, this does not in any way undermine the importance of developing and implementing an ICP, as if the health practitioner community as a whole is familiar with such tools as and when they commence their entry into the profession, they would usher in a powerful model for delivery of care. Clinical pathways thus bring in a refreshing approach to the dissemination of clinical excellence in palliative care. Within it one can develop a number of sub-models that would address specific requirements. This may help the patients in breathing their lasts in a dignified environment. It also contains the potential to set standards and for being used in quality assurances within a palliative care and or hospice setting. It also sets in motion a change in the mindset in the culture for the care of dying.

In essence, the critical pathways should and would lay emphasis on the delivery of a multitude of national priorities through networks and collaborations across the board that would include social care, local government, voluntary and independent sectors. Partnership working would call for working not only across agency boundaries but also professional boundaries. Of particular concern in this regard is the tendency to use partnership and participation in an interchangeable manner. It is indeed considered, a pitfall, if one were constrained to use that term, that to pursue post-bureaucratic analyses of professional practices. This is more than reflected in the current practices followed to prevent 'social exclusion'.

For instance, a single child in the current scheme of things may have to encounter multiple agencies spanning the education, health, social services and similar but multifarious

agencies that have the effect of only exacerbating an already existing contentious relationship.

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In a setting of this type, the senior level commitment to the multi-professional agency is considered to remain only at a rhetorical level on account of the fact that overarching departmental structures remain insulated from one another. The effect of this is that there is a wedge between micro and macro levels of collaborations. While at the micro level, there could be innovations that remain truncated as they are isolated in the macro level.

The working practices did not sustain in the case of short term projects as there was no mechanism for offering the expertise of the multi-agency professionals to subsequent inter-agency projects. The inter-agency working is also considered to promote the emergence of new hybrid professional types which has resulted in the creation of 'fluidity of roles' in which the practitioners have wade through a number of boundary issues, that may either internal or external or a combination of both of them. It also poses problems of cultural change.

The areas of concerns could then be summarized as the ones that relate to the conceptualization of inter-agency working, which places multiple demands upon the practitioners and clients (patients/careers). In this context, interagency working cannot be construed as a virtuous solution and or an ideal model of service delivery. It is also equated with 'partnership' tools and considered suitable for analyses of collaboration. The natural question

that crops up is that, “If the interprofessional working is a concept that is confronted with so many practical problems where its role in the health and social care system is, then what purpose does it serve?”

This section of the paper would argue the case in general and not relating to palliative care alone as the picture is to be seen in a broader perspective. In any context, it is seen as a remedy to the past failings of the health care system. It is something which would bring in sweeping changes in the delivery of caring in regard to at least that section of the population which needs it badly, namely, the adolescents.

It is of concern to note that mortality is still predominant in adolescents when compared with other groups with accidents and self-harm reported to be claiming as major causes of loss of lives. They also undergo significant mental health problems. The present mental and health services for children everywhere are seen to be inadequate to cope with their problems. There is also a diminished level of attendance by them to health care services. The reasons mentioned above are sufficient to bring in the point that there has to be better methods to attend to their health care needs. In a primary care setting, they relate to access, confidentiality, consent, and privacy. Young people have felt that they face barriers to the effective use of both primary and secondary health care services.

They pertain to lack of information, unfriendly services, sandwiched either with the children or elders in the hospitals and, in short, health services would have to pay greater attention to the special needs of them if the delivery health care aims at improving the emotional, psychological and physical health of the population. These solutions should be innovative, and also evidence-based.

Demographically, they are not a homogeneous group and have diverse special needs that

are associated with gender, ethnicity, social and educational disadvantage. The fact that services for young people with psychological and mental health problems have not changed much in the last three decades or so makes the introduction and implementation of interprofessional working an imperative if their requirements have to be met. This is all the more warranted because a single style of service may not attract the young people. As a result, specific local health service provisions should take into account all other relevant service provisions including the one that is multi-professional in nature.

The practitioners involved in such facilities should also be trained to take into account the specific needs of young people. The quality assurance standards should also be maintained. The development of the communication skills by the staff is considered to be of paramount importance and it yet another reason as to why interprofessional agency approach is advocated. The amount of people dedicated to finding the cure for cancer is going to proportionately affect how much the illness can be eradicated. If there is a critical mass of people dedicated to ending cancer forever, then the likelihood is that cancer will not be here to stay. With the advent of all the new technology, it is very possible that someday a cure will be here. However, having to deal with many issues, researchers may not be necessarily prepared or as well-funded as they should be in order to help aid them in their discoveries.

Cancer research must be better-funded and more publicly-supported. If it were, this would aid a great deal in helping cancer research come to the forefront of issues in the medical community. What is such a shame is that any illness is indeed curable if the cure is out there—if there is a formula, if there is a recipe, it can be done. We just need to find it.

The fact that these platinum-based drugs can give the cancer patients and their families hope for the present, and a promise for a brighter future in a cancer-free world—this is what

makes their value priceless. This is because no value can really be placed on human life. Truly—when one thinks of one's friend, one's father, one's sister, one's mother, one's cousin, one's brother—no one can replace those people in a person's family. No one person can be replaced. Things and places can be replaced, but people can't.

What people must realize, in order to get people more active and aware within cancer funding and research, is that their loved ones' lives may someday be in jeopardy, and they can do something to prevent that from happening. If people could see into the future and automatically know that one of their friends or family members was going to get cancer, perhaps they would be more inclined to be involved and active in the fundraising and the research for finding a cure. The need for funding and research within the fight against cancer is very real and urgent.

Without funding, there will be no advanced research occurring in the field of anti-cancer drug therapy. Without advanced research occurring in this field, whole bodies of knowledge will be lost over time. The longer research is left unattended, the more the theories get stagnant in the minds of researchers. While this research is new and fresh on researchers' minds, we should take advantage of this fact. While this area of research is still very popular, we should strive to make sure that it reminds high on the list of priorities of fundraisers and researchers around the globe. One can raise awareness in all different kinds of ways. For example, having social events that target raising money for cancer research is great ideas in order to both raise awareness and foster social networking.

Social networking is another wonderful idea in order to further one's cause. The use of Facebook and Twitter in order to get the word out about the importance of cancer research and funding to go towards it may be blogged about, written about on a status update, or be given a fan page in order to raise awareness (and cash) for research.

What is amazing is that one can use one's social networking influence online in order to influence ordinary events. There is one person on Twitter by the name of Drew Olanoff who started a revolutionary hashtag (or conversation thread) on Twitter called #beatcancer. Since Mr. Olanoff started the hashtag #beatcancer, he has raised millions of dollars for cancer research singlehandedly. This was an idea that he came up with after having been diagnosed with, and later beat, cancer. Not everyone is as lucky in his or her fights with cancer. Wonderfully, however, there is now much more money that was donated to cancer research due to Mr. Olanoff's selfless efforts. With the continued raising of awareness and an encouragement that the medical community do more in the field of cancer research, it is hoped that someday cancer will be known as the curable illness that was once considered incurable.

Mononuclear platinum square complexes, multinuclear platinum complexes, and inverse micelle synthesis are all important in understanding biological functions better. In the case of platinum complexes, one can better understand the intricacies of cancer research. With the advent of cisplatin, platinum drug research became all the rage starting with Farrell's discovery in the early '90s. After that, the usage of cisplatin exploded, as platinum-based drugs were vaunted into the spotlight, cisplatin having had marvelous success in clinical trials and in usage on actual patients after the clinical research was complete.

The benefit of knowing how different compounds do work under certain circumstances is priceless. Countless lives have been saved, and can continue to be saved, with the development of cancer research. If it were not for the contributions of thoughtful and energetic scientists, we might not have the advances in inorganic coordination chemistry that we do today. However, thankfully, due to the work of Nicholas Farrell and others, we can safely say that we are on the road to finding definitive cures, or the cure, for cancer.

That day where the cure for cancer is found has not come yet, but it is fast approaching. One day people will not have to worry about getting cancer because it will be a curable illness.

Until that day, however, we will have to depend upon the fundraisers to raise money for cancer research. We will have to depend upon the physicists, the chemists, and the biologists, in order to help coordinate knowledge and develop new kinds of drugs, both platinum-based and non-platinum-based. We need to use our collective knowledge in order to make a better tomorrow for our children today. In order to defeat cancer, we must realize that the difficulties we face are small if we just collaborate more.

For the scientific community, curing cancer will be its greatest accomplishment and will be no small feat. With determination, hard work, and research, the cure for cancer will someday no longer be just a dream but will be a reality.

REFERENCED FIGURES:

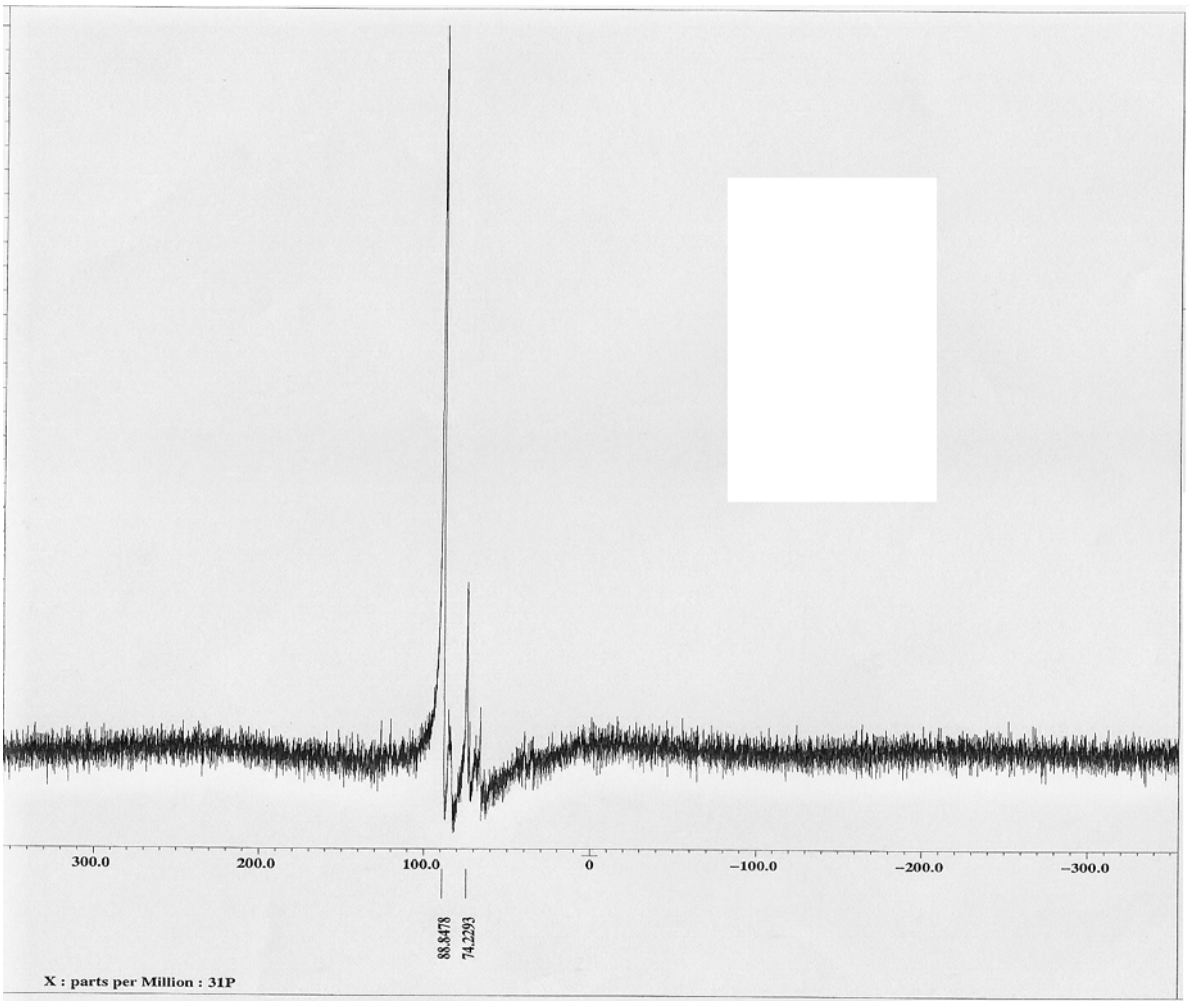
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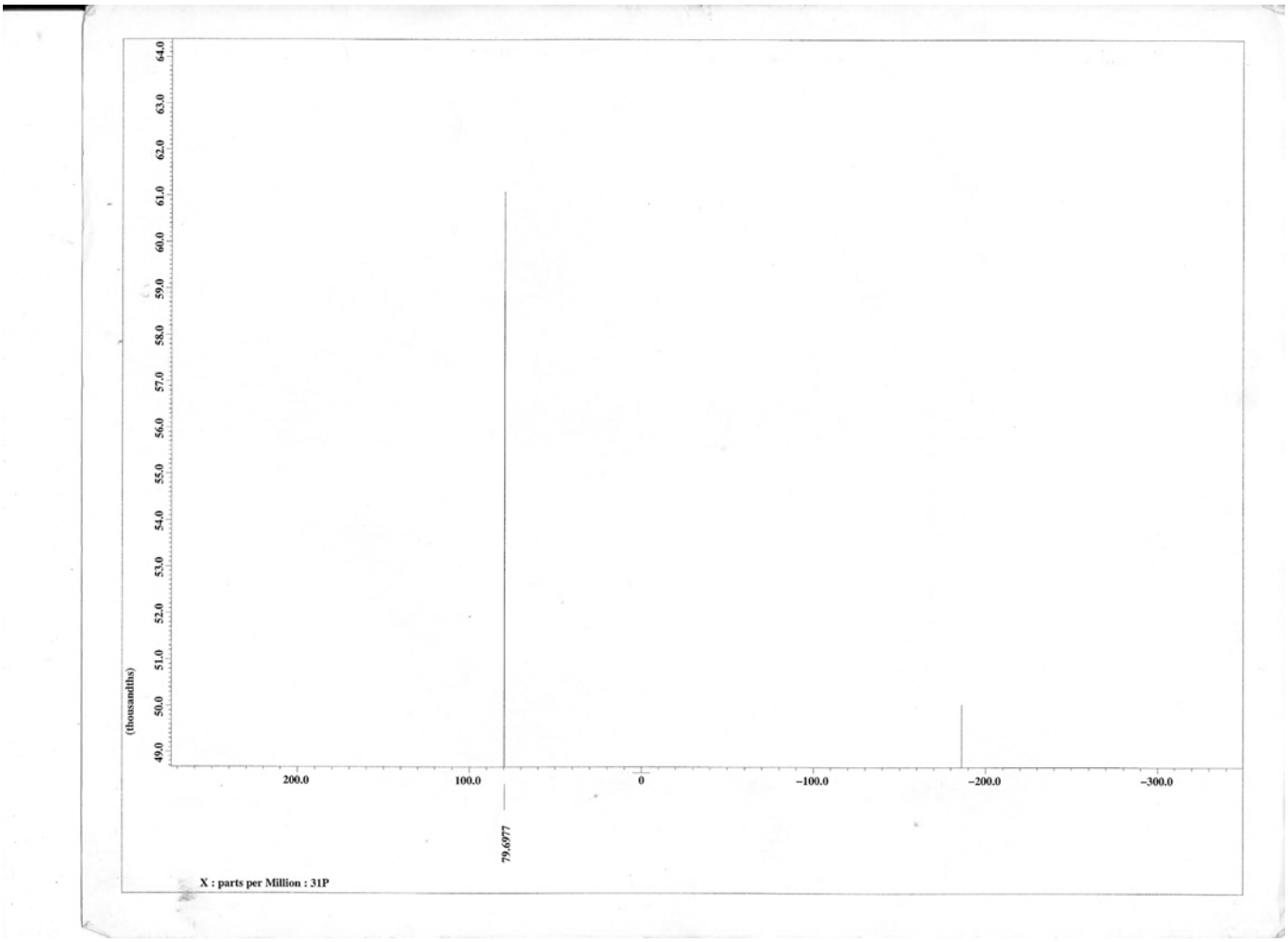
FIGURE 1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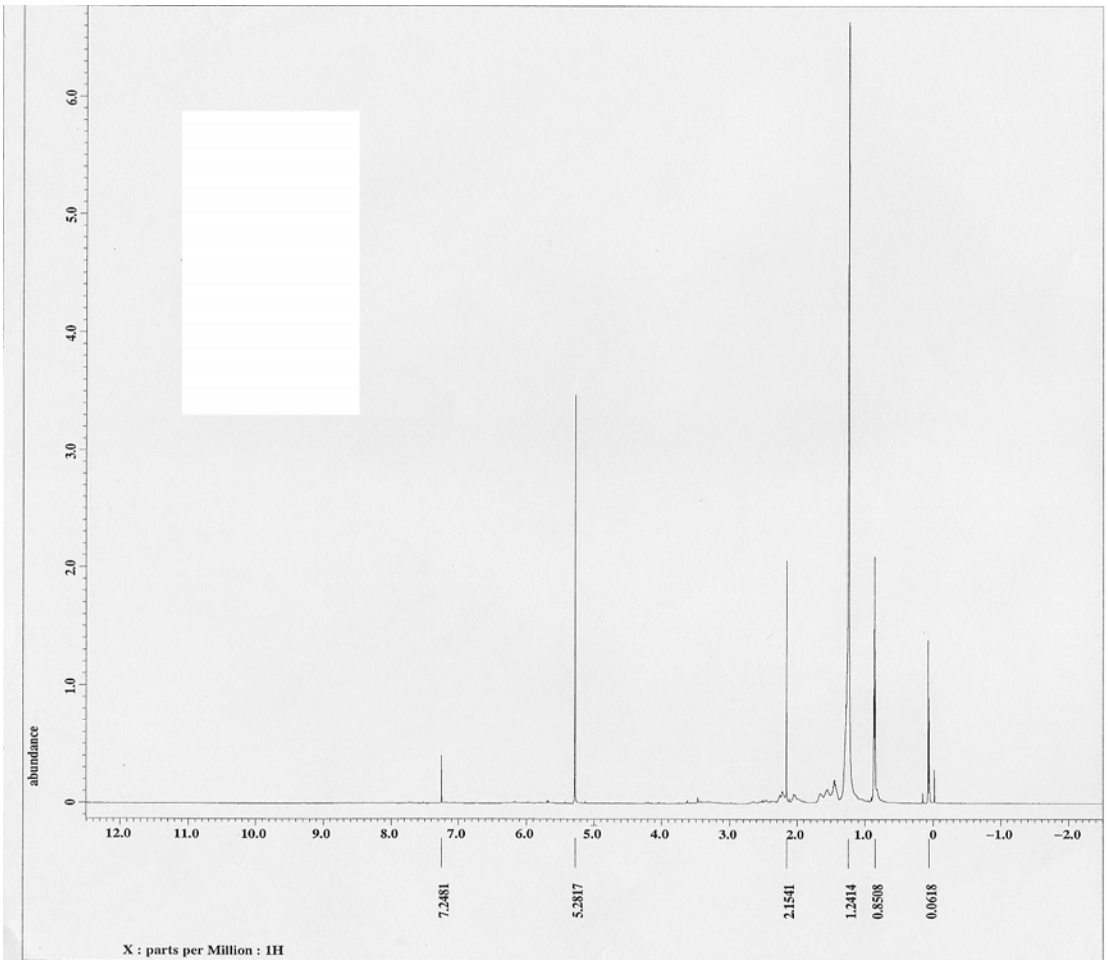
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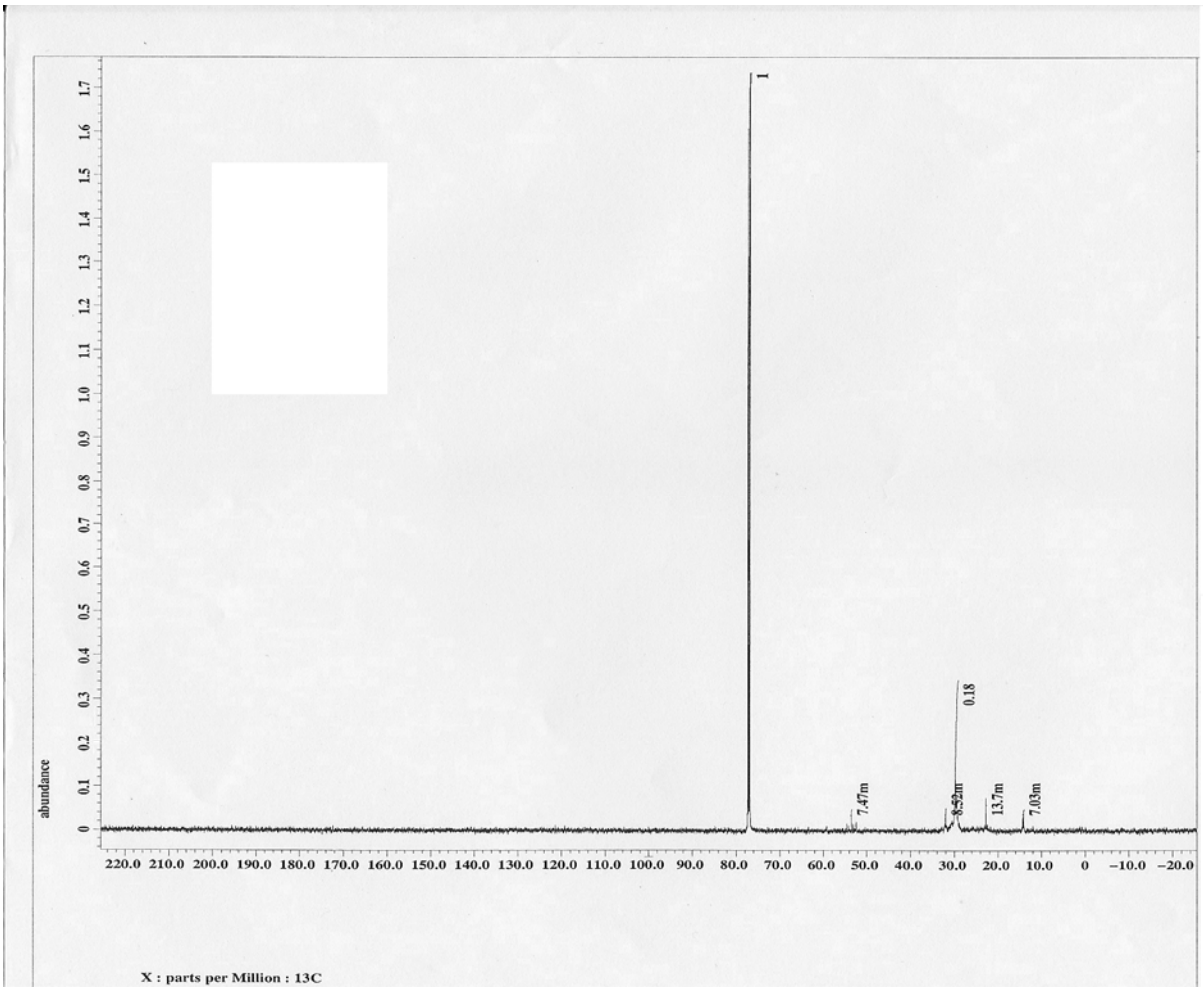

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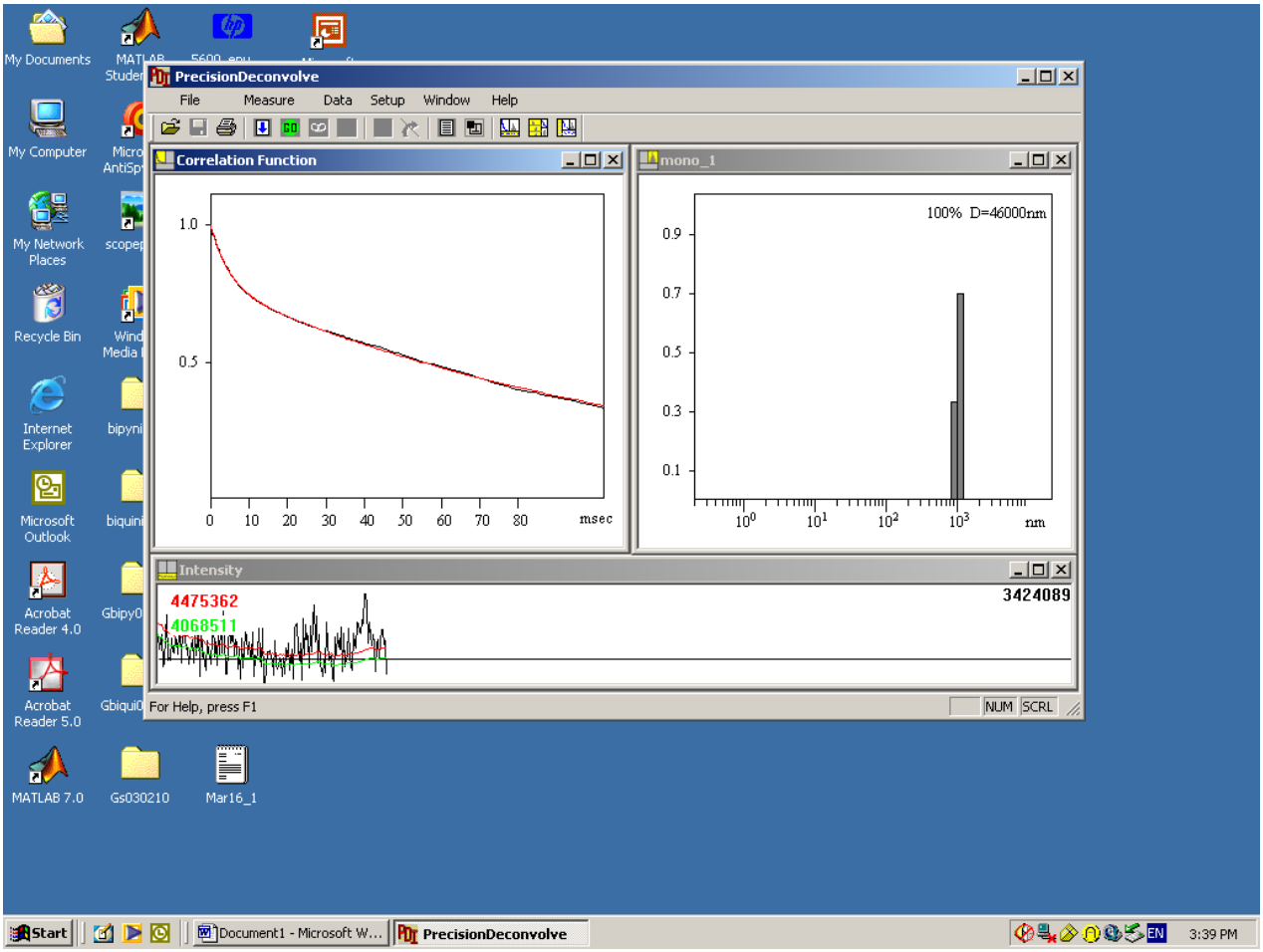
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FIGURE 5

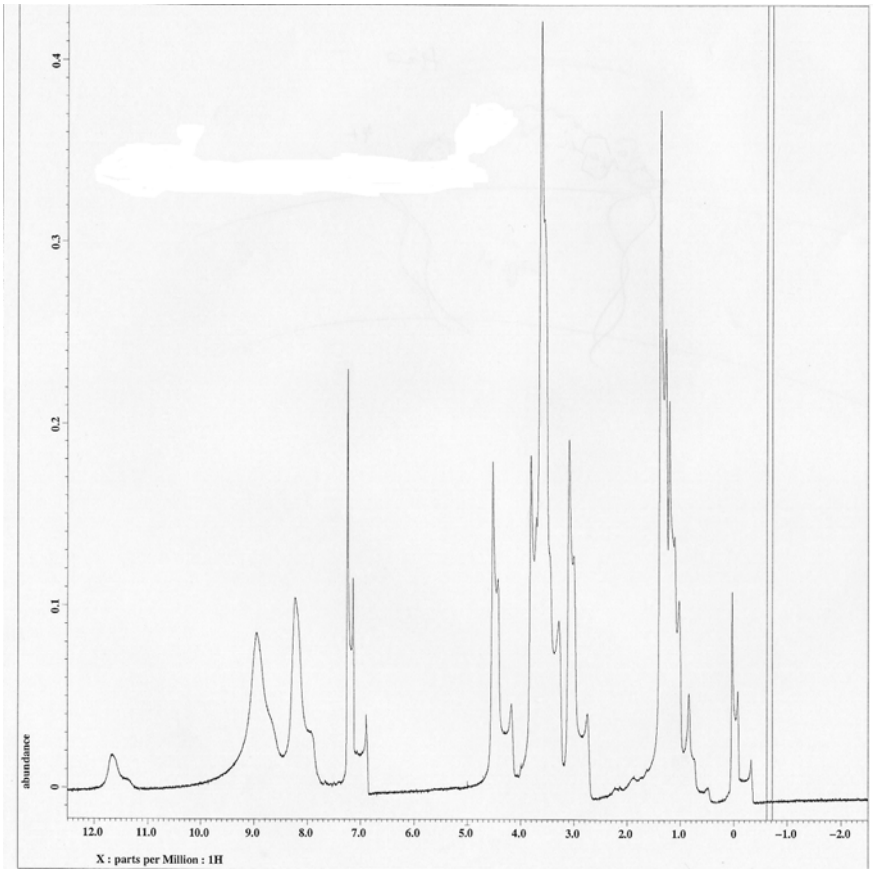
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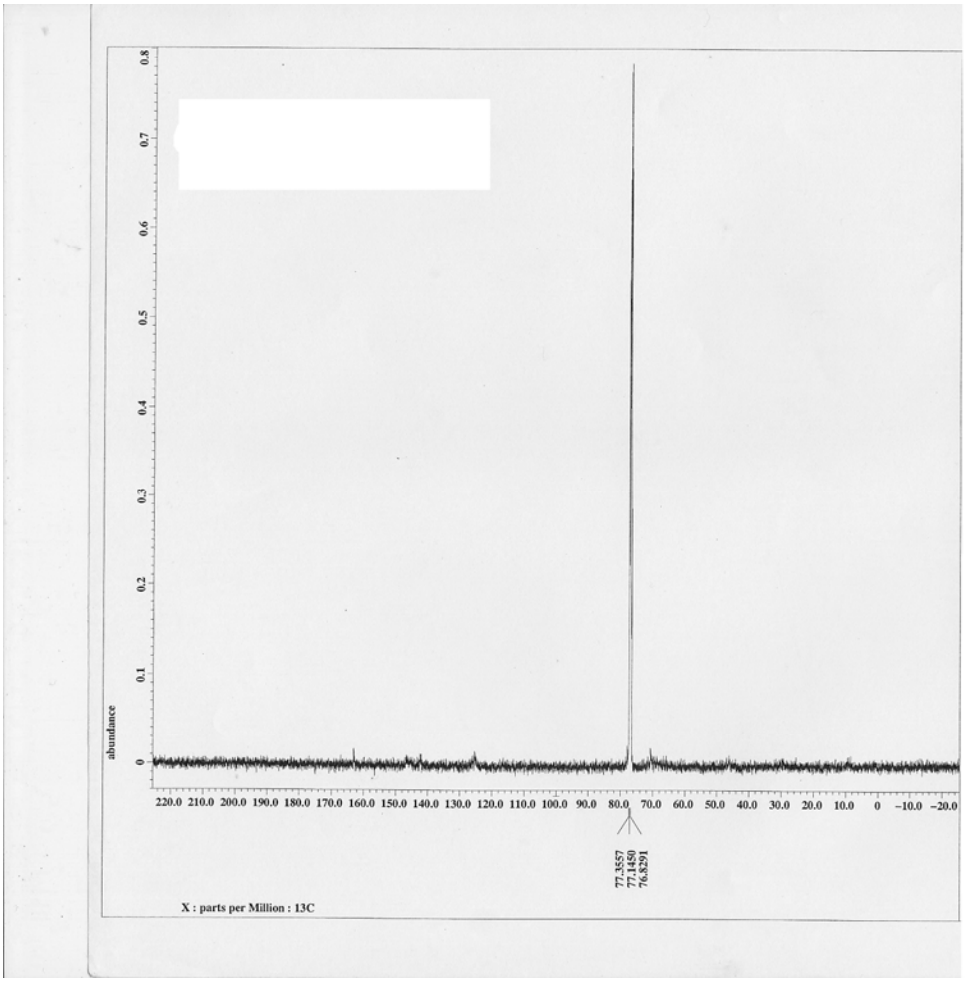
FIGURE 6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0.1
0
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0
77.3557
77.1450
76.8291
X : parts per Million : 13C

FIGURE 7

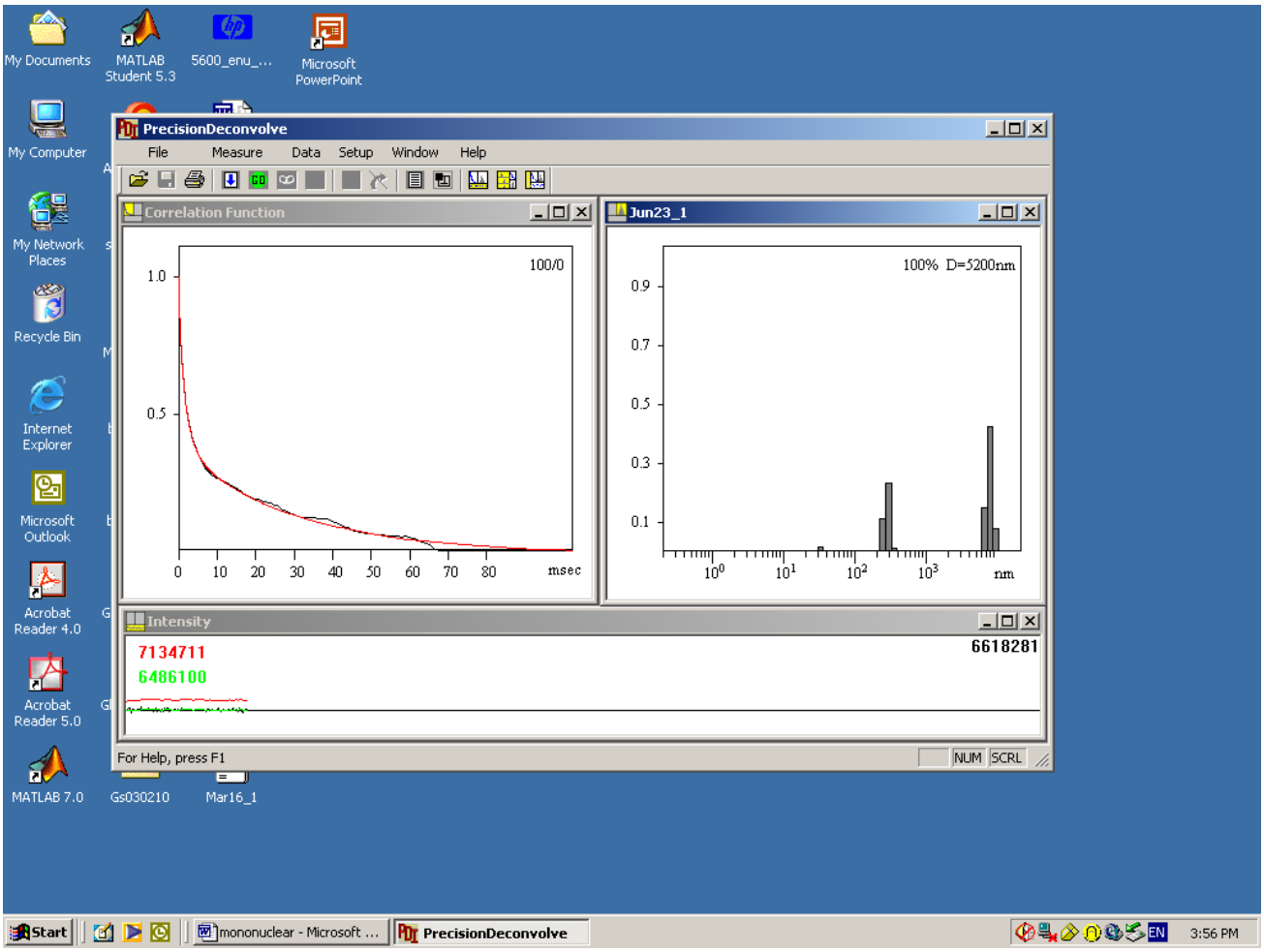
My Documents
MATLAB Student 5.3
5600_enu_...
Microsoft PowerPoint
My Computer
My Network Places
Recycle Bin
Internet Explorer
Microsoft Outlook
Acrobat Reader 4.0
Acrobat Reader 5.0
MATLAB 7.0
Gs030210
Mar16_1
PrecisionDeconvolve
File Measure Data Setup Window Help
Correlation Function
100/0
1.0
0.5
0 10 20 30 40 50 60 70 80
msec
Jun23_1
100% D=5200nm
0.9
0.7
0.5
0.3
0.1
10^0 10^1 10^2 10^3
nm
Intensity
7134711
6486100
6618281
For Help, press F1
NUM SCRL
Start
mononuclear - Microsoft ...
PrecisionDeconvolve
EN
3:56 PM

FIGURE 8

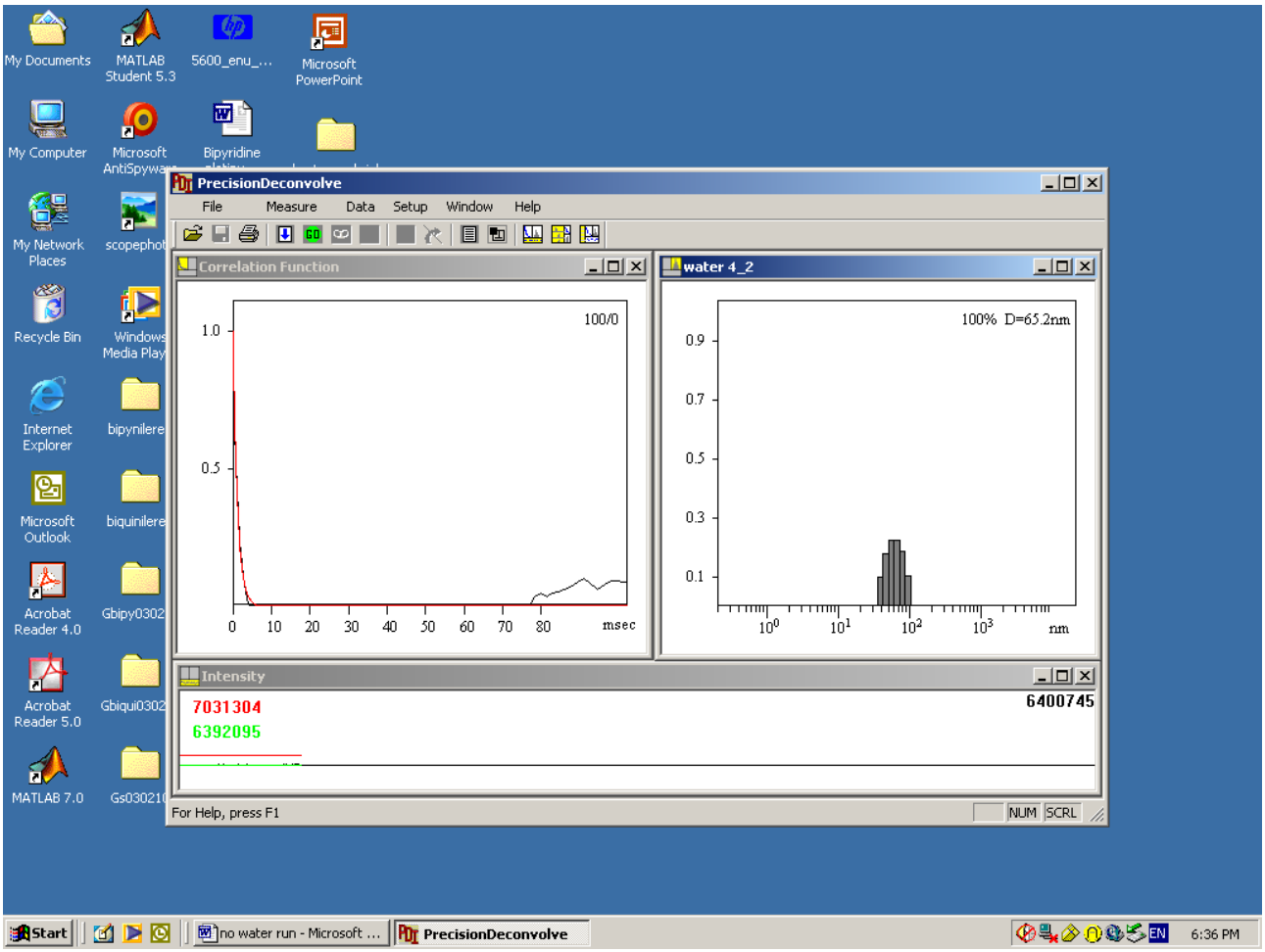
My Documents
MATLAB Student 5.3
5600_enu_...
Microsoft PowerPoint
My Computer
Microsoft AntiSpyware
Bipyridine
My Network Places
scopephot
Recycle Bin
Windows Media Play
Internet Explorer
bipynilere
Microsoft Outlook
biquinilere
Acrobat Reader 4.0
Gbipy0302
Acrobat Reader 5.0
Gbiqui0302
MATLAB 7.0
Gs030210
PrecisionDeconvolve
File
Measure
Data
Setup
Window
Help
Correlation Function
100/0
1.0
0.5
0
10
20
30
40
50
60
70
80
msec
water 4_2
100% D=65.2nm
0.9
0.7
0.5
0.3
0.1
nm
Intensity
7031304
6392095
6400745
For Help, press F1
NUM
SCRL
Start
no water run - Microsoft ...
PrecisionDeconvolve
6:36 PM

FIGURE 9

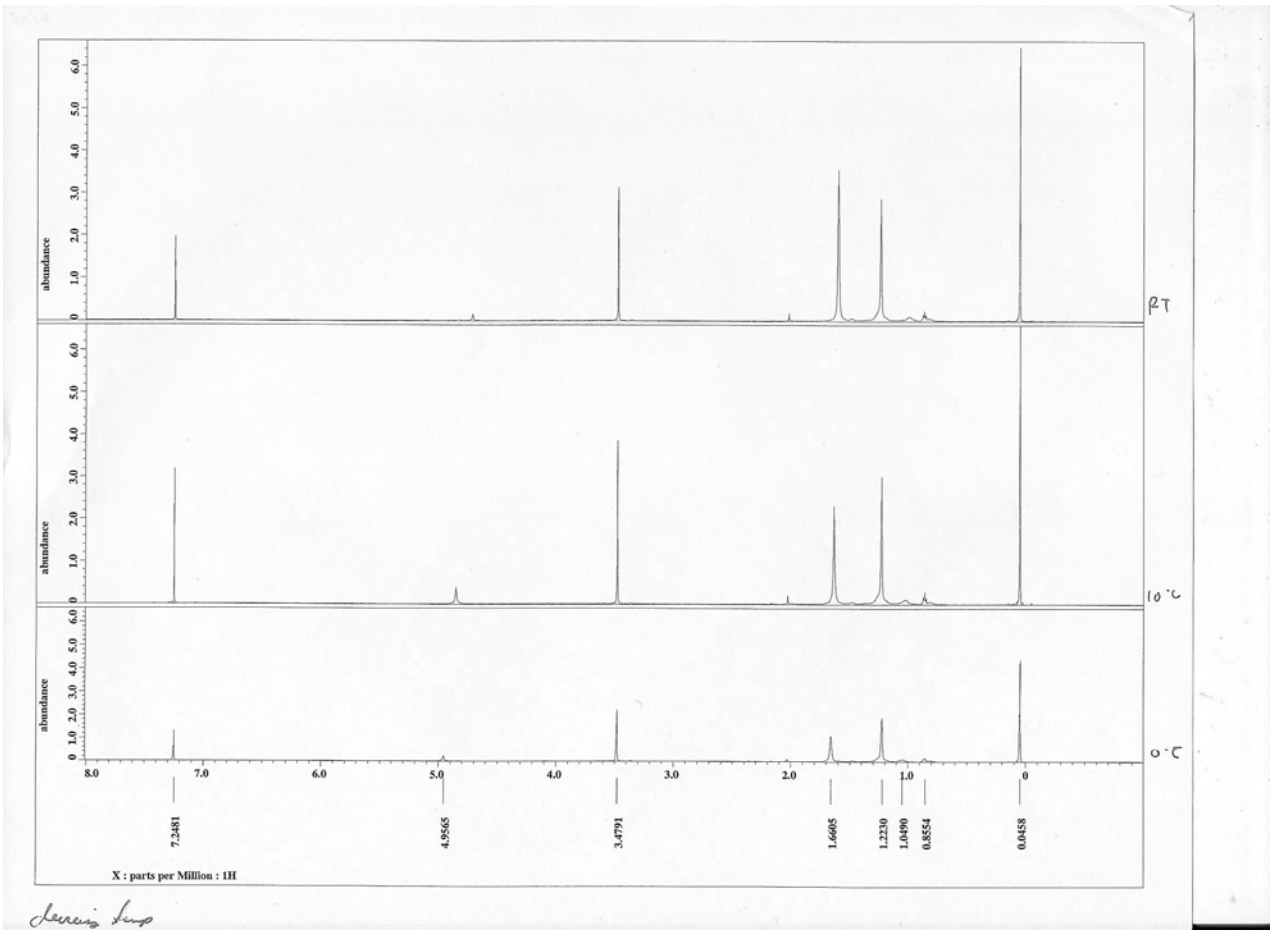
abundance
RT
10°C
0°C
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.2481
4.9565
3.4791
1.6605
1.2230
1.0490
0.8554
0.0458
X : parts per Million : 1H

FIGURE 10

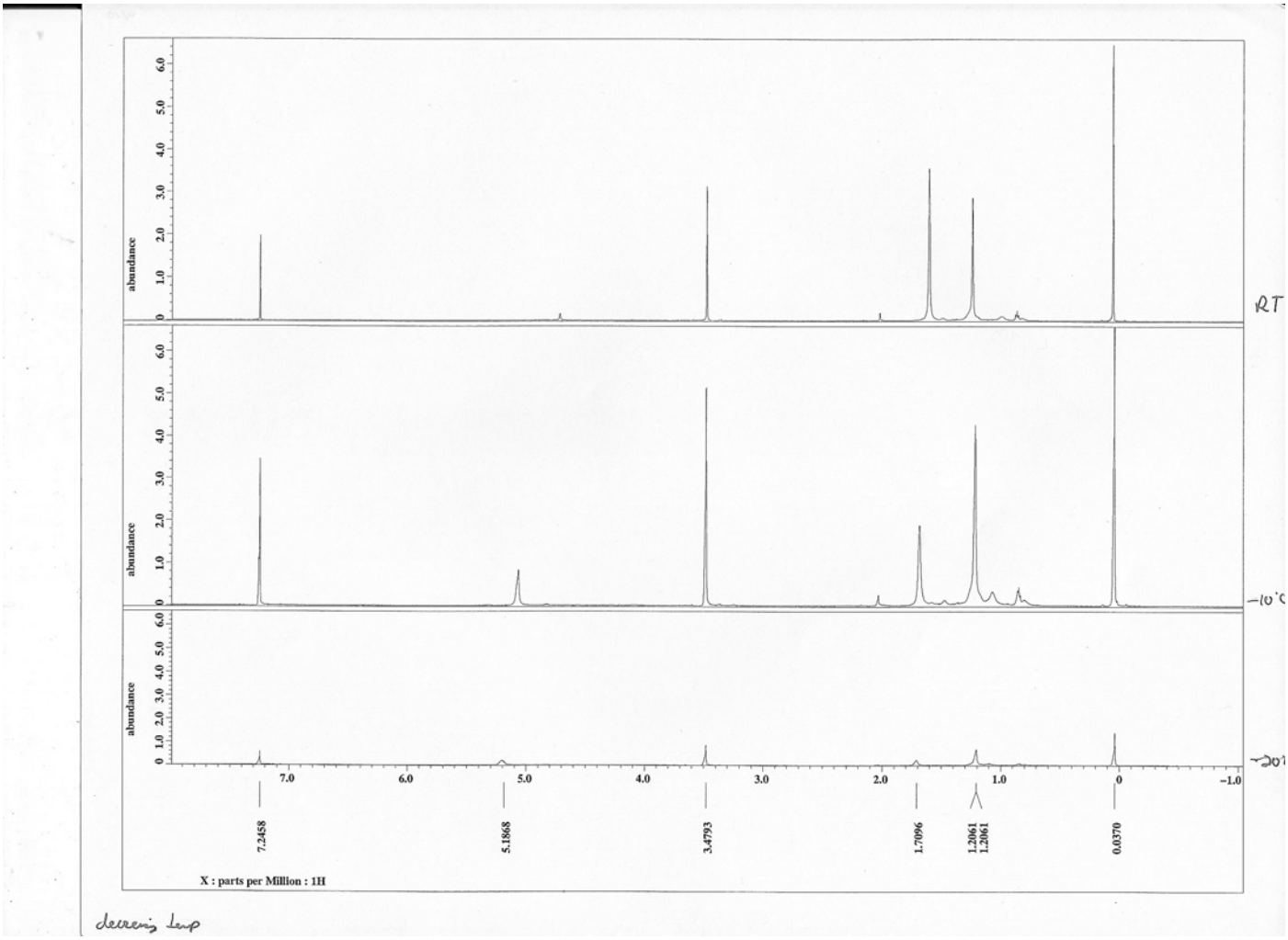
abundance
RT
abundance
-10°C
abundance
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
-1.0
7.2458
5.1868
3.4793
1.7096
1.2061
1.2061
0.0370
X : parts per Million : 1H

FIGURE 11

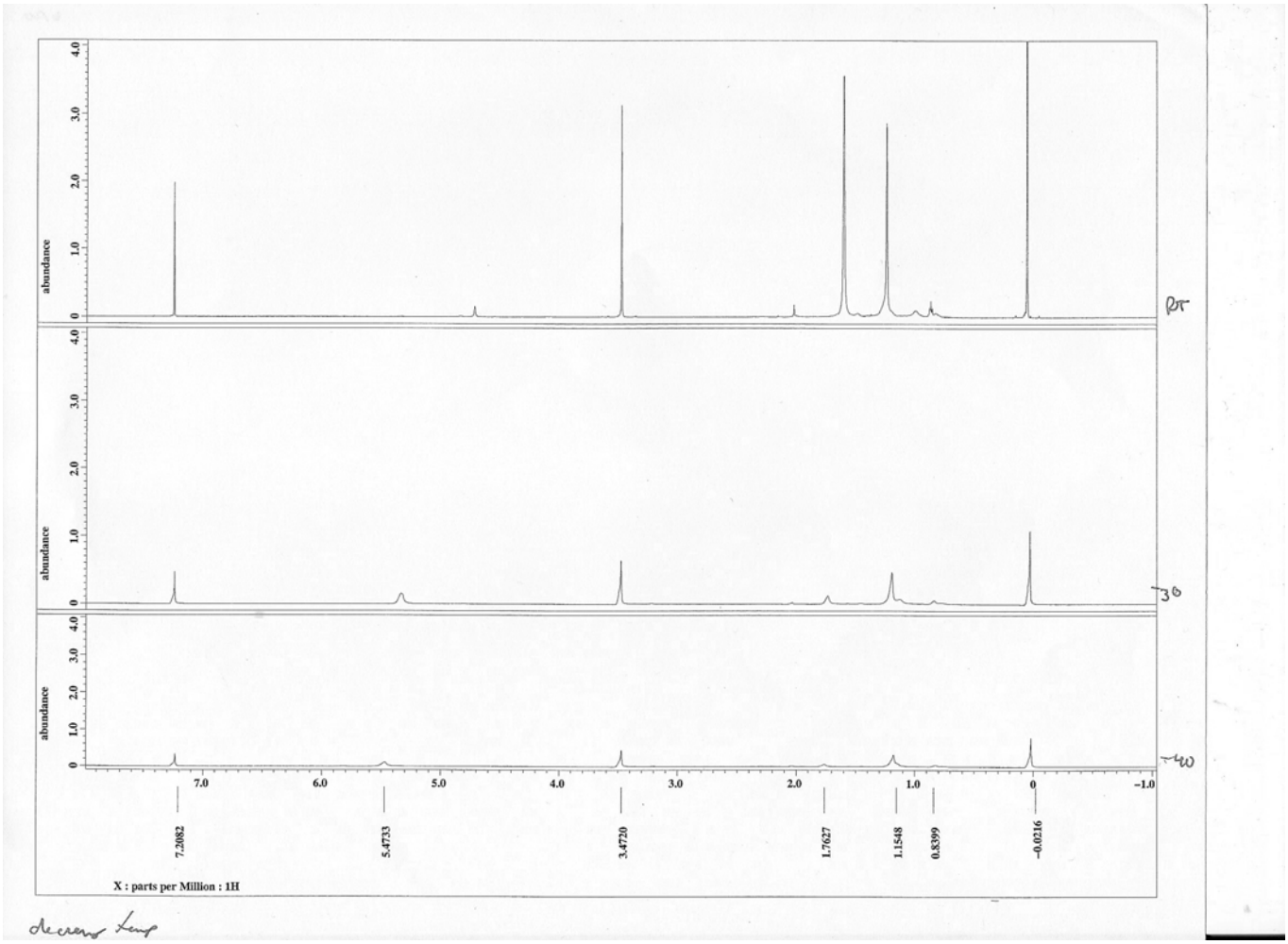
abundance
4.0
3.0
2.0
1.0
0
RT
30
40
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
−1.0
7.2082
5.4733
3.4720
1.7627
1.1548
0.8399
−0.0216
X : parts per Million : 1H

FIGURE 12

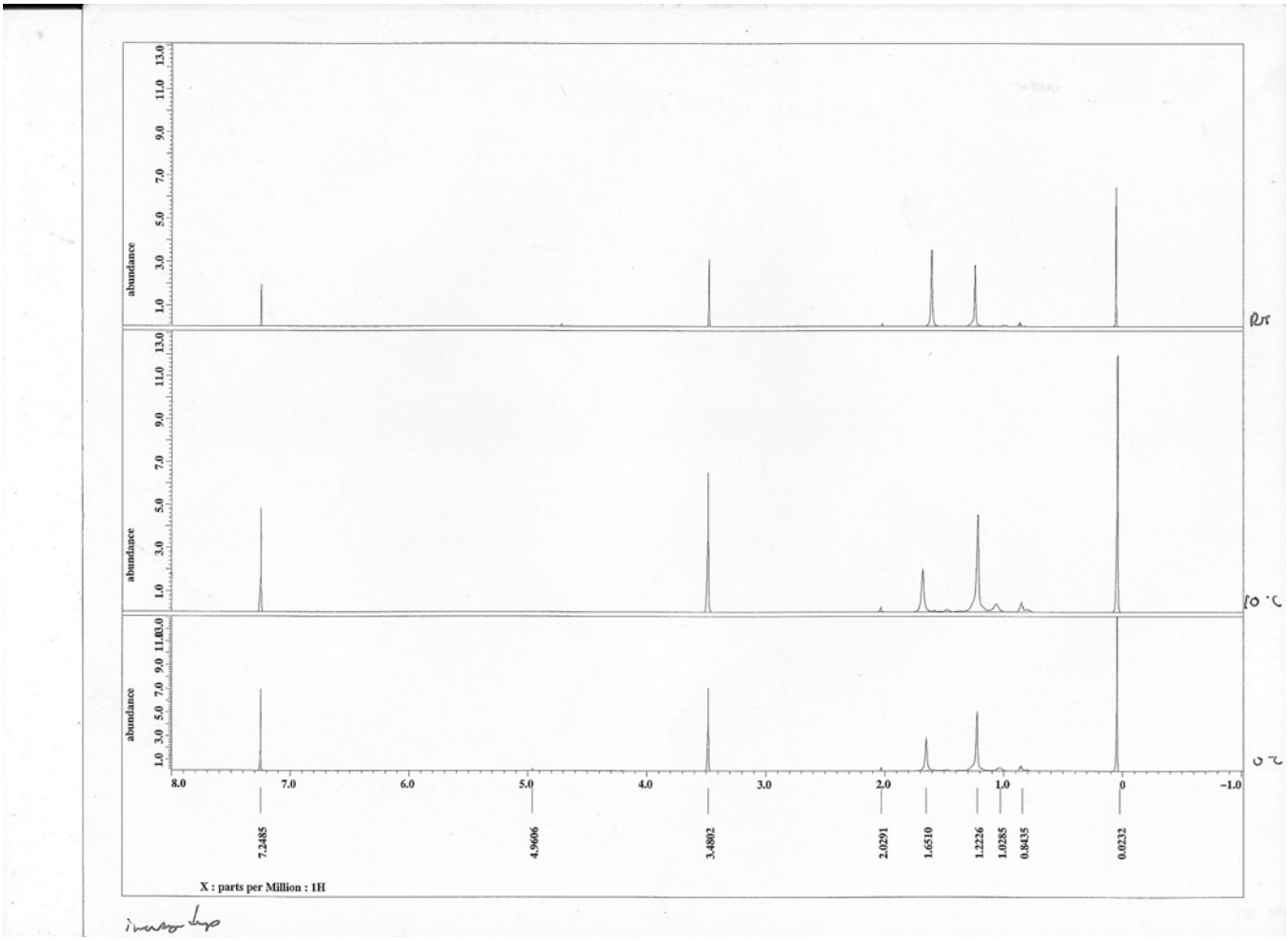
abundance
RT
50 °C
5 °C
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
−1.0
7.2485
4.9606
3.4802
2.0291
1.6510
1.2226
1.0285
0.8435
0.0232
X : parts per Million : 1H

FIGURE 13

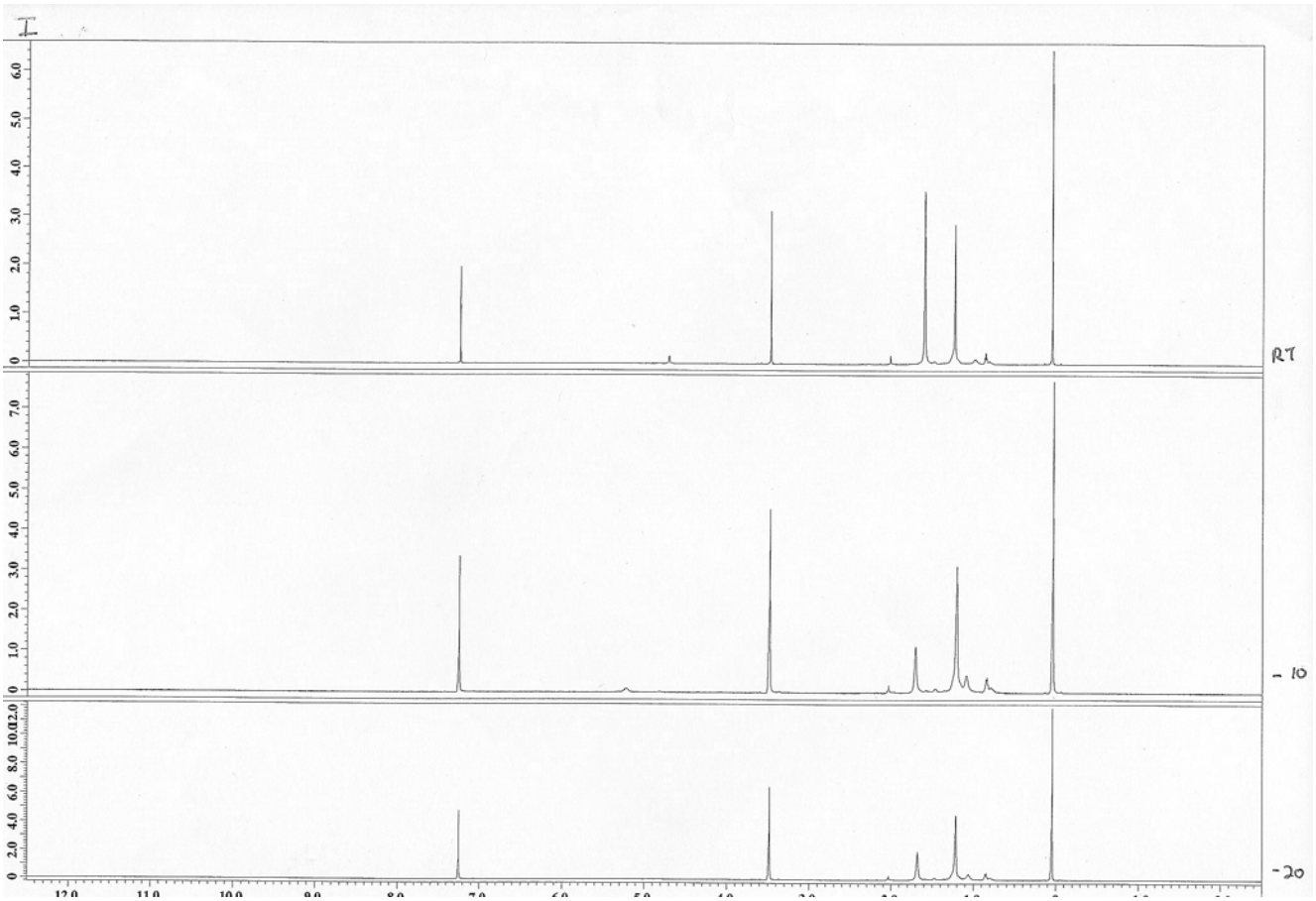

FIGURE 14

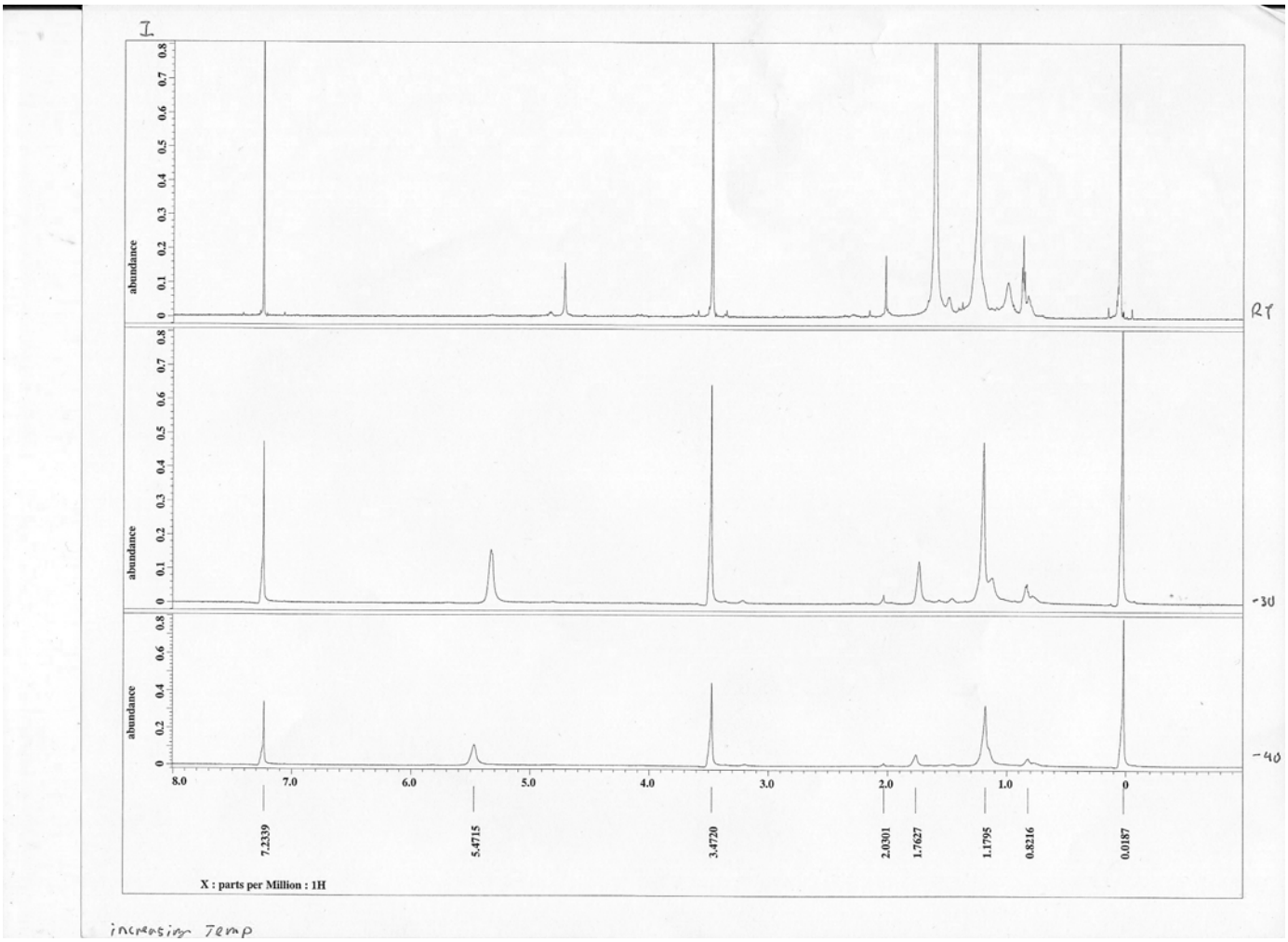
I
abundance
RT
-30
-40
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.2339
5.4715
3.4720
2.0301
1.7627
1.1795
0.8216
0.0187
X : parts per Million : 1H
increasing Temp

FIGURE 15

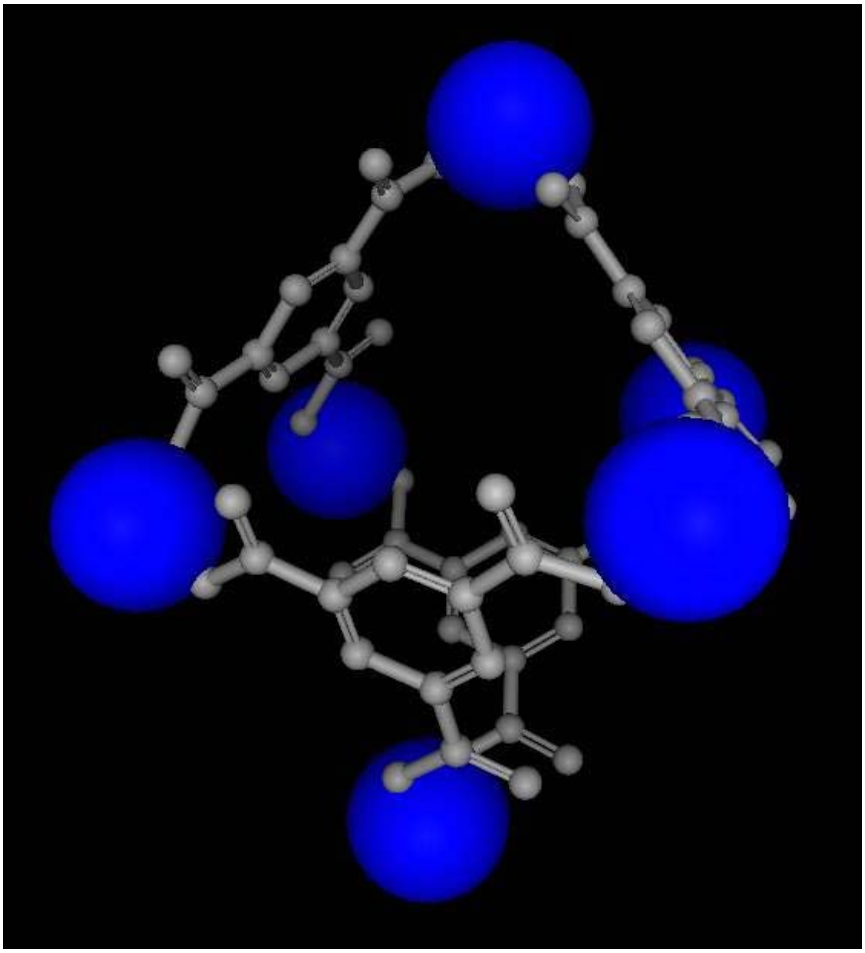

Figure 16

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CURRICULUM VITA

Robert Moreno was born Jaunary 7, 1980 in El Paso Texas, first son of Robert and Patricia Moreno. He graduated from Maxine L. Silva Health Magnet High School in the spring of 1998. After a break from academia which he spent travelling the eastern reaches of the world, he returned to El Paso and enrolled at the University of Texas at El Paso to pursue a B.S. Degree in Chemistry. As an undergraduate he began his research carrer with Dr. Beth Gardner with foci in inorganic chemistry and forensic science. HE was awarded an NSF fellowship under the NanoHub project during his tenure in her lab. As a graduate student he began working with Dr. Juan C. Noveron focusing on Bio-Inorganic synthesis. During his time in Dr. Noveron's lab he was awarded the NSF GK-12 Fellowship whereupon he taught eighth grade science for one year at Guillen Middle School.

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