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Synthesis of Hydrogenated Thiol-Silanes for Selective Reactions

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Engaged Learning Final Report

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Abstract

The intention of this experiment is to show the creation of multifunctional thiols from the reaction between various hydrochlorosilanes and mercaptoethanol in an attempt to utilize their distinct properties for practical applications. Multifunctional thiols have many useful applications including use in high-refractive-index lenses,[1] heavy metal chelation,[2] and degradable plastics.[3] Previous work,[5] in our lab has explored a class of reactions key to the synthesis of these compounds: the reaction between methylated chlorosilanes with mercaptoalcohols. We extended this reaction to include hydrogenated chlorosilanes. This allows us to produce multifunctional thiols with an additional functionalizable position at the hydrogen, allowing for greater flexibility in regards to practical applications. This functionalizable position allows the substituted chlorosilanes to undergo further reactivity with the possibility of forming more complex polymers and other important molecules with more widespread applications. The seemingly simple addition of the hydrogen to the chlorosilane led to unexpected results that differed significantly from those found with the reactions of the previously shown methylchlorosilanes.

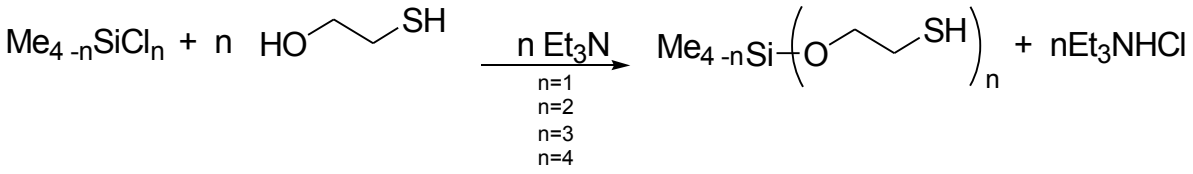
Background

Multifunctional thiols are compounds containing multiple thiol groups, where a “thiol” is a compound that has a carbon group attached to a sulfhydryl (-SH) group. Multifunctional thiols have been proven to have many diverse applications. Sulfur and silicon compounds are characterized by having high electronic polarizabilities, which in turn leads to high-refractive-indices. Such compounds can be woven into polymers to make excellent optical lenses because they are able to bend light to a greater degree with less material. This allows for numerous innovations including uses in lightweight glasses and contact lenses. Additionally, these polymers are known to produce very clear plastics, again making them excellent for optical applications. Sulfur has a very high affinity for

heavy metals such as mercury and arsenic, making sulfur compounds promising candidates for heavy metal chelation. Heavy metal chelation is the process of extracting dangerous toxins from the natural environment including drinking water and soil. Further, these polymers may degrade in the body allowing for medical applications such as drug delivery or as a sheath for the implantation of electrodes in the brain.[3]

Despite how useful these compounds have proven to be, commercially available multifunctional thiols are limited to a handful of mercaptoesters.[6] Previous work in our lab,[5] has explored a class of reactions key to the synthesis of these compounds; the reaction between methylated chlorosilanes with mercaptoalcohols **(Scheme 1)**.The reaction they developed is shown to be very efficient with a high product yield. They were able to form and isolate mono, di, tri, and tetra substituted multifunctional thiols.

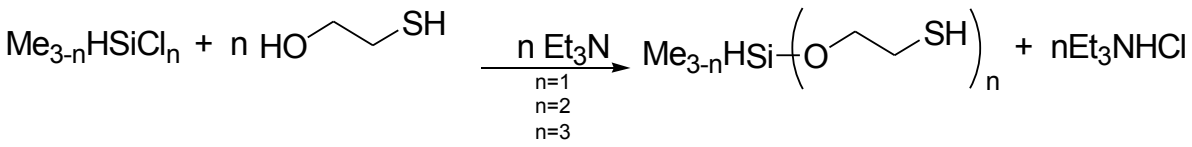
They found that simple mercaptoalcohols (such as 2-mercaptoethanol) react with chlorosilanes excessively through the alcohol and not the sulfhydryl group. This regioselectivity of the alcohol seems to be unique to silicon whereas other Group 14 elements (electrophilic carbon, germanium, tin, and lead) react with the sulfhydryl group.



Scheme 1: The reaction previously done in the lab. (From left to right) Adding a chlorosilane to a mercaptoethanol in the presence of triethylamine to form a multifunctional thiol and a hydrochloride salt.

In order to expand our previous work on these reactions, we attempted to extend this chemistry to hydrogenated chlorosilanes **(Scheme 2).** We quickly found that the simple addition of the hydrogen to the chlorosilanes entirely changed the chemistry of these

reactions. These reactions consistently resulted in messy outcomes with several different products formed and often converted to higher molecular weight products with time. Increasing order of substitution of the mercaptoethanol groups led to even messier products. We were able to form the mono and di- substituted product but the trisubtituted seemingly polymerizes immediately upon formation.



Scheme 2: The main difference from Scheme 1 is the addition of the hydrogen attached to the silicon. This hydrogen adds dual functionality to the thiol formed.

The main reason we wanted to make these compounds is their dual functionality. Not only can we functionalize at the sulfur groups,[7] but we can also functionalize at the silicon because there is a hydrogen present on the silicon[8] (see **figure 1** below). Hydrosilylation is a well-developed chemistry of the silicon-hydrogen bond that is now open to use in these materials. This opens up a wide avenue of further development of the fore mentioned materials.

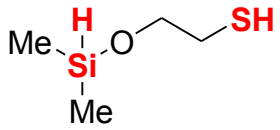
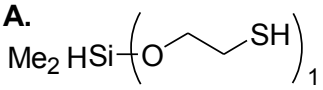


Figure 1: A picture of Product A Showing the two functionalizable positions: the S-H group and the Si-H.

Methodology

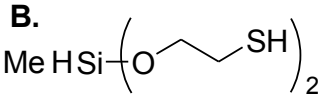
Following the procedure of the previous work,[5] I attempted to synthesize compounds A-C.

A.



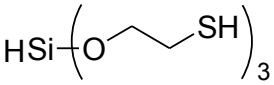
Monosubstituted

B.



Disubstituted

C.



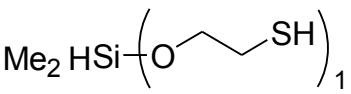
Trisubstituted

These reactions are performed under mild conditions that involve the combination of chlorosilane and mercaptoethanol in the presence of triethylamine and diethyl ether. The reaction is left to stir overnight at room temperature. The next day, the hydrochloride salt is removed using filtration methods. Excess solvent is removed under reduced pressures and the product is recovered via distillation. The purity and identity of the product is analyzed using gas chromatography mass spectrometry (GC/MS) and nuclear magnetic resonance (NMR) spectroscopy.

After the formation of these initial three products, we moved onto selective reactivity studies where we attempted to develop reaction conditions to selectively react with the functional sulfur group through thiolene reactions or the functional hydrogenated silanethrough hydrosilylation reactions.[7] This was mainly done through UV reactions that will be explained later in the paper.

Results:

A. Monosubstituted Product



Formation of Product

The monosubstituted product was formed under mild conditions that involved the combination of chlorodimethylsilane with mercaptoethanol in the presence of triethylamine (1:1:1 ratio)

and diethyl ether. The reaction was then left to stir overnight at room temperature. The next day, the hydrochloride salt was removed using vacuum filtration. Finally, the excess ether was removed by a rotovap machine where we reduced the pressure allowing the ether to evaporate and the product to be recovered. The purity and identity of the product is analyzed using gas chromatography mass spectrometry (GC/MS) and nuclear magnetic resonance (NMR) spectroscopy. The product was stored in the lab freezer.

Product Analysis

It was found that the monosubstituted product was formed, could be isolated, and was stable for up to eight months in the lab freezer (**Figure 2**). However, after eleven months, the product was found to have separated into two layers. We are unsure how to explain why this occurred. Between 8 and 11 months, we cleaned out our lab freezer so the products were left at room temperature and exposed to moisture in the atmosphere and this may have caused the separation to occur. We tried storing the product in the lab freezer and the dry box freezers but there was not a significant difference so products were stored in the lab freezer for ease.

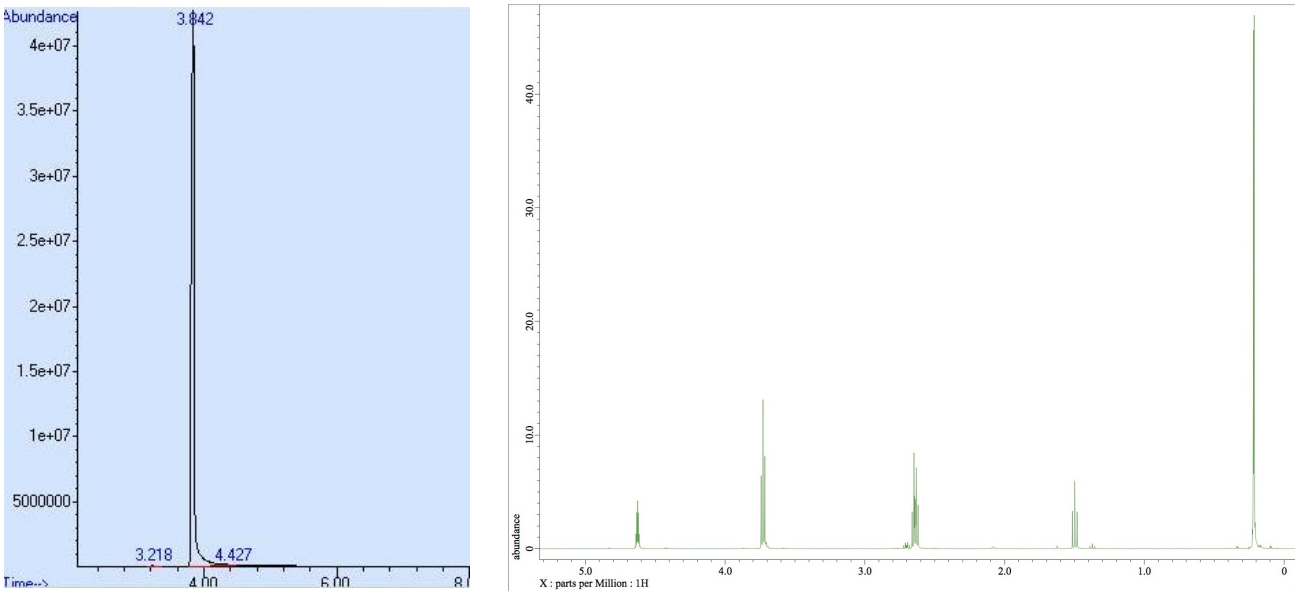
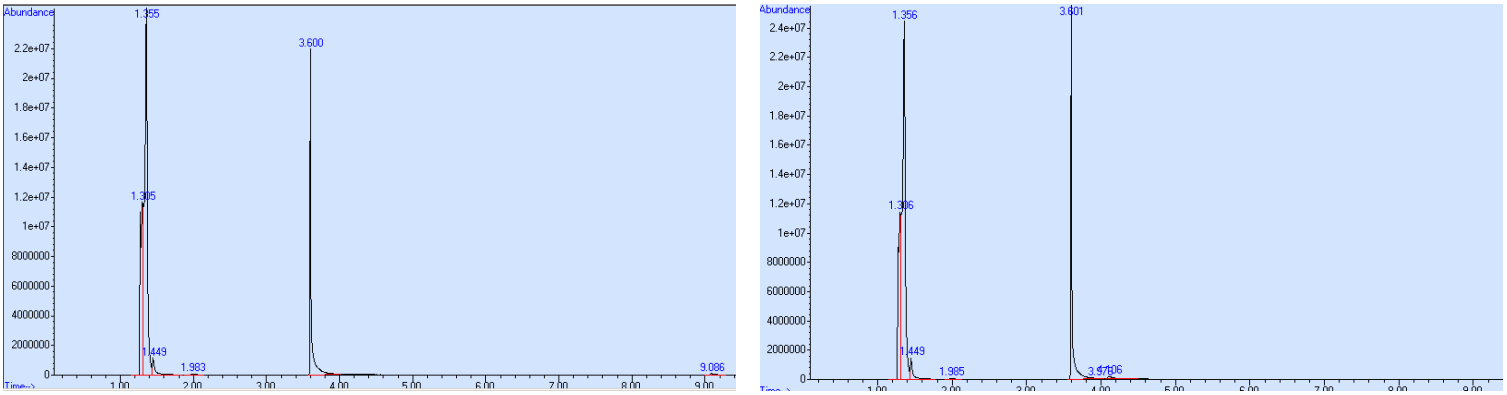


Figure 2: A GC (left) and H^1 NMR (right) of the mono-substituted product.

Formation of Higher Molecular Weight Products

These reactions (mono, di, and tri-substituted) tend to form higher molecular weight products in addition to the desired product. As you increase substitution of mercaptoethanol groups, the reactions get increasingly less clean. The mono substituted is the most clean reaction. On the first couple days after filtration and rotovap, the mono-substituted product does tend to form a higher molecular weight peak on the GC/MS at ~9.05 (although much smaller than the desired product peak at ~3.7). However, over a couple of days, the reaction clears up and the 3.7 peak product is all that remains. (**Figure 3**).

Figure 3: A GC of the mono-substituted product after filtration (left) and a GC of the same



product, two days later after sitting in freezer. Note the disappearance of the 9.051 peak.

Due to the tendency of the disubstituted product to convert to higher molecular weight products, we tested whether or not the monosubstituted product would also convert to higher molecular weight products (to the 9 peak) if left exposed to the air at room temperature. Unexpectedly, the product broke down and evaporated leaving mercaptoethanol behind.

Pyridine vs. Triethylamine

Triethylamine could potentially deprotonate the chlorosilane which would result in the formation of undesired products. Therefore, we tested if we would get a cleaner product by using pyridine as a base. The pKa of pyridine is 5.2 and that of triethylamine is 10.78. Therefore, we reasoned that pyridine, as a weaker base, would be less likely to

deprotonate the silane. We did side by side reactions with the only difference being the base and found that there was not a significant difference in the product between using pyridine or triethylamine. See GC in **Figure 4**.

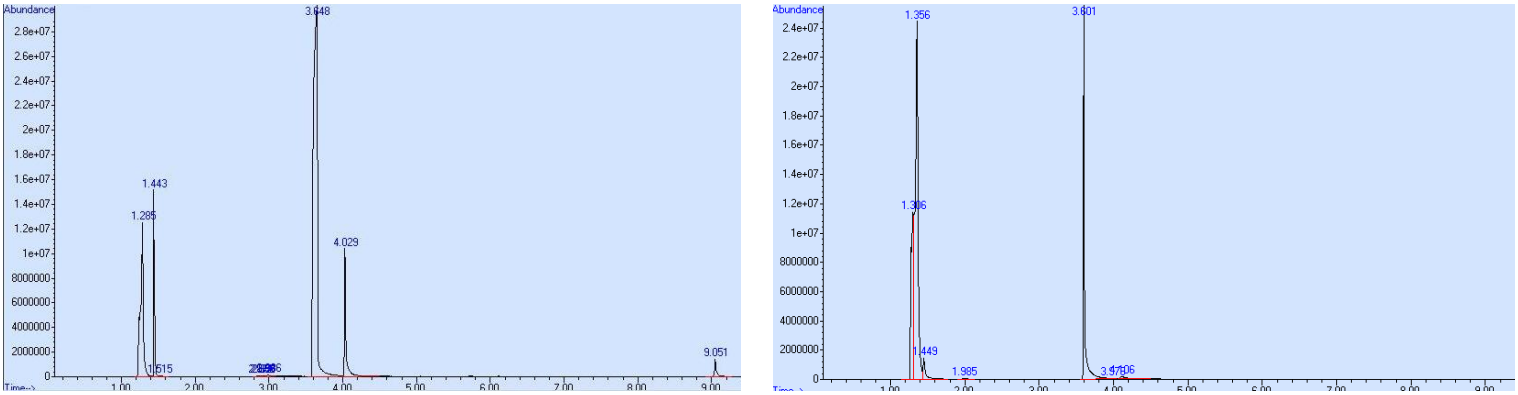
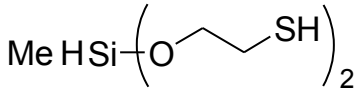


Figure 4: A GC of the mono-substituted product using triethylamine as a base (left) and pyridine as a base (right).

B-1 Disubstituted Product

Formation of Product



The disubstituted product was formed under mild conditions that involved the combination of dichloromethylsilane with mercaptoethanol in the presence of triethylamine (1:2:2 ratio) and diethyl ether. The reaction was left to stir overnight at room temperature. The next day, the product was filtered to remove the hydrochloride salt and exposed to low pressures to remove the diethyl ether. The purity and identity of the product was analyzed using gas chromatography (GC) and nuclear magnetic resonance (NMR) spectroscopy.

Analysis of Product

After letting the reaction run overnight, we found that the disubstituted product was formed but there was a mixture of higher molecular weight compounds formed as well. (**Figure 5** below). As time progressed, the desired product (~peak 7) converted to the ~8 peak and eventually all of the product converts to the ~9 peak. Through analysis of mass

spectrometry of the product, we are fairly certain that the ~9 peak is the trisubstituted product seen in lab work previously with the loss of a hydrogen.

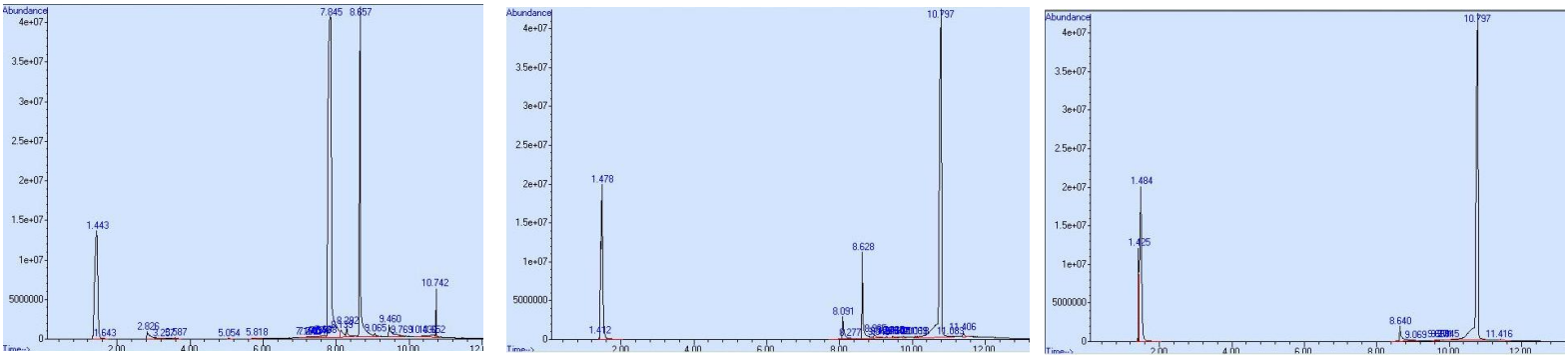
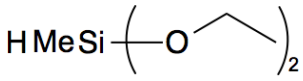


Figure 5: A GC of the disubstituted product immediately after filtration (left), three days later (middle), four days later (right).

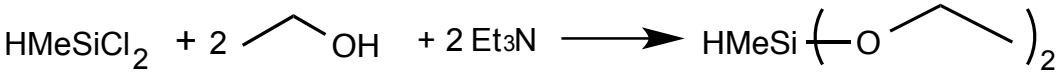
Excess Mercaptoethanol

We hypothesize that these conversions happen because excess mercaptoethanol in the reaction flask continues to react with the product formed. Therefore, we added excess mercaptoethanol to test if the conversion to the higher molecular weight products would form faster (1:3:2 ratio of silane:mercaptoethanol:triethylamine). As expected, the excess mercaptoethanol expedited the formation of higher molecular weight products.

B-2 Diethoxymethylsilane Product



To discover if this conversion to higher molecular weight products was specific to the sulfur mercaptoethanol side chains, we did the same reactions with absolute ethanol and the hydrogenated chlorosilanes in the presence of triethylamine and ether. The resulting product that formed, diethoxymethylsilane was messy in both NMR and GC/MS. However, we ordered some stock diethoxymethylsilane to run some tests and study its characteristics.



Scheme 3: (From left to right) Adding a chlorosilane to a absolute ethanol in the presence of triethylamine to form a multifunctional thiol. Instead of mercaptoethanol we are using absolute ethanol and forming diethoxymethylsilane.

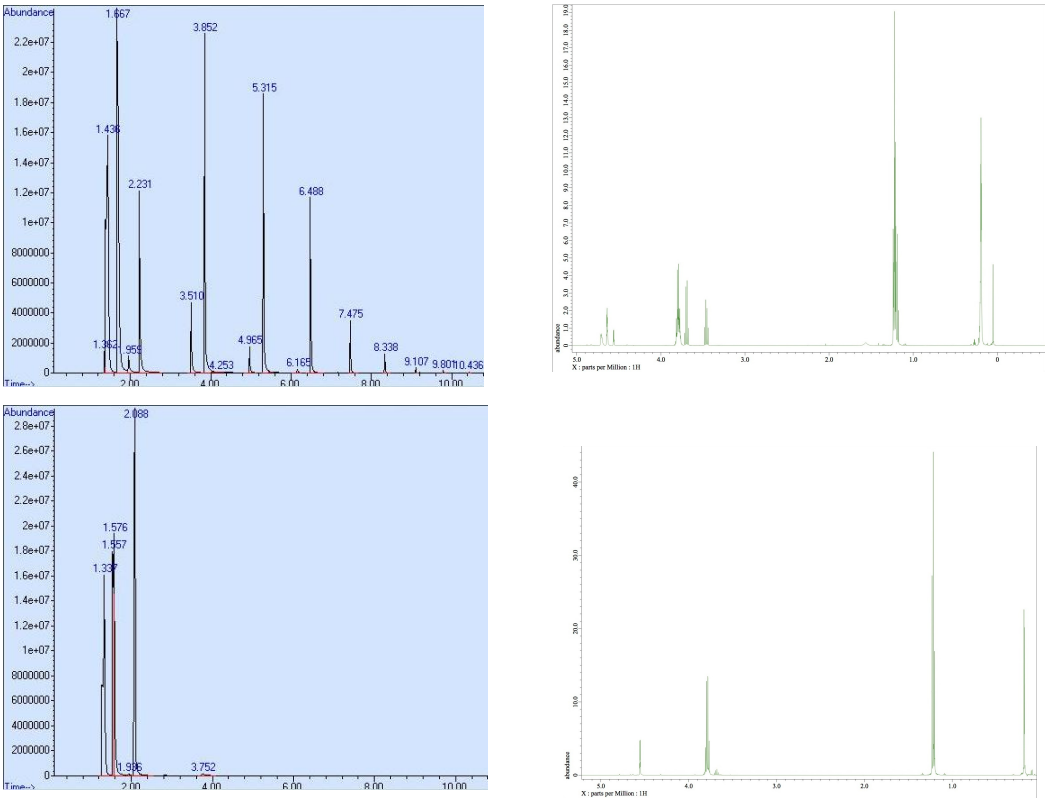


Figure 6:
Top row:
GC (left) and H^1 NMR (right) of lab made diethoxymethylsilane.

Bottom row:
GC (left) and H^1 NMR (right) of stock diethoxymethylsilane.

Stock Diethoxymethylsilane

When the stock diethoxymethylsilane arrived, we took a GC/MS and H^1 NMR to compare to our diethoxymethylsilane formed. The product was much cleaner as seen in **Figure 6** above. We transferred a small portion to one of our lab vials, placed it in the lab freezer and monitored it over a week. Over time, the product in our lab vial starter to decay similarly to the diethoxymethylsilane we tried to produce earlier but the product in the commercially bought bottle remained the same. This led us to question whether or not

our lab vials did not seal well and/or there was a reaction going on with other products in our freezer.

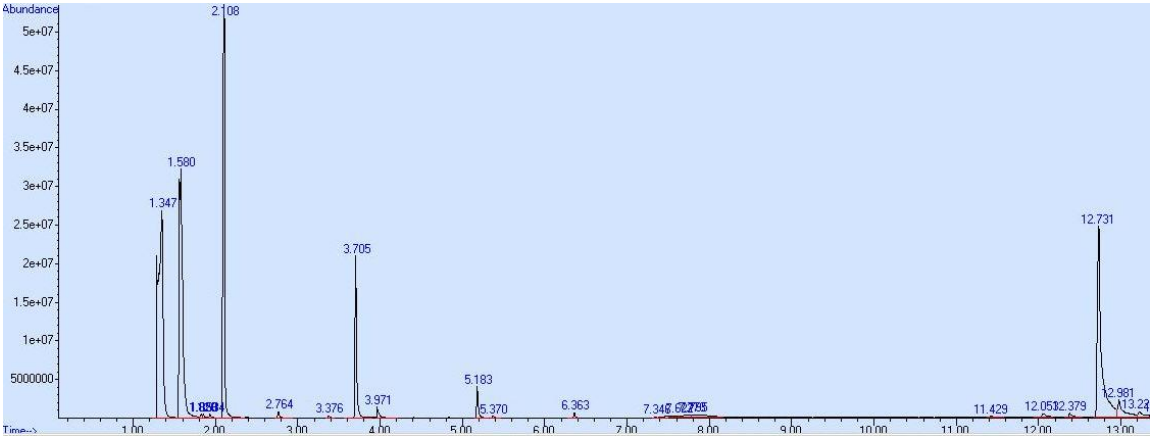


Figure 7: GC of stock diethoxymethylsilane in a vial (not its original bottle) after a week in lab freezer.

Rotovap

In the process of making the diethoxymethylsilane product, we rotovapped the solution to evaporate excess solvent. In order to see if this affected the stock diethoxymethylsilane, we added 5 drops of absolute ethanol and 5 drops of triethylamine to a 1 mL sample of the stock diethoxymethylsilane and rotovapped for 20 minutes. There was some change in the diethoxymethylsilane product but nothing significant in the GC/MS immediately after rotovap. (**Figure 8** below).

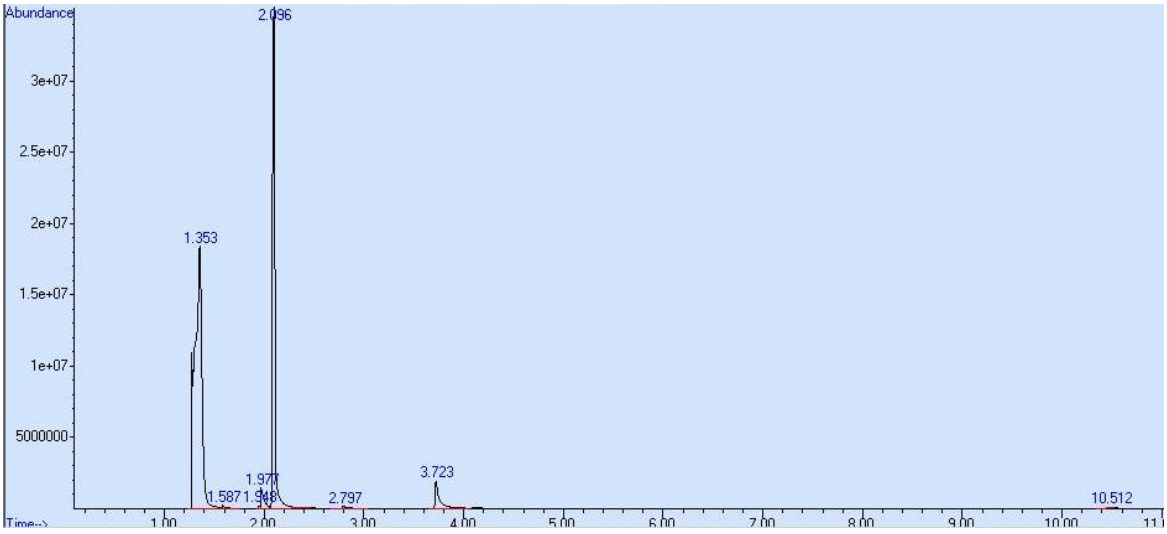
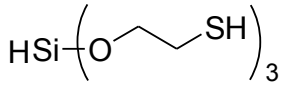


Figure 8: GC of diethoxymethylsilane after rotovap with triethylamine and absolute ethanol.

C. Trisubstituted Product

Formation of the Product



We attempted to form the tri-substituted product under mild conditions that involved the combination of trichlorosilane with mercaptoethanol in the presence of triethylamine (1:3:3 ratio) and diethyl ether. The reaction was then left to stir overnight at room temperature. The next day, product was filtered and distilled as previously described for mono- and disubstituted products. The purity and identity of the product was analyzed using gas chromatography (GC) and nuclear magnetic resonance (NMR) spectroscopy.

Analysis of Product

The filtrate and rotovapped product showed no trisubstituted product forming. We noted the general trend that the resulting compound was less stable with increasing mercaptoethanol side chains. Therefore, we were unable to form the tri-substituted product.

Pyridine vs. Triethylamine

Triethylamine could potentially deprotonate the chlorosilane which would cause the formation of products other than those desired. Therefore, tested whether or not we would get a cleaner product by using pyridine as a base. We set up a side by side reaction and, from the H^1 NMR, determined that the pyridine led to a cleaner reaction but our desired product was still not formed. (**Figure 9** below)

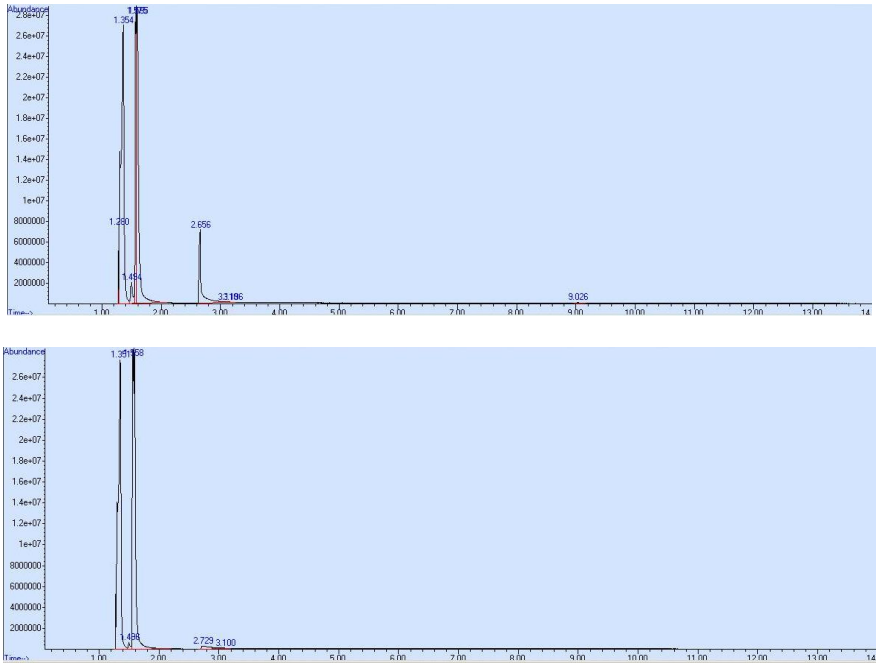
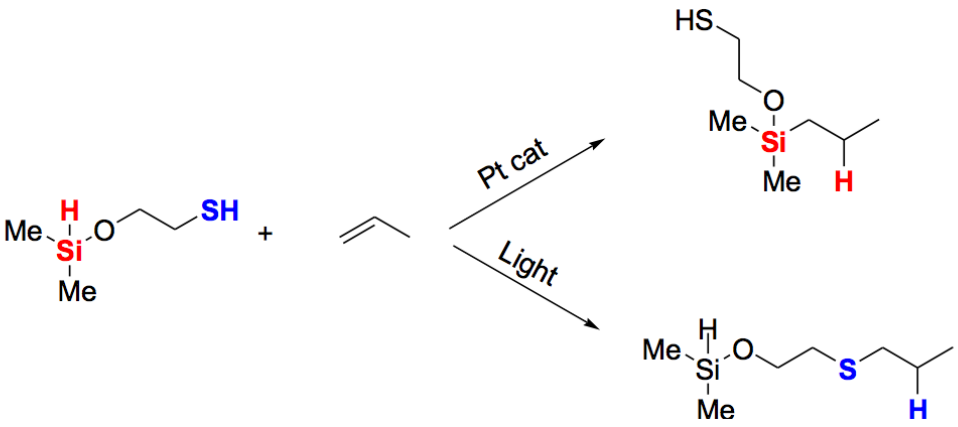


Figure 9: GC of trisubstituted product of pyridine (bottom) and triethylamine (top).

UV Reactions

After these three initial reactions were investigated, we also started to do selective reactivity studies where we attempted to develop reaction conditions to selectively react with the functional sulfur group through thiolene reactions[7] or the functional hydrogenated silane through hydrosilylation reactions **(Scheme 4 below)**. We started these reactions at the end of the summer and first tried to selectively react the sulfur group of the mercaptoethanol through a thiolene reaction with trimethylvinylsilane. We combined the monosubstituted product with trimethylvinylsilane in a (1:1) ratio in the presence of UV light for 3-4 hours. We are currently in the process of testing these results. We were only able to use the mono-substituted products for UV reactions because that was the only product that was stable enough to experiment with at this point.



Scheme 4: Showing the dual functionality of the thiol produced. The resulting end product depends on the reaction conditions.

Future Plans/ Learning Experience

Moving forward, we hope to better understand the appropriate reactions conditions that will lead to the formation of stable and clean mono-, di-, and trisubstituted hydrochlorosilanes. As described above, we were only successful in developing a stable mono substituted version. The disubstituted product was difficult to isolate and lead to messy results. And we were consistently unsuccessful in the synthesis of the trisubstituted product. Understanding the chemistry and specific reaction conditions that lead to a more stable product will aid in better researching subsequent reactions such as the UV reactions described above. Future work in this area will hopefully create these chlorosilanes with the functionalizable hydrogen and lead to the formation of complex polymers that will prove to be useful in a wide array of practical applications.

Throughout my time working in Dr. Son's lab, I have continued to gain valuable hands on experience. This project has thoroughly challenged me to think critically, to perform intently, and to interpret results that stretch beyond the scope of the sophomore organic chemistry level. These are all essential life skills that will follow me throughout my career moving forward into medical school. Additionally, I was able to develop leadership skills and communication skills as I was able to train a new student in the lab to run the reactions with me. Interactions with mentors and coworkers has opened a new

avenue of learning beyond the traditional college lecture.Through research, not only do I learn the basic science behind my classes more in depth but also the hard work and vigor behind the scenes in the discovery of the science. Undergraduate research has had a positive effect on my college experience. Research has ultimately stretched my intellectual outlook and empowered me to go beyond the classroom and think in an innovative manner. Whereas I look forward to the next step of my educational journey, I am also anxious to see where this science goes from here.

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