Selective, Radical-Mediated Additions of Thiols to Alkenes in the Presence of Protected Alkynes

by

Stuart Thomas Merriman Pasch
Class of 2014

A thesis submitted to the faculty of Wesleyan University in partial fulfillment of the requirements for the Degree of Bachelor of Arts with Departmental Honors in Chemistry

Middletown, Connecticut April, 2014
Acknowledgements

I would first like to thank Professor Northop for his seemingly endless patience and knowledge. You taught me everything and without you I would never have been able to accomplish this level of research. Since I arrived as a wide-eyed freshman you have been both my greatest resource as well as an inspiration, constantly reminding me why I love chemistry.

To the other members of the Northrop Lab: Rod, Merry, Umesh, Stephen, Charlie, Alex, and Rohit. Thank you for your daily patience and guidance. You were the support that helped me get through all of those tricky columns. I really enjoyed getting to know all of you.

Thank you so much mom and dad for your encouragement and logistical support. Shuttling me back to school so many times late at night was immeasurably helpful and meant so much.

Thank you to the Wesleyan University Department of Chemistry, especially Roslyn and Sarah, which has been so flexible and given me so many resources throughout this whole process. And finally I want to thank my readers Professors Bolton, Northrop, and Novick who, against all of their better judgment, kindly agreed to read my thesis.
Abstract

The addition of thiols to alkenes (thiol-ene reactions) and thiols to alkynes (thiol-yne reactions) is rapidly expanding field since it shows great promise as a powerful pathway for polymer and macromolecular synthesis. The current limitation for these reactions is the ability to carry out selective thiol-ene and thiol-yne additions, particularly within mixtures of several thiol, alkene, or alkyne components (ternary systems). Thiol additions in these competitive ternary systems result in complex mixtures of products. Previous studies have shown that sequential selective addition of a thiol to electron poor Michael acceptors is possible by first using basic conditions followed subsequently by a radical addition. Through the use of triisopropyl silyl protecting groups bound to terminal alkynes, it is possible to sterically disfavor the addition of thiols to alkynes while still allowing thiol-ene additions. This protocol will allow for the addition of two different thiols though a two step radical pathway. The two step radical addition allows for broader molecular tailoring of complex systems and synthetic flexibility in the choice of different substrates as it is not limited by the electron density of the reacting alkene.
# Table of Contents

Acknowledgements ................................................................................................................................. i

Abstract ...................................................................................................................................................... ii

Table of Contents ........................................................................................................................................ iii

**Chapter 1: Introduction and Background** ............................................................................................... 1

  1.1 History and Importance of Click Chemistry ....................................................................................... 2
  1.2.1 The Evolution of Click Reactions: CuAAC Reactions ................................................................. 6
  1.2.2 The Evolution of Click Reactions: Thiol-ene and Thiol-yne Reactions ............................... 8
  1.3 Limitations and Expansion of Thiol-ene and Thiol-yne Mechanisms ............................................. 11
  1.4 Our Approach ..................................................................................................................................... 13

**Chapter 2: Results and Discussion** .................................................................................................... 15

  2.1.0 Choice of Test Substrates .............................................................................................................. 16
    2.1.1 Synthesis of Di-ene 1 ............................................................................................................... 18
    2.1.2 Synthesis of Maleimide 2 ........................................................................................................ 19
  2.2 Test of Two Triisopropyl Silyl Protected Molecules ........................................................................ 21

**Chapter 3: Conclusion and Future Work** ............................................................................................. 28

Experimental ................................................................................................................................................ 33

Spectroscopic Data ...................................................................................................................................... 43

Bibliography .................................................................................................................................................. 52
Chapter 1: Introduction and Background
1.1 History and Importance of Click Chemistry

The ideal chemical reaction is specific to one functional group, highly efficient, and performed without the need of harsh reaction conditions. Most chemical reactions are do not meet any of these qualifications. Recently “click” reactions have been defined to be reactions that do possess these “ideal” reaction characteristics. The following definition of click chemistry, described originally by Sharpless\(^1\) in 2001, was codified mostly in terms of forming carbon-heteroatom bonds that are prevalent in natural systems: “The reaction must be modular, wide in scope, give very high yields, generate only inoffensive byproducts that can be removed by nonchromatographic methods, and be stereospecific (but not necessarily enantioselective). The required process characteristics include simple reaction conditions (ideally, the process should be insensitive to oxygen and water), readily available starting materials and reagents, the use of no solvent or a solvent that is benign (such as water) or easily removed, and simple product isolation. Purification if required must be by nonchromatographic methods, such as crystallization or distillation, and the product must be stable under physiological conditions. […] Click processes proceed rapidly to completion and also tend to be highly selective for a single product: we think of these reactions as being ‘spring-loaded’ for a single trajectory.”\(^2\) It was this definition that led to the development of the field of click chemistry.

Many of the substrates used in click chemistry are well known but it is the way in which these substrates are combined, particularly the catalysts and conditions used, that give this new classification of reactions. As a result the reaction schemes
of click chemistry have been applied to many areas of chemical development that are beyond the scope of the original biological and biomedical focus. Macromolecular and materials chemistry have been particularly impacted by advances in click chemistry. Given important differences in the reactivity of polydisperse macromolecules as compared to discrete small molecules, the definition of click chemistry had to be modified to account for the new synthetic conditions of macromolecular polymer systems (Figure 1).

**Figure 1.** Overlap of Click Chemistry Definitions
(from reference\(^2\))

Two key aspects that must be considered when expanding the original definition of click chemistry to macromolecular synthesis are reactant stoichiometry and large scale purification.\(^2\) Both of these conditions are well exemplified in the
synthesis of dendrimers. A dendrimer is a branching macromolecular polymer that grows layer by layer from a central core (Figure 2).

![Diagram of dendrimer growth]

**Figure 2.** Exponential Growth of Dendrimers With Each Generation

Due to the high specificity of click pathways, click chemistry is useful for dendrimer growth. To ensure symmetrical growth, dendrimer synthesis requires precise reactant stoichiometry to ensure that each individual reaction goes to completion. It is also important that a minimal excess of reactant is used to reduce the possibility of forming unwanted side products. Because of the large number of reactions occurring simultaneously, any reaction inefficiency will have a large affect in the overall yield of the product. If the efficiency of the dendrimer growth reaction is 95.0% per functional group, then after 16 reactions the final yield drops to a mere 44.0%. Thus reactions with efficiencies of 99.9% are necessary to ensure a high yielding and monodisperse product (Table 1).

<table>
<thead>
<tr>
<th>Number Reactions</th>
<th>80%</th>
<th>90%</th>
<th>95%</th>
<th>99%</th>
<th>99.9%</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>64%</td>
<td>81%</td>
<td>90.3%</td>
<td>98.0%</td>
<td>99.8%</td>
</tr>
<tr>
<td>4</td>
<td>41%</td>
<td>65.6%</td>
<td>81.5%</td>
<td>96.1%</td>
<td>99.6%</td>
</tr>
<tr>
<td>8</td>
<td>16.8%</td>
<td>43.1%</td>
<td>66.3%</td>
<td>92.3%</td>
<td>99.2%</td>
</tr>
<tr>
<td>16</td>
<td>2.8%</td>
<td>18.5%</td>
<td>44.0%</td>
<td>85.2%</td>
<td>98.4%</td>
</tr>
</tbody>
</table>

**Table 1.** The Effects of Reaction Efficiency on Dendrimer Growth

Large scale purification is also a necessary consideration because as the dendrimers grow in size, traditional purification methods such as flash chromatography become
unable to effectively remove impurities. Rather than invent new methods of purification, different click reaction methods must be developed that can avoid tedious purification protocols all together (e.g. solvent free reaction methods that allow for simple precipitation purification of macromolecules). The current click chemistry protocols are both useful and reliable but this field of research is still being developed, and as a result there is still much to be discovered.\textsuperscript{5,6} Many of the current methods are still limited by specific reaction conditions and substrate requirements. The research herein explore a less restrictive reaction pathway.
1.2.1 The Evolution of Click Reactions: CuAAC Reactions

The advent of click chemistry was not so much a discovery of new functional group transformations but more of a new application of preexisting pathways. Some of the original click substrates have been known for a long time, but these systems were originally inefficient and not enantioselective (Figure 3A). The first “click” reaction was the copper(I) catalyzed alkyne-azide cyclo-addition (CuAAC). Sharpless discovered that with the addition of a copper(I) catalyst this reaction not only became much quicker, but it also gave a highly regioselective product (Figure 3B).

A. 1,3-Dipolar Cycloaddition of Azides and Alkynes

![1,3-Dipolar Cycloaddition of Azides and Alkynes](image1)

reaction rate increases when R² and R³ are electron withdrawing groups
both enantiomers are formed

B. Copper(I) Catalyzed Azide-Alkyne Cycloaddition (CuAAC)

![Copper(I) Catalyzed Azide-Alkyne Cycloaddition (CuAAC)](image2)

only one enantiomer is formed

**Figure 3.** Comparison of Catalyzed and Uncatalyzed Cycloaddition (adapted from reference8)

The CuAAC reaction is thought of as the quintessential click reaction because it is extremely reliable and it was the most widely adopted early on. This pathway is favorable for substrates that are soluble in water or other polar solvents, but in some
cases it is possible under solvent free, neat, conditions. This pathway is limited only to the reactions of alkynes with azides and thus does not provide any versatility in substrate availability. Additionally this protocol is less favorable for any systems that are unable to solubilize the necessary copper(I) catalyst.\textsuperscript{1,9} Thus, the synthesis of some large non-polar macromolecular systems are less accessible by this route. While CuAAC has been successfully and widely adapted to macromolecules and materials chemistry, other click protocols have shown even greater synthetic utility in these areas. Reactions of thiols with alkenes (thiol-ene click) and with alkynes (thiol-yne click), for example, are fast becoming the most desirable methods of materials synthesis using click chemistry.\textsuperscript{1,10,11,12}
1.2.2 The Evolution of Click Reactions: Thiol-ene and Thiol-yne Reactions

Similar to alkyne-azide reactions, the reaction of thiols with alkenes and alkynes is not a new development. Since the early 1900’s thiols have been reacted with alkenes and alkynes to make polymers. Thiol-ene methods, however, fell out of fashion in favor of other methods in the 1930’s-1940’s. Since that time many of these alternative methods have been pushed seemingly to their limits of development. Around the year 2000, thiol-ene/yne chemistry was brought back into popular use with the advent of click chemistry. Due to a wide variety in possible catalysts as well as substrates, thiol-ene and thiol-yne click chemistry has had a broad impact on the synthesis of materials in many different chemical applications: hydrogels and micellar drug delivery, dental restorative and vaccine development, high refractive index optical materials, and lithographic patterning. Additionally the thiol-ene/yne mechanism does not require the use of a copper(I) catalyst, which can be toxic in biological applications.

The catalyzed thiol-ene/yne reaction is highly efficient and highly selective. Figure 4 shows the mechanism of radical initiated thiol-ene and thiol-yne reactions. While only the radical mechanism is shown it should be noted that the reaction can also be catalyzed by certain bases or nucleophiles as well as some solvent promoted conditions. The mechanism involves the formation of a thiol radical (thiyl), from the abstraction of a hydrogen atom initiated by a photocatalyst. This thiyl then attacks an alkene forming a C-S bond and a carbon centered radical. The newly formed carbon radical then abstracts a proton from another thiol resulting in an anti-Markovnikov thiol ether product and another thiyl radical, thus repeating
the cycle (Figure 4A). In the case of the thiol-yne mechanism two thiols are added to give a 1,2-diaddition product formed through a vinyl sulfide intermediate (Figure 4B). \(^7,12,30\)

**A. Mechanism for radicalmediate thiol-ene chemistry**

![Mechanism of thiol-ene reaction](image)

**B. Mechanism for radicalmediate thiol-yne chemistry**

![Mechanism of thiol-yne reaction](image)

**Figure 4.** Mechanism of Thiol-ene and Thiol-yne Reactions  
(Note ‘I’ represents an Initiator)
One prominent advantage of thiol-ene and thiol-yne reactions is that strong C-S bonds can be formed easily under a variety of different conditions (radical, base, nucleophile catalyst, solvated or solvent free, irradiated with light or without, etc.) at ambient temperatures. The ability to form cross-linked or branching molecules by means of the di-thiol addition to alkynes provides further versatility. As a result these systems potentially have a wide application in many different areas of material science.

Commercial applications of thiol-ene chemistry includes photolithography and nanoscale printing. Because the thiol-ene and thiol-yne reactions can be catalyzed by specific UV frequencies, the location of the thiol-ene or thiol-yne can be controlled. Different shapes can be patterned by using an opaque material to block light from areas of the thiol-ene substrates. It is also possible to generate thiol-ene or thiol-yne versions of “soft” lithography (Figure 5). Because these compounds are organic they might have significant benefits over more rigid inorganic photolithography which are required to be more crystalline. In the more immediate future these highly tailored compounds can be applied to macromolecular synthesis.

Figure 5. Thiol-ene Soft Lithography (from reference\textsuperscript{24})
1.3 Limitations and Expansion of Thiol-ene and Thiol-yne Mechanisms

Despite the extensive and ever increasing utility of thiol-ene and thiol-yne reactions across multiple areas of polymer and materials chemistry, there are currently very few means of carrying out selective thiol-ene or thiol-yne reactions. The ability to achieve selective thiol-ene and thiol-yne reactions, particularly within mixtures of several thiol, alkene, or alkyne components (i.e. ternary systems), will be a significant advance that allows greater synthetic control and modularity, leading to an enhanced ability to tailor materials properties.

Recent developments in thiol-ene and thiol-yne chemistry have shown that the reaction of one thiol with one alkene or alkyne in the presence of another is possible only under certain conditions. Electron-withdrawing alkene groups, such as Michael acceptors, are much more reactive under basic conditions. Provided that these electron poor alkenes are paired with electron rich alkynes, it is possible to selectively add thiols to the alkenes under base catalyzed conditions. Subsequent thiol-yne reactions can then occur via a radical pathway.

A more broadly applicable scheme for thiol-ene and thiol-yne reactions, however, would be by a two step radical pathway. The base initiated mechanism often requires some solvent and an electron poor alkene but the radical pathway is viable for essentially any alkene and can be carried out under solvent free conditions using only a photo initiator and light. The difficulty lies in the competitive addition between thiol-ene and thiol-yne additions. A potential solution is to use steric to disfavor one of these functional groups. It is known that both thiol additions occur quickly to terminal alkynes (Scheme 1A), but the reactivity of thiols with an internal
alkyne is generally slower due to a reversible first addition (Scheme 1B).\textsuperscript{30} Additionally it is theorized that the activation energy for radical addition increases with the size of the –R group attached to the alkyne (Figure 6). With the use of a large enough protecting group it might be possible to completely disfavor the addition of thiols to alkynes in the presence of more accessible alkenes.

**Scheme 1.** Reaction Pathways for Internal and Terminal Alkynes

**Figure 6.** Proposed Variation of Activation Energies of Thiol-yné Radical Additions to Silyl Protected Alkynes
1.4 Our Approach

We aim to discover conditions that allow the selective addition of thiol to alkenes (or alkynes) in the presence of another alkyne under purely radical initiated conditions. Under such conditions selective thiol-ene and thiol-yne reactions would no longer be restricted to only electron poor Michael acceptors that determine selectivity. To achieve this goal, we hypothesize that silyl protecting groups, such as triisopropyl silyl (TIPS), can be used to sterically restrict radical reactivity to alkynes, thus imparting selectivity.

Two molecules (Figure 7) were used to test the radical initiated selective thiol addition to alkenes in the presence of protected alkynes. The diallyl-BMPA-TIPS propargyl ether, 1, was synthesized from 2,2-bis(hydroxymethyl)propionic acid (BMPA). This compound was selected because allyl groups react rapidly in thiol-ene reactions. A second target molecule, 2, was made using maleimide as a starting material. Compound 2 was chosen because the maleimide group will react slowly unlike the allyl groups in compound 1. The choice of highly reactive allyl groups

![Figure 7. Target Compounds 1 and 2](image-url)
and a less reactive maleimide will allow the range and scope of selectivity to be tested.

If the thiol-yne reaction can be disfavored through the use of protecting groups, then multiple thiol-ene and thiol-yne reactions can be catalyzed sequentially providing a pathway to tailor individual components and assemble them in a predictable fashion. This molecular tailoring could be used in any number of systems that involve macromolecular construction from individual component parts. Once these pieces have been assembled, the durability of the thiol-ene and thiol-yne bond will prevent any additional reactions from taking place. This research will investigate whether incorporating a large enough protecting group makes it possible to shut down a thiol-yne reaction in the presence of a thiol-ene reaction.
Chapter 2: Results and Discussion
2.1.0 Choice of Test Substrates

Target molecules 1 and 2 were chosen to represent two ends of the spectrum in the kinetics of thion-ene reactivity: thiol-maleimide radical reactions are slow, while thiol-allyl radical reactions are rapid. These two molecules were also chosen because of their small size and short synthetic route. Initially, a trimethyl silyl group (TMS) was chosen as the protecting group for the alkyne. Early investigations showed that TMS could likely work to disfavor thiol-yne radical addition to alkynes (Scheme Exp1 of the experimental section). We found, however, that TMS groups were too labile to successfully carry out many other reactions (Scheme Exp2 of the experimental section). Therefore we switched to the more stable TIPS group.

Scheme 2. TIPS Addition Methods

Two methods for incorporating a triisopropyl silyl (TIPS) group were investigated. In the first method the alkyne was synthesized on the substrate before the addition of the protecting group (Scheme 2). This two step method had very low yields as it required both the synthesis of the alkyne as well as the addition of a large protecting group. Protecting a substrate bound alkyne with TMS was found to be
possible (Scheme Exp3 of the experimental section) yielding 29.3% but the addition of TIPS on the same substrate (Scheme Exp4 of the experimental section) was not effective. With necessity of using the larger TIPS group a different approach was needed. It was found that TIPS acetylene could be used to prepare alcohol 3 with high yield, and the resulting alcohol could be added to a substrate with moderate success. Thus it is more effective to add the alkyne and the protecting group as a preassembled unit. This reduces the number of low yielding steps.
2.1.1 Synthesis of Di-ene 1

Scheme 3. Synthesis of 1

First di-allyl 4 was synthesized by addition of allyl bromide to a BMPA substrate using sodium hydroxide in toluene. Compound 4 was isolated in 95.5% yield without requiring further purification. The TIPS protected alkyne was added using a DCC coupling of 4 to TIPS alcohol 3 under dry inert conditions. The test molecule, diallyl-DMPA-TIPS propargyl ether 1, was purified and collected by flash chromatography using 3% ethyl acetate in hexanes. The pure product (4, 82.4% yield) was confirmed using $^1$H NMR spectroscopy as well as ESI mass spectroscopy. The total yield of compound 1 from starting materials was 78.7%.
2.1.2 Synthesis of Maleimide 2

First, under constant volume conditions, furan was used to protect the carbon-carbon double bond on the maleimide. The use of constant volume ensures that only one enantiomer of furan-maleimide 5 is formed. After heating to 100 °C in ether overnight the product (5) was filtered and collected as a white solid with a 97.0% yield. The solid was confirmed as the desired product by using $^1$H NMR spectroscopy. Next, TIPS propargyl alcohol 3 was added onto the diimide using DIAD and triphenyl phosphene in dry THF. The product (6) was purified by flash chromatography using a hexanes and ethyl acetate solution. It was found that DIAD byproducts move with the same Rf value as the intended product, so any excess DIAD was carried over into the next step. The furan-maleimide 5 was formed using reversible addition and as a result the furan can be removed using heat in toluene. The DIAD from the previous step was successfully removed by flash chromatography because of the change in mobility of test molecule, TIPS maleimide 2. The product was collected with a yield of 60.0% and confirmed by $^1$H NMR spectroscopy as well.

**Scheme 4. Synthesis of 2**
as ESI mass spectroscopy. The total yield of compound 2 from starting materials was 58.2%.
2.2 Test of Two Triisopropyl Silyl Protected Molecules

The reaction of both molecules 1 and 2 was investigated with the same initial thiol, methyl-3-mercaptopropionate (7). Each compound was allowed to react with thiol 7, mixing the reagents in the presence of 2,2-Dimethoxy-2-phenylacetophenone (DMPA) and irradiated with 365 nm light. The standard usage of DMPA is 2% catalyst by total mass of the reactants. These reactions did not require a workup because they were run in solvent free, neat, conditions.

The addition of thiol to compound 1 (Scheme 5) was monitored over four hours by observing the loss of the alkene protons H_d and H_e, at 5.87 and 5.20 ppm respectively each with integrations of four protons, by ^1H NMR spectroscopy. Once the alkene peak was no longer present, the reaction was purified by flash chromatography.

Scheme 5. Synthesis of 10
Figure 8. $^1$H NMR spectroscopy of the Formation of 8

After compound 8 was purified, protons $H_a$ and $H_b$, which correspond to the protected alkyne, remained singlets at 1.06 and 4.71 ppm respectively (Figure 8), indicating no reaction between the thiol and TIPS-protected alkyne had taken place. The complete lack of the alkene multiplets at 5.87 and 5.20 ppm suggest that all of the alkene was consumed during the reaction. Proton $H_c$, originally a doublet of doublet of triplets, is now a pentet integrating to four protons around 1.8 ppm. The terminal alkene proton $H_f$, has moved upfield from 5.20 to 2.59 ppm because it is now adjacent to a sulfur atom. The integral of the methoxy peak at 3.70 ppm corresponds to six protons and this indicates the presence of two equivalents of thiol. The lack of a terminal alkyne further supports that the TIPS group was not removed during the reaction or purification. A mass peak of 649.3 g/mol was observed by ESI mass spectroscopy and agrees with the predicted molecular weight. This confirms that the
TIPS protecting group is still bound to the alkyne while the alkene was successfully reacted with thiol with a 35.5% yield.

![Diagram of chemical structures and NMR spectra](image)

**Figure 9.** $^1$H NMR spectroscopy of the Formation of 9 and 10

The TIPS protecting group on compound 8 was successfully cleaved using 1.0 M TBAF in THF for 20 hours at room temperature. After a workup of ether extraction and a water/brine wash the product was purified using flash...
chromatography. A solution of 5:1 hexanes:ethyl acetate was used followed by a flush with 3:1 hexanes:ethyl acetate. The flush was collected and the solvent was removed by rotary evaporation to give a viscous oil (9). The lack of the large TIPS peak, $H_a$, at 1.06 ppm confirms that the TIPS group was cleaved (Figure 9). The presence of $H_i$ at 2.48 with an integration of one suggests that there is now a proton attached to the alkyne, this further confirms the removal of the protecting group. Additionally the singlet that was at 4.70 ppm, representing $H_b$, has been split into a doublet from long range coupling with terminal alkyne proton $H_i$. A mass peak of 493.2 g/mol observed by ESI mass spectrometry agrees with the predicted mass of 9. This spectroscopic data confirms that a TIPS protecting group was not only sturdy enough to protect the alkyne in compound 8, but it was also labile enough that it was still able to be removed in compound 9 with a yield of 81.2%.

A second thiol was added to the unprotected alkyne of compound 9. Thiol 11, 1-hexanethiol, was added over four hours using 2% DMPA catalyst by total mass of the reactants. The addition of thiol was observed by the loss of $H_b$ and $H_i$ at 4.70 and 2.48 ppm respectively (Figure 9). The multiplets between 4.00 and 4.50 ppm with a total integration of two suggest that $H_b$ is split due to the non-specific addition of thiol. The peak at 3.00 ppm with integration of one proton corresponds to $H_j$, the only single proton present in compound 11. Proton $H_i$ is observed in the multiplet at 2.78 ppm. The evidence for the presence of this proton is that the integration of the peak at 2.78 increased from four to six protons from the previous spectra. A mass peak of 729.4 g/mol observed by ESI mass spectrometry agrees with the predicted mass of 10. This confirms the collection of product with a 79.2% yield. This second
addition of thiol proves that it is possible to selectively and sequentially add two different thiols onto a single substrate only through the use of a radical mechanism. The overall yield of the radical additions was 22.8%, giving an overall yield from starting materials of 18.0%.

Scheme 6. Synthesis of 12

The addition of thiol to compound 2 (Scheme 6) was monitored by $^1$H NMR spectroscopy over five hours. The loss of H$_k$ at 6.75 ppm confirms that the alkene has been entirely consumed (Figure 10). The H$_r$ peak around 3.8 ppm is split into a multiplet because the two protons of H$_q$ are unequal due to chirality. Additionally there is still the presence of a TIPS group and no peak corresponding to an alkyne proton. Thus this compound was most likely synthesized. There are, however, two unknown singlets that appear around 2.1 ppm in the $^1$H NMR spectra that suggests that this product is not entirely pure. A mass peak of 412.2 g/mol agrees with the predicted values for 12. While compound 12 was unable to be fully purified the spectral data suggests that the target compound was successfully made. Further purification is necessary before the TIPS group is removed.
Once compound is successfully purified the TIPS group will be cleaved using TBAF and THF (Scheme 7). Note compound 13 has been successfully made by a base catalyzed pathway before. Once the alkyne has been deprotected it is possible to add a second thiol to the alkyne by the radical mechanism. This will show that the thiol can still be selectively added to a less reactive maleimide while in the presence of a TIPS-protected alkyne.

Figure 10. $^1$H NMR spectroscopy of the Formation of 12

Once compound is successfully purified the TIPS group will be cleaved using TBAF and THF (Scheme 7). Note compound 13 has been successfully made by a base catalyzed pathway before. Once the alkyne has been deprotected it is possible to add a second thiol to the alkyne by the radical mechanism. This will show that the thiol can still be selectively added to a less reactive maleimide while in the presence of a TIPS-protected alkyne.
Scheme 7. Future Reactions of 2
Chapter 3: Conclusion and Future Work
The use of a TIPS group to sterically protect the alkyne in di-ene compound 8 proves that it is possible to use sterics to drive the selective addition of thiols to alkenes in ternary systems. Not only was this successful but the overall yield of these materials was high, 78.7% yield to compound 1 from starting materials and 18.0% from starting materials to complete synthesis of 10, for unoptimized and preliminary methods. While it is unfortunate that the maleimide, 2, has yet to be satisfactorily be purified, there is very strong spectroscopic evidence that the target molecule was made. Future steps for this reaction involve the cleaving of the TIPS group to expose the alkyne and then the second addition of a thiol.

The successful addition of a thiol to an unprotected alkene in the presence of a TIPS protected alkyne demonstrates that there is still much to be discovered in the field of radical mediated thiol-ene/thiol-yne chemistry. While alternative base catalyzed mechanisms can also allow for selectivity in competitive thiol-ene/thiol-yne reactions, they are limited by the necessity of electron poor Michal acceptors. It is possible to synthesize compound 13 using a base catalyzed mechanism, but it does not provide the versatility to synthesize compound 8. Thus, while the base catalyzed mechanism has been more closely studied, it is not the final direction of thiol-ene/yne synthesis.
The next step of this research will be using the TIPS protecting groups to cross link many monomer units (Figure 11) in a two step process. For example, a compound bearing two alkenes and a TIPS-protected alkyne (such as \( \text{1} \)) can be made in large yields over a short period of time. Through the use of a dithiol, the monomer units could be polymerized to give linear polymers with pendant TIPS-protected alkynes. Then, the TIPS could be cleaved and the polymer could be further functionalized by dithiol or substituted using a mono thiol. The ability to functionalize the alkynes after polymerization could result in a much wider range of available uses for these polymers.

**Figure 11. Uses of Two Step Radical Addition**
Mechanically Interlocked Molecules

Another potential application of this system is in rotoxane synthesis. Rotoxanes are macromolecules where a macrocyclic molecule encircles a linear guest molecule and is unable to dethread because of sterically imposing “stopper” groups at each end of the guest (Figure 12). One of the common methods for synthesizing rotoxanes is known as threading followed by stopping. In this method the guest is threaded through the macrocycle by thermodynamics, driven by noncovalent interactions between the macrocycle and the guest (e.g. dialkyl ammonium guests and crown ether rings), before stopper groups are quickly and efficiently added, typically using some sort of click reaction (Figure 13). One key limitation of this protocol under previous thiol-ene and thiol-yne conditions was the necessity of a basic catalyst. Base catalyzed click reactions could destabilize the interactions between host and guest and decrease the favorability of host-guest formation. The use of
radical additions can allow for a reaction protocol in which no base is needed and there would be no disruption of the charge separation. This would allow for more diversity in this set of reactions.

**Figure 13. Structural View of Rotoxanes**

A hypothetical use of selective thiol-ene/thiol-yne reactions in the synthesis of mechanically interlocked polymers is shown in figure 13. In this example, a selective thiol-ene reaction is used to form a mechanically interlocked rotoxane bearing four TIPS-protected alkynes: two off the stoppers of the guest and two off the macrocycle. Deprotection of the TIPS-groups followed by cross-linking with a tetrathiol produces a cross-linked polymer joined by multiple mechanical bonds. It is thought that the added flexibility provided by the translational motion of the macrocycle will allow the cross-linked polymer to retain its strength while exhibiting greater flexibility.
Experimental

Scheme 2. TIPS Addition Methods

Preparation of 3: To a flame dried 100 ml Schlenk flask THF (40 ml) dried with bubbled N₂ and molecular sieves was added. TIPS propargyl (1.93 g, 10.57 mmol) was added and the flask was cooled to -78 °C. To the cooled flask 2.5 M BuLi in hexanes (5.7 ml, 13.74 mmol) was added. To a separate flask paraformaldehyde (0.634 g, 21.13 mmol) was added and flushed with N₂. The dried THF (25 ml) was transferred to the paraformaldehyde flask and then contents were moved to the Shlenk flask by syringe. The reaction was stirred overnight and quenched with 10% HCl before being transferred to a separatory funnel. The product was extracted with 2 x 50 ml of ether. The combined ether extracts were washed with Na₂CO₃ and then back extracted with 2 x 30 ml of additional ether. The combined ether extracts were then dried MgSO₄, filtered, and solvents were removed by rotary evaporation. The product was purified with flash chromatography using 2:1 hexanes:ether. ¹H NMR spectroscopy of the product (2.11 g, 94.0% yield) agreed with values from the literature.³⁴

Preparation of 4: (From Scheme 3) To a flask 2,2-Bis(hydroxymethyl)propionic acid (BMPA) (4.0 g, 29.8 mmol) was dissolved in toluene (60ml, making a 0.5 M solution). Then with slow stirring NaOH (11.92 g, 298 mmol) was added. The allyl-bromide (25.2 g, 208 mmol) was then added and the solution was refluxed overnight.
with vigorous stirring. The solution was then cooled to room temperature and 50 ml of water was added. HCl was added to reduced to the pH of the solution to 1. The toluene was then washed with 2 x 50 ml of water. The organic layer was then dried with MgSO₄, filtered and solvents were removed by rotary evaporation. No further purification was needed. ¹H NMR spectroscopy of the product (6.10 g, 95.5% yield) was consistent with literature values.³⁵

Preparation of 1: (From Scheme 3) To a 3-arm flask 4 (1.31 g, 6.12 mmol), 3 (1.00 g, 4.708 mmol), and DPTS (0.416 g, 1.412 mmol) was added and flushed with N₂. In a separate flask DCC (1.262 g, 6.12 mmol) was added and flushed with N₂ gas. To each flask 10 ml of dry THF was added and the DCC was added to the 3-arm flask with a syringe. The reaction was stirred overnight. The solution was passed through a fritted filter and washed in a separatory funnel with NaHCO₃, brine, water. The crude material was then dried with MgSO₄, filtered, and solvents were removed by rotary evaporation. The crude material was purified with flash chromatography using 3% ethyl acetate in hexanes. The product (1.6 g, 82.4% yield) was collected and confirmed using ¹H NMR spectroscopy. APCI-MS (m/z) [MH]⁺ calculated for C₂₃H₄₁O₄Si, 409.2769 g/mol; found 409.2763 g/mol (ppm error = -1.4); ¹H NMR (300 MHz, CDCl₃) δ ppm 5.87 (ddt, J=17.30, 10.48, 5.46 Hz, 2 H), 5.11 - 5.31 (m, 4 H), 4.74 (s, 2 H), 3.99 (dt, J=5.28, 1.47 Hz, 4 H), 3.53 - 3.63 (m, 4 H), 1.23 (s, 3 H), 1.07 (s, 21 H). ¹³C NMR (CDCl₃, 75 MHz): 173.61, 134.76, 116.43, 101.09, 87.98, 72.23, 71.75, 52.8, 48.37, 18.44, 17.82, 11.02 ppm.

Preparation of 5: (From Scheme 4) Maleimide (5.0 g, 51.51 mmol) and furan (14.03 g, 206.04 mmol) were added to a 250 ml pressure flask along with 80 ml of ether.
The flask was heated to 100 °C and stirred overnight. A pure white solid product (8.25 g, 97% yield) was collected with filter paper. No further purification was needed. $^1$H NMR spectroscopy of the product was consistent with literature values.$^{32}$

Preparation of 6: (From Scheme 4) To a 250 ml 3-arm flask 5 (0.950 g, 5.750 mmol), 3 (1.3434 g, 6.325 mmol), PPh$_3$ (1.6590 g, 6.325 mmol) were added. The system was cooled to 0 °C and flushed with N$_2$. Then DIAD (1.279 g, 6.325 mmol) was added along with dry THF (56.5 ml, making a 0.1 M solution) before the system was warmed to room temperature stirring for 24 hours. Flash chromatography was used to purify the product using one column volume of 4:1 hexanes:ethyl acetate and then switched to 2:1 hexanes:ethyl acetate. The DIAD was avoided but some excess DIAD ran with the product. Collected a contaminated product (2.067 g) as shown by $^1$H NMR spectroscopy.

Preparation of 2: (From Scheme 4) The DIAD contaminated 6 (2.067 g total) was added to a 500 ml flask with toluene (200 ml). The solution was refluxed overnight without a condenser. The toluene was removed by rotary evaporation. The product was purified by flash chromatography using 5:1 hexanes:ethyl acetate. A pure product was collected (1.0 g, 60% yield). $^1$H NMR spectroscopy of the product was consistent with literature values.$^{36}$

Preparation of 8: (From Scheme 5) To a vial 1 (510.2 mg, 1.236 mmol) and 7 (356.6 mg, 2.968 mmol) was added. Additionally 2% of the total mass of the reactants of DMPA was added (17.3 mg). The vial was placed under 365 nm light and stirred for 4 hours. The product was purified by flash chromatography using 5:1 hexanes:ethyl acetate. The pure product (286.7 mg, 35.5% yield) was confirmed by $^1$H NMR
spectroscopy. APCI-MS (m/z) [MH]$^+$ calculated for C$_{31}$H$_{57}$O$_8$Si$_2$, 649.3259 g/mol; found 649.3253 g/mol (ppm error = -0.9); $^1$H NMR (300 MHz, CDCl$_3$) d ppm 4.71 (s, 2 H), 3.70 (s, 6 H), 3.44 - 3.58 (m, 8 H), 2.77 (t, $J$=7.00 Hz, 4 H), 2.59 (m, $J$=7.90, 7.90, 7.90 Hz, 8 H), 1.81 (quin, $J$=6.52 Hz, 4 H), 1.18 (s, 3 H), 1.06 (s, 21 H). $^{13}$C NMR (CDCl$_3$, 75 MHz): 173.64, 172.35, 101.05, 72.28, 69.61, 52.83, 51.75, 48.41, 34.57, 29.48, 28.7, 26.89, 18.48, 11.03 ppm.

Preparation of 9: (From Scheme 5) To a 100 ml flask 8 (286.7 mg, 0.4391 mmol) was dissolved in THF (4.29 ml, making a 0.1 M solution). Then 1.0 M TBAF in THF with 5% water (0.5269 ml, 0.5269 mmol) was added and the reaction was stirred for 20 hours. To the flask 50 ml of ether was added. The ether was washed in a separatory funnel with 25 ml of water and then brine. The ether layer was dried over MgSO$_4$, filtered, and solvents were removed by rotary evaporation. The deprotected alkyne 9 was purified by flash chromatography first using 4 column volumes of 5:1 hexanes:ethyl acetate before flushing with 3:1 hexanes:ethyl acetate. A pure oil (175.7 mg, 81.2% yield) was collected and confirmed by $^1$H NMR spectroscopy. APCI-MS (m/z) [MH]$^+$ calculated for C$_{22}$H$_{37}$O$_8$S$_2$, 493.1924 g/mol; found 493.1934 g/mol (ppm error = 1.9); $^1$H NMR (300 MHz, CDCl$_3$) d ppm 4.70 (d, $J$=2.35 Hz, 2 H), 3.71 (s, 6 H), 3.46 - 3.55 (m, 8 H), 2.78 (t, $J$=7.00 Hz, 4 H), 2.54 - 2.66 (m, 8 H), 2.48 (t, $J$=2.35 Hz, 1 H), 1.82 (quin, $J$=6.60 Hz, 4 H), 1.21 (s, 3 H). $^{13}$C NMR (CDCl$_3$, 75 MHz): 72.49, 69.66, 51.77, 34.61, 29.52, 28.75, 26.92 ppm. Note the sample was not concentrated enough to observe any additional carbon shifts.

Preparation of 10: (From Scheme 5) To a vial 9 (175.7 mg, 0.357 mmol) and 1-hexanethiol, 11, (168.7 mg, 1.427 mmol) was added. Additionally 2% of the total
mass of the reactants of DMPA was added (6.88 mg). The vial was placed under 365 nm light and stirred for 4 hours. The product was purified by flash chromatography using 5:1 hexanes:ethyl acetate. The pure product (207.5 mg, 79.7% yield) was confirmed by $^1$H NMR spectroscopy. APCI-MS (m/z) [MH]$^+$ calculated for C$_{34}$H$_{65}$O$_8$S$_4$, 729.3557 g/mol; found 729.3551 g/mol (ppm error = -0.8); $^1$H NMR (300 MHz, CDCl$_3$) d ppm 4.40 (dd, J=11.29, 4.54 Hz, 1 H), 4.20 (dd, J=11.14, 6.74 Hz, 1 H), 3.70 (s, 6 H), 3.45 - 3.56 (m, 8 H), 2.97 - 3.04 (m, 1 H), 2.73 - 2.83 (m, 6 H), 2.52 - 2.66 (m, 12 H), 1.82 (quin, J=6.52 Hz, 4 H), 1.52 - 1.65 (m, 4 H), 1.22 - 1.44 (m, 12 H), 1.20 (s, 3 H), 0.89 (t, J=6.45 Hz, 6 H). $^{13}$C NMR (CDCl$_3$, 75 MHz): 174.23, 172.35, 72.56, 69.66, 65.26, 51.76, 48.53, 44.68, 34.7, 34.59, 33.33, 31.62, 31.43, 31.39, 29.79, 29.67, 29.5, 28.74, 28.53, 26.9, 22.53, 17.9, 14.02 ppm. Preparation of 12: (From Scheme 6) To a vial 2 (520.0 mg, 1.784 mmol) and methyl-3-mercaptopropionate, 7, (257.3 mg, 2.141 mmol) was added. Additionally 2% of the total mass of the reactants of DMPA was added (15.5 mg). The vial was placed under 365 nm light and stirred for 5 hours. The product was purified by flash chromatography using 5:1 hexanes:ethyl acetate. This Product is yet to be fully purified. APCI-MS (m/z) [MH]$^+$ calculated for C$_{20}$H$_{34}$NO$_4$SiS, 412.1972 g/mol; found 412.197 g/mol (ppm error = -0.6); $^1$H NMR (300 MHz, CDCl$_3$) d ppm 4.30 (s, 2 H), 3.77 - 3.86 (m, 1 H), 3.72 (s, 3 H), 3.08 - 3.28 (m, 2 H), 3.00 (dt, J=13.63, 6.96 Hz, 2 H), 2.66 - 2.78 (m, 2 H), 2.44 - 2.57 (m, 1 H). No $^{13}$C NMR spectroscopy was taken due to a lack of satisfactory purification.
**Exp1. Synthesis of 18**

Preparation of 16: To a vial 25 (83.7 mg, 0.223 mmol) and methyl-3-mercaptopropionate, 7, (35 mg, 0.290 mmol) was added. Additionally 2% of the total mass of the reactants of DMPA was added (2.4 mg). The vial was placed under 365 nm light and stirred for 5 hours. The product was purified by flash chromatography using 10:1 hexanes:ethyl acetate. The product (30 mg, 27% yield) was confirmed by $^1$H NMR spectroscopy.

Preparation of 17: To a vial 16 (30 mg, 0.061 mmol) and potassium carbonate (34 mg, 0.243 mmol) was dissolved in 1:1 dichloromethane:methanol (2 ml). The reaction was stirred for 1.5 hours before 20 ml of water was added. The product was then extracted with 3 x 20 ml of dichloromethane. The combined dichloromethane extracts were washed with 20 ml of water and brine and then dried with MgSO$_4$, filtered, and solvents were removed by rotary evaporation. $^1$H NMR spectroscopy and thin layer chromatography show complete consumption of the starting material. There was not enough material for complete purification and the crude material was carried directly into preparation of 18.
Preparation of 18: To a vial unpurified 17 (21.4 mg) and 7 (44.2 mg, 0.366 mmol) was added. Additionally 2% of the total mass of the reactants of DMPA was added (1.3 mg). The vial was placed under 365 nm light and stirred for 5 hours. Flash chromatography was attempted using 10:1 hexanes:DCM but due to the small amount of material no product was observed by $^1$H NMR spectroscopy.

![Chemical structure of compounds 19, 20, and 21](image)

Exp2. Failed TMS Reaction

Preparation of 20: To a 100 ml flask phenol, 19, (0.5 g, 2.74 mmol) was dissolved in acetonitrile (15 ml). Then TMS propargyl bromide (0.786 g, 4.11 mmol), K$_2$CO$_3$ (1.13 g, 8.22 mmol), and catalytic KI were added. The reaction was refluxed at 80 °C overnight. The acetonitrile was removed by rotary evaporation and then extracted with 3 x 50 ml dichloromethane. The product was dried with MgSO$_4$, filtered, and solvents were removed by rotary evaporation. The product was purified by flash chromatography using 4:1 dichloromethane:hexanes. The product (0.8 g, 99% yield) was gathered and confirmed by $^1$H NMR spectroscopy.

Preparation of 21: To a 100 ml flask 20 (0.363 g, 1.24 mmol) was dissolved in methanol (13 ml, making a 0.1 M solution). To this solution NaBH$_4$ (0.141 g, 3.72 mmol) was dissolved and the solution was stirred at 0 °C for 1 hour. The reaction was quenched with water and the methanol was removed under reduced pressure. The product was extracted with 3 x 40 ml of ethyl acetate and then the combined extracts were washed with 40 ml of water and 40 ml of brine. The ethyl acetate was
dried with MgSO₄, filtered, and solvents were removed by rotary evaporation. ¹H NMR spectroscopy indicated that the TMS group fell off during the reaction. This reaction failed.


Preparation of 23: To a 250 ml 3-arm flask lithium aluminum hydride (0.926 g, 24.37 mmol) was added. To a dropping funnel compound, 22, (2.0g, 12.18 mmol) was added. The system was flushed with N₂. To the lithium aluminum hydride anhydrous diethyl ether (61.0 ml, making a 0.4 M solution) and anhydrous THF (24.4 ml, making a 0.5 M solution) were added. The system was cooled over to 0 °C and the THF solution was added slowly. Once all of the THF was added the system was warmed to room temperature and stirred overnight. The reaction was then refluxed for 40 minutes. The flask was placed in a 0 °C bath and cold water was to quench the reaction. Ether was added and decanted off five times. The ether was dried over MgSO₄, filtered, and rotovapped. ¹H NMR spectroscopy showed pure product³⁷ (1.9 g, 99 % yield) without the need of additional purification.
Preparation of 24: To a 100 ml 3-arm flask 23 (1.8 g, 11.68 mmol) was added. The system was flushed with N₂. DMF (20 ml) was added and the system was cooled to 0 °C. NaH (0.840 g, 35.04 mmol) was then added and the reaction was stirred for 1 hour before propargyl bromide (80% in toluene, 4.168 g, 35.04 mmol) was added. The reaction was stirred for 48 hours with a condensor. The compound was purified using 4:1 hexanes:ethyl acetate by flash chromatography. Pure product (1.292 g, 48.0% yield) was collected and verified by ¹H NMR spectroscopy.³⁸

Preparation of 25: To a flame dried Schlenk flask 24 (0.29 g, 1.26 mmol) was added. THF (10 ml) dried over molecular sieves was added. The flask was placed in a -78 °C bath and 2.5 M BuLi in hexanes (1.512 ml, 3.78 mmol) was added. After 1 hour of stirring TMSCl (0.548 g, 5.04 mmol) was added and the solution was warmed to room temperature. The reaction was stirred overnight. Aqueous ammonium chloride was added to quench and the product was extracted 3 x 30 ml with ethyl acetate. The product was dried with MgSO₄, filtered, and solvents were removed by rotary evaporation. The product was purified by flash chromatography using 20:1 hexanes:ethyl acetate. A pure product (0.1382 g, 29.3% yield) was collected and confirmed by ¹H NMR spectroscopy.

Exp4. Failed TIPS Addition

Preparation of 26: To a flame dried Schlenk flask 24 (0.5 g, 2.171 mmol) was added. THF (20 ml) dried over molecular sieves was added. The flask was placed in a -78 °C bath and 2.5 M BuLi in hexanes (2.605 ml, 6.513 mmol) was added. After 1
hour of stirring TIPSCI (1.67 g, 8.684 mmol) was added and the solution was warmed to room temperature. The reaction was stirred for 36 hours. Aqueous ammonium chloride was added to quench and the product was extracted 3 x 30 ml with ethyl acetate. The product was dried with MgSO₄, filtered, and solvents were removed by rotary evaporation. Flash chromatography was used with 3% DCM in hexanes but not product was able to be found. Thus this reaction failed.
Spectroscopic Data

NMR 1. $^{13}$C NMR (CDCl$_3$, 75 MHz)

NMR 8. $^{13}$C NMR (CDCl$_3$, 75 MHz)
NMR 9. $^{13}$C NMR (CDCl$_3$, 75 MHz)

NMR 10. $^{13}$C NMR (CDCl$_3$, 75 MHz)
NMR 16. $^1$H NMR (CDCl$_3$, 300 MHz)

NMR 20. $^1$H NMR (CDCl$_3$, 300 MHz)
NMR 25. $^1$H NMR (CDCl$_3$, 300 MHz)
**Measured Mass**

409.2763

<table>
<thead>
<tr>
<th>Element</th>
<th>Low Limit</th>
<th>High Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>18</td>
<td>28</td>
</tr>
<tr>
<td>H</td>
<td>30</td>
<td>50</td>
</tr>
<tr>
<td>O</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Si</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Formula</th>
<th>Calculated Mass</th>
<th>mDaError</th>
<th>ppmError</th>
<th>RDB</th>
</tr>
</thead>
<tbody>
<tr>
<td>C23 H41 O4 Si</td>
<td>409.2769</td>
<td>-0.6</td>
<td>-1.4</td>
<td>4.5</td>
</tr>
</tbody>
</table>

**MS 1. APCI-MS (m/z) [MH]^+**
**Measured Mass**

649.3253

<table>
<thead>
<tr>
<th>Element</th>
<th>Low Limit</th>
<th>High Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>26</td>
<td>36</td>
</tr>
<tr>
<td>H</td>
<td>45</td>
<td>65</td>
</tr>
<tr>
<td>O</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>S</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Si</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Formula</th>
<th>Calculated Mass</th>
<th>mDaError</th>
<th>ppmError</th>
<th>RDB</th>
</tr>
</thead>
<tbody>
<tr>
<td>C30 H57 O9 Si2 S</td>
<td>649.3256</td>
<td>-0.3</td>
<td>-0.5</td>
<td>4.5</td>
</tr>
<tr>
<td>C31 H57 O8 Si S2</td>
<td>649.3259</td>
<td>-0.6</td>
<td>-0.9</td>
<td>4.5</td>
</tr>
<tr>
<td>C35 H53 O7 S2</td>
<td>649.3227</td>
<td>2.6</td>
<td>4.0</td>
<td>9.5</td>
</tr>
<tr>
<td>C34 H53 O8 Si S</td>
<td>649.3225</td>
<td>2.8</td>
<td>4.3</td>
<td>9.5</td>
</tr>
<tr>
<td>C33 H53 O9 Si2</td>
<td>649.3223</td>
<td>3.0</td>
<td>4.7</td>
<td>9.5</td>
</tr>
</tbody>
</table>

**MS 8. APCI-MS (m/z) [MH]^+**
MS 9. APCI-MS (m/z) [MH]$^+$

<table>
<thead>
<tr>
<th>Element</th>
<th>Low Limit</th>
<th>High Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>17</td>
<td>3627</td>
</tr>
<tr>
<td>H</td>
<td>25</td>
<td>45</td>
</tr>
<tr>
<td>O</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>S</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Formula</th>
<th>Calculated Mass</th>
<th>mDaError</th>
<th>ppmError</th>
<th>RDB</th>
</tr>
</thead>
<tbody>
<tr>
<td>C22 H37 O8 S2</td>
<td>493.1924</td>
<td>1.0</td>
<td>1.9</td>
<td>4.5</td>
</tr>
</tbody>
</table>
### Measured Mass

<table>
<thead>
<tr>
<th>Element</th>
<th>Low Limit</th>
<th>High Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>29</td>
<td>39</td>
</tr>
<tr>
<td>H</td>
<td>55</td>
<td>75</td>
</tr>
<tr>
<td>O</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>S</td>
<td>3</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Formula</th>
<th>Calculated Mass</th>
<th>mDaError</th>
<th>ppmError</th>
<th>RDB</th>
</tr>
</thead>
<tbody>
<tr>
<td>C34 H65 O8 S4</td>
<td>729.3557</td>
<td>0.6</td>
<td>-0.8</td>
<td>2.5</td>
</tr>
<tr>
<td>C37 H61 O8 S3</td>
<td>729.3523</td>
<td>2.8</td>
<td>3.8</td>
<td>7.5</td>
</tr>
</tbody>
</table>

**MS 10. APCI-MS (m/z) [MH]^+**
Measured Mass

<table>
<thead>
<tr>
<th>Element</th>
<th>Low Limit</th>
<th>High Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>15</td>
<td>25</td>
</tr>
<tr>
<td>H</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>O</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>N</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>S</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Si</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Formula</th>
<th>Calculated Mass</th>
<th>mDaError</th>
<th>ppmError</th>
<th>RDB</th>
</tr>
</thead>
<tbody>
<tr>
<td>C19 H34 N O5 Si2</td>
<td>412.1970</td>
<td>0.0</td>
<td>0.0</td>
<td>5.5</td>
</tr>
<tr>
<td>C20 H34 N O4 Si S</td>
<td>412.1972</td>
<td>-0.2</td>
<td>-0.6</td>
<td>5.5</td>
</tr>
<tr>
<td>C21 H34 N O3 S2</td>
<td>412.1975</td>
<td>-0.5</td>
<td>-1.1</td>
<td>5.5</td>
</tr>
<tr>
<td>C17 H40 O3 Si2 S2</td>
<td>412.1952</td>
<td>1.8</td>
<td>4.4</td>
<td>0</td>
</tr>
</tbody>
</table>

**MS 12. APCI-MS (m/z) [MH]+**
Bibliography


