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Sensory materials that respond to chemical and mechanical stimuli are under development in many laboratories. There are many significant uses of polydiacetylene compounds as sensory material. They have been applied to drug delivery, drug design, biomolecule development, cosmetics, and national security. In this study, experiments were carried out toward the development of a novel sensory material based on the established synthetic research on polydiacetylene compounds. Synthetic routes toward sensory materials with different head groups, different carbon chains lengths, and the incorporation of molecular imprints were explored.

Diacetylene moieties, which can be used for polymer vesicle formation, were prepared by two main routes. In one route, 1-iodo-1-octyne and 1-iodo-1-dodecyne were prepared as starting materials for the synthesis of two diacetylene compounds (Diacetylene I and Diacetylene II). In the other route, a mesityl alkyne was used to prepare 5-iodo-1-pentyne, which was then used to prepare a triethylamino alkyne. This in turn was used to synthesize a diacetylene (Diacetylene III). Although each diacetylene product was formed, purification by column chromatography was found to be difficult. Experiments in vesicle formation, with and without molecular imprints, were also carried out using commercially available diacetylenes .

THE SYNTHESIS OF A POLYDIACETYLENE TO CREATE A NOVEL SENSORY MATERIAL

by
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Approved by

_____
Committee Chair

“To my mom and dad

for instilling in me the belief

that if you have the

strength and the courage

to work hard and achieve,

nothing will stand in your way

when you reach for the stars.”

APPROVAL PAGE

This thesis has been approved by the following committee of the

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TABLE OF CONTENTS

Page

CHAPTER

I. INTRODUCTION 1

Statement of Problem 1
Objective 7

II. REVIEW OF LITERATURE 12

Polymer Vesicles 12
Vesicle Structure 13
Polymer Compounds 16
Molecular Imprinting 18

III. EXPERIMENTAL 22

IV. RESULTS AND DISCUSSION 33

Iodoacetylenes 33
Molecular Imprinted Compounds 41

V. CONCLUSION 45

REFERENCES 46

CHAPTER I

INTRODUCTION

Statement of Problem

The development of a novel active sensory material is a growing field of study because of the many applications possible. For example, some popular methods used in conjunction with sensory materials are quartz crystal microbalance, electrochemical, and surface plasmon resonance. In all of these methods the materials are passive participants in the transduction of electrons. With an active material the actual material itself acts as the transducer. Therefore, the interest in active material is high because it has no need for an outside source to stimulate it into a responsive form. In general, materials expand depending on the temperature or pressure; some materials deform if an electromagnetic field is applied to them. Materials that respond to an electromagnetic field are called active materials. Ideally, active materials can change their shape, stiffness, transparency, and color in response to a signal. Currently, structures from active materials are used in switches, sensors, actuators, etc.

In contrast, passive materials have the need for an outside source to stimulate it into a responsive form. Therefore, the benefits of developing active materials essentially rest with the fact that creating active materials are economically more feasible. Most cost reduction occurs in not having to use the equipment and chemical reagents needed to activate the passive material. This also decreases the cost because man-hours are not

required for the activation of the material. Another benefit of active materials is in the variety of pathways that have been developed to make them. A new area of research for active materials in the last twenty years is in the application of polydiacetylenes (PDAs) for sensory materials.[1]

Sensory Materials:

In general, sensory materials give a measurable response to stimuli. A stimulus is something that elicits or influences a change in a material. Stimuli can be categorized based on its response:

1. Chemoreceptive- material that responds to chemicals
2. Mechanoreceptive- material that responds to light, radiation, or motion

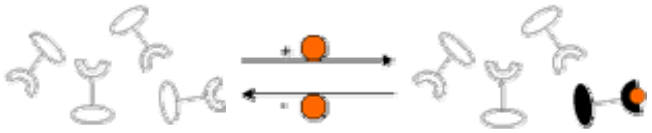
Many different types of sensory materials have been developed employing the chemoreceptive and mechanoreceptive responses. Some of the active sensory materials that are being developed are thermo-elastic materials in the form of fiber optic sensors, shape memory alloys in the form of photo-elastic sensors, and polydiacetylene materials in the form of chemosensors.[1]

Chemosensory materials are the subject of many investigations. A chemosensor is a molecular device designed to detect a specific molecule or class of molecules. The efficiency of a chemosensor can be defined as the relationship between the bound analyte and the "empty" receptor as illustrated in Scheme I.[1]

Scheme I[1]

Traditional Chemosensor:

Sensitivity related to equilibrium constant $K(eq) = \frac{(\text{Bound Receptor})}{(\text{Unbound Receptor})(\text{Analyte})}$



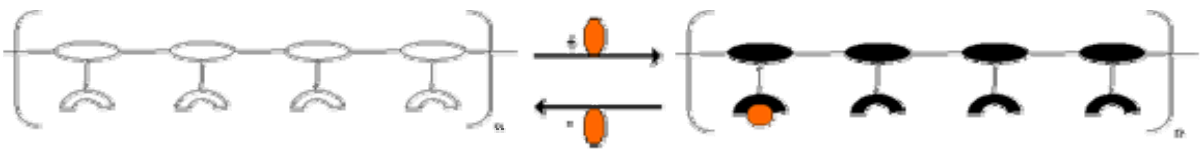
As seen in the Scheme, sensitivity is related to the equilibrium constant *K(eq)*. When the equilibrium between the analyte and receptor is rapid, sensors can be produced that provide a real-time response. The response will continuously vary with the concentration of the analyte. However, the sensitivity is limited because only bound analyte gives a response.

The traditional chemosensor has been modified to provide better sensitivity through signal amplification. Signal amplification occurs when the signal is enhanced in someway and can lead to better sensitivity. A modification to the traditional chemosensor, such as linking, amplifies the signal and thereby provides an overall more sensitive sensor. Scheme II illustrates the amplification of the signal due to a collective response using the "molecular wire approach.[1]"

Scheme II[1]

Receptors Wired in Series:

Amplification due to a collective system response.



The “molecular wire approach” enhances the sensitivity of chemosensors in effect by “wiring chemosensory molecules in series.[1]” In Scheme II a single event of binding of the analyte in a supermolecular polyreceptor system produces a response larger than that afforded by a similar interaction in an analogous small monoreceptor system (Scheme I). Because the receptors are wired in series only fractional occupancy is required to get the system to respond, thus signal amplification occurs. The amplification is due to the collective system response of the receptors. This method is a universal method by which to obtain signal amplification relative to single molecule systems. Polymer vesicles are supermolecules that are used to form chemosensors because they can readily use the “molecular wire approach for sensory signal amplification.[1]”

More specifically, conjugated polymers (CPs) are great examples of materials that have properties that utilize the “molecular wire approach for sensory signal amplification.[1]” The most distinctive property of CPs is that in their neutral states they exhibit semiconductive to insulating levels of conductivity but can be made conductive by doping. Doping in the case of CPs is different from that of semiconductor systems. In the case of CPs doping refers to the oxidation or reduction of the π-electronic system. Doping by oxidation is referred to p-doping and doping by reduction is called n- doping. To maintain electroneutrality, doping requires the incorporation of a counterion. The natural or doped conductivity of CPs contributes to the signal amplification process because it allows for better electronic communication to occur within the CPs. Specifically, the conductivity allows the electrons to move more freely and therefore produces a better signal compared to a nonconductive material.[1, 2]

Imagine that the molecular wire in Scheme II is capable of conducting an electrical current. Analyte binding produces a resistive element in the wire. Signal enhancement occurs when a single binding event influences the conductivity of the whole molecular wire. Amplification is also due to the fact that binding constants of all receptors are additive.[1, 2]

The CP's structure and composition have a direct effect on the sensitivity of the conductivity and thus the signal amplification. If the wire in Scheme II has kinks it can disrupt the flow of the electrons and thus the signal. There are many ways this can occur. For example, in polyacetylenes the conductivity is disrupted when the number of saturated sites is maximized. In other words, the saturation of the molecular wire causes a kink and the signal will be disrupted. The saturated sites represent resistive elements that impede the electrical transport in the system. Therefore to maximize the signal for CPs the procedure followed is to minimize the sites of saturation.[1, 2]

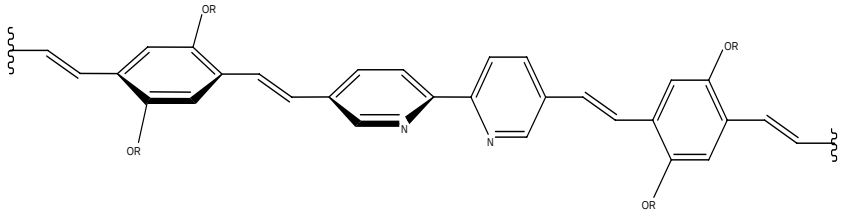
Conformational defects can also reduce the electronic delocalization and are known to produce kinks (resistive elements) in the wire. This was determined when polyacetylenes were made more soluble by adding side chains to the backbone. This resulted in compounds that were nonplanar and had very low conductivity.[1] Nonplanarity can reduce the conjugation along the polymer backbone but can also serve to decrease the electronic communication between polymer chains. The following analogy helps to understand the electronic communication effect:

"Flat sheets of paper pack efficiently with high degrees of contact between neighboring sheets; however, the physical packing of sheets of paper that have been crinkled is much

less efficient. Hence, the intermolecular charge transport between polymers chains will be greatly reduced in nonplanar structures.[1]" Therefore to protect the CPs from kinks the procedure is to carefully choose side chains which do not disrupt the planarity of the polymer backbone. Figure I shows how the properties discussed were utilized to develop a molecular wire with this ideal properties.[1, 2]

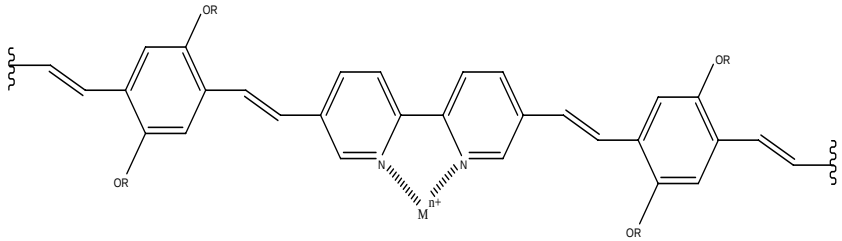
Figure I. Ideal Molecular Wire Approach[2]

UNBOUND: NONPLANAR



$- M^{n+} \rightleftharpoons + M^{n+}$

BOUND: PLANAR



In the unbound example the molecular wire is a bulky conjugated polymer that is not in a planar form. After the addition of a metal analyte (doping) the compound becomes planar

by coordination with the metal. In the unbound state the compound has a natural resistance or kink that does not allow electrons to move freely. After the analyte is bound the conformation becomes planar and the electrons can move freely. The kink is removed and conductivity is allowed.[2]

Objective

The development of novel sensory material in the form of a polymer vesicle is one application of polydiacetylene compounds. Polydiacetylene compounds as sensory material have been applied to drug delivery, drug design, and development of better biomolecules, cosmetics, and national security for detectors of hazardous materials. It is proposed that with the use of the established synthetic research on polydiacetylene compounds, a novel sensory material can be developed.[3]

The objective of the study carried out here is to develop a novel sensory material based on polydiacetylenes in the form of a polymer vesicle. The longer range goal of this research is to develop a synthetic strategy for the application of polydiacetylenes in sensory materials. To this end we sought to synthetically develop and test the best procedures to easily create and modify diacetylenes in the following ways:

1) Determine the easiest method of synthesis for different head groups

2) Determine the easiest method of synthesis for different carbon chain lengths

3) Determine the easiest method of synthesis for incorporating molecular imprints

In the listed research objectives above specific observations were made and cited for each of the experimental modifications. The specific observations are summarized in the following questions:

What effect does the modification have on the polymer vesicle formation?

What effect does the modification have on the ability to sense?

What effect does the modification have on the stability of the compound?

The diacetylene moiety used in this study is a polydiacetylene (PDA). PDAs have been intensely investigated as biological sensors because of the unique color change that occurs upon stimulation.[3] An advantage of using PDAs is that the color change is in the visible region. The stimuli can be a variety of environmental perturbations, such as pH, temperature, and ligand/receptor interactions. When the PDA is in the form of a polymer vesicle, stimulation occurs when events happen remote to the conjugated system. While in other CP systems changes in the conjugated backbone are required for effective sensory response, PDA's show a response when sensory events occur at remote locations relative to the conjugated backbone. This is called a remote stimuli response and is another advantage of a PDA sensor.[3,4]

The unique color change is usually from blue to red but can vary depending upon conditions. The differences in color likely arise from the differences in packing efficiencies between the monomers. Poor packing results in oligomers with less extensive conjugation that absorb shorter wavelengths. The most intensely blue solutions typically result from strongly hydrogen-bonded head groups or other modifications incorporating amide functionalities. Efficient packing of the chains alone does not necessarily indicate formation of long conjugated lengths as evidenced by the orange color of vesicles of alcohol derivative. Similarly, larger head groups such as those containing carbohydrates

hinder the solid-state polymerization due to the increased distance between diacetylene units.[6]

The color and chromism of the materials is one of the more intriguing aspects of polydiacetylene chemistry. The color of the material, and therefore the energy of electronic excitations, can be dependent upon many factors. These factors include the original packing state of the monomers and the exposure of the polymeric material to environmental perturbations such as heat (thermochromism), mechanical stress (mechanochromism), or solvent (solvatochromism).[6] Of all the chromisms, the thermochromic transition of polydiacetylene has been the most thoroughly studied.[6] Much of the PDA literature is committed to developing an understanding of the thermochromic blue to red color transition.[3, 4, 6] Some basic understandings emerge from this work:

(1) The blue to red transition is associated with a conformational change of the PDA backbone from planar to nonplanar.[6]

(2) Side chain conformation appears to play a critical role in the planar to nonplanar conformational change of the eneyne backbone.[6]

However, determining the exact molecular interactions between the side chains and their effect on the backbone remains an active area of research.[3, 4, 6]

In accordance, an advantage of having the PDA sensor in vesicle form is due to the conformation of the vesicle. The vesicle is interlinked and “wired in series” and demonstrates the “molecular wire in series for signal amplification” approach discussed

earlier.[1,2] These unique properties lead to the ability of the PDA sensor to sensitively detect stimuli and for the detection to be easily distinguished by the naked eye. [3, 4]

To achieve the objectives of the study, the diacetylene moiety shown in Figure II was modified.

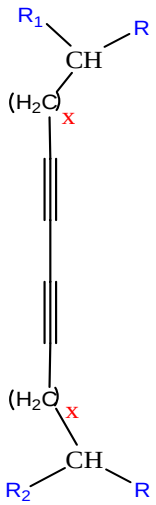
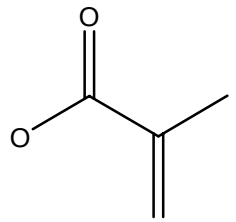


Figure II. Diacetylene Moiety: **(R_1=Polar group, R_2=Nonpolar group, R=Any, X= # Carbons)**[7,8,9]

The diacetylene moiety was manipulated so that the R_1 polar group was one of the following possible groups:[7, 8, 9]

R_1= COOH, $N^+(CH_3)_3$, $CONHNH_2$

The R_2 nonpolar group did not vary much, often using the following group:

R_2= 

The X which represents the length of the carbon chain was varied with each experimental application, with the following range of carbons in any combination:[7, 8 ,9]

X= 2, 3, 4, 5, 6, 7,

The diacetylene moiety was treated with UV light to create a polymer vesicle. As stated before, the goal of this research was to develop a synthetic strategy for the application of polydiacetylenes in sensory materials, through the variation of the above groups.

CHAPTER II

REVIEW OF LITERATURE

Polymer Vesicles

Vesicles are microscopic sacs that enclose a volume with a molecularly thin membrane. The membranes are generally self-directed assemblies of amphiphilic molecules. These membranes can also be motivated to assemble by an outside stimulus. Amphiphilic molecules have a dual hydrophilic-hydrophobic character. Biological amphiphiles form vesicles central to cell function and are principally lipids of molecular weight less than l kilodalton. These lipid structures are referred to as biomembranes. In dilute solutions block copolymers, that mimic lipid amphiphilicity, can self-assemble into vesicles. In contrast to lipids, polymer molecular weights can be orders of magnitude greater that those of the lipids. These structures are called polymer vesicles.[10]

Polymer vesicles have the ability to assemble in response to outside stimuli. As described in the sensory material section these stimuli can take on two forms:

1. Mechanical Stimuli: create a response through light, radiation, heat, motion

2. Chemical Stimuli: create a response through chemical interactions

This means a polymer vesicle can be stimulated to assemble by either mechanical or chemical means.[10]

Vesicle Structure

Vesicles form in response to the energy minimization gained from interactions between the hydrophobic tails or excluding the hydrophobic tail from the hydrophilic solvent. The hydrophobic tail is situated toward the inside and protected from the outside aqueous environment. This leaves the hydrophilic end to interact with the outside environment. In the case of the polymer vesicle two amphiphiles will maneuver themselves so that they are protected as seen in Figure III.[11] The hydrophobic tails, in gray, of each amphiphile interact and leave the outside and inside hydrophilic ends, in black, to interact with the environment.[11]

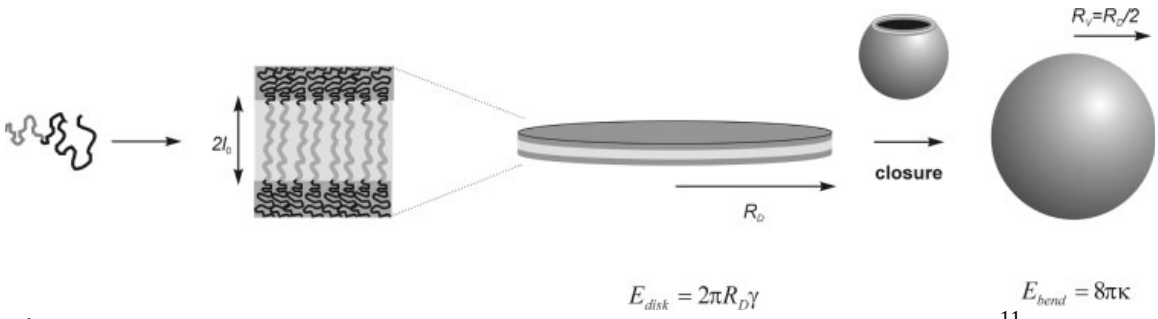


Figure III. Schematic illustration of the formation of bilayers and their closure to vesicles.[11]

The double layer is formed and creates the three regions that can be seen in Figure IV below.[12] Figure IV is a schematic representation of the three different parts of a vesicle available for template polymerization, which means it is the backbone necessary for polymerization to occur: a) the aqueous core; b) the lipid plus/minus water interface; c) the hydrophobic layer.[12]

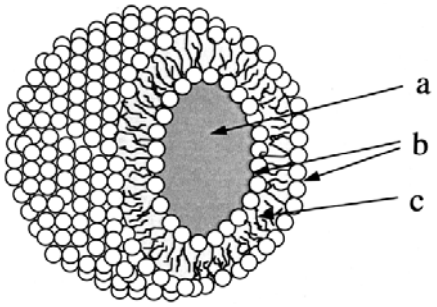


Figure IV. Vesicle structure: a) aqueous core; b) lipid-water interface; c) hydrophobic layer [12]

After the amphiphile or monomer units are aligned in the correct vesicle formation, the monomer units can either self assemble into the vesicle structure or can be stimulated by an outside source to form the vesicle structure. In both cases interlinking occurs between the monomer/amphiphile units to create the spherical polymer vesicle seen in Figures III and IV. The crosslinking means that covalent bonds form between the monomer units. Crosslinking only occurs in the synthetic polymer vesicles in which a crosslinking agent is used. The crosslinking helps the vesicle to maintain its spherical shape.[11, 12]

An example of the process of how the monomer or amphiphile undergoes the reaction to form the vesicle is seen in Figure V.[3, 4] In Figure V the first reaction shows how the diacetylene units (monomers) align themselves into the hydrophobic-hydrophilic formation. The second step shows that with stimulus from UV light, the diacetylenes are polymerized into the polymer and the polymer vesicle can take shape. Note that in Figure V the beginning and end of the chain reactions are shown. The chain reaction actually occurs twice (2X) as denoted in Figure V. These diacetylenes link up into a sphere so that

as the last molecule in the polymer links up with the first molecule in the polymer the chain reaction is set off again to get the final 1,4 linked polymer vesicle.[3,4]

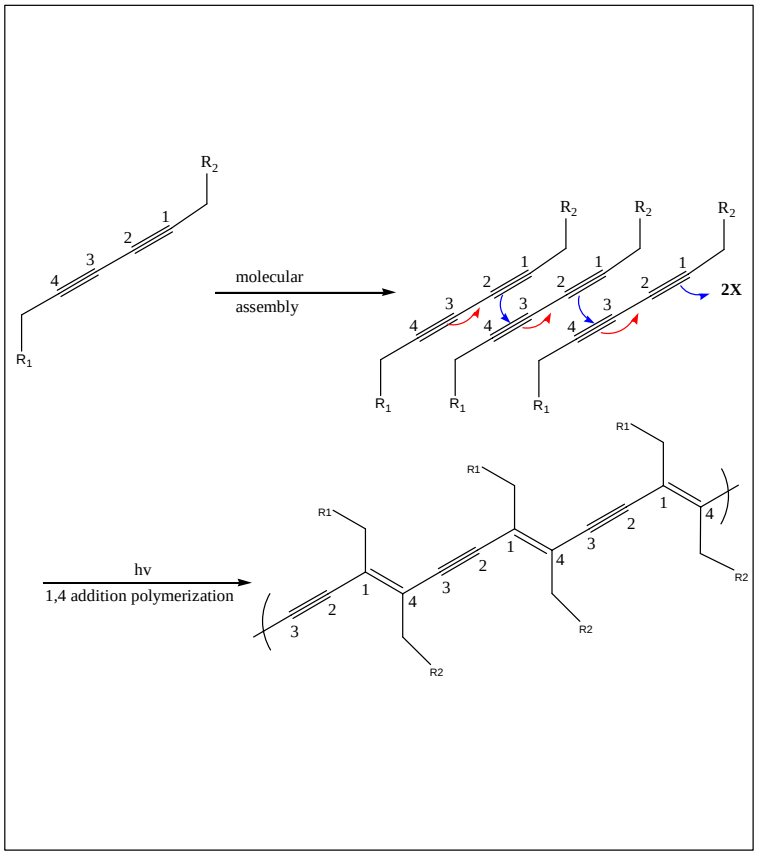


Figure V. General reaction scheme for photopolymerization of diactylenes: (R1 = functionalized alkyl chain, R2= alkyl chain) [3,4,5]

The diacetylene polymerization mechanism is quite different from that of many other polymer systems that usually polymerize in solution or in the liquid state. Only when the material is in a highly ordered state will diacetylene polymerization occur. To allow propagation of the linear chain polymerization through the ordered phase, an optimal packing of the diacetylene units is required.[6] The side groups attached to the

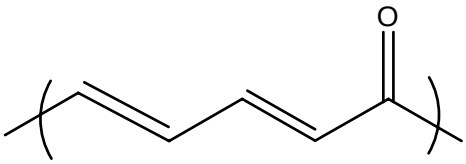
diacetylene units determine the packing of monomers in a crystalline lattice and hence can be tailored by choosing the appropriate substituents or head groups.[6] As shown in Figure V, the polymeric backbone formed is composed of alternating double and triple bonds. Accordingly, the extent of conjugation depends on its monomer conformation. As discussed before, in an optimal conformation, which is substantially controlled by the side chains, the conjugated polymer absorbs light at approximately 650 nm, giving it a blue appearance that is easily visible to the eye. If the effective conjugation length is reduced due to strain and torsion imposed onto the backbone, the absorption maximum is shifted to about 550 nm corresponding to a red color. As stated before, the strain or torsion occurs though perturbations such as pH change, temperature change, and ligand-receptor binding.[3, 4, 5, 6]

Polymer Compounds

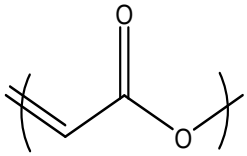
There are many polymer compounds that have been used to synthesize the polymer vesicles. There are many concerns that accompany the choice of which polymer to choose. The application of the polymer vesicle will be the main determinate of which compound will be chosen. Structural features of vesicles as well as properties including stability, fluidity, and intermembrane dynamics are greatly influenced by characteristics of the polymers. One of the key elements that affect the synthesis of the polymer vesicle is stability of structure. Polymer vesicles are known to be more stable than their unpolymerized counterparts. Over the last 20 years a large number of polymerizable amphiphiles have been successfully applied bearing the following moieties shown in Figure VI.[13]

Vinyl

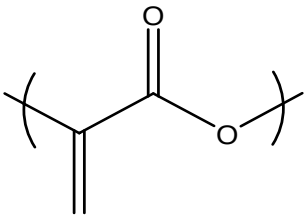
Dienoyl



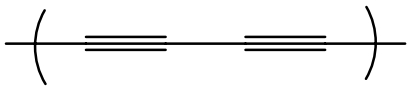
Acrylate



Methacrylate



Diacetylene



Acetylene

Styryl

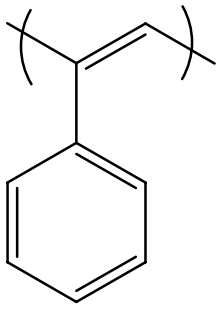


Figure VI: Diacetylene moieties successfully applied to the formation of a stable polymer vesicle.[4]

Molecular Imprinting

Molecular imprinting is a technique for the fabrication of sensory materials that have the capability to specifically recognize a chemical species. Molecular imprinting has become, over the past decade, a favorably accepted tool for the research and development of artificial recognition compounds. Generally, the preparation of molecularly imprinted polymers (MIP) consists of the following four steps:[14]

1) Self assembly of the monomers around the target molecule
2) Polymerization in the presence of a cross-linker
3) Removal of the target molecule by extraction procedures
4) Rebinding of a specific target molecule

These steps are represented in Figure VII below:[14]

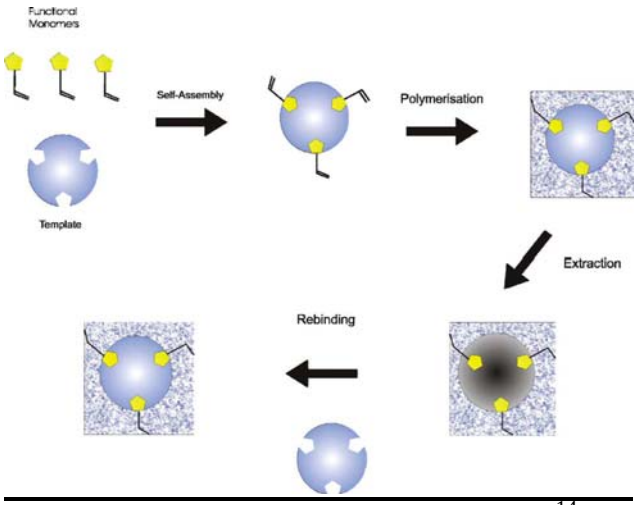


Figure VII. Steps for Molecular Imprinting[14]

Molecular imprinting can be achieved by either noncovalent or covalent interactions. Mosbach established the most widely used strategy based on noncovalent interactions

between specific functional groups on the polymerizable monomers and the template in order to position the monomers in a specific spatial orientation prior to polymerization.[14, 15] After polymerization and removal of the template, the functional groups of the polymeric matrix can then bind the specific target through the same noncovalent interactions. As long as the target has the same noncovalent interaction and characteristics as the original template had then any target is possible. In other words, the ensuing imprints possess a chemical (spatial arrangements or complementary functionality) and steric (size and shape) memory for the template. These enable MIPs to rebind the same target molecule from a mixture of a different target molecules provided that the binding sites of the molecular receptors and the template/target complement each other in size, shape, and chemical functionality. Using the noncovalent imprinting strategy high affinity binding sites can be created. The limitation of noncovalent MIPs is that the template and target must form a sufficient number of noncovalent intermolecular interactions.[14, 15]

A covalent molecular imprinting method was introduced by Wulff. Between a polymerizable monomer and a template molecule a reversible covalent bond is formed. The covalent bonds are cleaved to liberate the template and afterward reformed in order to selectively bond the target. Covalent imprinting is very stable and selective. A limitation of covalent MIPs is that the number of functional groups that can react with the template in the imprint is limited. Very rigid imprint formation occurs at high concentrations. Due to the limited interactions the cleavage and rebinding may be limited and problematic.[14, 15, 16]

In order to counteract the problems with both the noncovalent and covalent MIPs, compounds that can form both noncovalent and covalent bonding have been utilized. Some functional monomers, such as methacrylic acid (MAA) and Cu[1–4-vinylbenzyl]-1,4,7-triazacyclononane]SO4 (STACNCu), have been employed to achieve highly specific affinity and stable MIPs.[14] The most widely used functional monomer is MAA because it can form hydrogen bonds with a number of chemical structures and the binding and removal of target molecules can be performed under mild conditions. Two functional groups are usually present on the functional monomer. At one end of the monomer is a functional group that interacts with the template through noncovalent interactions (e.g., van der Waals forces, hydrophobic interactions, or hydrogen bonding) or reversible covalent interactions.[14] At the other end of the monomer, which does not interact with the template, is a functional group that is able to covalently bind/react with the cross-linker.[15] The monomers around the template are polymerized by the covalent cross-linker, which holds them in place after the template is removed.[15] One problem encountered is that it becomes nearly impossible to remove the template from the imprint when the entire binding site is concealed by the polymer. It is believed that the problem may be minimized by selecting the appropriate cross-linker and concentration.[14] One solution generally used is to apply an excess of cross-linking agent to increase the rigidity of the imprinted matrix. Unfortunately, this sometimes has an adverse effect on the interaction between the template and the matrix, which results in a low recognition capacity. Ethyleneglycol dimethacrylate (EDMA) and trimethylolpropane trimethacrylate are the most commonly employed cross-linkers.[14, 15, 16]

Despite certain limitations MIPs exhibit many promising properties. MIPs are especially unique in their recognition characteristics, which are not affected by acid, base, heat or organic phase treatment. This ability makes MIPs widely used in chromatographic separation, solid phase extraction, catalysis, binding assays, and sensors.[16] In view of the challenges in environmental applications, medicine, food process industries, molecular biology, security, and defense areas there is a great need for analytical methods with high sensitivity and good veracity.[16] Owing to their specificity towards the target molecules and high stability against physicochemical perturbations, molecularly imprinted polymers have been widely employed for these diverse applications.[16] Ultimately, by applying the materials and techniques discussed and manipulating the synthetic routes used, information can be gained in the application of MIPs and PDAs as sensory materials.

CHAPTER III

EXPERIMENTAL

Formation of iodoacetylene: 1-iodo-1-octyne

A mixture of 1-octyne (10.00 g), butyl lithium (1.2 equiv, 68.00 mL), and iodine (1.5 equiv, 34.40 g) was added to a round bottom flask in ethyl ether solvent (200 mL) under nitrogen as follows. First, the 1-octyne solution was added to 200 mL ether in the round bottom flask, which was then placed into liquid nitrogen. Butyl lithium solution (1.6 M) was added slowly drop wise. The solution stirred for thirty minutes at room temperature. It was then put back into liquid nitrogen and the iodine solution was added slowly. It was allowed to stir for thirty minutes at room temperature. The solution was diluted with ether and washed three times with 10% sodium thiosulfate (in aqueous solvent) until excess iodine was removed and the solution turned clear. It was dried on magnesium sulfate and suction filtered. Excess solvent was removed using the rotovap. Lastly, an NMR spectrum was obtained to confirm that the product was 1-iodo-1-octyne; ^{1}H-NMR (CH_3Cl_2-d) 2.4 (t, 2H, CH_2), 2.2 (t, 2H, CH_2), 1.3 (s, 10H, CH_3), 1.6 (t, 3H, CH_3).

Formation of iodoacetylene: 1-iodo-1-dodecyne

A mixture of 1-dodecyne (5 mL), butyl lithium (1.2 equiv, 11.1 mL), and iodine (1.5 equiv, 8.75 g) was added to a round bottom flask in ethyl ether solvent (100 mL) under nitrogen as follows. First, the 1-dodecyne solution was added to 200 mL ether in

the round bottom flask, which was then placed into liquid nitrogen. Butyl lithium solution (1.6 M) was added slowly drop wise. The solution stirred for thirty minutes at room temperature. It was then put back into liquid nitrogen and the iodine solution was added slowly. It was allowed to stir for thirty minutes at room temperature. The solution was diluted with ether and washed three times with 10% sodium thiosulfate (in aqueous solvent) until excess iodine was removed and the solution turned clear. It was dried on magnesium sulfate and suction filtered. Excess solvent was removed using the rotovap. Lastly, an NMR spectrum was obtained to confirm that the product was 1-iodo-1-dodecyne. Impurities were found and column chromatography was employed to remove the impurities. In this case, dry silica was poured into an 18 inch column and hexane was used as the solvent. Twenty mL fractions were collected and all fractions that were found to be pure by thin layer chromatography (TLC) were combined and excess solvent was removed with the rotovap. An NMR spectrum was obtained to confirm product was 1-iodo-1-dodecyne; ^{1}H-NMR (CH_3Cl_2-d) 2.4 (t, 2H, CH_2), 2.2 (t, 2H, CH_2), 1.3 (s, 14H, CH_3), 1.6 (t, 3H, CH_3).

Alternative Synthesis of 1-iodo-1-octyne:

Methanol (300 mL) was added to a round bottom flask with a stir bar. The flask was then placed on an ice bath. Sodium metal (3.00 grams) was cut and put into a hexane bath immediately. Slowly all pieces of the 3.00 grams of sodium metal were transferred to the methanol and dissolved. 1-octyne (19.40 mL) was added slowly to the flask. Finally, iodine (30.00 g) was slowly added to complete the reaction. It stirred overnight

under nitrogen. The solution was treated with 10% sodium thiosulfate (aqueous) to remove excess iodine and until the solution became clear. It was then extracted with dichloromethane. The product was finally dried on magnesium sulfate and suction filtered. Excess solvent was removed using the rotovap. Lastly, an NMR spectrum was obtained to confirm that the product was 1-iodo-1-octyne; ^{1}H-NMR (CH_3Cl_2-d) 2.4 (t, 2H, CH_2), 2.2 (t, 2H, CH_2), 1.3 (s, 10H, CH_3), 1.6 (t, 3H, CH_3).

Formation of iodoacetylene: 1-iodo-1-nonyne

A mixture of 1-nonyne (10 g), butyl lithium (1.2 equiv, 38.6 mL), iodine (1.5 equiv, 30.4 g) was added to a round bottom flask in ethyl ether solvent (200 mL) under nitrogen as follows. First, the 1-nonyne solution was added to 200 mL ether in the round bottom flask, which was then placed into liquid nitrogen. Butyl lithium solution (1.6 M) was added slowly drop wise. The solution stirred for thirty minutes at room temperature. It was then put back into liquid nitrogen and the iodine solution was added slowly. It was allowed to stir for thirty minutes at room temperature. The solution was diluted with ether and washed three times with 10% sodium thiosulfate (aqueous) until excess iodine was removed and the solution became clear. It was dried on magnesium sulfate and suction filtered. Excess solvent was removed using the rotovap. Lastly, an NMR spectrum was obtained to confirm that the product was 1-iodo-1-nonyne. Impurities were found and column chromatography was employed to remove the impurities. In this case, dry silica was poured into a column (18 inch) and hexane was used as the solvent. Twenty mL fractions were collected and all fractions that were found to be pure by TLC were

combined and excess solvent was removed with the rotovap. After the excess solvent was removed no product remained. Therefore no NMR spectrum could be obtained.

Coupling of iodoacetylene with 5-hexyn-1-ol: Diacetylene I

A mixture of 1-iodo-1-octyne (1 g), 5-hexyn-1-ol (0.603 mL), $(PPh_3)_2PdCl_2$ (0.09 g), copper iodide (0.024 g), and DIPA (1.20 mL) (diisopropyl amine) was added to 100 mL tetrahydrofuran (THF). The mixture was stirred under nitrogen at room temperature for 1.5 hours. The solution was then diluted with ethyl ether and washed with 10% HCl (aqueous) twice. It was then washed with brine solution (aqueous NaCl) twice. The solution was dried over magnesium sulfate and suction filtered. Excess solvent was removed using the rotovap. The NMR spectrum showed that the compound had some impurities. This procedure was repeated several times before it was successful. The first time the synthesis was carried out the product was lost, and the second time the product did not react properly. Finally, the third time the NMR spectrum showed that the product was present but impure and so the product was then column purified on a silica column with 10% ethyl acetate/hexane. The fractions that contained the product, as shown by TLC, were combined and the solvent removed using the rotovap. Unfortunately, after removal of the solvent not enough sample was left for confirmation by NMR of a pure product.

Coupling of 1-iodo-5-hexynoic acid with 1-octyne: Diactylene II

A mixture of 1-iodo-5-hexynoic acid (1 g), 1-octyne (0.886 g), $(PPh_3)_2PdCl_2$ (0.128 g), copper iodide (0.0384 g), and DIPA (1.71 mL) was added to 100 mL THF. The mixture was allowed to stir under nitrogen at room temperature for 1.5 hours. The solution was then diluted with ethyl ether and washed with 10% HCl (aqueous) twice. It was then washed with brine solution (aqueous NaCl) twice. The solution was dried over magnesium sulfate and suction filtered. Excess solvent was removed using the rotovap. The NMR spectrum showed impurities and column chromatography was carried out using a 50% ethyl acetate/ 50% hexanes mixture to elute the product. As no product was recovered, successive elution with 20%, 30%, 40%, and 50% ethyl acetate with hexane as solvent was used, although without success.

Formation of Mesityl Acetylene Unit: Acetylene Compound I

A mixture of 4-pentyn-1-ol (5.56 mL), mesityl chloride (4.60 mL), and triethylamine (8.35 mL) was added to a round bottom flask with 100 mL dichloromethane at room temperature. The solution was heated and stirred under reflux for two hours. The solution was then poured into another flask that was on ice. Next, it was washed 3 times with 100 mL deionized water and then washed 3 times with 100 mL sodium bicarbonate solution. The solution was washed again 3 times with 100 mL deionized water, then dried on magnesium sulfate and suction filtered. Excess solvent was removed using the rotovap. Lastly, an NMR spectrum was obtained to confirm that

the product was the target compound; ^{1}H-NMR (CH_3Cl_2-d) 3.0 (s, 3H, CH_3), 4.4 (t, 2H, CH_2), 1.9 (q, 2H, CH_2), 2.4 (m, 2H, CH_2), 2.0 (t, 1H, CH).

Formation of iodoacetylene: 5-iodo-1-pentyne

A mixture of Acetylene Compound I (6.43 g) and sodium iodide (17.82 g) was added to a round bottom flask with 120 mL acetone. The solution was stirred and refluxed overnight. Finally, the solution was filtered and concentrated using the rotovap. An NMR spectrum confirmed that the 5-iodo-1-pentyne was formed; ^{1}H-NMR (CH_3Cl_2-d) 3.3 (t, 2H, CH_2), 2.3 (t, 2H, CH_2), 2.0 (m, 2H, CH_2), 2.0 (m, 2H, CH_2).

Formation of Triethyl Ammonium Acetylene Unit: Acetylene Compound II

A mixture of 5-iodo-1-pentyne (11.42 g) and 100 ml acetonitrile were added to a round bottom flask and stirred till combined. Slowly and dropwise 60 mL of triethyl amine (TEA) was added to the round bottom flask. The solution was heated and refluxed overnight. The solution was washed and extracted 3 times with 200 mL ethyl ether. The product was concentrated and NMR spectroscopy confirmed the presence of product with excess acetonitrile as impurities. Recrystallization was used to remove the excess solvent. In the first attempt at recrystallization the solid product was added to ethyl acetate but it would not dissolve. In the second attempt at recrystallization the solution was added to ethanol and heated with a heat gun to dissolve. An NMR spectrum showed that this method was not successful at removing the excess acetonitrile. Despite the impurity further experiments were carried out with this product.

Coupling of Acetylene Compound II with 1-iodo-octyne: Diacetylene III

A mixture of 1-iodo-octyne (3.48 gram), acetylene compound II (1.87 g), $(PPh_3)_2PdCl_2$ (0.31 g), copper iodide (0.084 g), and DIPA (4.14 mL) was added to 100 mL THF. The mixture was allowed to stir under nitrogen at room temperature overnight. The solution was then diluted with ethyl ether but some solids would not dissolve even when using the heat gun. The solution was refluxed for 1 hour but still some components did not dissolve. The ether was removed and instead the mixture was worked up in dichloromethane and washed with 10% HCl (aqueous) twice. It was then washed with brine solution (aqueous NaCl) twice. The solution was dried over magnesium sulfate and suction filtered. Excess solvent was removed with the rotovap. The NMR spectrum showed impurities, so column chromatography with packed silica and detection by TLC were used to separate the product from the impurities. First 3% methanol/dichloromethane was used as the column solvent. The methanol concentration was then increased to 10% after about 20 fractions were collected. Only 3 fractions showed product by TLC. Those fractions were combined and concentrated using the rotovap. The NMR spectrum showed that the compound was not the desired product. This synthetic route was carried out again with the same reactants but refluxed for 3 hours instead of one. In the end, the yield was too small to run a column so the synthesis was repeated again using 3 times the starting material as used before. Column chromatography was carried out using this larger amount of product, which also showed impurities. 3% methanol/ dichloromethane was initially used to elute the column and this was later increased to 20% methanol/ dichloromethane, without success. Finally 100%

dichloromethane was used to elute the column. No fractions containing product were ever collected from the column.

Formation of polymer vesicles with 10, 12 pentacosadiynoic acid:[17]

A diacetylene moiety (10, 12 pentacosadiynoic acid) was purchased from Sigma Aldrich and used for formation of polymer vesicles with and without a molecular imprint. To five vials (100 mL each) deionized water was added to 2/3 of the way full. Then 100.00 mg of 10, 12 pentacosadiynoic acid was added to each vial. The vials were capped and submerged into a water bath set at 70°C and sonicated for 30 minutes until the milky color of the solution dissipated. The absence of the milky color indicates that the 10, 12 pentacosadiynoic acid was fully dissolved in the solution. The vials were then put into a 4°C refrigerator overnight. They were then exposed to UV light for about 30 seconds. 3 of the 5 vials turned a pale blue, while the others turned a milky blue color and were discarded. The clear blue color indicated vesicle formation. To remove water from the newly formed vesicles the solutions were transferred to round bottom flasks and concentrated using the rotovap. Several rotovap temperatures, 80^{o}C, 50 ^{o}C, and 47 ^{o}C, were used in an attempt to control polymer degradation with variable results. To remove water quickly the rotovap heater for the first round bottom flask was set at 80°C. The 80°C temperature was too hot for the polymer vesicles and resulted in the vesicles turning red, indicating a sensory material that was useless for further study. The next round bottom flask was set at 50°C, but these vesicles turned a semi-red color. The last round bottom was set at 47°C to remove part of the water and then placed under a

vacuum to remove the rest of the water overnight. The polymer vesicles were then resuspended in deionized water and NMR spectroscopy performed. The NMR spectrum only showed a water peak and formation of product could not be confirmed.

Formation of a molecularly imprinted compound:[16]

Set of 4 vials obtained along with the octadecyl methacrylate compound shown below in Figure VIII:

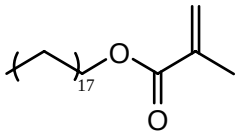


Figure VIII. Octadecyl Methacrylate

To a set of 4 vials a mixture of acetonitrile (1.5 mL), methacrylic acid (MAA) (0.11 g), the octadecyl methacrylate(0.04 g), 2,2'-azo-bis-isobutyronitrile (AIBN) (0.02 g), caffeine (0.03 g), and ethylene glycol dimethacrylate (EGDMA) (1.20 mL) was added and then each vial was flooded with nitrogen for 1 minute and capped. The vials were heated in a 70°C water bath for 10 hours. Excess solvent was removed with the rotovap and 5 mL of methanol were added to each vial. The solution was then vacuum filtered and a solid was obtained from each vial.

Esterification of stearic acid:

In a round bottom flask stearic acid (5.00 g), ethanol (50.10 mL), sulfuric acid (2.50 mL) were mixed at 70°C and refluxed overnight. The solution was concentrated and dissolved in ethyl ether. Next, the solution was washed 3 times with 100 mL

deionized water. It was then washed 3 times with 100 mL saturated sodium bicarbonate and washed with deionized water again. The solution was dried with magnesium sulfate and filtered. Finally, it was concentrated on the rotovap and confirmation of the product was given by the NMR; ^{1}H-NMR (CH_3Cl_2-d) 4.0 (t, 2H, CH_2), 2.3 (t, 2H, CH_2), 1.3 (m, 3H, CH_3), 0.9 (t, 3H, CH_3).

Esterification of 10, 12 pentacosadiynoic acid:

In a round bottom flask 10,12 pentacosadiynoic acid (10.00 g), ethanol (150.00 mL), and sulfuric acid (7.50 mL) were mixed and refluxed overnight at 90°C. The solution was concentrated and dissolved in ethyl ether. Next, the solution was washed 3 times with 100 mL deionized water. It was then washed 3 times with 100 mL saturated sodium bicarbonate and washed with deionized water again. The solution was dried with magnesium sulfate and filtered. Finally, it was concentrated on the rotovap and confirmation of the product was given by the NMR; ^{1}H-NMR (CH_3Cl_2-d) 4.0 (t, 2H, CH_2), 2.3 (t, 2H, CH_2), 1.3 (m, 3H, CH_3), 0.9 (t, 3H, CH_3).

Analytical methods:

During all aspects of the research the main analytical technique used to confirm results of our synthesis was NMR spectroscopy. Specifically proton NMR (^{1}H-NMR) was the technique used for identification purposes. A Jeol 500 MHz NMR spectrometer (JNM-ECA500) was used to confirm products. Most of the samples were prepared in d-chloroform, d-water, or d-methanol.

For purification purposes gravity column chromatography was utilized when the NMR spectrum showed impurities. Packed 200 mesh silica was loaded into a glass chromatography tube (18 inches). The fractions from the column were collected and TLC was used to confirm the fraction that contained the purified product.

CHAPTER IV

RESULTS AND DISCUSSION

As stated, two main projects were pursued, the synthesis of the iodoacetylenes and the formation of the molecularly imprinted compound. Several iodoacetylenes were prepared with partial success in purification. Similarly there was partial success in preparing imprinted compounds, as there was evidence that they formed, although purification was problematic.

Iodoacetylenes

The first thesis project was to synthesize several iodoacetylenes with the intention of forming a diacetylene moiety. Reactions were carried out between 1-octyne, 1-nonyne, or 1-dodecyne and iodine to form the target compounds. Figure IX shows the compounds that were successfully synthesized (1-iodo-1-dodecyne,1-iodo-1-octyne).

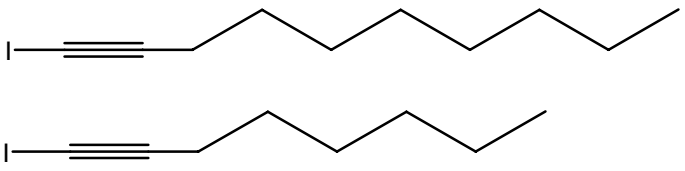
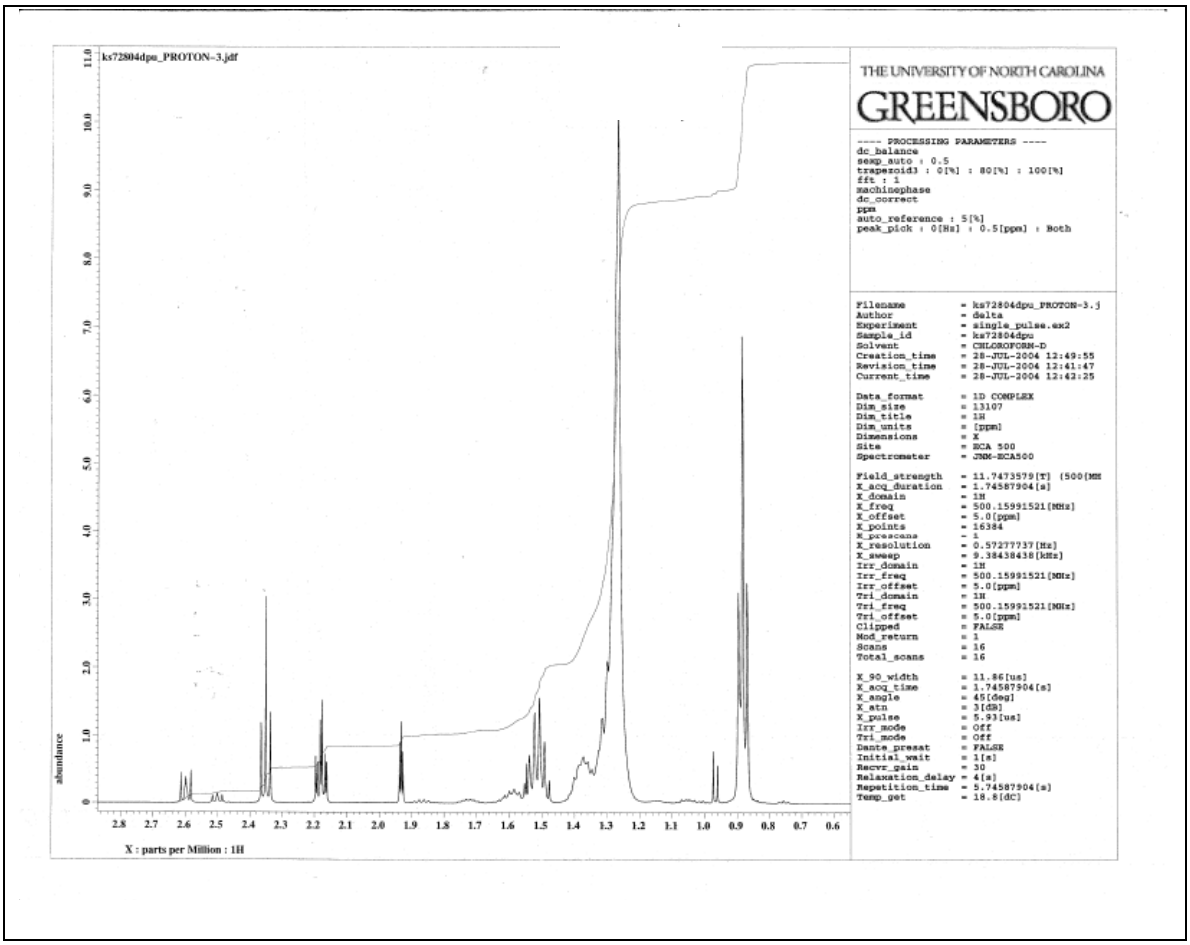


Figure IX. Top: 1-iodo-1-dodecyne, **Bottom:** 1-iodo-1-octyne

Two methods of synthesis were used for the formation of 1-iodo-1-octyne. An alternative synthesis procedure to make 1-iodo-1-octyne was followed because it required fewer steps and was faster than the first method. This route was used many times to make several batches for experimental use.

NMR spectroscopy was used to confirm that the products were successfully synthesized. NMR Spectrum I shows the spectrum for 1-iodo-1-dodecyne.



NMR SPECTRUM 1. 1-iodo-1-dodecyne

The next step in the thesis project was to couple an iodoacetylene with another compound to form the diacetylene product. To achieve this, 1-iodo-1-octyne was coupled with 5-hexyn-1-ol. Figure X shows the target product that was desired (Diacetylene 1).

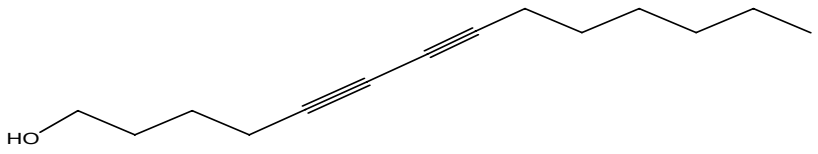


Figure X. Diacetylene 1: Coupled product of 1-iodo-1-octyne and 5-hexyn-1-ol

The NMR spectrum showed that the compound had some impurities. Although this experiment was repeated three times, the product was not recovered. Not enough product was left after the solvent was removed to confirm the presence of the product by NMR.

The same coupling route used to form a diacetylene moiety in the previous experiment was used to produce a second diacetylene moiety, by coupling 1-iodo-5-hexynoic acid and 1-octyne. Figure XI shows the target compound of this synthesis (Diaceylene II).

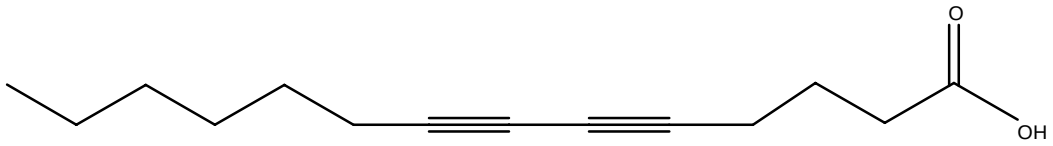


Figure XI. Diacetylene II: Coupled product of 1-iodo-5-hexynoic acid and 1-octyne

The NMR spectrum showed that the compound had some impurities. Column chromatography and TLC did not successfully separate the product from the impurities. The product was apparently lost on the column. No product came off as determined by TLC.

Another synthesis was employed for a different coupling compound. This reaction was between 4-pentyn-1-ol and mesityl chloride. Figure XII shows the intended target compound for this synthesis (Acetylene Compound I).

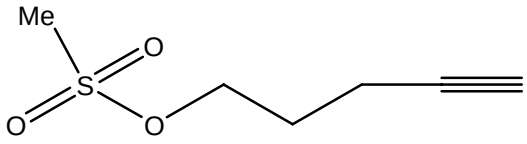
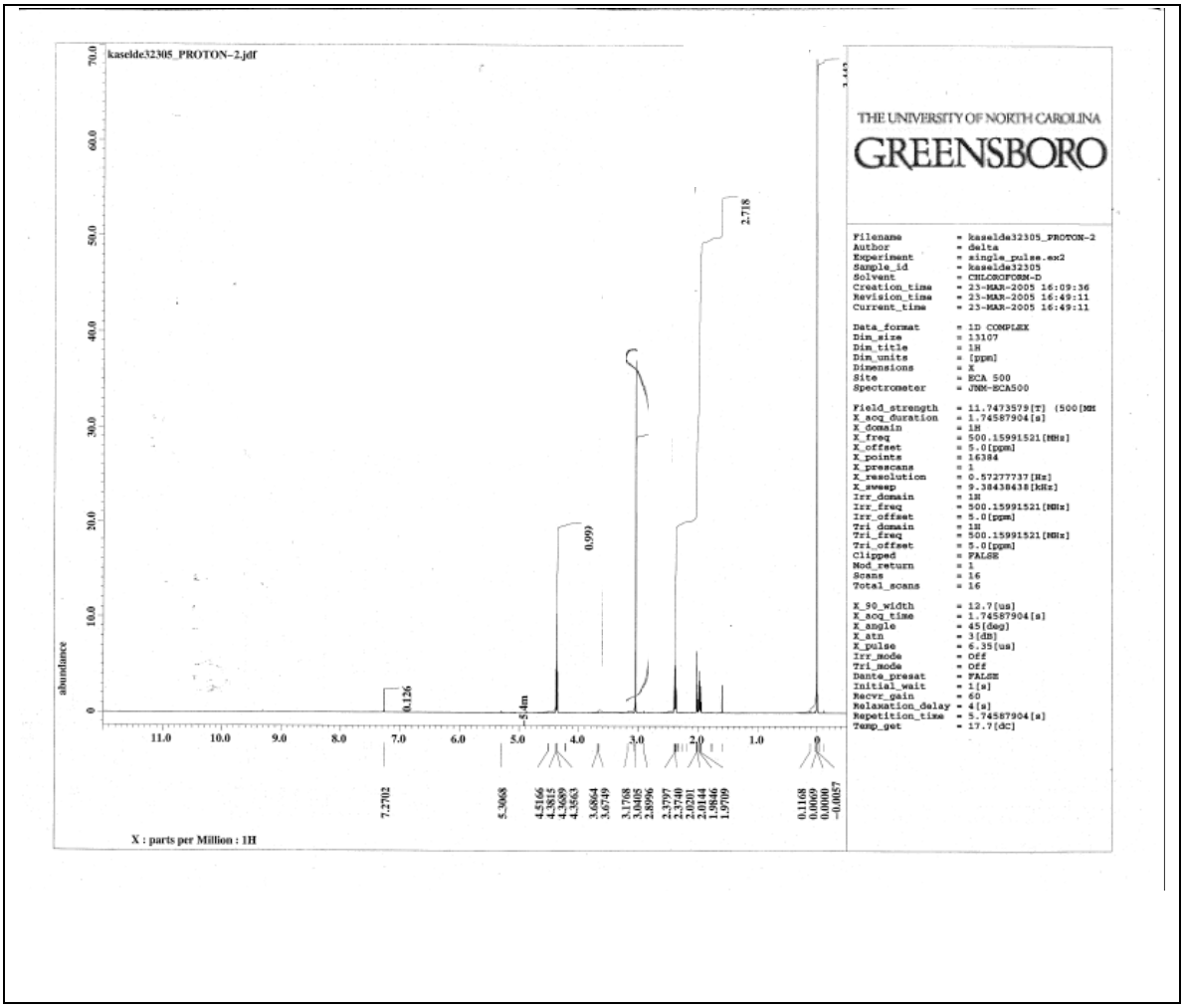


Figure XII. Acetylene Compound I: Target product for the reaction between 4-pentyn-1-ol and mesityl chloride

The NMR spectrum confirmed that the target product was synthesized (NMR Spectrum II) so the product was used for further synthesis.



NMR SPECTRUM II. Acetylene Compound I

In continuation of synthesizing a new coupling compound, the next step was to replace the mesityl group of the Acetylene Compound I with an iodine group to form 5-iodo-1-pentyne. The target compound (5-iodo-1-pentyne) is shown in Figure XIII.

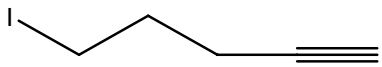


Figure XIII. Target compound 5-iodo-1-pentyne

The NMR spectrum showed that the mesityl group was completely removed, as indicated by the absence of the methyl group peaks. Further synthesis continued using the new product as reactant.

In the last synthesis to create a new coupling compound, reaction was carried out between the 5-iodo-1-pentyne (figure XIII) and triethylamine. Figure XIV shows the target compound for this synthesis **(**Acetylene Compound II).

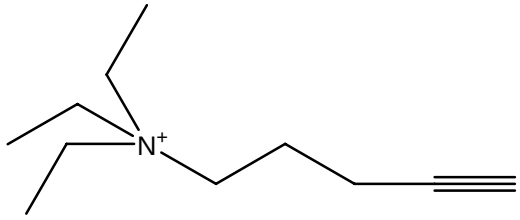
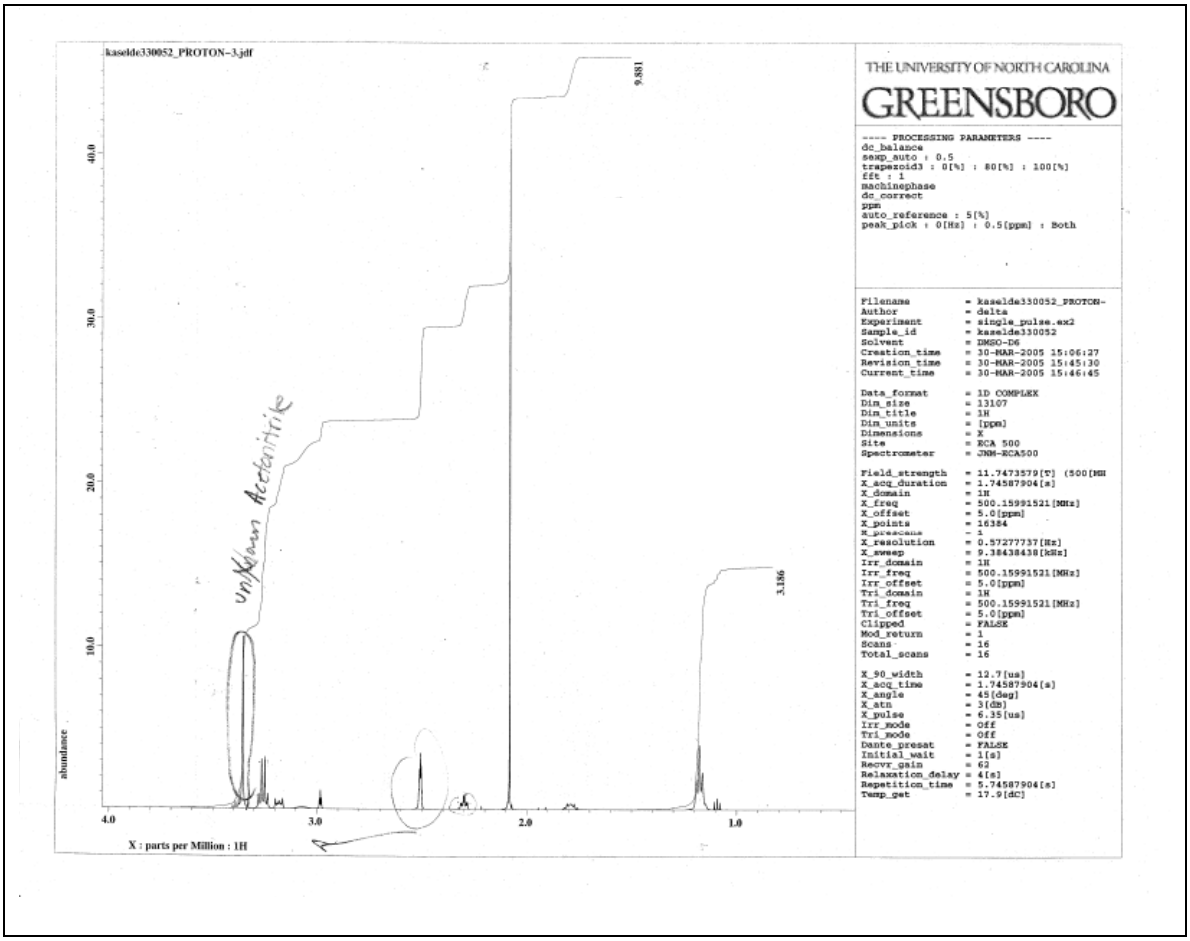


Figure XIV. Acetylene Compound II: Target Coupling Compound

NMR spectroscopy confirmed the formation of Acetylene Compound II, but an impurity, which was believed to be acetonitrile, was also present. The product was

recrystallized, but this was not successful at removing the impurity, as judged by NMR (NMR Spectrum III).



NMR SPECTRUM III. Acetylene Compound II

Despite the presence of an impurity, which was believed to be excess acetonitrile, the impure product was used in a reaction to synthesize Diacetylene III, shown in Figure XV. The reaction was carried out between the impure coupling compound Acetylene Compound II and 1-iodo-1-octyne that had been synthesized previously.

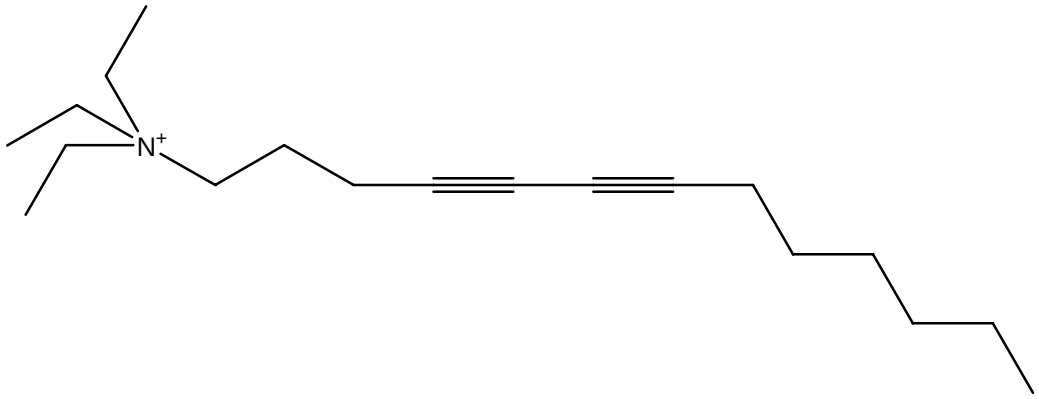
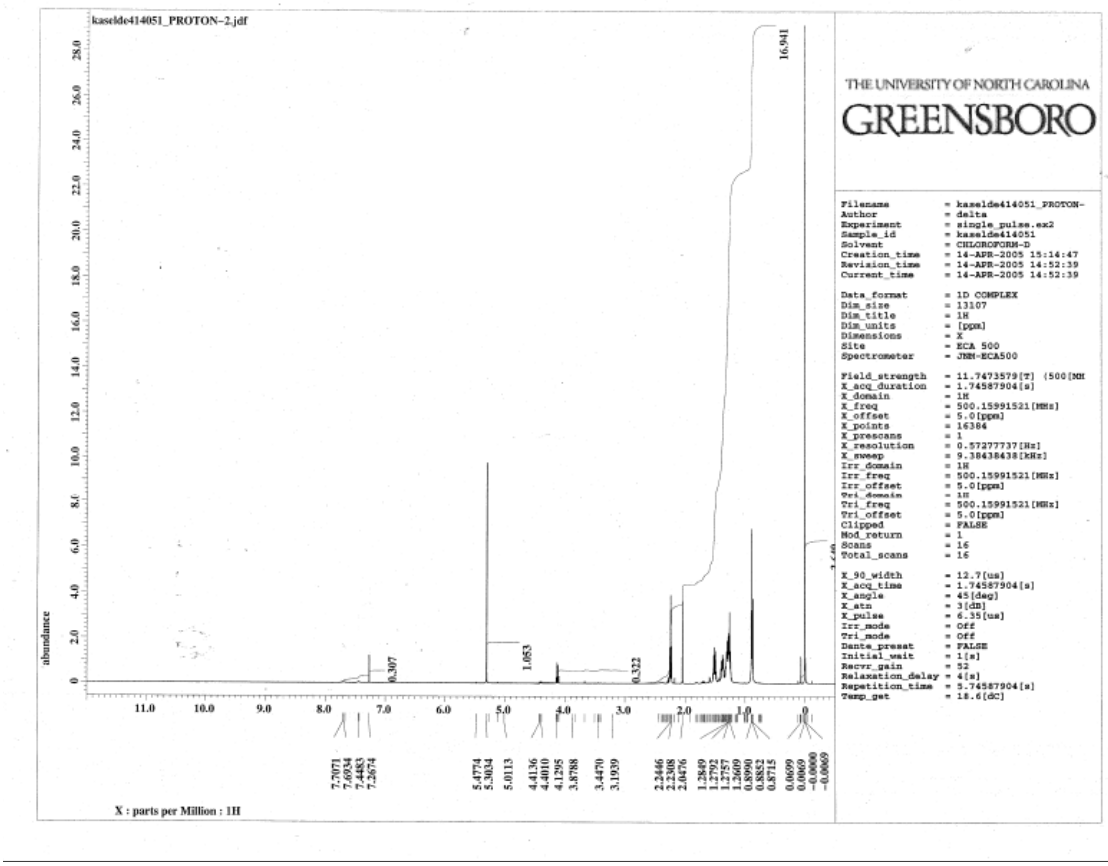


Figure XV. Diacetylene III: Target Diacetylene Compound

The NMR spectrum showed that the product had some impurities. Column chromatography was carried out and fractions that showed product by TLC were concentrated. However NMR spectroscopy showed that the target coupled compound (Diacetylene III) was not obtained.

The coupling route used for the above compound was used again but the reaction mixture was refluxed for a longer time in order to synthesize Diacetylene III shown in Figure XV. The NMR spectrum of the product showed it to be impure (NMR Spectrum IV). Column chromatography was not successful in purifying the product.



NMR SPECTRUM IV. Diacetylene III

Molecular Imprinted Compounds

The second major project involved the formation of polymer vesicles and polymer vesicles with molecular imprints. Polymer vesicles were formed using a commercially available diacetylene (10,12-pentacosadiynoic acid) as described in Experimental. Visual observation of a blue solution confirmed vesicle formation, but NMR spectroscopy was required to validate the presence of vesicles. In the many trials of making the polymer vesicles some problems were encountered in this confirmation process. In order to carry

out NMR spectroscopy the water needed to be removed. Unfortunately, the only feature the NMR spectra showed was a water peak. This synthesis was repeated many times varying temperatures to obtain the best blue color indicating vesicle formation and varying the resuspension processes, which included carrying out the reaction in D_2O. However, none of the adjustments were able to solve the problem of the water peak versus the vesicle peaks and vesicle formation was not confirmed by NMR, only by visual observation.[17]

Next, the formation of a molecularly imprinted polymer vesicle was experimented with in order to test the remote stimuli response of the polydiacetylene in vesicle formation. The same vesicle formation procedures were used but with the addition of the molecular imprinting compound shown in Figure VIII. In the first attempt none of the vials showed a blue color. The experiment was carried out again using D_2O as solvent and increasing the 10, 12 pentacosadiynoic acid to three times the original amount. The solution turned blue after UV exposure for 30 sec. This confirmed vesicle formation and to confirm the presence of the molecular imprinted vesicle an NMR spectrum was obtained. However, the same result as before was found in that the concentration of the water was overwhelming and the presence of the molecular imprinted compound could not be confirmed by NMR spectroscopy.[16]

Another route for polymer vesicle formation was investigated because of a unique characteristic we observed for certain diacetylene moieties. In the research sources previously investigated it was believed that the color change from blue to red was irreversible, indicating that once the stimulus was applied and the color change occurred

that the polymer vesicle was no longer an active sensor. [19] However, it was found in the literature that when a hydrazide group was attached to the diacetylene moiety this blue to red color change became reversible and the polymer vesicle could become an active sensor again.[19] This instantly became an area of synthesis to be explored with the goal of synthesizing two new hydrazide compounds. The target compounds for this project (Hydrazide Compounds I and II) are shown in Figure XVI.[18, 19]

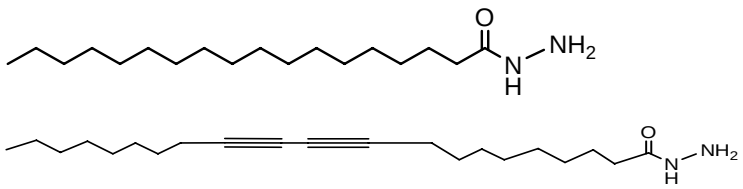


Figure XVI. Hydrazide Compounds I and II: Target Hydrazide Compounds

In order to synthesize these two target compounds esterification of stearic acid and 10, 12 pentacosadiynoic acid were implemented. In both cases synthesis was confirmed by NMR spectroscopy. Reaction was then carried out between these ester products and hydrazine hydrates to form the target hydrazide Compound I seen in Figure XVI. For the stearic acid hydrazide product NMR spectroscopy showed that the reaction had not gone to completion, even after refluxing at a higher temperature for longer time. For the 10, 12 pentacosadiynoic acid hydrazide Compound II, the NMR spectrum and TLC showed that very little product had formed. The NMR spectrum of the product obtained from the second synthesis showed impurities that could possibly have been

excess ethanol.[18, 19] Upon further analysis and after some other experiments had been carried out with this compound it was found that comparative spectra of a hydrazide compound in the literature did not match the NMR spectra obtained. Therefore, the subsequent reactions that were performed were carried out with a compound that had been incorrectly identified. These reactions included making a polymer vesicle following the same procedures described in the experimental section.

CHAPTER V

CONCLUSION

In the end, three iodoactylenes (1-iodo-1-dodecyne, 1-iodo-1-octyne, 5-iodo-1-pentyne), and two acetylenes (Acetylene Compounds I and II) were successfully synthesized. All these compounds were successfully employed in further experiments to make different diacetylene moieties (Diacetylenes I through III) that can be used for vesicle formation. According to the NMR spectra the reactions were a success. On the other hand, further experiments will need to be carried out to develop better purification techniques to produce viable products. Next, polymer vesicles with and without molecular imprints were successfully synthesized with the help of commercially available starting materials. The polymer vesicles were confirmed by visual observation and with more time better purification methods can be worked out to obtain the desired products.

The experimental successes and failures both contributed to the goal of creating a synthetic strategy for the application of polydiacetylenes in sensory materials. The synthetic strategy employed for most experiments worked to a degree and, with more time and understanding, a viable polydiacetylene can be synthesized. Overall, major headway can be accomplished with better purification and analytical techniques. Ultimately, these successes will help to lead to a polymer vesicle that can be used as a novel sensory material.

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