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# Gemini metallo-Surfactants: Chemical and Physical Properties

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# GEMINI METALLO-SURFACTANTS: CHEMICAL and PHYSICAL PROPERTIES

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by

Erich I. Valenzuela

2011

## **Dedication**

I would like to dedicate this thesis defense with a lot of love to my beautiful wife Alethia who supported throughout my studies and motivated me to keep studying and kept pushing me forward in those hard times. I would also like to dedicate this thesis defense to my precious daughter Xitlali who with a smile she would make my day and would give me strength to keep going. I would as well share this achievement with my parents Jose Antonio Rito Valenzuela Villalba and Maria del Rosario Alcantar Enriquez who went through a lot of sacrifices in order to give an excellent education to all their children. To my brothers and sisters: Jr, Jonathan, Brian, Marcus, Chayo, Chuy, Mayra, David, Gilo, and Velia for making me smile with their crazy comments.

# GEMINI METALLO-SURFACTANTS: CHEMICAL and PHYSICAL PROPERTIES

By

Erich I. Valenzuela

Thesis

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The University of Texas at El Paso

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## Abstract

Gemini surfactants are amphiphilic molecules that consist of two surfactant molecules chemically joined together by a spacer group. These molecules tend to self-assemble into vesicles at much lower concentrations than traditional surfactants and have found many applications in catalysis, adsorption applications, drug-delivery, nanoscale technology, and biotechnology. In this thesis, the synthesis, characterization and physical properties of a new type of Gemini surfactant derived from dinuclear Cu(II) metal complexes is presented. We call these molecules Gemini Metal-Organic Surfactants (GMOs).

Three newly developed new GMOs (compounds **1-3**) are composed of Cu(II) ions ligated to a lipid-functionalized triamine group and the metals are bridged by a bipyridyl spacer group. The head groups of the resulting GMOs were characterized via X-ray crystallography. The GMO self-assemble in water into stable metallo-liposomes, which were characterized with mass spectrometry (MS), Infrared (IR), fluorescent optical microscopy and atomic force microscopy. The Critical Micelle Concentration (CMC) of the GMOs were determined with Nile Red-stained Fluorescent Optical Microscopy as a function of concentration and the results were  $1.9 \times 10^{-4} \text{M}$  for **1**,  $4.1 \times 10^{-4} \text{M}$  for **2**, and  $4.9 \times 10^{-4} \text{M}$  for **3**.

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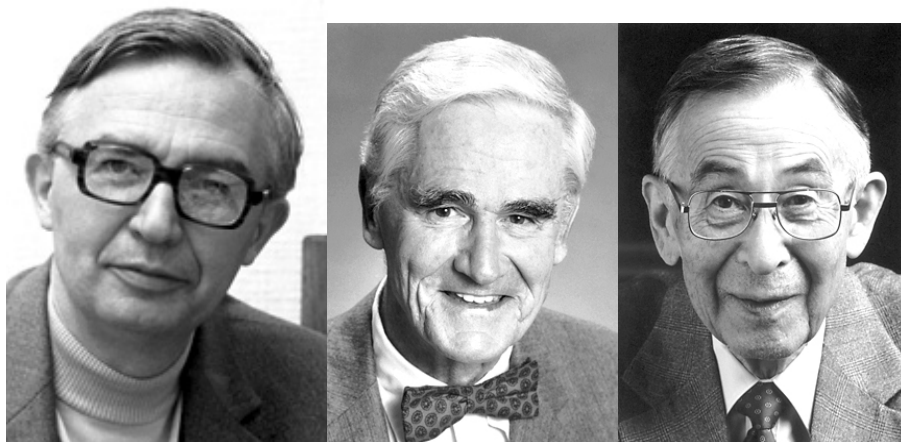
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## Chapter 1. Introduction

Chemistry has traditionally focused on the formation of molecules from atoms, but until recently the focus has shifted to the study of supramolecular structures, which are structures beyond the molecule and form superstructures. This thesis focuses on a new kind of supramolecular structures derived from small molecules.

Throughout the years chemistry has been divided into many branches in order to have a more methodically, deeply, organized, and detailed understanding of how atoms and molecules work and how we can benefit from it. There are many branches of chemistry out there like, Astrochemistry, Biochemistry, Electrochemistry, Environmental chemistry, Organic chemistry and many more, but there is only one branch that studies in detail the non-covalent bonding between molecules, and that is Supramolecular chemistry.<sup>1</sup>

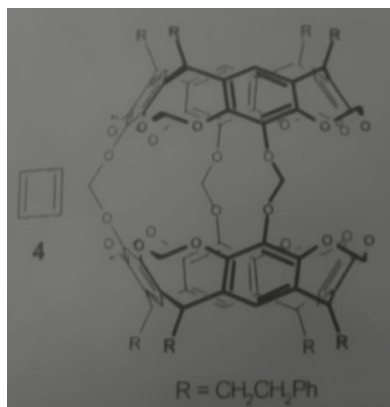
Supramolecular chemistry is a young but fast growing branch of chemistry. Its concept was presented by French chemist Jean-Marie Lehn, who along with Donald J. Cram and Charles J. Pedersen (who did not have a PhD at that time), obtained the Nobel Prize in chemistry in 1987.<sup>2</sup> According to Lehn, Supramolecular chemistry “is chemistry beyond the molecule”.<sup>3</sup> In other words, the definition of supramolecular chemistry is based on the non-covalent interactions between molecules.<sup>4</sup>



**Figure 1.1.** Jean-Marie Lhen on the picture on the left, in the middle its Donald J. Cram, and on the right picture is Charles J. Petersen.<sup>4</sup>

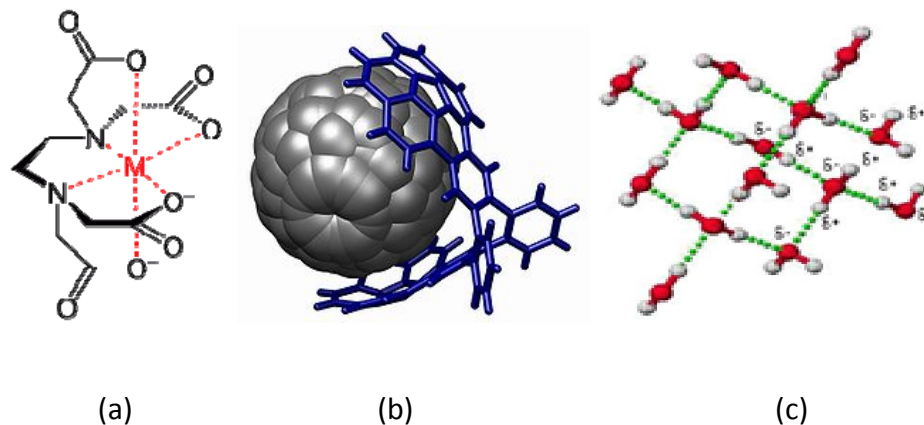
Non-bonding interactions can refer to those interactions that not necessarily are covalent bonding. They are characterized by having much more smaller energies in comparison with covalent bond energies that can go from 200-400KJ/mol. An example of these would be the London dispersion forces, ion-induced dipoles, dipole-dipole interactions, electrostatic interactions, or hydrogen bonding which all have energies lower than 80KJ/mol.<sup>4</sup>

Non-bonding interacting atoms can go into geometrical arrangements that could fit the topology of the molecules, becoming frameworks of non-interactive bonding. An example of this is could be a “molecular flask”. Cyclobutadiene is a very unstable molecule under normal conditions but inside a molecular flask, it is stabilized and can remain stable for months.<sup>5</sup>



**Figure 1.2.** shows the molecular flask in which cyclobutadiene can be stabilize longer than normal at room temperature.<sup>4</sup>

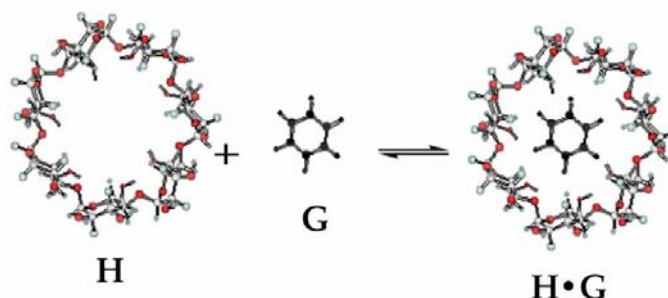
In order to have non-covalent bonding, pre-organization and self-organization or self-assembly of the molecules have to occur. Pre-organization of the molecules denotes that the molecules have a spontaneous arrangement with respect to each other to facilitate chemical reactions<sup>6</sup>. The key element that forces pre-organization by spatial arrangement is known as a template.<sup>7,8,9</sup> Molecular self-assembly is based on the topology of the molecules, non-covalent interaction between them and the “template effect” that is divided into two categories; the kinetic template effect that describes how the molecule is being affected in a direct form by the metal-ion that controls the steric course of the sequence of the reaction, and the thermodynamic template effect that involves the perturbation of an already existing equilibrium in an organic system obtaining a high yield on the desired metal complex product.<sup>10</sup>



**Figure 1.3.** Examples of non-covalent interactions that make self-assembly possible. (a) coordination bonding (b)  $\pi$ - $\pi$  stacking and (c) H-bonding.<sup>11,12,13</sup>

Supramolecular chemistry encompasses different sizes of molecules, which is the reason why the study of it can be divided into three different size domains. The three main domains used in the organization for the study of supramolecular chemistry are: the host-guest domain, the aggregate science, and the crystal engineering domain. For example, mesoscopic structures<sup>14, 15</sup> which ranges are in between the micro and macro scale as do biological assemblies and polymers.

The host-guest domain involves two or more molecules a “host” and a “guest” that are involved in pure non-covalent interactions for a supramolecular complex. According to Cram<sup>4</sup> the host could be a molecule or ion that has a binding site that converges into a complex while a guest is any molecule or ion whose binding sites diverge in the complex.<sup>16</sup> It can be say that hosts are normally microcyclic organic molecules (i.e. crown ethers<sup>17</sup>, the hexokinase enzyme,<sup>18</sup> the foldamers<sup>19</sup>) whereas metal ions or neutral organic molecules can serve as guests.

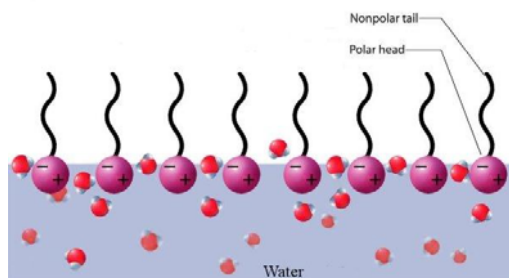


**Figure 1.4.** Host-guest molecules interacting by hydrophobic interactions,  $\pi$ - $\pi$  stacking, ion-ion interactions, and Hydrogen bonding.<sup>20</sup>

Crystal engineering is in simple words, obtaining crystals with desire properties.<sup>21, 22</sup> sadly, with the technology today in general, it is still impossible to do this. A model used for packing molecules into a crystal and obtaining its properties was proposed by Kitajgorodsky<sup>23</sup> but he was not able to predict the crystal structure. This is because intermolecular forces such as hydrogen bonding, Van der Waals, charge-transfer, and electrostatic forces dominate the charge for both the crystallization and the complex formation and they are very dependent in direction and distance from one interaction to another. One statistical analysis of thousands of crystal structures was performed in order to study the influence of weak intermolecular interactions on molecular structure from the Cambridge Data Base. The analysis showed that typical building blocks forming patterns could be recognized. Consequently, it was determined that theoretically obtaining supramolecular aggregates or crystal with foreseeable spatial structures and desirable properties was possible.<sup>24, 25</sup>

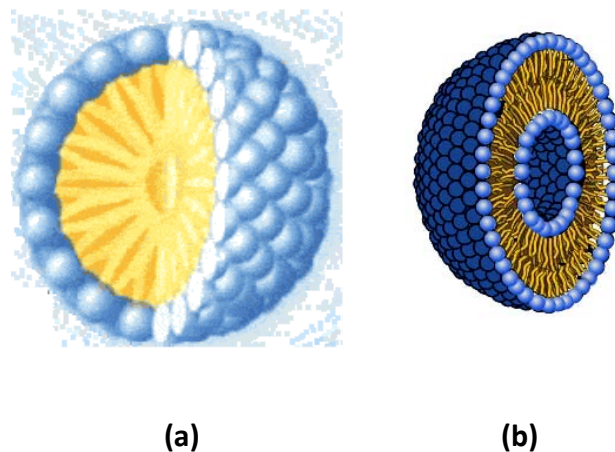
Aggregate sciences focus more on the bigger molecular assemblies than the host-guest domain. Such molecules “aggregate” with themselves in order to make bigger structures. These molecules include the Langmuir and Langmuir-Blodgett layers, liposomes, and micelles.

Langmuir and Langmuir–Blodgett layers are films according to Fuhrhop and Köning as amphiphilic monolayers in water. They do not necessarily emphasize the hydrophobic effect on the molecular assemblies, but represent a separation between solid-liquid phases or liquid-solid phases in water.<sup>26</sup> When they are on a water surface, the polar part of the amphiphilic molecule interacts with water while the hydrophobic part of the same molecule is repelled.



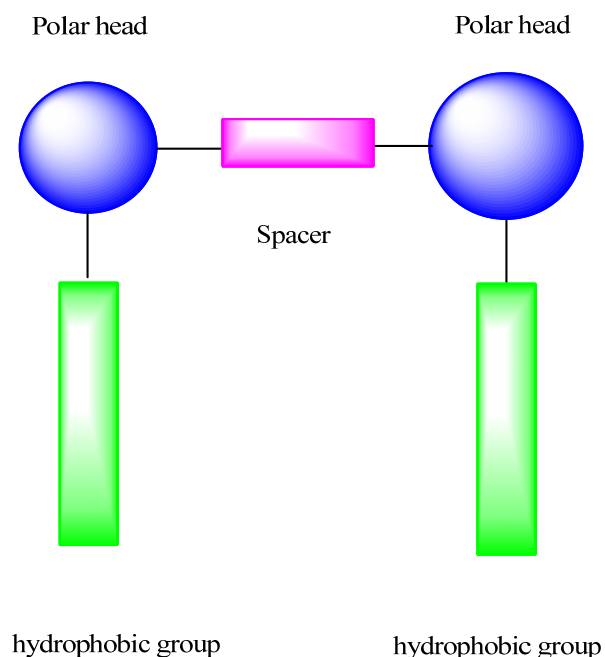
**Figure 1.5.** Langmuir and Langmuir –Blodgett layers.<sup>27</sup>

Micelles and liposomes are formed by amphiphilic molecules, or molecules that have a “head” group that can be cationic, anionic, or non-ionic, and a hydrophobic “tail”. The interactions are based on the hydrophobic effect with involves the interaction of polar molecules with polar molecules and non-polar molecules with non-polar molecules. The difference between a micelle and a liposome consist of the bilayer of the liposome. Liposomes tend to aggregate in sphere-like monolayers having an outside and inside the polar head with a hydrophobic tail in between them. Micelles are monolayer sphere-like similar to the liposomes, but their polar head only interacts with water while the hydrophobic tail cocoons inside the micelle. There is also a reverse micelle where the interaction involves the non-polar solvents (i.e. alkanes) interacting with the amphiphilic molecule instead of water.



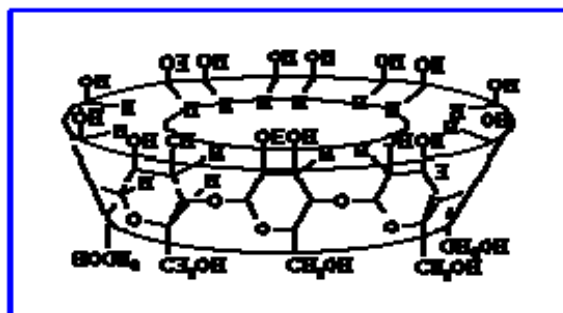
**Figure 1.6.** Illustration of (a)micelle (b) liposome.<sup>28,29</sup>

Also in this area there is a new fascinating type of dimer, the Gemini surfactant. Gemini surfactants are amphiphilic molecules made of two ionic head groups that can be either cationic, or anionic and two aliphatic chains<sup>30</sup> linked by either a fluxional or rigid spacer.<sup>31,32,33</sup> They have been of great interest because of their lower CMC values compared to the conventional surfactants of equivalent chain length,<sup>34</sup> less sensitivity to the polarity of short spacers,<sup>35</sup> and they could be used as vehicles in drug delivery. Because of the hydrophobic interaction, Gemini surfactants with a spacer of 16 carbon atoms (16C) or more reduce CMC almost ten-fold in comparison to shorter spacers (3C-8C),<sup>36</sup> this produces less skin irritation with increased concentration of the surfactant monomer in solution and it is useful in cosmetics.<sup>37,38,39</sup>



**Figure 1.7.** Gemini Surfactant.

Supramolecular systems have many applications today. For example, when photoelectric stimuli are applied they have varied amplitude which was original proposed by Nobel laureate Richard Feynman in 1959<sup>40</sup>. He proposed that hypothetical devices so called Drexler instruments<sup>41</sup> could be used in the future as biodegradable medical devices small enough to fit in a cell and replicate themselves.<sup>42</sup> In Pharmaceuticals, complexing a drug with cyclodextrin has opened new doors with medical applications. This is because cyclodextrin encapsulates drugs making them more soluble, stabilizing them and preventing them from decomposing by moisture or light.<sup>43</sup>



**Figure 1.8.** Encapsulation of cyclodextrin. The Hydroxyl groups are projecting outside the capsule making it water soluble while the hydrogens attached to the glucose, are pointing to the interior making it non-polar and able to interact with non-polar drugs.<sup>44</sup>

## 1.1 Statement of Problems

Non-covalent interactions are the key elements for supramolecular chemistry. Even one simple non-covalent interaction like,  $\pi$ - $\pi$  stacking, hydrogen bonding, electrostatics could change the way a reaction proceeds, or make the analysis of the molecule hard to predict or even analyze.

Nuclear Magnetic Resonance (NMR) studies can be done to most of the molecules in order to find the correlation certain atoms have between themselves and in the molecule. It is a spectroscopic tool for obtaining the chemical structure of simple and complex molecules as well. One of the problems that arise with Copper(II) complexes is that due to its diamagnetic structure, NMR spectrometric analysis cannot be obtained most of the time.

This work addresses this issue by obtaining different analysis other than NMR in order to obtain a characterization of a diethylene triamine Gemini-metallo Surfactant as monomers as well as in their aggregated form in water.

## 1.2 Objectives

The objectives for this study are:

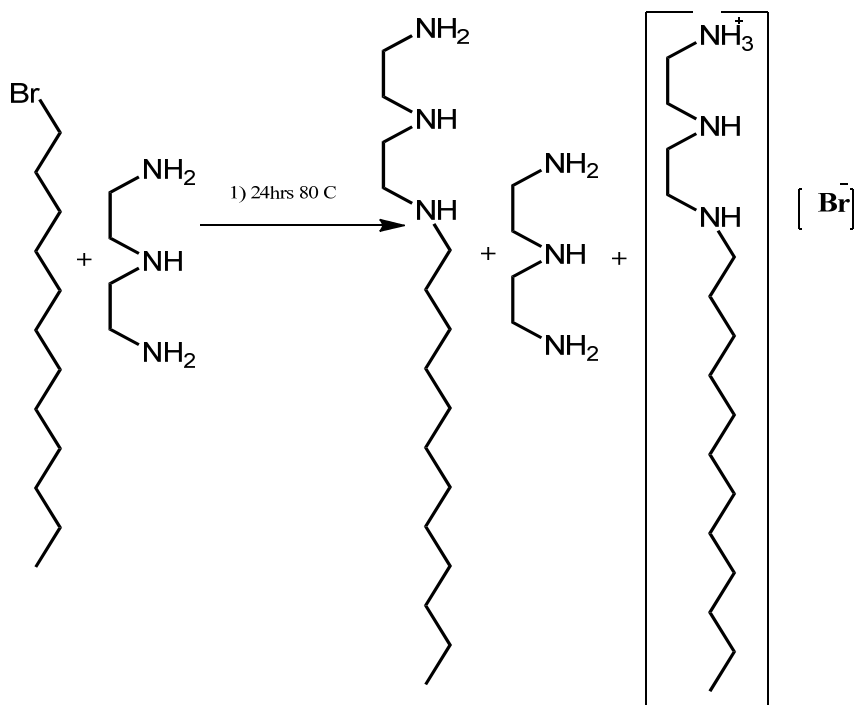
1. To synthesize and crystallize the body of the metallo-Gemini surfactant that it is formulated from diethylene triamine and the corresponding copper spacers: Chloride, 4,4'-Bipyridine, and (E)-1,2-di(pyridin-4-yl)ethane.
2. To repeat the synthesis of such molecules but with a functionalize carbon chain attached in order to obtain the desire metallo-Gemini surfactant and characterized it via M.S and D.S.C
3. To obtain the CMC and optical microscope images of the metallo-Gemini surfactant when this is emulsified in water.

## Chapter 2. Synthesis and Characterization of the Gemini-Metallo Surfactant

Copper is an essential element in the human body<sup>45</sup> (the daily requirement for adults is 900mcg).<sup>46</sup> It is a vital part of proteins such as ceruloplasmin as well as enzymes like c-oxidase that generates an electrical gradient used by the mitochondria to create ATP.<sup>47</sup> Copper also plays a major role in Wilson disease, Thalassemia, Sickle cell anemia<sup>48,49,50,51,52,53</sup> and Alzheimer's and has some interesting anti-inflammatory properties,<sup>54,55,56,57,58</sup> and is found as part of the active metabolites of clinically used anti-arthritic agents.<sup>59,60,61,62</sup> These copper complexes could be useful for any of this applications, but in order to find out what properties they have, we have to characterize them.

### 2.1 Ligand design and characterization

Diethylene triamine (DETA) is a hygroscopic liquid that is soluble in polar solvents.<sup>63</sup> Normally it is used in coordination reactions as a tridentate ligand forming complexes such as  $\text{Co}(\text{NO}_2)_3$ .<sup>64</sup> The amine complex is stored under argon at all times in order to avoid nitrogen oxidation<sup>65</sup>. The neat amphiphilic reaction was reflux for 24 hrs. using DETA as a limiting reagent. The byproduct would then be a primary amine attached by ion-ion interactions to the bromide atom.



**Figure 2.1.1** Synthesis of functionalized DETA.

### 2.1.1 NMR Spectrometry

The <sup>1</sup>H, <sup>13</sup>C spectrometric analysis of the functionalized amines were done with deuterated acetonitrile in a 600MHz NMR instrument. In the <sup>1</sup>H analysis, the expected multiplet from the amine protons can be observed at 2.38 ppm, as well as another multiplet signal at 2.24 ppm that corresponds to protons of the ethenes next to the secondary amines. Another multiplet signal can be observed at 1.13 ppm corresponding to the protons of the aliphatic chain with exception of the last carbon. The triplet at 0.602 ppm corresponds to the last methyl group.

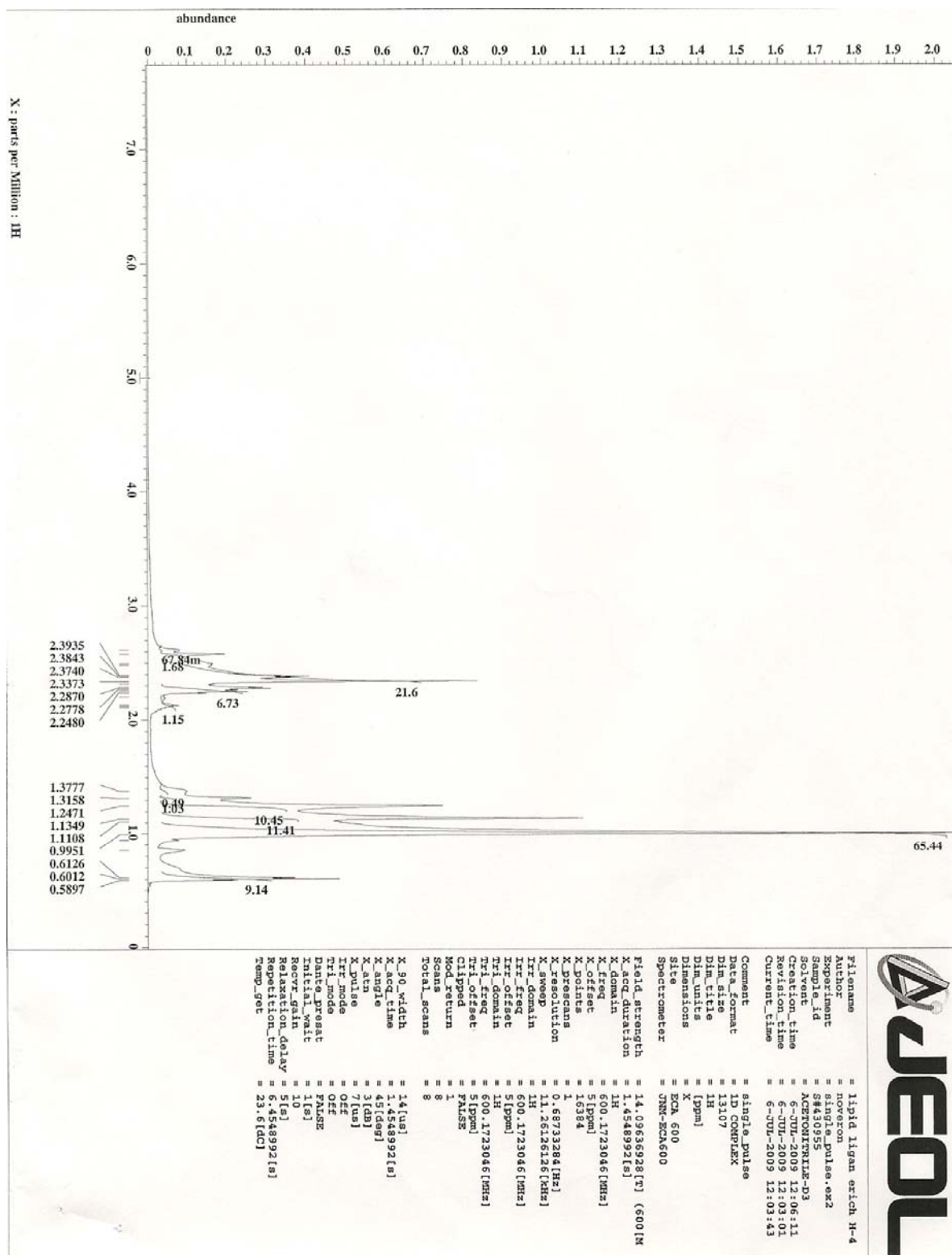
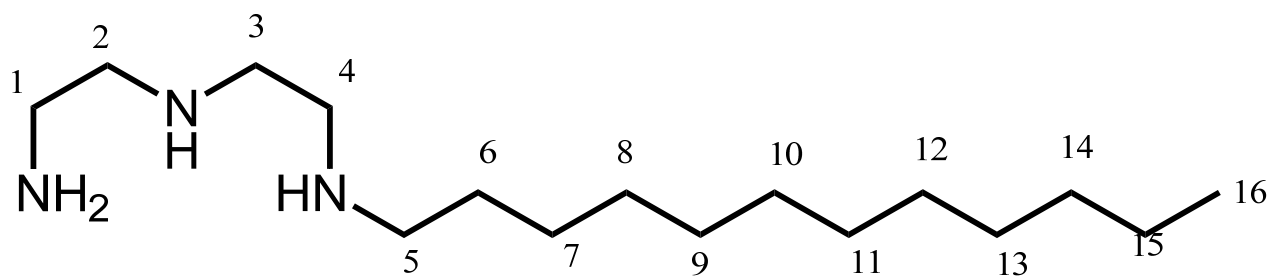


Figure 2.1.1.1  $^1\text{H}$  NMR characterization

The  $^{13}\text{C}$  NMR of the ligand is shown in figure 2.1.1.3. The 117 ppm signal corresponds to the deuterated acetonitrile. The signal at around 52.55 ppm is Carbon 2. Carbon 3, 4, and 5 are seen at 49.59 ppm. The signal that is found at 41.68 ppm corresponds to Carbon 1. At 31.79 ppm carbon 14 can be located next to signals around 29.62 ppm corresponding to carbons 6 and 1-13. The carbon 7 signal is seen at 27.32 ppm and the carbon 16 signal is located at 13.62 ppm.



**Figure 2.1.1.2** Sketch of functionalized DETA with label Carbons.

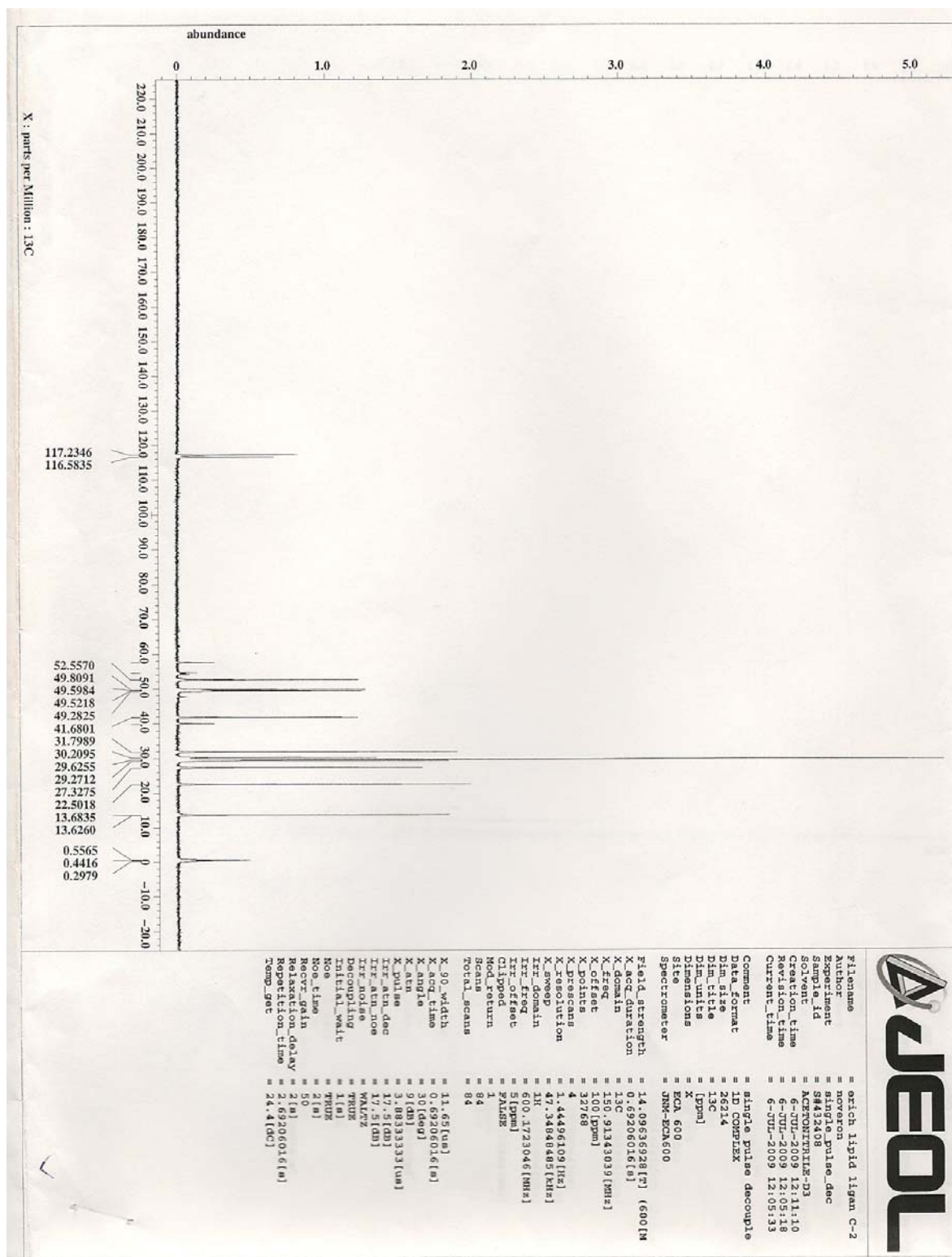


Figure 2.1.1.3  $^{13}\text{C}$  NMR of the ligand

## 2.2 Synthesis and characterization of functionalized Cu(Cl)<sub>2</sub> DETA

Due to the paramagnetic nature of Copper chloride, it was hard to characterize. Copper chloride was first characterized using Electron Paramagnetic Resonance (EPR). Yevgeny Zavoisky in 1944 was the first one to characterize this complex using EPR.<sup>66,67</sup> Chlorination of aromatic hydrocarbons is possible in a high yield when using copper chloride in a polar solvent in the presence of aluminum oxide chlorinating at the alpha position of the carbonyl compound.<sup>68</sup> In the synthesis of organic compounds,<sup>69</sup> it can be used in the chlorination of aromatic hydrocarbons as well.

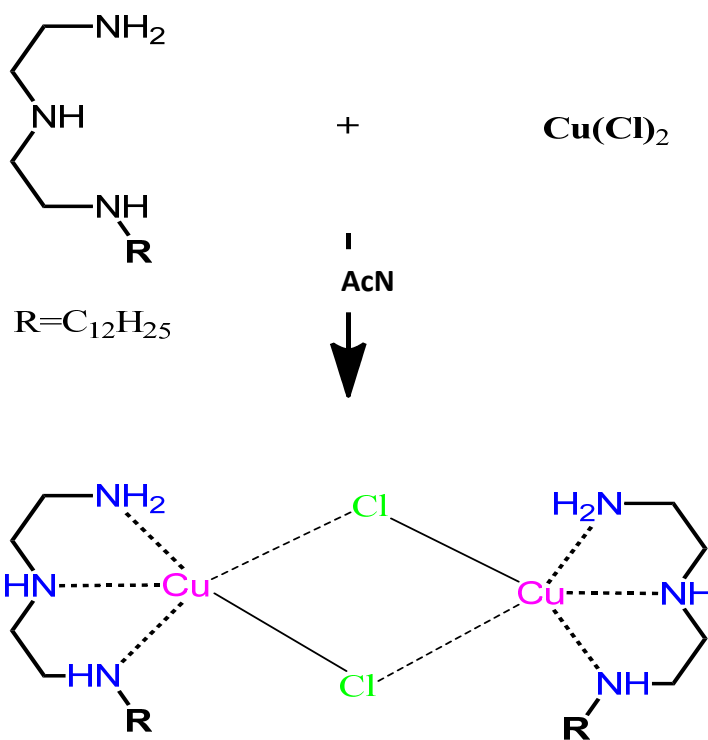
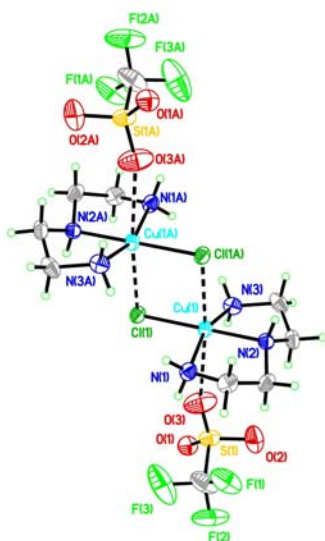


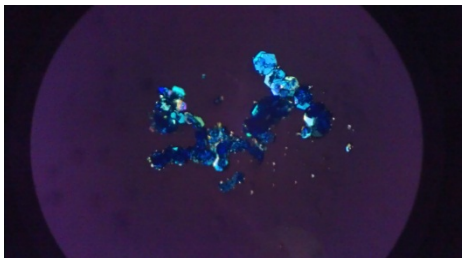
Figure 2.2.1. Reaction procedure of the Copper Chloride complex.

### 2.2.1. X-Ray Crystallography

The following coordination reaction was run with DETA alone as well as with the functionalized DETA, the crystal structure of DETA in coordination with copper chloride has been reported<sup>70</sup>, but it was important to be able to crystallize the structure. The crystal structure of Cu(Cl)<sub>2</sub> DETA obtained is shown in Figure 2.2.1.1. The reaction with functionalized DETA and Cu(Cl)<sub>2</sub> is shown in Figure 2.2.1.



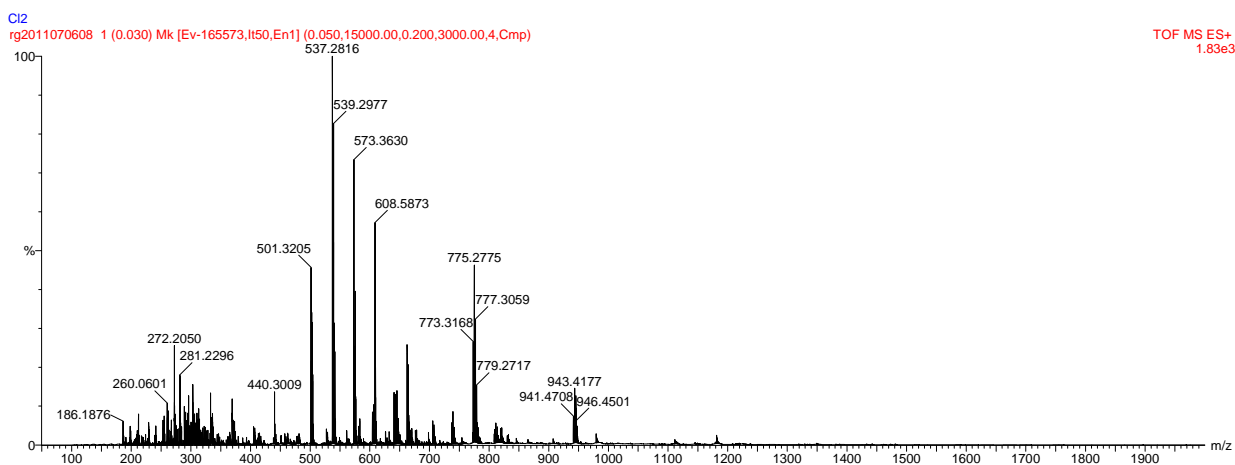
**Figure 2.2.1.1** Crystal structure for  $\text{Cu}(\text{Cl})_2 \cdot \text{DETA}$



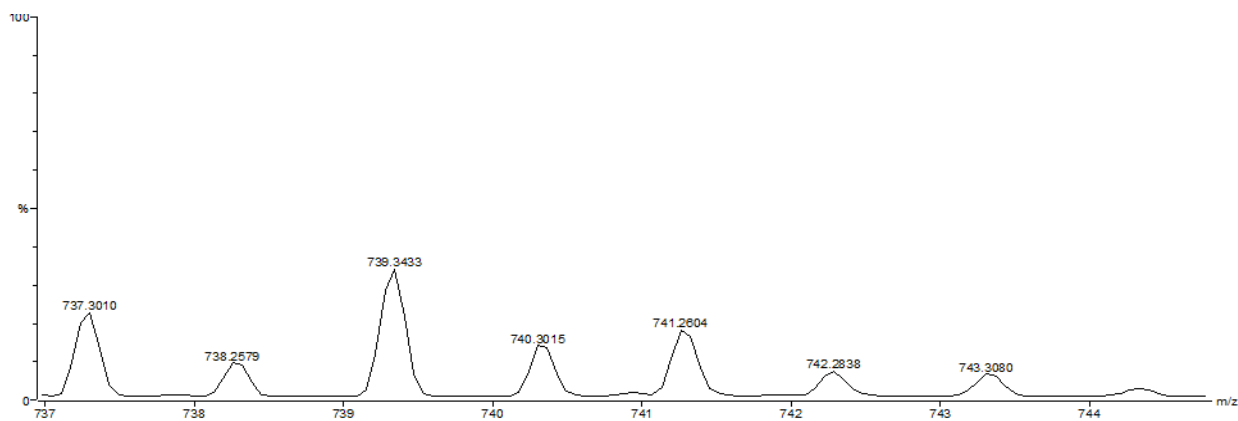
**Figure 2.2.1.2**  $\text{Cu}(\text{Cl})_2$  dimer crystal

### 2.2.2 Mass Spectrometry

Mass Spectrometry is a technique that measures the mass of the molecule with respect to its charge.<sup>71</sup> The instrument used was the Micromass Quadrupole Time of flight. Since it is expected that the amphiphilic molecule has charge 2+, it would be probable that the parent ion would be around 370m/z since its total weight is 740m/z. The original weight fragment was also expected. The sample was run in positive mode and the peaks obtained from the sample referred to the M+1, and M+2 which were located with a spectra magnification of 6X. This enlargement was needed due to the low concentration of the solution as well as the low sensitivity of the instrument.



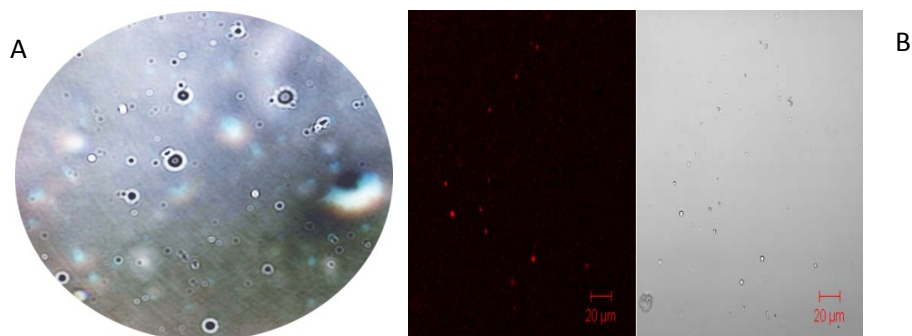
**Figure 2.2.2.1** Mass Spectra of the Copper Chloride complex confirming the M+1, M+2, and M+3 peaks of the molecule



**Figure 2.2.2.2.** Isotropic distribution for the binuclear Cu(II)Cl<sub>2</sub> complex at M+1.

### 2.2.3. Optical and UV- microscopy

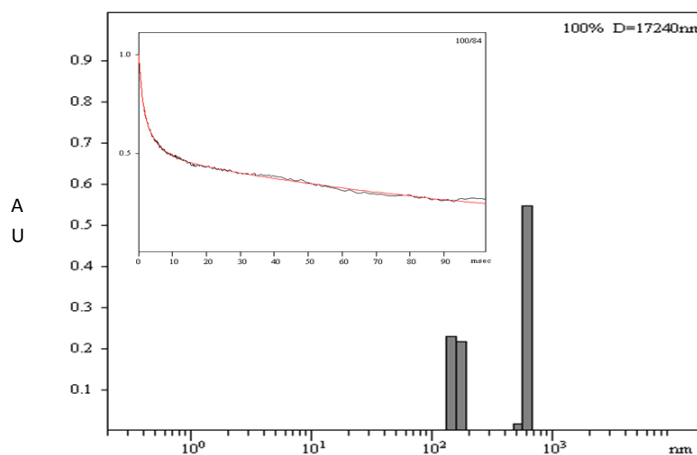
Optical microscopy was used in order to look at the aggregation of the micelles. Millimolar quantities of the complex were dissolved in water in order to obtain the micelle complexes. The molecules were stained with Nile Red, which is a lipophilic stain that fluoresces in the presence of hydrophobic interactions<sup>72</sup> giving an emission of excitation at 245 nm and emits at 525 nm in the presence of lipophilic molecules.<sup>73</sup>



**Figure 2.2.3.1** (A) Aggregation of the copper-Gemini surfactant in water forming micelles. (B) Metallo Gemini surfactant stained with 5  $\mu\text{mL}$ .

## 2.2.4 Dynamic Light Scattering

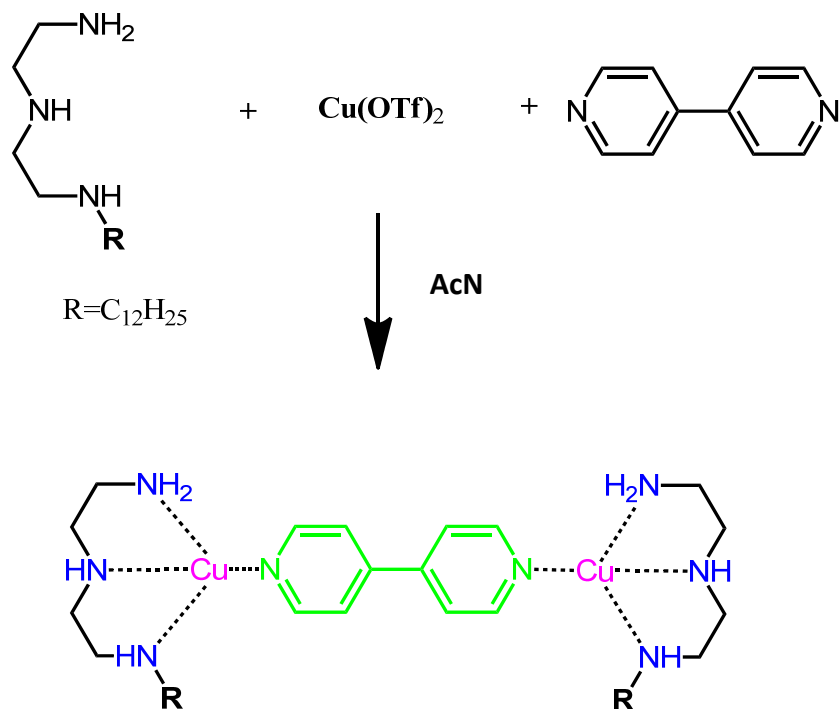
Dynamic Light Scattering (DLS) is a technique that is used to determine the size distribution of polymers in solution or particles in suspension.<sup>74</sup> A laser is used to excite the particles in the vessel. Once it hits the particles in suspension, the laser would scatter the wavelength depending on the size of the particles in suspension, and that data is collected in the instrument, and then the average particle's size is obtained. This copper complex has three different aggregations of particle sizes; the average particle size is noted on the upper right side of Figure 2.2.3.2.



**Figure 2.2.3.2.** DLS of functionalized  $\text{Cu}(\text{Cl})_2$  DETA

### 2.3. Synthesis of functionalized 4, 4'-Bipyridine

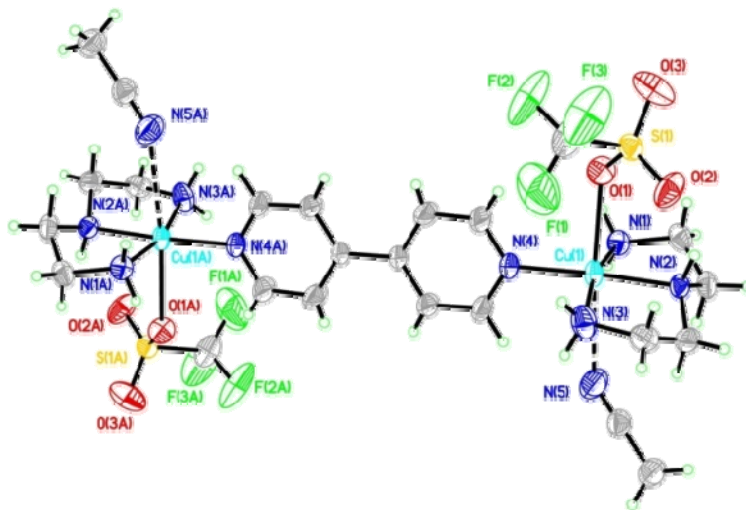
Due to its ability to bridge between metal centers, 4, 4'-Bipyridine has been of great interest in coordination reactions.<sup>75</sup> This reaction uses copper triflate as a salt instead of copper chloride. The reactants were put in a round bottle flask and stirred with 10mL of acetonitrile. The stoichiometric ratios were 2:1:2 adding first the DETA then the copper triflate and at the end the 4, 4'-Bipyridine, all reagents were left to react for half hour.



**Figure 2.3.1.** Reaction procedure of functionalized DETA 4, 4'-Bipyridine.

### 2.3.1. X-Ray Crystallography

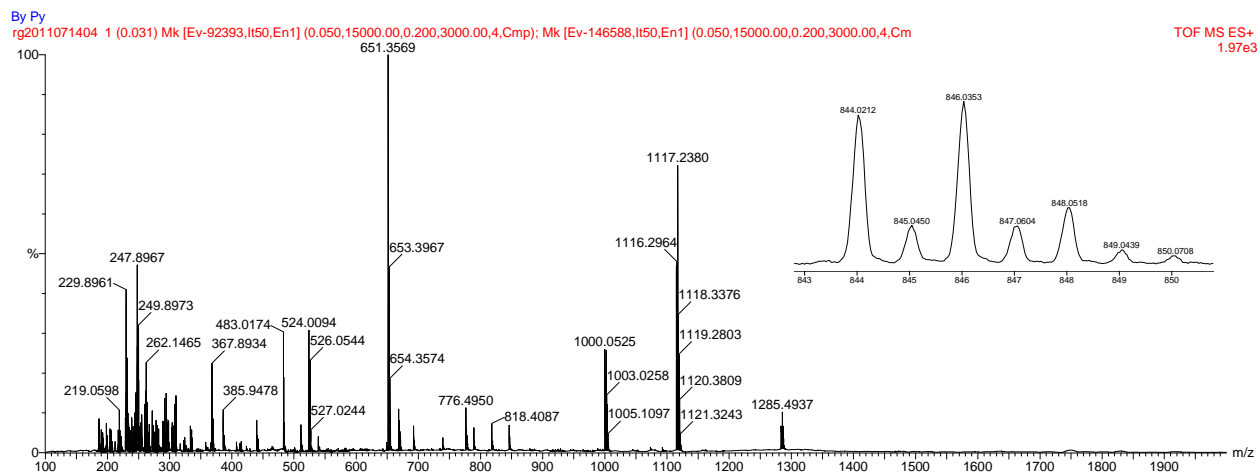
A solution containing stoichiometric amounts DETA,  $Cu(OTf)_2$ , and 4, 4'-Bipyridine were prepared with acetonitrile. After 30 min of stirring, the solution was crystallized under ether diffusion. The X-Ray crystal structure of the Gemini was done at room temperature.



**Figure 2.3.1.1.** Crystal structure of the dimer with 4, 4'-Bipyridine as the spacer.

### 2.3.2. Mass Spectrometry

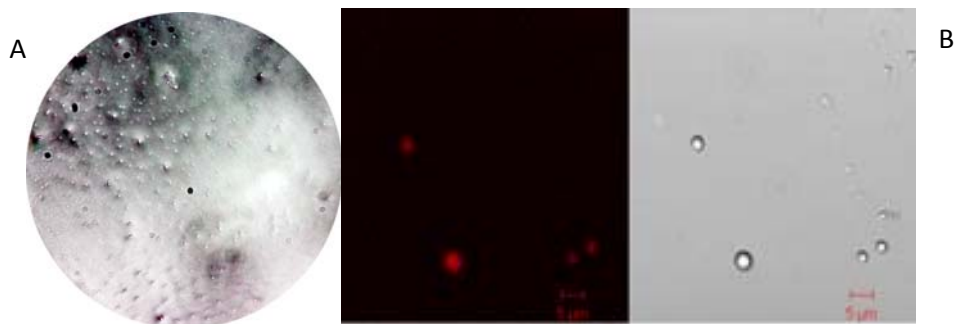
Mass Spectrometry of the metallo-Gemini complex was taken with Micromass Q-ToF instrument by WATERS. The analysis shows a signal for of M+1 and M+2 of the molecular weight of the complex at 847m/z in the isotropic distribution.



**Figure 2.3.2.1.** Mass spectra of the 4, 4'-Bipyridine metallo-Gemini surfactant.

### 2.3.3. Optical and UV- microscopy

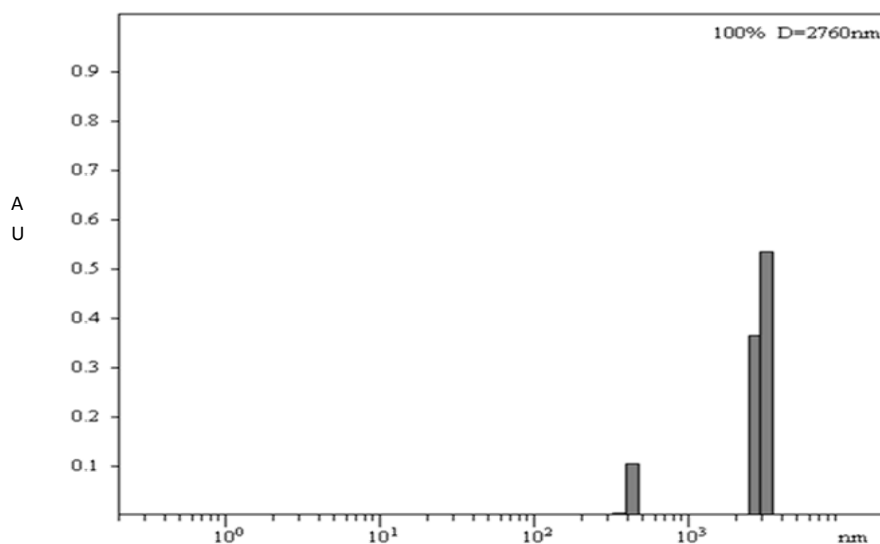
A 10mM concentration of the complex was prepared with 5mL of distilled water to emulsify. Due to the hydrophobic effect, the aggregations of the molecules into micelles were possible. These micelles were observed under optical microscope as well as detailed analyzed with Nile Red fluorescence in the UV-microscope.



**Figure 2.3.3.1.** (A) Micelle formation in water. (B) micelles stained with Nile Red fluorescing.

### 2.3.4 Dynamic Light Scattering

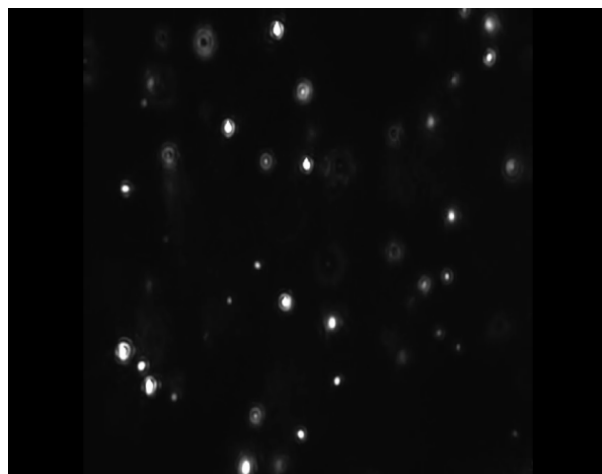
DLS of the metallo-Gemini surfactant was obtained getting as a result an average particle size of 3480nm. As it can be observed in Figure 2.3.4.1, there are three different aggregations of molecules. Two of them of very comparable size while the other a larger size; this may explain a multi-micellar layer property that these amphiphilic molecules have sometimes. Another reason is the absorbance of possible dust particles at 300nm which could be the explanation for the odd signal observed in the photo outside the range of the sample. .



**Figure 2.3.4.1.** Light scattering showing a particle's average of 2.7microns

### 2.3.5 Nanoparticle Tracking Analysis

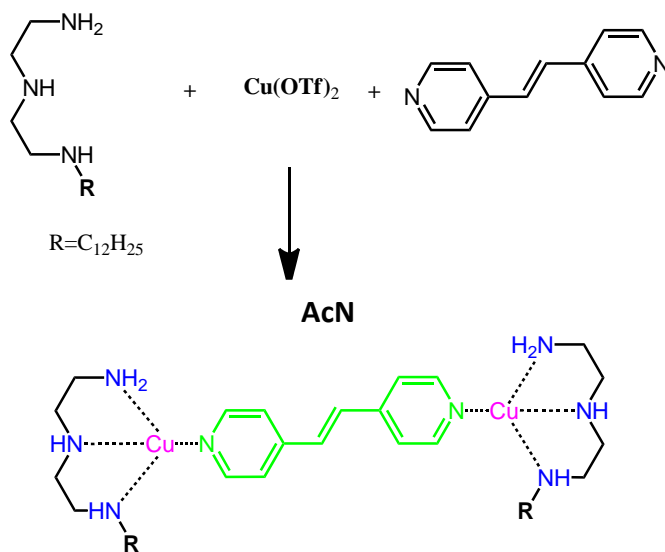
Nanoparticle Tracking Analysis (NTA) it's a technique that visualizes nanoparticles in movement in a liquid environment.<sup>76</sup> The metallo-Gemini surfactants were dissolved in 0.1mL of acetonitrile and were aggregated using sonication in 5mL of water. Figure 2.3.5.1 is a still picture of the actual video analysis. As it can be observed from the image, the presence of micelles in water is confirmed with the help of the NTA. It also can be observed that the micellar sizes as well as the shape are analogous to each other confirming the level purity of the compound. The hollow that it is observed in Figure 2.3.5.1 is an effect that happens because of the vaporization of the solvent.



**Figure 2.3.5.1.** Synthesis and characterization of (E)-1,2-di(pyridin-4-yl)ethane

## 2.4 Synthesis and characterization of (E)-1,2-di(pyridin-4-yl)ethane

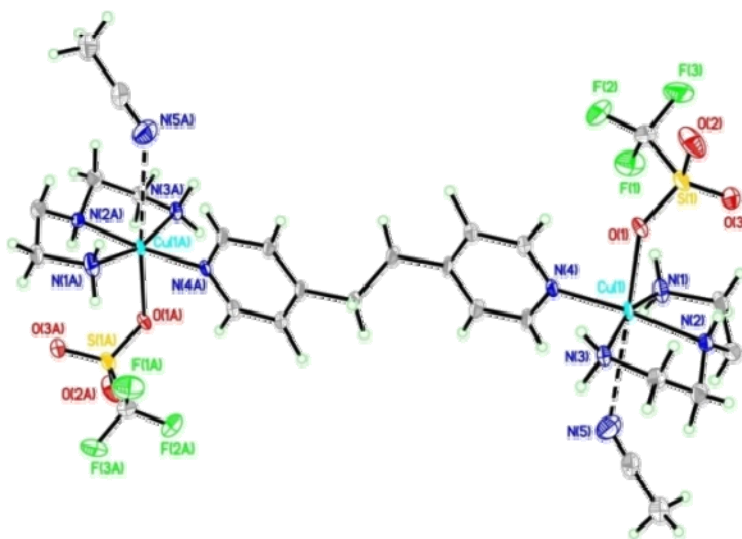
N-donor co-ligands play a key role in the self-assembly coordination as co-ligands.<sup>77</sup> This metallo-Gemini complex was synthesized the in the same conditions as the previous one.



**Figure 2.4.1** Synthesis of the metallo-Gemini surfactant with (E)-1,2-di(pyridin-4-yl)ethane as a bridge.

### 2.4.1. X-Ray Crystallography

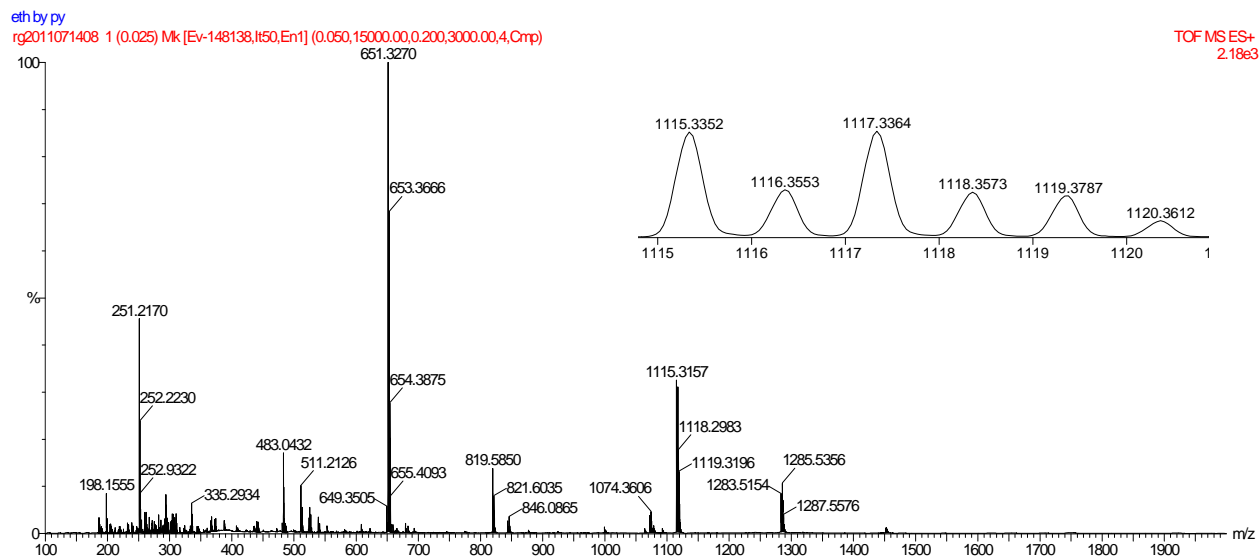
Crystallization of the dimer was obtained under the same conditions as the previous one.



**Figure 2.4.1.1.** Crystal structure of the (E)-1,2-di(pyridin-4-yl)ethane complex.

### 2.4.2. Mass Spectrometry

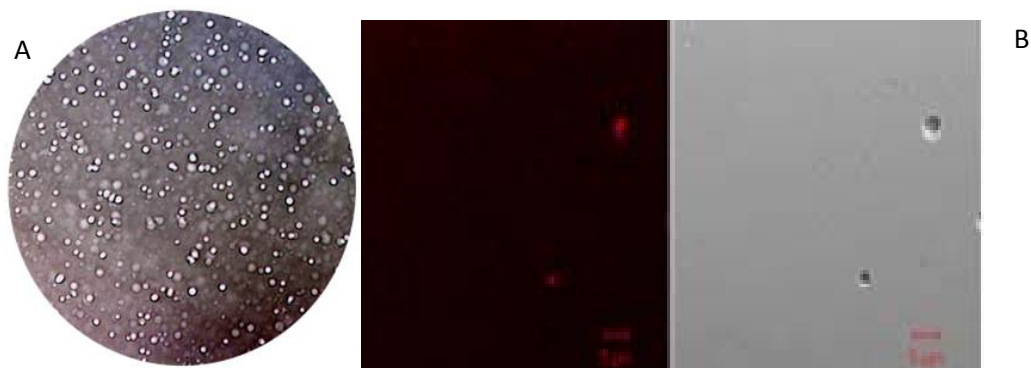
The Mass Spectrometry analysis shows the respective peaks for the atomic mass of the sample. The desired signals that indicated the mass of the complex was 1118m/z which it can be observed it appeared in the isotropic distribution. As stated above, because of the loss of sensitivity by the instrument and of the low concentration of the metal complex, a magnification of the region where the isotropic distribution was seen, was performed and shown as an insert.



**Figure 2.4.2.1.** Mass Spectra of the (E)-1,2-di(pyridin-4-yl)ethane Metallo-Gemini Surfactant.

### 2.4.3. Optical and UV- microscopy

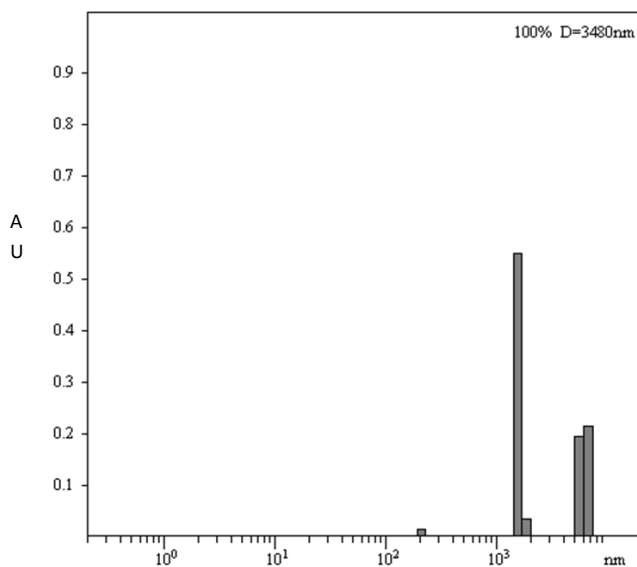
A sample was prepared in Acetonitrile and sonicated with water in order to form the micelles. Afterwards, the micelles were then observed under the optical microscope where a “colony” was visible. Using a UV-microscope, the micelles were then stained with Nile Red so the hydrophobic properties could be observed under UV-light.



**Figure 2.4.3.1.** (A) picture taken from an optical microscope of the micelles. (B) Micelles stained with Nile Red.

#### 2.4.4 Dynamic Light Scattering

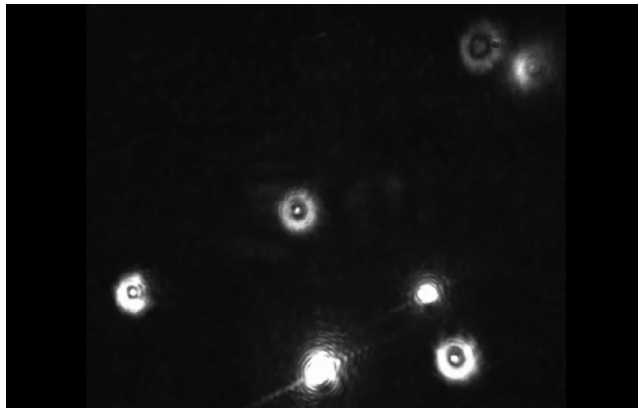
DLS of the (E)-1,2-di(pyridin-4-yl)ethane was taken in a millimolar concentration. The sample was prepared at room temperatures in an organic polar solvent and sonicated for 5min before analysis is performed.



**Figure 2.4.4.1.** DLS of the (E)-1,2-di(pyridin-4-yl)ethane metallo-Gemini complex

### 2.4.5 Nanoparticle Tracking Analysis

This analysis shows that indeed there is aggregation of the metallo-Gemini surfactants into micelles due to the hydrophobic effect. Figure 2.4.5.1



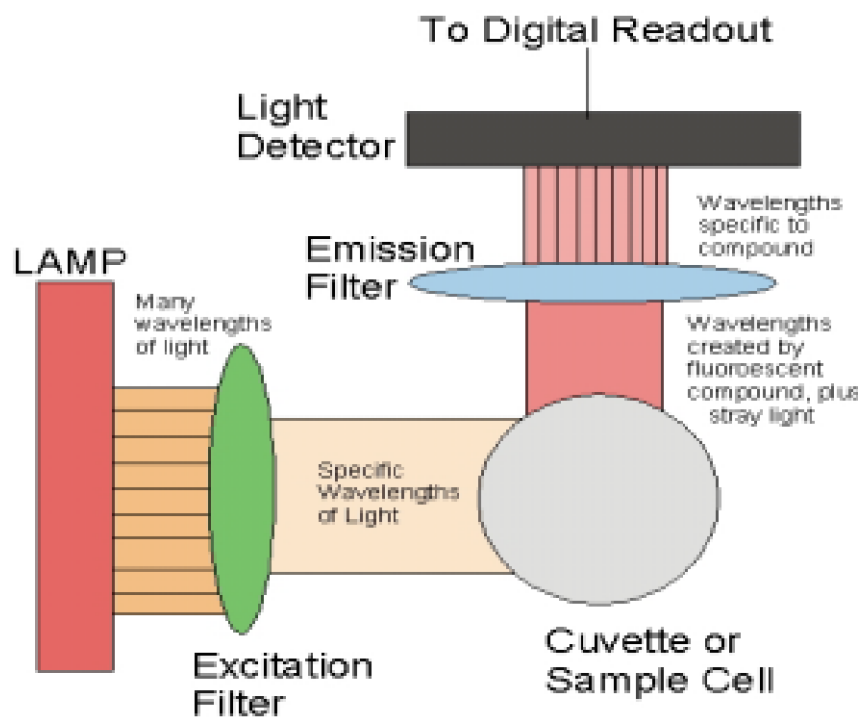
**Figure 2.4.5.1.** Image of the vesicles taken using NTA.

## **Chapter 3. Physical properties of the Gemini-Metallo Surfactant**

### **3.1 Critical Micelle Concentration (CMC)**

Critical Micelle Concentration (CMC) is an important tool to characterized physical properties of a surfactant. CMC is defined as the concentration of surfactants above which micelles form and extra surfactants added to the system go to micelles.<sup>78</sup> When the surfactants are about to reach CMC the surface tension changes, because it is subject to the concentration of the surfactant. The value of the CMC is dependable of pressure, temperature, the medium, whether this medium is ionic or not.

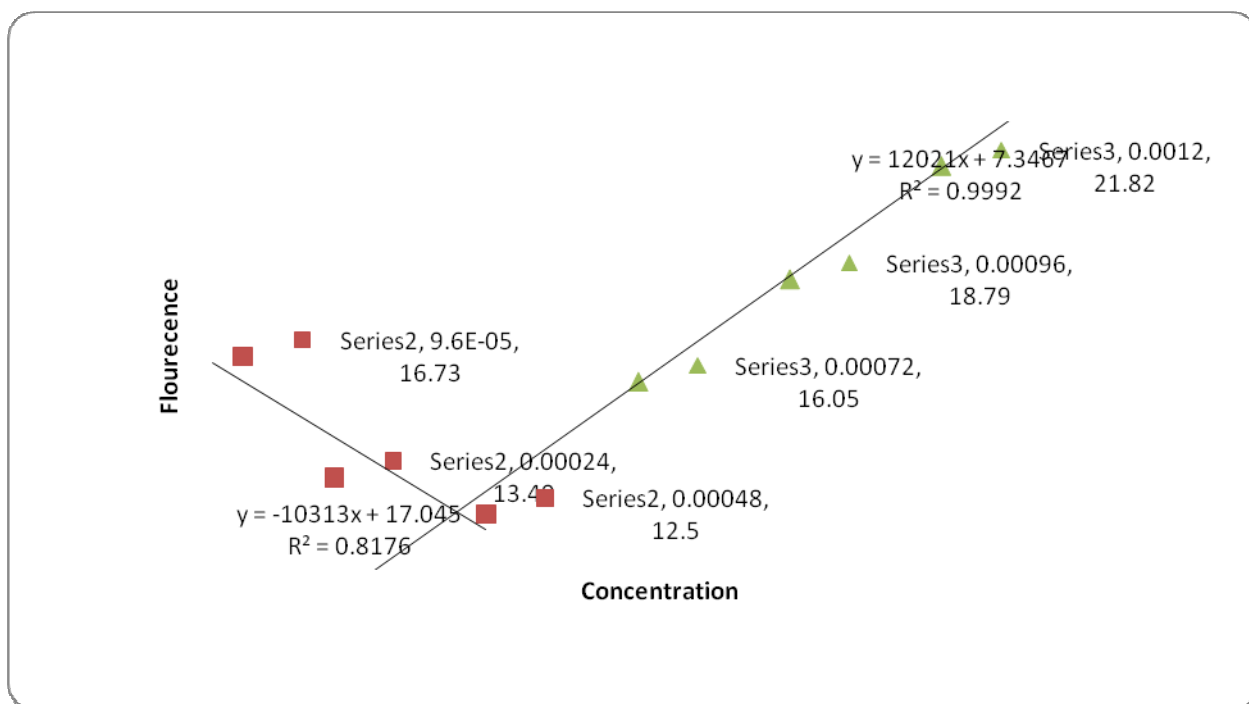
The micellar meditations were prepared with at the same concentration. The instrument used to analyze the aggregation of the molecules was the Fluoroskan Ascent by Labsystems. Once the sample is put into the instrument, an excitation energy from a laser is used to excite the particles. The laser passes through an excitation filter before hitting the particles. Then the particles that have absorbed the dye will have an excitation at the fluorescent wavelength. This excitation passes through another filter and then is the level of emission is detected. .<sup>79</sup>



**Figure 3.1.1** Fluorometer scheme.<sup>79</sup>

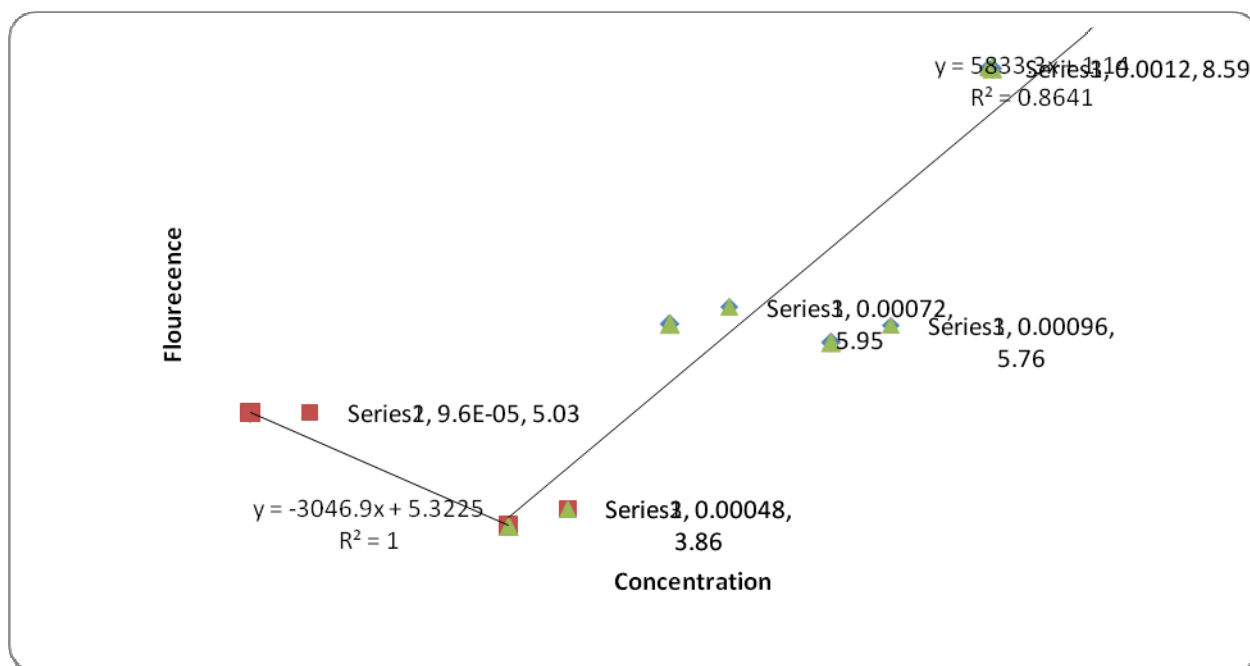
All three samples were prepared using the same methodology. Alike concentrations of the three compounds were prepared for the analysis. The total final volume used for the analysis was 50 $\mu$ L with a different volume of water added to the metallo-Gemini complex. The first particles that were analyzed where the Cu(Cl)<sub>2</sub>DETA complexes. As it can be observed in Figure 3.1.2, the minimal concentration at which the micelle forms it's about  $1.9 \times 10^{-4}$  M.





**Figure 3.1.3** CMC of metallo-Gemini surfactant with 4, 4'-Bipyridine as a bridge.

As it can be observed in Figure 3.1.4, the values for the CMC are close to  $5.1 \times 10^{-4}$  M. these values are higher comparing to both the copper chloride and the 4, 4'-Bipyridine Gemini surfactant. As stated before, this could be due to the size of the spacer, the larger the spacer, the higher the concentration that the micelles would aggregate. Also it can be observed that the fluorescent values are a slightly lower at the starting point as compared to the one of 4, 4'-Bipyridine, this could be a result of the distances between the two pyridine molecules. The pyridines in the complex 4, 4'-Bipyridine are parallel one to another and they are closer to the ones of (E)-1,2-di(pyridin-4-yl)ethane.



**Figure 3.1.4** CMC of metallo-Gemini surfactant with (E)-1,2-di(pyridin-4-yl)ethane as a bridge.

### 3.2 Scanning Electron Microscopy (SEM)

SEM is a type of electron microscope instrument that scans a sample with a high energy beam of electrons. The electrons interact with the atoms and produce signals containing information about the topography of the sample and other properties such as electrical conductivity.<sup>80</sup>

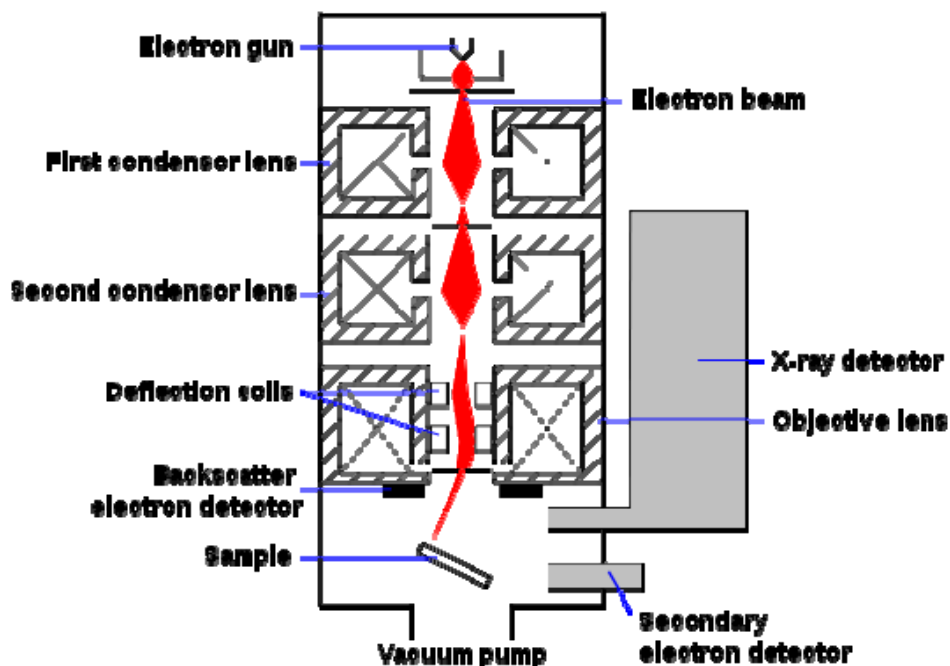
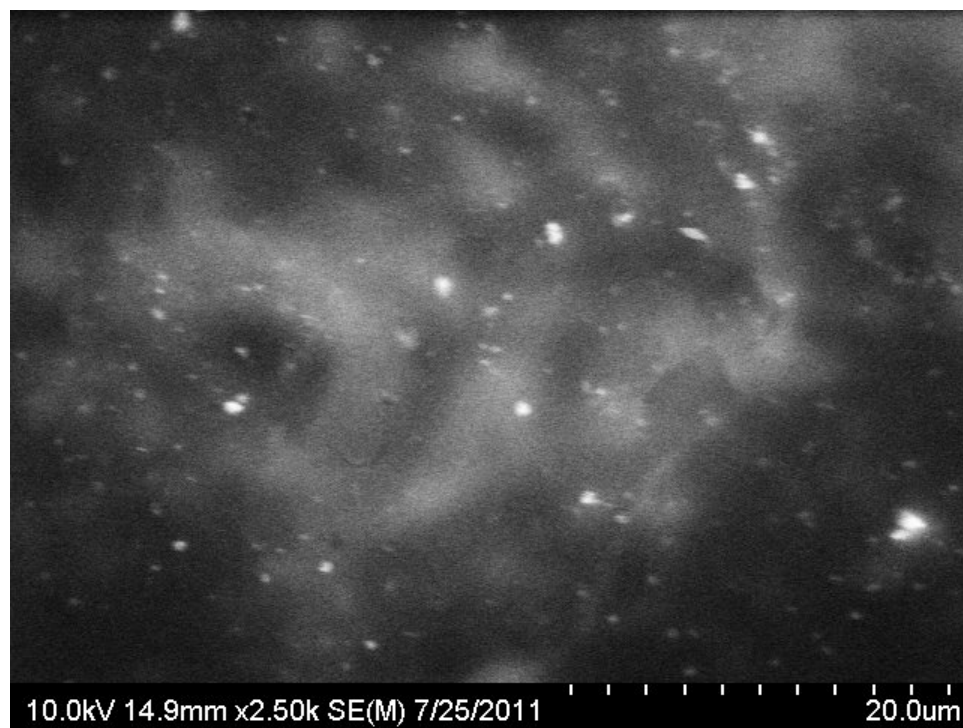


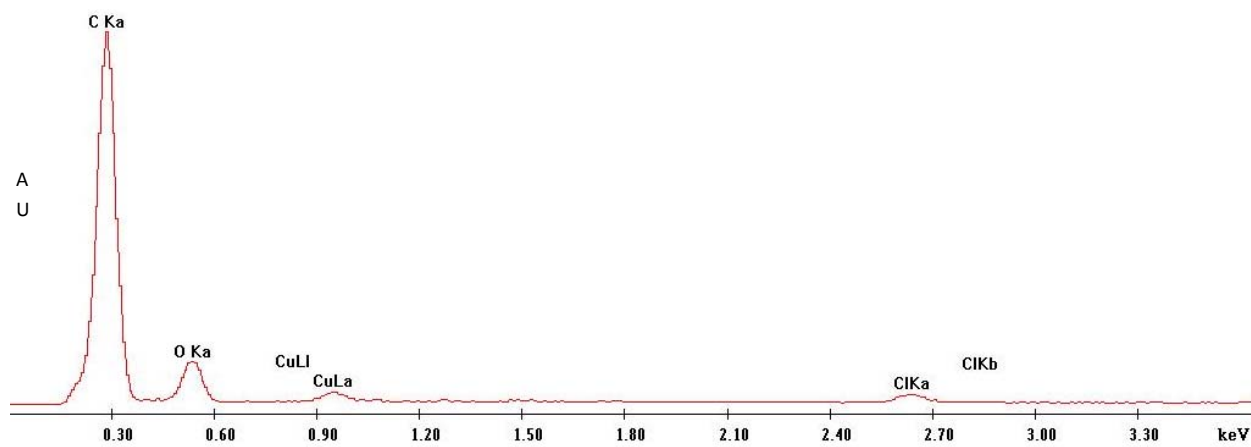
Figure 3.2.1. SEM<sup>81</sup>

Max Knoll was the first person to obtain an image on a SEM instrument, he showed electron channeling contrast in an image of silicon steel.<sup>82</sup> Well ahead, Manfred von Ardenne improved the physical principles and beam specimen interactions on the SEM.<sup>83,84</sup> There are two different types of signals that SEM can produce secondary electrons, which can produce high resolution images on a sample surface up to 1 nm in size, and back-scattered electrons (BSE) analysis which is more useful in analytical purposes. BSE signal was used in this analysis due to the capacity of giving not only an image of the topology of the substance but as well an elemental composition of such.

1 mM solution of functionalized  $\text{Cu}(\text{Cl})_2$  complex was prepared and put into the instrument in order to get the analysis.

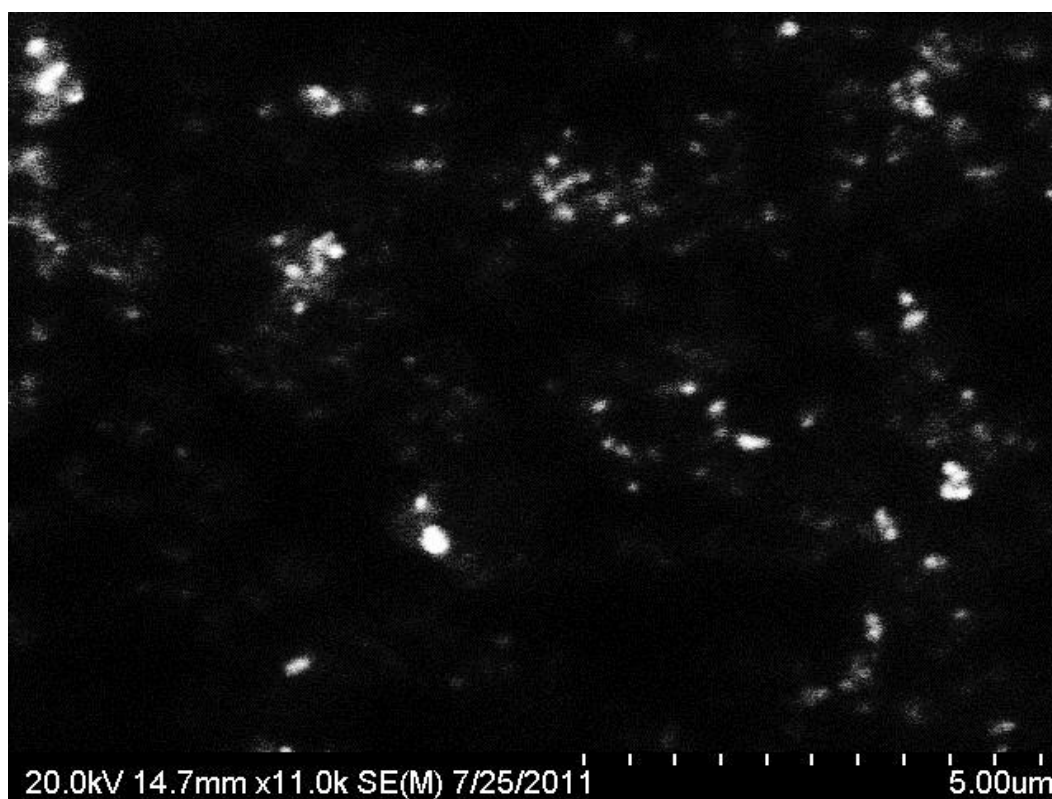


**Figure 3.2.2.** SEM of functionalized  $\text{Cu}(\text{Cl})_2$  liposomes.

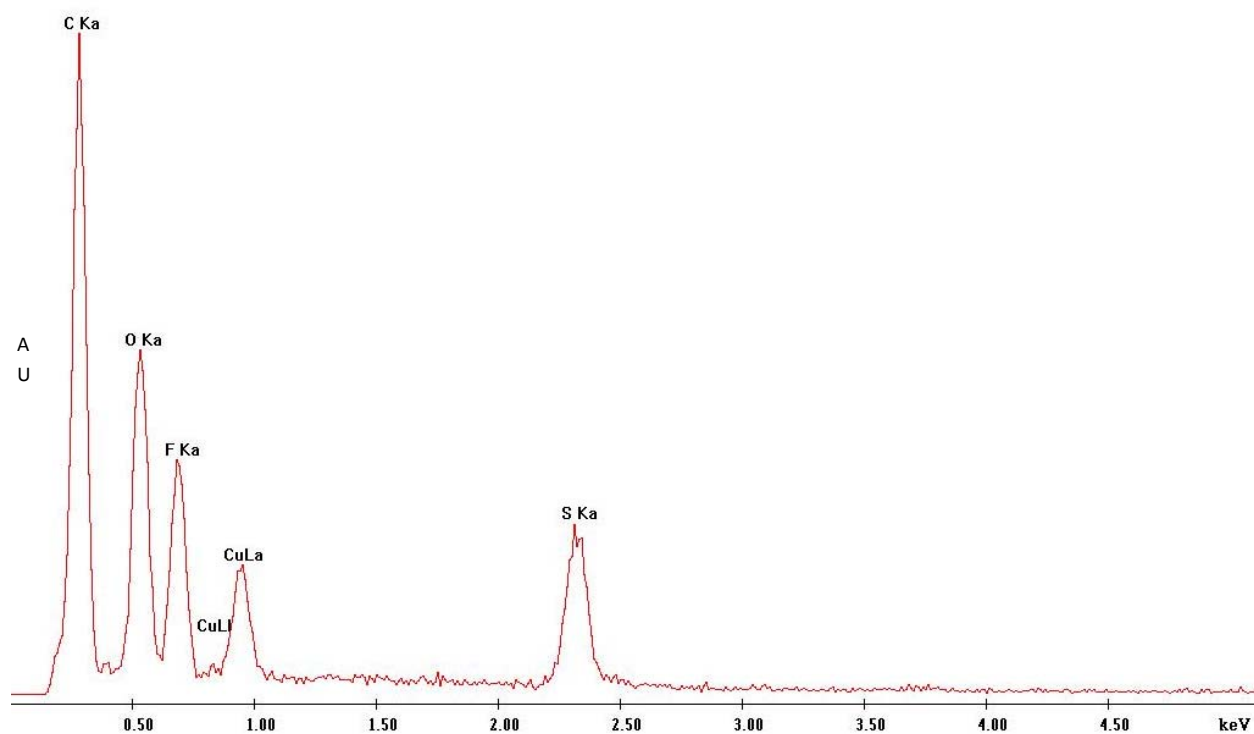


**Figure 3.2.3.** Elemental analysis of functionalized  $\text{Cu}(\text{Cl})_2$  liposomes

It can be observed in figure 3.2.2. SEM spectra of functionalized  $\text{Cu}(\text{Cl})_2$  complex. It can be clear in the spectra, sphere like particles appeared in an abundance population which confirms that the topology of the liposomes. The elemental analysis of the compound shows signals at 8.50keV indication Oxygen abundance from the counter ion triflate, a signal at 8.93keV of the copper as well as a signal at 2.65keV corresponding the chloride spacer. It also can be noticed a strong signal at 0.30ekV for the carbon film used to put the sample on.

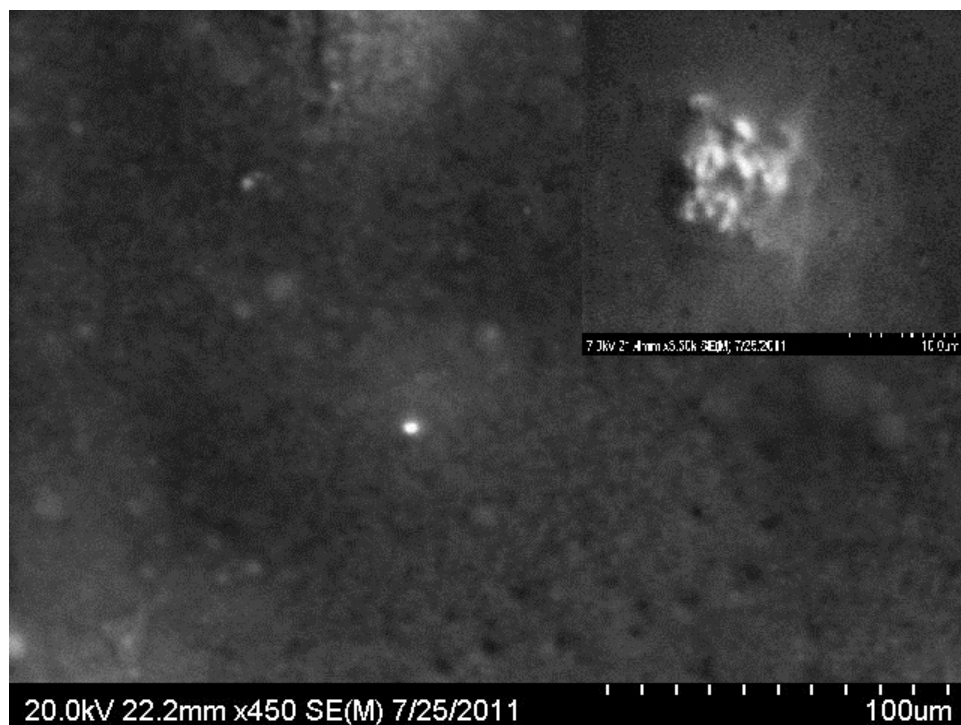


**Figure 3.2.4.** SEM of functionalized 4,4'- bipyridine liposomes.

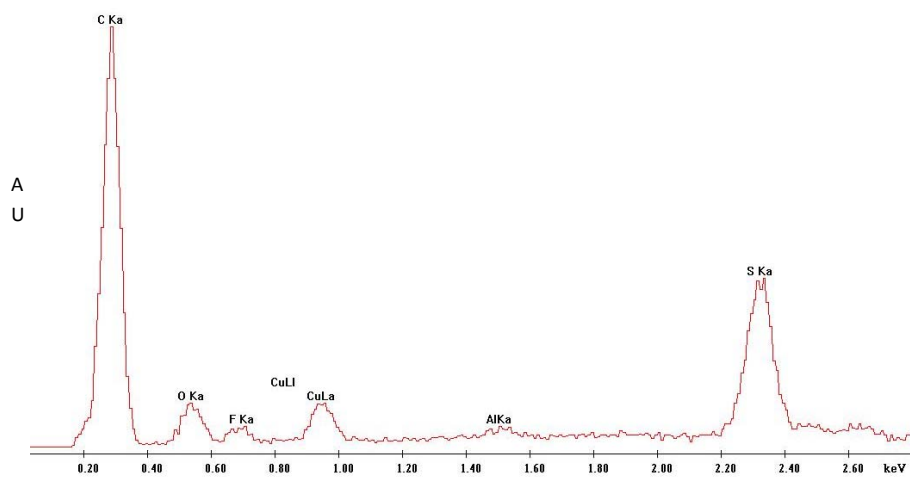


**Figure 3.2.5.** Elemental analysis of functionalized 4,4'-bipyridine liposomes.

Figure 3.2.4 shows an abundant population of liposomes under SEM. It can be observed the approximately liposome size is about  $0.5\mu\text{m}$ . Figure 3.2.6 demonstrates the elemental analysis of the complex displaying at 0.50keV a signal for Oxygen which comes from the triflate counter ion, a signal at 0.65 corresponding to fluorides as well from the triflate, 0.90keV signal from copper and a signal at 2.45keV corresponding to sulfur. A signal at 0.30ekV corresponds to the carbon of the surface where the sample was put on.



**Figure 3.2.6** SEM of functionalized (E)-1,2-di(pyridin-4-yl)ethene liposomes.



**Figure 3.2.7.** Elemental analysis of functionalized (E)-1,2-di(pyridin-4-yl)ethene liposomes.

Figure 3.2.6 shows a single liposome using SEM. It can be observed the shape of the liposome not been entirely spherical. An explanation for this could be that the liposomes have to be under vacuum all of the time due to the process of the analysis. If vacuum is disturbed, the direction of the electron beam hitting particles to be analyzed could be disrupted, resulting less than spherical structures. Another explanation for this explosion of the liposome could be a result of dryness of the sample analyzed, and since liposomes tend to aggregate due to the hydrophobic effect and the analysis requires a solid sampling. The lack of water surrounding the liposome plus the extra pressure caused by the vacuum could easily make a liposome appear less spherical.

Figure 3.2.7 shows the elemental analysis for the functionalized (E)-1,2-di(pyridin-4-yl)ethene liposomes. It can be observed as well as the previous analysis the signal at 0.5ekV of the oxygen, a signal at around 0.70ekV corresponding to the fluorine atoms, a signal at around 0.95ekV corresponding to a copper ion, as well as a signal at 2.35ekV linking the sulfur ion. It also is observed an aluminum signal at 1.50ekV for the aluminum chip where the sample was placed, as well as a signal at 0.30ekV of the carbon surface

## Conclusions

New and innovating supramolecular self-assembly metallo-Gemini surfactants were synthesized in good yield. The products were generated by X-Ray Crystallography and their physical properties and self-assembly studied in detail.

Three newly developed new GMOs (compounds **1-3**) are composed of Cu(II) ions ligated to a lipid-functionalized triamine group and the metals are bridged by a bipyridyl spacer group. The head groups of the resulting GMOs were characterized via X-ray crystallography. The GMO self-assemble in water into stable metallo-liposomes, which were characterized by mass spectrometry (MS), Infrared (IR), fluorescent optical microscopy and atomic force microscopy. The Critical Micelle Concentration (CMC) of the GMOs were determined with Nile Red-stained Fluorescent Optical Microscope as a function of concentration and the results were  $1.9 \times 10^{-4} \text{M}$  for **1**,  $4.1 \times 10^{-4} \text{M}$  for **2**, and  $4.9 \times 10^{-4} \text{M}$  for **3**.

Self-assembly metallo-Gemini surfactant is a young and still developing studied area. Three new copper based metallo-Gemini surfactants were obtained during this investigation, all of them in coordination with a tridentate diethylene triamine functionalized with a twelve carbon lipophilic chain. The three metallo-Gemini surfactants were satisfactorily synthesized and characterized with: optical and fluorescent microscopy, Mass Spectrometry analysis, and Dynamic Light Scattering.

Future work of GMOs involves the study of the biological properties associated with cellular toxicity, drug-delivery potential and as Cu(II) sequestering agents.

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## Appendix

### A.1 Supporting information for chapter 2

#### A.1 Supporting information for chapter 2

**Experimental section.** All chemicals used were commercially supplied. NMR spectra were recorded using JOEL ECA 600 spectrometer. Mass Spectrometry analysis was conducted on the Micromass Quadruple Time of Flight (Q-Tof). Critical Micelle Concentration work was done on

**Synthesis of N1-(2-aminoethyl)-N2-dodecylethane-1,2-diamine.** DETA (40mL, 0.37mol) was dissolved put in a 100mL three neck round bottle flask stirring in a reflux system at 80°C under Argon gas. While mixture stirred, 1-Bromo dodecane was added (19.14mL, 0.074mol) drop wise to the neat solution, the solution was left to stir for 24hrs. two different layers were form after the stirring, with a syringe the top layers was sucked out of the flask then put into another flask that was under Argon where distillation of the excess DETA was perform under vacuum system at 80°C.  $^1\text{H}$  and  $^{13}\text{C}$  NMR are provided in chapter 2.

**Synthesis of functionalized  $\text{Cu}(\text{Cl})_2$  DETA.** In a round bottle flask 10mL of Acetonitrile were added along with a stirring bar on a stirring plate.

**Synthesis of functionalized 4, 4'-Bipyridine.** In a round bottle flask 10mL of Acetonitrile were added along with a stirring bar on a stirring plate. Then N1-(2-aminoethyl)-N2-dodecylethane-1,2-diamine was added (0.136mL,  $5 \times 10^{-4}$  mols) along with  $\text{Cu}(\text{Otf})_2$  ( 0.09g ,  $2.5 \times 10^{-4}$  mols) and left for stirring for half an hour. 4, 4'-Bipyridine was added (0.39g,  $5 \times 10^{-4}$  mols) and left for stirring for another half hour. In case of oxidation of the ligand with  $\text{CO}_2$  (a precipitation would occur), a purification method based on solubility with diethyl ether can be done due to its solubility with the desired product.

**Synthesis of functionalized (E)-1,2-di(pyridin-4-yl)ethane.** The same procedure as 4,4-bipyridine was done in stoichiometric amounts.

**X-Ray Crystallography.** X-ray crystallography was obtained from the three dinuclear compounds. They were covered in an oil solution and transferred to a Nonius KappaCCD diffractometer equipped with Mo  $\text{K}\alpha$  radiation with a wavelength of  $\lambda = 0.71073 \text{ \AA}$ . All crystals were solved at 298°F and were grown under ether diffusion. Crystals and structures refinement data are listed in tables A.1.1 to A.3.1.9.

**Table A.1.1.** Crystal data and structure refinement for  $\text{Cu}(\text{Cl})_2$  crystal

Identification code	159ha1ms
Empirical formula	$\text{C}_5 \text{H}_{13} \text{Cl Cu F}_3 \text{N}_3 \text{O}_3 \text{S}$

Formula weight	351.23	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 11.7938(14) Å	$\beta = 90^\circ$ .
b = 7.8157(9) Å	$\beta = 96.9250(10)^\circ$ .	
c = 13.9070(16) Å	$\gamma = 90^\circ$ .	
Volume	1272.6(3) Å <sup>3</sup>	
Z	4	
Density (calculated)	1.833 Mg/m <sup>3</sup>	
Absorption coefficient	2.127 mm <sup>-1</sup>	
F(000)	708	
Crystal size	0.30 x 0.20 x 0.03 mm <sup>3</sup>	
Theta range for data collection	1.74 to 24.99°.	
Index ranges	-14<= <i>h</i> <=13, -9<= <i>k</i> <=9, -16<= <i>l</i> <=16	
Reflections collected	11963	
Independent reflections	2246 [R(int) = 0.0311]	
Completeness to theta = 24.99°	100.0 %	
Absorption correction	None	
Max. and min. transmission	0.9389 and 0.5679	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	2246 / 10 / 154	
Goodness-of-fit on F <sup>2</sup>	1.480	
Final R indices [ <i>I</i> >2sigma( <i>I</i> )]	R1 = 0.0565, wR2 = 0.1835	
R indices (all data)	R1 = 0.0602, wR2 = 0.1896	
Largest diff. peak and hole	1.395 and -0.893 e.Å <sup>-3</sup>	

**Table A.1.2.** Bond lengths [Å] and angles Cu(Cl)<sub>2</sub> crystal

Cu(1)-N(1)	1.995(4)
Cu(1)-N(2)	2.011(4)
Cu(1)-N(3)	1.989(4)
Cu(1)-Cl(1)	2.2879(13)
Cu(1)-Cl(1)_ $\Sigma$ 1	2.7837(13)
Cu(1)-O(3)	2.705(6)

Cu(1)···Cu(1)_ $\Sigma$ 1	3.6318(11)
S(1)-O(3)	1.385(6)
S(1)-O(1)	1.409(4)
S(1)-O(2)	1.480(5)
S(1)-C(5)	1.770(9)
C(5)-F(2)	1.269(9)
C(5)-F(1)	1.282(8)
C(5)-F(3)	1.371(10)
N(1)-C(1)	1.491(7)
N(2)-C(3)	1.471(7)
N(2)-C(2)	1.472(7)
N(3)-C(4)	1.505(7)
C(1)-C(2)	1.487(8)
C(3)-C(4)	1.469(9)
N(3)-Cu(1)-N(1)	159.8(2)
N(3)-Cu(1)-N(2)	84.36(18)
N(1)-Cu(1)-N(2)	84.18(19)
N(3)-Cu(1)-Cl(1)	96.71(14)
N(1)-Cu(1)-Cl(1)	94.99(14)
N(2)-Cu(1)-Cl(1)	178.72(12)
Cl(1)-Cu(1)-Cl(1)_ $\Sigma$ 1	89.07(4)
Cu(1)-Cl(1)-Cu(1)_ $\Sigma$ 1	90.93(4)
O(3)-S(1)-O(1)	118.0(3)
O(3)-S(1)-O(2)	109.0(5)
O(1)-S(1)-O(2)	111.3(3)
O(3)-S(1)-C(5)	108.1(4)
O(1)-S(1)-C(5)	108.4(3)
O(2)-S(1)-C(5)	100.6(4)
F(2)-C(5)-F(1)	110.3(8)
F(2)-C(5)-F(3)	102.1(7)
F(1)-C(5)-F(3)	108.6(8)
F(2)-C(5)-S(1)	115.1(7)
F(1)-C(5)-S(1)	114.2(6)
F(3)-C(5)-S(1)	105.5(7)
C(1)-N(1)-Cu(1)	109.9(3)
C(3)-N(2)-C(2)	117.3(4)

C(3)-N(2)-Cu(1)	108.0(3)
C(2)-N(2)-Cu(1)	108.4(3)
C(4)-N(3)-Cu(1)	108.8(3)
C(2)-C(1)-N(1)	107.5(4)
N(2)-C(2)-C(1)	108.0(4)
C(4)-C(3)-N(2)	107.4(5)
C(3)-C(4)-N(3)	107.5(4)

**Table A.1.3.** Torsion angles [°] for Cu(Cl)<sub>2</sub> crystal

O(3)-S(1)-C(5)-F(2)	176.9(7)
O(1)-S(1)-C(5)-F(2)	47.9(8)
O(2)-S(1)-C(5)-F(2)	-68.9(7)
O(3)-S(1)-C(5)-F(1)	-54.1(9)
O(1)-S(1)-C(5)-F(1)	176.9(7)
O(2)-S(1)-C(5)-F(1)	60.1(8)
O(3)-S(1)-C(5)-F(3)	65.1(7)
O(1)-S(1)-C(5)-F(3)	-63.9(6)
O(2)-S(1)-C(5)-F(3)	179.3(6)
N(3)-Cu(1)-N(1)-C(1)	66.2(7)
N(2)-Cu(1)-N(1)-C(1)	10.5(4)
Cl(1)-Cu(1)-N(1)-C(1)	-168.5(4)
N(3)-Cu(1)-N(2)-C(3)	-17.9(4)
N(1)-Cu(1)-N(2)-C(3)	145.5(4)
Cl(1)-Cu(1)-N(2)-C(3)	-164(5)
N(3)-Cu(1)-N(2)-C(2)	-146.0(3)
N(1)-Cu(1)-N(2)-C(2)	17.4(3)
Cl(1)-Cu(1)-N(2)-C(2)	67(6)
N(1)-Cu(1)-N(3)-C(4)	-66.4(7)
N(2)-Cu(1)-N(3)-C(4)	-10.8(4)
Cl(1)-Cu(1)-N(3)-C(4)	168.5(4)
Cu(1)-N(1)-C(1)-C(2)	-36.1(6)
C(3)-N(2)-C(2)-C(1)	-164.6(4)
Cu(1)-N(2)-C(2)-C(1)	-42.1(5)
N(1)-C(1)-C(2)-N(2)	51.3(6)
C(2)-N(2)-C(3)-C(4)	166.5(5)

Cu(1)-N(2)-C(3)-C(4)	43.7(5)
Cu(1)-Cl(1)-Cu(1)_S1-Cl(1)_S1	0.00
N(2)-C(3)-C(4)-N(3)	-53.5(6)
Cu(1)-N(3)-C(4)-C(3)	37.7(5)

**Table A.1.4.** Crystal data and structure refinement for 4,4'-bipyridine complex

Identification code	046jn1t	
Empirical formula	C <sub>26</sub> H <sub>40</sub> Cu <sub>2</sub> F <sub>12</sub> N <sub>10</sub> O <sub>12</sub> S <sub>4</sub>	
Formula weight	1168.00	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 9.1863(18) Å	α = 90°.
	b = 20.414(4) Å	β = 91.746(4)°.
	c = 11.923(2) Å	γ = 90°.
Volume	2234.9(8) Å <sup>3</sup>	
Z	2	
Density (calculated)	1.736 Mg/m <sup>3</sup>	
Absorption coefficient	1.254 mm <sup>-1</sup>	
F(000)	1184	
Theta range for data collection	1.98 to 26.60°.	
Index ranges	-11 ≤ h ≤ 11, -25 ≤ k ≤ 25, -15 ≤ l ≤ 15	
Reflections collected	23882	
Independent reflections	4680 [R(int) = 0.0337]	
Completeness to theta = 26.60°	100.0 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	4680 / 12 / 347	
Goodness-of-fit on F <sup>2</sup>	1.205	
Final R indices [I > 2σ(I)]	R1 = 0.0509, wR2 = 0.1494	
R indices (all data)	R1 = 0.0581, wR2 = 0.1568	

Largest diff. peak and hole

0.690 and -0.352 e.Å<sup>-3</sup>

**Table A.1.5.** Bond lengths [Å] and angles [°] for 4,4'-bipyridine complex

Cu(1)-N(1)	1.992(3)
Cu(1)-N(3)	1.995(3)
Cu(1)-N(2)	2.005(2)
Cu(1)-N(4)	2.027(2)
Cu(1)-N(5)	2.991(5)
N(1)-C(1)	1.475(4)
N(1)-H(1N1)	0.9000
N(1)-H(2N1)	0.9000
N(2)-C(3)	1.468(4)
N(2)-C(2)	1.472(4)
N(2)-H(1N2)	0.9100
N(3)-C(4)	1.477(5)
N(3)-H(2N3)	0.9000
N(3)-H(1N3)	0.9000
N(4)-C(5)	1.306(5)
N(4)-C(9)	1.309(4)
C(1)-C(2)	1.500(5)
C(1)-H(1A)	0.92(4)
C(1)-H(1B)	0.95(5)
C(2)-H(2A)	0.95(4)
C(2)-H(2B)	1.00(5)
C(3)-C(4)	1.480(6)
C(3)-H(3A)	0.90(4)
C(3)-H(3B)	1.00(5)
C(4)-H(4A)	0.94(4)
C(4)-H(4B)	0.76(4)
C(5)-C(6)	1.371(5)
C(5)-H(5)	0.80(6)
C(6)-C(7)	1.364(5)
C(6)-H(6)	0.73(5)
C(7)-C(8)	1.357(4)
C(7)-C(7)#1	1.489(5)
C(8)-C(9)	1.372(5)

C(8)-H(8)	0.86(5)
C(9)-H(9)	0.98(5)
C(10)-N(5)	1.128(5)
C(10)-C(11)	1.425(5)
C(11)-H(11A)	0.9600
C(11)-H(11B)	0.9600
C(11)-H(11C)	0.9600
S(1)-O(3)	1.405(3)
S(1)-O(2)	1.430(3)
S(1)-O(1)	1.439(2)
S(1)-C(12)	1.802(5)
C(12)-F(2)	1.292(5)
C(12)-F(1)	1.303(6)
C(12)-F(3)	1.313(5)
S(2)-O(5)	1.414(3)
S(2)-O(4)	1.423(3)
S(2)-O(6)	1.426(3)
S(2)-C(13)	1.798(5)
C(13)-F(6)	1.269(6)
C(13)-F(5)	1.321(6)
C(13)-F(4)	1.346(6)
N(1)-Cu(1)-N(3)	165.10(13)
N(1)-Cu(1)-N(2)	84.80(10)
N(3)-Cu(1)-N(2)	83.79(11)
N(1)-Cu(1)-N(4)	94.39(10)
N(3)-Cu(1)-N(4)	96.32(11)
N(2)-Cu(1)-N(4)	175.99(10)
Cu(1)-N(5)-C(10)	142.81(13)
C(1)-N(1)-Cu(1)	108.9(2)
C(1)-N(1)-H(1N1)	109.9
Cu(1)-N(1)-H(1N1)	109.9
C(1)-N(1)-H(2N1)	109.9
Cu(1)-N(1)-H(2N1)	109.9
H(1N1)-N(1)-H(2N1)	108.3
C(3)-N(2)-C(2)	117.5(3)
C(3)-N(2)-Cu(1)	107.51(19)

C(2)-N(2)-Cu(1)	107.61(18)
C(3)-N(2)-H(1N2)	108.0
C(2)-N(2)-H(1N2)	108.0
Cu(1)-N(2)-H(1N2)	108.0
C(4)-N(3)-Cu(1)	110.5(2)
C(4)-N(3)-H(2N3)	109.5
Cu(1)-N(3)-H(2N3)	109.5
C(4)-N(3)-H(1N3)	109.5
Cu(1)-N(3)-H(1N3)	109.5
H(2N3)-N(3)-H(1N3)	108.1
C(5)-N(4)-C(9)	115.8(3)
C(5)-N(4)-Cu(1)	123.4(2)
C(9)-N(4)-Cu(1)	120.7(2)
N(1)-C(1)-C(2)	108.3(3)
N(1)-C(1)-H(1A)	104(2)
C(2)-C(1)-H(1A)	113(2)
N(1)-C(1)-H(1B)	115(3)
C(2)-C(1)-H(1B)	110(3)
H(1A)-C(1)-H(1B)	106(3)
N(2)-C(2)-C(1)	106.6(3)
N(2)-C(2)-H(2A)	107(2)
C(1)-C(2)-H(2A)	120(2)
N(2)-C(2)-H(2B)	103(3)
C(1)-C(2)-H(2B)	114(3)
H(2A)-C(2)-H(2B)	104(3)
N(2)-C(3)-C(4)	107.6(3)
N(2)-C(3)-H(3A)	119(3)
C(4)-C(3)-H(3A)	108(3)
N(2)-C(3)-H(3B)	108(3)
C(4)-C(3)-H(3B)	109(3)
H(3A)-C(3)-H(3B)	104(4)
N(3)-C(4)-C(3)	108.7(3)
N(3)-C(4)-H(4A)	107(2)
C(3)-C(4)-H(4A)	112(2)
N(3)-C(4)-H(4B)	108(3)
C(3)-C(4)-H(4B)	112(3)

H(4A)-C(4)-H(4B)	110(4)
N(4)-C(5)-C(6)	124.1(4)
N(4)-C(5)-H(5)	116(5)
C(6)-C(5)-H(5)	120(5)
C(7)-C(6)-C(5)	120.5(4)
C(7)-C(6)-H(6)	132(4)
C(5)-C(6)-H(6)	107(4)
C(8)-C(7)-C(6)	115.0(3)
C(8)-C(7)-C(7)#1	122.1(3)
C(6)-C(7)-C(7)#1	123.0(3)
C(7)-C(8)-C(9)	121.2(3)
C(7)-C(8)-H(8)	118(4)
C(9)-C(8)-H(8)	120(4)
N(4)-C(9)-C(8)	123.4(3)
N(4)-C(9)-H(9)	117(3)
C(8)-C(9)-H(9)	119(3)
N(5)-C(10)-C(11)	178.3(4)
C(10)-C(11)-H(11A)	109.5
C(10)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	109.5
C(10)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11C)	109.5
H(11B)-C(11)-H(11C)	109.5
O(3)-S(1)-O(2)	116.7(2)
O(3)-S(1)-O(1)	115.6(2)
O(2)-S(1)-O(1)	113.72(16)
O(3)-S(1)-C(12)	102.6(3)
O(2)-S(1)-C(12)	102.5(2)
O(1)-S(1)-C(12)	102.98(19)
F(2)-C(12)-F(1)	108.1(5)
F(2)-C(12)-F(3)	105.4(4)
F(1)-C(12)-F(3)	108.2(5)
F(2)-C(12)-S(1)	112.6(3)
F(1)-C(12)-S(1)	111.2(4)
F(3)-C(12)-S(1)	111.0(3)
O(5)-S(2)-O(4)	113.2(2)

O(5)-S(2)-O(6)	115.8(2)
O(4)-S(2)-O(6)	113.36(19)
O(5)-S(2)-C(13)	106.2(3)
O(4)-S(2)-C(13)	103.5(2)
O(6)-S(2)-C(13)	103.2(2)
F(6)-C(13)-F(5)	110.0(5)
F(6)-C(13)-F(4)	106.0(5)
F(5)-C(13)-F(4)	104.6(5)
F(6)-C(13)-S(2)	113.9(4)
F(5)-C(13)-S(2)	112.6(4)
F(4)-C(13)-S(2)	109.2(3)

**Table A.1.6.** Torsion angles [°] for 4,4'-bipyridine complex.

N(3)-Cu(1)-N(1)-C(1)	-49.5(5)
N(2)-Cu(1)-N(1)-C(1)	-9.4(2)
N(4)-Cu(1)-N(1)-C(1)	174.6(2)
N(1)-Cu(1)-N(2)-C(3)	-147.1(2)
N(3)-Cu(1)-N(2)-C(3)	23.3(2)
N(4)-Cu(1)-N(2)-C(3)	-68.6(15)
N(1)-Cu(1)-N(2)-C(2)	-19.7(2)
N(3)-Cu(1)-N(2)-C(2)	150.7(2)
N(4)-Cu(1)-N(2)-C(2)	58.9(15)
N(1)-Cu(1)-N(3)-C(4)	43.9(6)
N(2)-Cu(1)-N(3)-C(4)	3.7(3)
N(4)-Cu(1)-N(3)-C(4)	179.7(3)
N(1)-Cu(1)-N(4)-C(5)	-82.5(4)
N(3)-Cu(1)-N(4)-C(5)	107.8(4)
N(2)-Cu(1)-N(4)-C(5)	-160.7(14)
N(1)-Cu(1)-N(4)-C(9)	94.4(3)
N(3)-Cu(1)-N(4)-C(9)	-75.2(3)
N(2)-Cu(1)-N(4)-C(9)	16.2(16)
Cu(1)-N(1)-C(1)-C(2)	36.3(3)
C(3)-N(2)-C(2)-C(1)	165.5(3)
Cu(1)-N(2)-C(2)-C(1)	44.1(3)
N(1)-C(1)-C(2)-N(2)	-53.3(3)

C(2)-N(2)-C(3)-C(4)	-167.3(3)
Cu(1)-N(2)-C(3)-C(4)	-45.8(3)
Cu(1)-N(3)-C(4)-C(3)	-30.0(4)
N(2)-C(3)-C(4)-N(3)	49.9(4)
C(9)-N(4)-C(5)-C(6)	-0.5(7)
Cu(1)-N(4)-C(5)-C(6)	176.6(4)
N(4)-C(5)-C(6)-C(7)	1.0(9)
C(5)-C(6)-C(7)-C(8)	-1.1(7)
C(5)-C(6)-C(7)-C(7)#1	179.8(5)
C(6)-C(7)-C(8)-C(9)	0.8(6)
C(7)#1-C(7)-C(8)-C(9)	179.9(4)
C(5)-N(4)-C(9)-C(8)	0.2(6)
Cu(1)-N(4)-C(9)-C(8)	-177.0(4)
C(7)-C(8)-C(9)-N(4)	-0.4(7)
O(3)-S(1)-C(12)-F(2)	55.9(4)
O(2)-S(1)-C(12)-F(2)	177.3(4)
O(1)-S(1)-C(12)-F(2)	-64.5(4)
O(3)-S(1)-C(12)-F(1)	177.4(4)
O(2)-S(1)-C(12)-F(1)	-61.3(4)
O(1)-S(1)-C(12)-F(1)	57.0(4)
O(3)-S(1)-C(12)-F(3)	-62.0(4)
O(2)-S(1)-C(12)-F(3)	59.3(4)
O(1)-S(1)-C(12)-F(3)	177.6(4)
O(5)-S(2)-C(13)-F(6)	57.6(5)
O(4)-S(2)-C(13)-F(6)	177.0(5)
O(6)-S(2)-C(13)-F(6)	-64.6(5)
O(5)-S(2)-C(13)-F(5)	-68.5(5)
O(4)-S(2)-C(13)-F(5)	50.9(5)
O(6)-S(2)-C(13)-F(5)	169.3(4)
O(5)-S(2)-C(13)-F(4)	175.8(4)
O(4)-S(2)-C(13)-F(4)	-64.8(4)
O(6)-S(2)-C(13)-F(4)	53.6(4)

**Table A.1.7.** Crystal data and structure refinement for (E)-1,2-di(pyridin-4-yl)ethane complex

Identification code	058aj1ms	
Empirical formula	C <sub>28</sub> H <sub>42</sub> Cu <sub>2</sub> F <sub>12</sub> N <sub>10</sub> O <sub>12</sub> S <sub>4</sub>	
Formula weight	1194.04	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 8.735(4) Å	$\beta = 90^\circ$ .
	b = 21.922(9) Å	$\beta = 90.203(12)^\circ$ .
	c = 12.148(5) Å	$\beta = 90^\circ$ .
Volume	2326.2(17) Å <sup>3</sup>	
Z	2	
Density (calculated)	1.705 Mg/m <sup>3</sup>	
Absorption coefficient	1.207 mm <sup>-1</sup>	
F(000)	1212	
Theta range for data collection	1.92 to 27.04°.	
Index ranges	-11 ≤ h ≤ 11, -28 ≤ k ≤ 28, -15 ≤ l ≤ 15	
Reflections collected	24889	
Independent reflections	5092 [R(int) = 0.2026]	
Completeness to theta = 27.04°	99.9 %	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	5092 / 0 / 364	
Goodness-of-fit on F <sup>2</sup>	1.098	
Final R indices [I > 2sigma(I)]	R1 = 0.0838, wR2 = 0.1996	
R indices (all data)	R1 = 0.1079, wR2 = 0.2161	
Largest diff. peak and hole	1.055 and -1.370 e.Å <sup>-3</sup>	

**Table A.1.8.** Bond lengths [Å] and angles [°] for (E)-1,2-di(pyridin-4-yl)ethane complex

Cu(1)-N(3)	1.986(5)
Cu(1)-N(1)	1.991(5)
Cu(1)-N(2)	1.994(5)
Cu(1)-N(4)	1.995(4)
Cu(1)-O(1)	2.390(4)
N(1)-C(1)	1.482(7)
N(1)-H(1N)	0.9200
N(1)-H(2N)	0.9200
N(2)-C(2)	1.459(7)
N(2)-C(3)	1.465(8)
N(2)-H(3N)	0.72(7)
N(3)-C(4)	1.473(7)
N(3)-H(4N)	0.9200
N(3)-H(5N)	0.9200
C(1)-C(2)	1.472(9)
C(1)-H(1A)	0.89(6)
C(1)-H(1B)	1.17(6)
C(2)-H(2B)	0.86(6)
C(3)-C(4)	1.485(8)
C(3)-H(3A)	0.71(6)
C(3)-H(3B)	1.10(6)
N(4)-C(5)	1.324(7)
N(4)-C(9)	1.327(7)
N(5)-Cu(1)	3.207(5)
C(4)-H(4A)	1.13(7)
C(4)-H(4B)	1.03(7)
C(5)-C(6)	1.387(8)
C(5)-H(5)	0.98(6)
C(6)-C(7)	1.380(8)
C(6)-H(6)	1.16(10)
C(7)-C(8)	1.382(7)
C(7)-C(10)	1.490(7)
C(8)-C(9)	1.370(7)
C(8)-H(8)	0.98(6)
C(9)-H(9)	0.90(6)

C(10)-C(10)#1	1.538(11)
C(10)-H(10A)	1.04(7)
C(10)-H(10B)	0.91(7)
S(1)-O(2)	1.427(5)
S(1)-O(3)	1.432(4)
S(1)-O(1)	1.435(4)
S(1)-C(11)	1.821(7)
C(11)-F(2)	1.316(7)
C(11)-F(1)	1.320(8)
C(11)-F(3)	1.326(7)
N(5)-C(13)	1.126(8)
C(13)-C(14)	1.439(9)
C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800
C(14)-H(14C)	0.9800
S(2)-O(4)	1.437(4)
S(2)-O(5)	1.440(4)
S(2)-O(6)	1.452(4)
S(2)-C(12)	1.812(6)
C(12)-F(5)	1.310(8)
C(12)-F(6)	1.312(7)
C(12)-F(4)	1.331(8)
N(3)-Cu(1)-N(1)	162.9(2)
N(3)-Cu(1)-N(2)	85.31(19)
N(1)-Cu(1)-N(2)	84.03(19)
N(3)-Cu(1)-N(4)	93.67(18)
N(1)-Cu(1)-N(4)	95.46(19)
N(2)-Cu(1)-N(4)	173.7(2)
N(3)-Cu(1)-O(1)	87.60(17)
N(1)-Cu(1)-O(1)	106.52(19)
N(2)-Cu(1)-O(1)	94.21(18)
N(4)-Cu(1)-O(1)	91.96(16)
O(1)-Cu(1)-N(5)	169.74(18)
C(1)-N(1)-Cu(1)	109.6(4)
C(1)-N(1)-H(1N)	109.8
Cu(1)-N(1)-H(1N)	109.8

C(1)-N(1)-H(2N)	109.8
Cu(1)-N(1)-H(2N)	109.8
H(1N)-N(1)-H(2N)	108.2
C(2)-N(2)-C(3)	117.8(5)
C(2)-N(2)-Cu(1)	108.1(4)
C(3)-N(2)-Cu(1)	107.1(3)
C(2)-N(2)-H(3N)	110(5)
C(3)-N(2)-H(3N)	115(5)
Cu(1)-N(2)-H(3N)	96(5)
C(4)-N(3)-Cu(1)	108.3(3)
C(4)-N(3)-H(4N)	110.0
Cu(1)-N(3)-H(4N)	110.0
C(4)-N(3)-H(5N)	110.0
Cu(1)-N(3)-H(5N)	110.0
H(4N)-N(3)-H(5N)	108.4
C(2)-C(1)-N(1)	108.2(5)
C(2)-C(1)-H(1A)	110(4)
N(1)-C(1)-H(1A)	112(4)
C(2)-C(1)-H(1B)	111(3)
N(1)-C(1)-H(1B)	103(3)
H(1A)-C(1)-H(1B)	112(5)
N(2)-C(2)-C(1)	107.5(5)
N(2)-C(2)-H(2B)	104(4)
C(1)-C(2)-H(2B)	111(4)
N(2)-C(3)-C(4)	107.7(5)
N(2)-C(3)-H(3A)	108(5)
C(4)-C(3)-H(3A)	115(5)
N(2)-C(3)-H(3B)	104(3)
C(4)-C(3)-H(3B)	119(3)
H(3A)-C(3)-H(3B)	102(6)
C(5)-N(4)-C(9)	118.2(5)
C(5)-N(4)-Cu(1)	123.8(4)
C(9)-N(4)-Cu(1)	117.9(4)
N(3)-C(4)-C(3)	108.0(5)
N(3)-C(4)-H(4A)	112(3)
C(3)-C(4)-H(4A)	115(3)

N(3)-C(4)-H(4B)	113(4)
C(3)-C(4)-H(4B)	120(4)
H(4A)-C(4)-H(4B)	87(5)
N(4)-C(5)-C(6)	122.6(6)
N(4)-C(5)-H(5)	117(3)
C(6)-C(5)-H(5)	120(3)
C(7)-C(6)-C(5)	118.8(5)
C(7)-C(6)-H(6)	121(5)
C(5)-C(6)-H(6)	120(5)
C(6)-C(7)-C(8)	118.3(5)
C(6)-C(7)-C(10)	120.7(5)
C(8)-C(7)-C(10)	121.1(5)
C(9)-C(8)-C(7)	119.0(5)
C(9)-C(8)-H(8)	118(3)
C(7)-C(8)-H(8)	123(3)
N(4)-C(9)-C(8)	123.1(5)
N(4)-C(9)-H(9)	126(4)
C(8)-C(9)-H(9)	111(4)
C(7)-C(10)-C(10)#1	110.3(6)
C(7)-C(10)-H(10A)	100(4)
C(10)#1-C(10)-H(10A)	106(3)
C(7)-C(10)-H(10B)	109(5)
C(10)#1-C(10)-H(10B)	113(5)
H(10A)-C(10)-H(10B)	117(6)
C(13)-N(5)-Cu(1)	141.9(4)
O(2)-S(1)-O(3)	117.2(3)
O(2)-S(1)-O(1)	114.8(3)
O(3)-S(1)-O(1)	113.7(3)
O(2)-S(1)-C(11)	103.2(3)
O(3)-S(1)-C(11)	102.2(3)
O(1)-S(1)-C(11)	103.0(3)
S(1)-O(1)-Cu(1)	127.7(2)
F(2)-C(11)-F(1)	107.6(6)
F(2)-C(11)-F(3)	108.5(5)
F(1)-C(11)-F(3)	108.3(6)
F(2)-C(11)-S(1)	110.4(5)

F(1)-C(11)-S(1)	111.5(4)
F(3)-C(11)-S(1)	110.5(5)
N(5)-C(13)-C(14)	178.8(7)
C(13)-C(14)-H(14A)	109.5
C(13)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(13)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
O(4)-S(2)-O(5)	115.5(2)
O(4)-S(2)-O(6)	115.0(3)
O(5)-S(2)-O(6)	113.9(3)
O(4)-S(2)-C(12)	104.5(3)
O(5)-S(2)-C(12)	103.1(3)
O(6)-S(2)-C(12)	102.7(3)
F(5)-C(12)-F(6)	107.9(6)
F(5)-C(12)-F(4)	108.2(6)
F(6)-C(12)-F(4)	107.3(6)
F(5)-C(12)-S(2)	112.5(5)
F(6)-C(12)-S(2)	110.3(5)
F(4)-C(12)-S(2)	110.5(5)

**Table A.1.9.** Torsion angles [°] for (E)-1,2-di(pyridin-4-yl)ethane complex.

N(3)-Cu(1)-N(1)-C(1)	58.9(8)
N(2)-Cu(1)-N(1)-C(1)	7.1(4)
N(4)-Cu(1)-N(1)-C(1)	-179.2(4)
O(1)-Cu(1)-N(1)-C(1)	-85.6(4)
N(3)-Cu(1)-N(2)-C(2)	-145.7(4)
N(1)-Cu(1)-N(2)-C(2)	20.8(4)
N(4)-Cu(1)-N(2)-C(2)	-64.8(19)
O(1)-Cu(1)-N(2)-C(2)	127.0(4)
N(3)-Cu(1)-N(2)-C(3)	-17.8(4)
N(1)-Cu(1)-N(2)-C(3)	148.7(4)
N(4)-Cu(1)-N(2)-C(3)	63.1(19)
O(1)-Cu(1)-N(2)-C(3)	-105.1(4)

N(1)-Cu(1)-N(3)-C(4)	-62.5(8)
N(2)-Cu(1)-N(3)-C(4)	-10.9(4)
N(4)-Cu(1)-N(3)-C(4)	175.4(4)
O(1)-Cu(1)-N(3)-C(4)	83.6(4)
Cu(1)-N(1)-C(1)-C(2)	-33.6(6)
C(3)-N(2)-C(2)-C(1)	-166.3(5)
Cu(1)-N(2)-C(2)-C(1)	-44.8(5)
N(1)-C(1)-C(2)-N(2)	51.5(6)
C(2)-N(2)-C(3)-C(4)	164.9(5)
Cu(1)-N(2)-C(3)-C(4)	42.9(5)
N(3)-Cu(1)-N(4)-C(5)	-81.4(5)
N(1)-Cu(1)-N(4)-C(5)	113.1(5)
N(2)-Cu(1)-N(4)-C(5)	-161.8(16)
O(1)-Cu(1)-N(4)-C(5)	6.3(5)
N(3)-Cu(1)-N(4)-C(9)	95.5(4)
N(1)-Cu(1)-N(4)-C(9)	-70.0(4)
N(2)-Cu(1)-N(4)-C(9)	15(2)
O(1)-Cu(1)-N(4)-C(9)	-176.8(4)
Cu(1)-N(3)-C(4)-C(3)	37.3(5)
N(2)-C(3)-C(4)-N(3)	-53.5(6)
C(9)-N(4)-C(5)-C(6)	0.0(8)
Cu(1)-N(4)-C(5)-C(6)	176.8(4)
N(4)-C(5)-C(6)-C(7)	-0.6(9)
C(5)-C(6)-C(7)-C(8)	2.0(8)
C(5)-C(6)-C(7)-C(10)	-177.8(5)
C(6)-C(7)-C(8)-C(9)	-2.7(8)
C(10)-C(7)-C(8)-C(9)	177.1(5)
C(5)-N(4)-C(9)-C(8)	-0.7(8)
Cu(1)-N(4)-C(9)-C(8)	-177.7(4)
C(7)-C(8)-C(9)-N(4)	2.1(9)
C(6)-C(7)-C(10)-C(10)#1	110.2(7)
C(8)-C(7)-C(10)-C(10)#1	-69.6(9)
O(2)-S(1)-O(1)-Cu(1)	162.0(3)
O(3)-S(1)-O(1)-Cu(1)	23.2(4)
C(11)-S(1)-O(1)-Cu(1)	-86.5(3)
N(3)-Cu(1)-O(1)-S(1)	-147.9(3)

N(1)-Cu(1)-O(1)-S(1)	22.2(3)
N(2)-Cu(1)-O(1)-S(1)	-62.8(3)
N(4)-Cu(1)-O(1)-S(1)	118.5(3)
O(2)-S(1)-C(11)-F(2)	55.8(5)
O(3)-S(1)-C(11)-F(2)	177.8(4)
O(1)-S(1)-C(11)-F(2)	-64.0(5)
O(2)-S(1)-C(11)-F(1)	175.3(4)
O(3)-S(1)-C(11)-F(1)	-62.7(5)
O(1)-S(1)-C(11)-F(1)	55.5(5)
O(2)-S(1)-C(11)-F(3)	-64.2(5)
O(3)-S(1)-C(11)-F(3)	57.8(5)
O(1)-S(1)-C(11)-F(3)	176.0(4)
O(4)-S(2)-C(12)-F(5)	-175.6(4)
O(5)-S(2)-C(12)-F(5)	63.3(5)
O(6)-S(2)-C(12)-F(5)	-55.2(5)
O(4)-S(2)-C(12)-F(6)	-55.0(6)
O(5)-S(2)-C(12)-F(6)	-176.1(5)
O(6)-S(2)-C(12)-F(6)	65.3(6)
O(4)-S(2)-C(12)-F(4)	63.4(5)
O(5)-S(2)-C(12)-F(4)	-57.7(5)
O(6)-S(2)-C(12)-F(4)	-176.2(5)

**Dynamic Light Scattering (DLS).** Determination of DLS was performed on a PD2000 DLS Plus and Precision Detector at 298°F with a 90° scattering angle at 1mM aqueous concentration. Analyzation of data obtained was done with Precision Deconvolve Version 4.5 were size distribution data was obtained.

## A.2. Supporting information for chapter 3

**Critical Micelle Concentration Analysis.** CMC analysis of the three Gemini-metallo surfactants was done dyeing the liposomes with a fluorescent lipophilic molecule, the Nile Red. The analysis was performed in the Fluroskan Accent F1 flurometer by Thermo Electron Corporation with an emission wavelength of 530nm of emission and 640nm of absorption. The integration time was at 100ms. 20μL of Nile Red was added to 108 different microcells varying the concentration of the three binuclear Cu(II) complexes

using as stock solution 1mM concentration of each. The total volume adjusted with water in each micro cell was of 50 $\mu$ L taking in consideration the remaining of water.

**Scanning Electron Microscope (SEM).** All three Gemini-metallo surfactants were prepared at 1mM aqueous solution. Then the liposomes where put into a carbon surface film on an aluminum chip that was put inside the (SEM) instrument where the analysis took place.

## **Curriculum Vitae**

Erich Ivan Valenzuela Alcantar was born in August 7, 1985 in Queretaro, Queretaro. He was born out of a big family consisting of 7 brothers and 3 sisters. His parents Jose Antonio Rito Valenzuela and Maria del Rosario Alcantar Enriquez were always busy either working outside home or doing house chores all day so he was in charge of taking care of the smaller siblings he have. His dad was an English teacher and he wanted Erich to learn English in the United States so he sent him to El Paso Texas where he started his career in chemistry at the University of Texas at El Paso (UTEP). Being an international student he couldn't work outside campus so he first obtained a job in Contemporary Services Corporation (CSC) where he worked for about a year. Later on he grasped the opportunity to work as a math and science tutor for a couple of years. After that, he got the opportunity to work as an organic peer leader for the last years of his bachelors.

One year before graduation he encountered the opportunity to do research in an inorganic laboratory where he started doing first as a summer internship and later on he stayed for the rest of the year. While doing research he got the opportunity to go to National Conference held in Salt Lake City Utah where he presented a poster research.

One semester before graduation from his bachelors, he worked one semester as Research Assistant in UTEP and in fall 2009 he started to pursue his master degree in Chemistry. During that time, presented his initial research on Metallo-Gemini Surfactants at National Conference held in San Francisco, California.

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