2022

Unique Reactions of Sulfoxonium Ylides

MARISSA ALLEGREZZA

Unique Reactions of Sulfoxonium Ylides

A Major Qualifying Project Proposal
submitted to the Faculty of Worcester
Polytechnic Institute in partial fulfilment
of the requirements for the degree of
Bachelor of Science

By

Marissa Allegrezza

Date:

03/03/2022

Report Submitted to:

Professor Anita E. Mattson
Worcester Polytechnic Institute

Abstract

Herein two metal-free synthesis reactions with sulfoxonium ylides are reported, one being the O-H insertion of benzoic acids into sulfoxonium ylides and the other being cycloproponation of quinolones via a sulfoxonium ylide. An expansive scope of sulfoxonium ylides were used to demonstrate that enantioselective methods of synthesis via hydrogen bond donor catalysis is plausible for both of these unique sulfoxonium ylide reactions. A total of 33 new O-H inserted compounds were synthesized and 8 cycloproponated ones over the completion of these projects.

Chapter 1: O-H Insertions

1.1 Insertion Reactions:

Insertion reactions are some of the most widely used mechanisms in organic synthesis due to their ability to be manipulated into various organic compounds. To date, research on insertion chemistry with X-H bonds (with X= N, S, O, C) has been primarily focused on either the insertion of α-diazocarbonyls or transition metal catalyzed insertion reactions. [1] An α-diazocarbonyl is an organic compound with a nitrogen atom double bonded to a central carbon and another nitrogen atom, as seen in Figure 1.

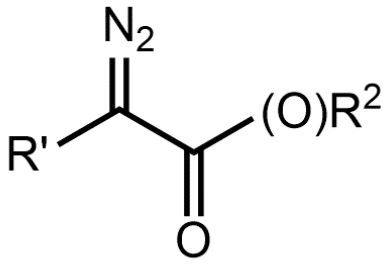


Figure 1: Example of α -diazocarbonyl

Although this work focused on O-H insertions, it is important to note examples of other X-H insertion reactions that have paved the way for the research we are conducting now. In 2012, the Zhou Group published a paper regarding a variety of X-H insertions. One that gave high yields and moderate to high enantioselectivity was the copper-catalyzed asymmetric N-H insertion of α-diazopropionates (Figure 2). Here, 5 mol percent of CuCl combined with a chiral spiro-bisoxazoline ligand produced high enantioselectivity requiring only 1 mol percent of the chiral ligand. The highest enantioselectivity reported, with an electron-withdrawing group in the *para*-position or the addition of another benzene group off the backbone, was 98% *ee*.[2]

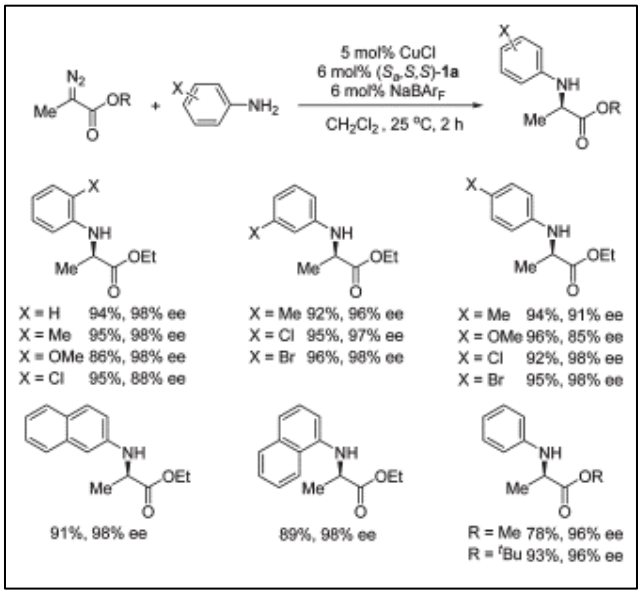


Figure 2: Copper-Catalyzed Asymmetric N-H Insertion of α -Diazopropionates.[2]

In 2016, the first asymmetric catalytic insertion of α-diazocarbonyl compounds into O-H bonds was reported. This publication described an enantioselective approach to achieve insertions of α-diazoesters and α-diazoketones into O−H bonds of carboxylic acids with high yields and enantiomeric excess. To achieve 99% yields and enantioselectivity up to (97.5:2.5 er) 95% *ee*, the group used a $Rh_2(OAc)_4$ metal complex and a guanidine catalyst, which can be seen in Figure 3. The utilization of the chiral guanidine allowed the proton transfer to proceed in a highly enantioselective manner, as opposed to a chiral amino amide or cinchonine, where they saw decreased enantioselectivity and increased reaction times.[3]

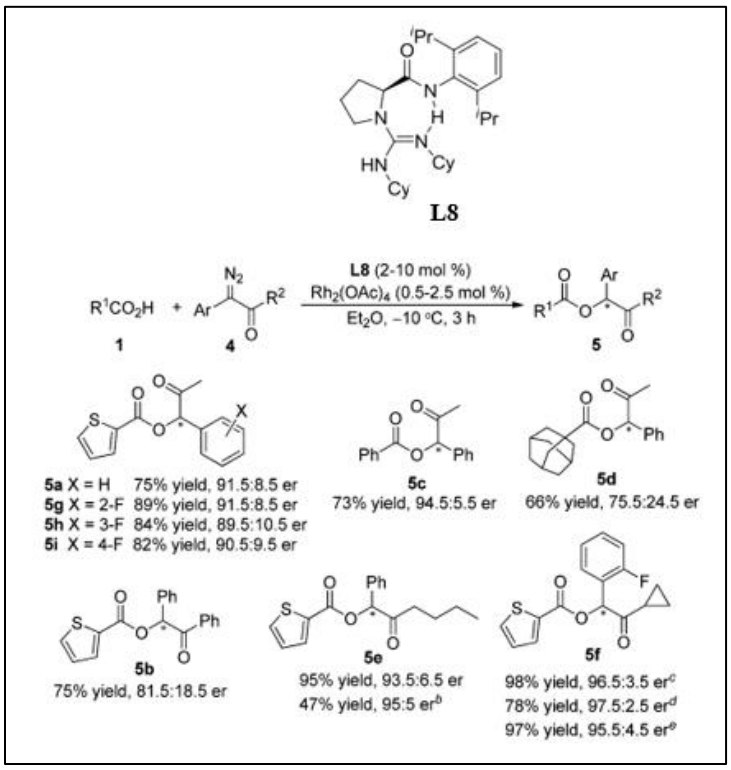


Figure 3: Substrate Scope of Asymmetric O−H Insertion of α-Diazoketones with Carboxylic Acids. [3]

Additionally, insertion reactions have shown their importance in drug discovery and their motifs can be seen in some natural and synthetic medicinal compounds. A very popular example of N-H insertion chemistry is with the synthesis of B-lactam antibiotics. The introduction of antibiotics in the 1950's, brought with it synthesis challenges. It took nearly a decade of long and broad investigations surrounding the chemical synthesis of penicillin before a suitable mechanism was discovered which was thanks to the application of intramolecular N-H carbene insertion chemistry. This solution paved way for synthesis of numerous fused natural and synthetic B-lactam antibiotics.[4] Some examples of medicinal agents synthesized via this method are displayed in Figure 4.

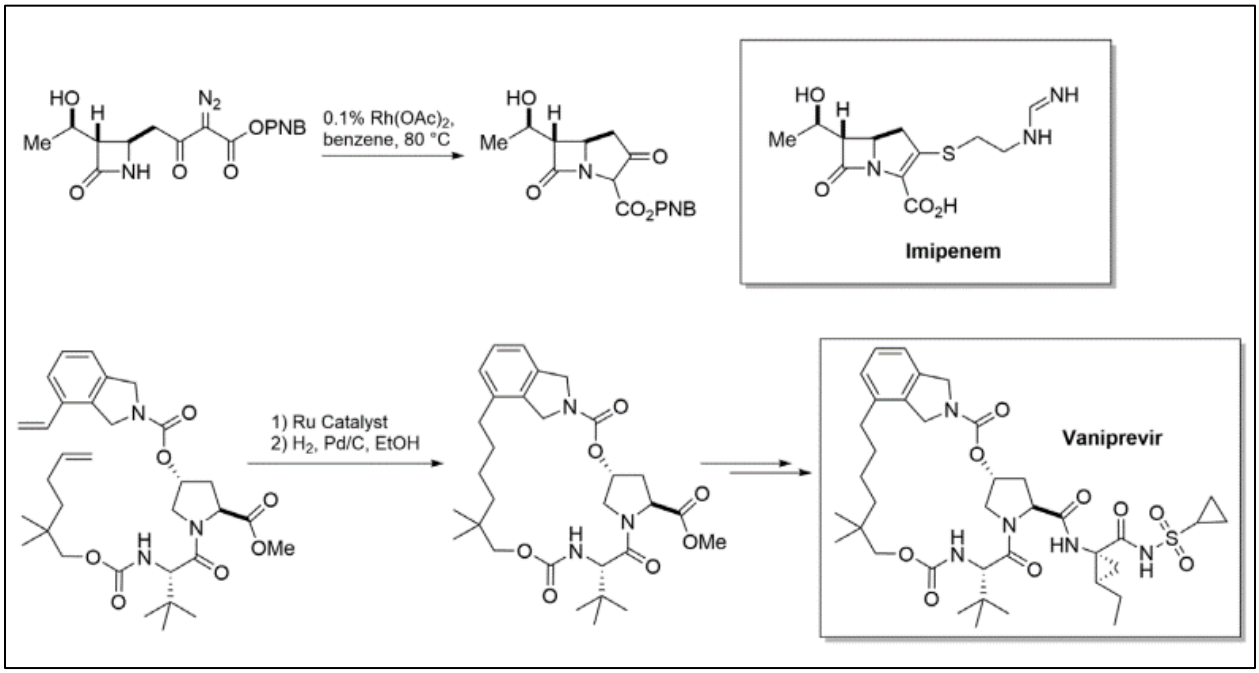


Figure 4: Intramolecular N-H carbenoid insertion chemistry application in fused B-lactams. [4]

1.2 Enantioselective Catalysis:

Chiral transition metal-based catalysts have two important components, the central metal and the chiral ligand. Transition metal catalyzed reactions proceed through a reactive intermediate known as a metal carbene (Figure 5), which can undergo a wide variety of catalytic reactions. Much research has confirmed that the electronic character of the metal carbene is directly related to the chemo-, regio-, and stereoselective outcome of the reaction, thus when paired with a suitable catalyst, the reaction may induce enantioselective activity.[5] Catalytic reactions that proceed via a metal carbene intermediate commonly use a diazo compound as the precursor, as seen in the papers referenced in Chapter 1 Section 1. One such reaction is the

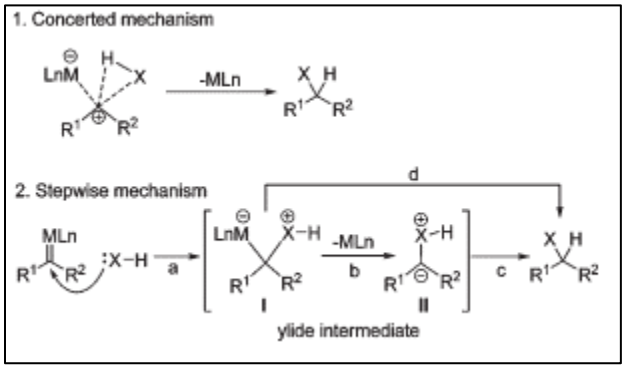


Figure 5: Proposed mechanisms for formation of a metal carbene. [2]

insertion into an X-H bond, which is done through these reactive intermediates.(5)

An accepted mechanism for the formation of a metal carbene involves a metal-mediated decomposition of the α-diazocarbonyl, which allows for the now, electron-deficient metal carbene, to insert into the respective X-H bond. The other accepted mechanism detailed in this paper is a stepwise process where an ylide is formed and then a 1,2-proton transfer happens. Both mechanism are detailed in Figure 5.(2)

1.3 Hydrogen Bond Donor Catalysis:

An area that is less studied involves metal free insertion reactions. Few papers have been published that detail successful enantioselective insertion via metal-free catalysis. One paper by the Mattson Group detailed successful metal-free S-H and O-H insertions of a-aryldiazoacetates via urea-induced acid amplification. The group proposed that the reaction proceeded because of a urea-induced protonation of the organic compound to enhance acidity rather than of catalytic activation of the diazo, which then promotes the insertion.(5)

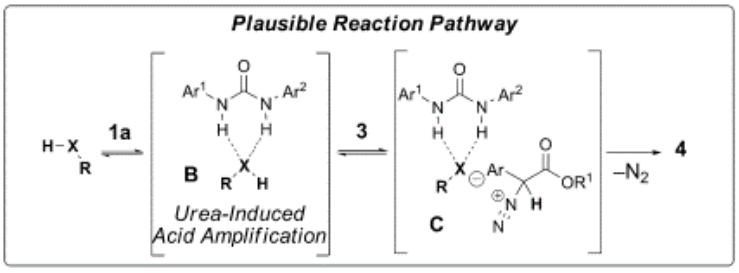


Figure 6: Urea induced protonation. (7)

The urea-induced protonation shown in Figure 6, achieves enantioselectivity because of what is known as hydrogen bond donor catalysis. The promising results of using these methods are quickly making a name for itself in the organic field. Another paper published in 2014 by the same group states that the ultimate goal of implementing Hydrogen Bond Donor catalysis is to overcome the reactivity problems that are commonly seen with Lewis acid and transition metal mediated catalysis.(7)

Successful hydrogen bond donor organocatalysts are molecules whose two hydrogen bonds allow them to act as Lewis acids. The catalytic activity stems from the bidentate complex of the substrate binding, which orients and activates the molecule by lowering the lowest unoccupied molecular orbital (*LUMO*), of the dieneophile when it binds with the catalyst.(8)

1.4 Sulfoxonium Ylides:

The first stable sulfur based ylides, described by Ingold and Jessop in 1930, became the building blocks for the synthesis of dimethylsulfonium and dimethylsulfonium ylides done by Johnson and LaCount, Franzen, and Corey and Chaykovsky in the 1960's.[1] Since then, sulfur based ylides have received increasing attention due to their ability to enable safer execution of insertion chemistry compared to the more commonly used a-diazocarbonyls.

Recent advancements in organic chemistry have led to increased interest in sulfoxonium ylides as opposed to diazo compounds because, though having many useful applications in the field of organic chemistry they present drawbacks that limit their uses.[1] Sulfoxonium ylides are bench top stable at room temperature and do not produce rapid exotherms of N_2 gas, instead producing dimethyl sulfoxide (DMSO) as the byproduct.[9]

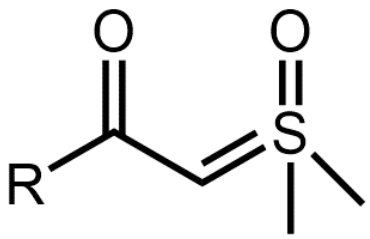


Figure 7: Example structure of sulfoxonium ylide.

Until the work of the Mattson Group in 2018, where they used hydrogen bond donor catalysis to produce enantioselective insertions of ylides into S-H bonds, there had been no enantioselective insertion reactions using sulfoxonium ylides and hydrogen bond donor catalysis. Prior, most methods involved either the use of a diazo compound or were catalyzed by a transition metal. In this paper, *Enantioselective S-H Insertion Reactions of a-Carbonyl Sulfoxonium Ylides,* Alexandria Leveille and Patricia Momo found in an initial catalyst screen that a thiourea catalyst at room temperature in toluene, gave 50% *ee*. Upon further optimization they found that when using chloroform as the solvent at -28ºC, they could obtain products with up to 95% *ee*, as shown in Figure 8. [10]

Inspired by the success of Alexandria and Patricia and their work on metal free enantioselective S-H insertions using sulfoxonium ylides opposed to diazo compounds, the group proposed the investigation of hydrogen bond donor catalyzed O-H insertion reactions with sulfoxonium ylides.

1.5 Experimental:

Catalyst Screen O-H Insertions:

We initially began this project by conducting a catalyst screen in chloroform at room temperature with a 10 mol percent catalyst load. Through screening seventeen catalysts, the pyrene thiourea, which is highlighted in Table 1, was the only one that gave a semi-reasonable hit in *ee*. With this being our only option, we decided to use this catalyst and begin further optimizations.

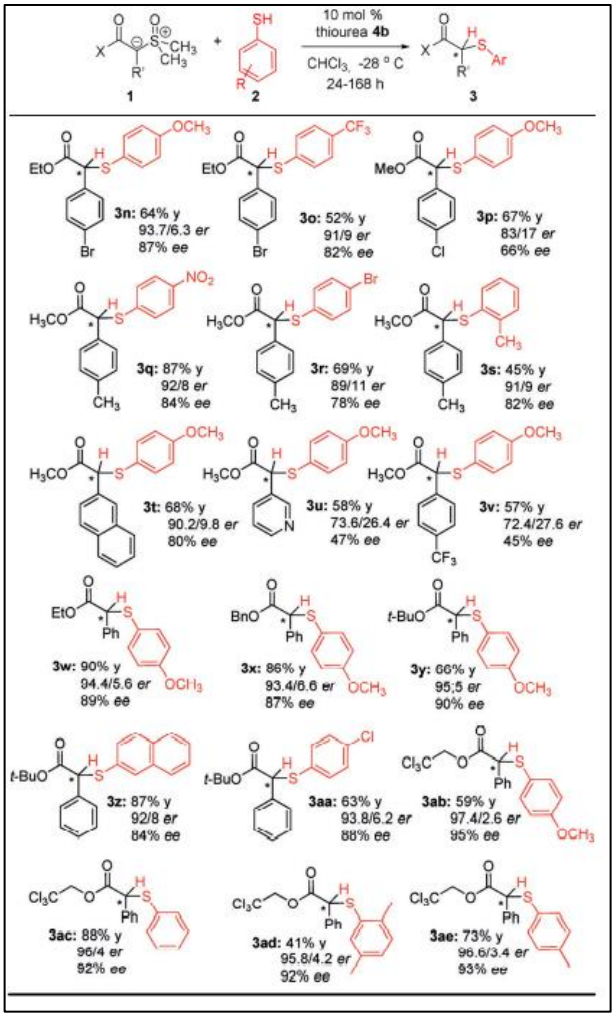
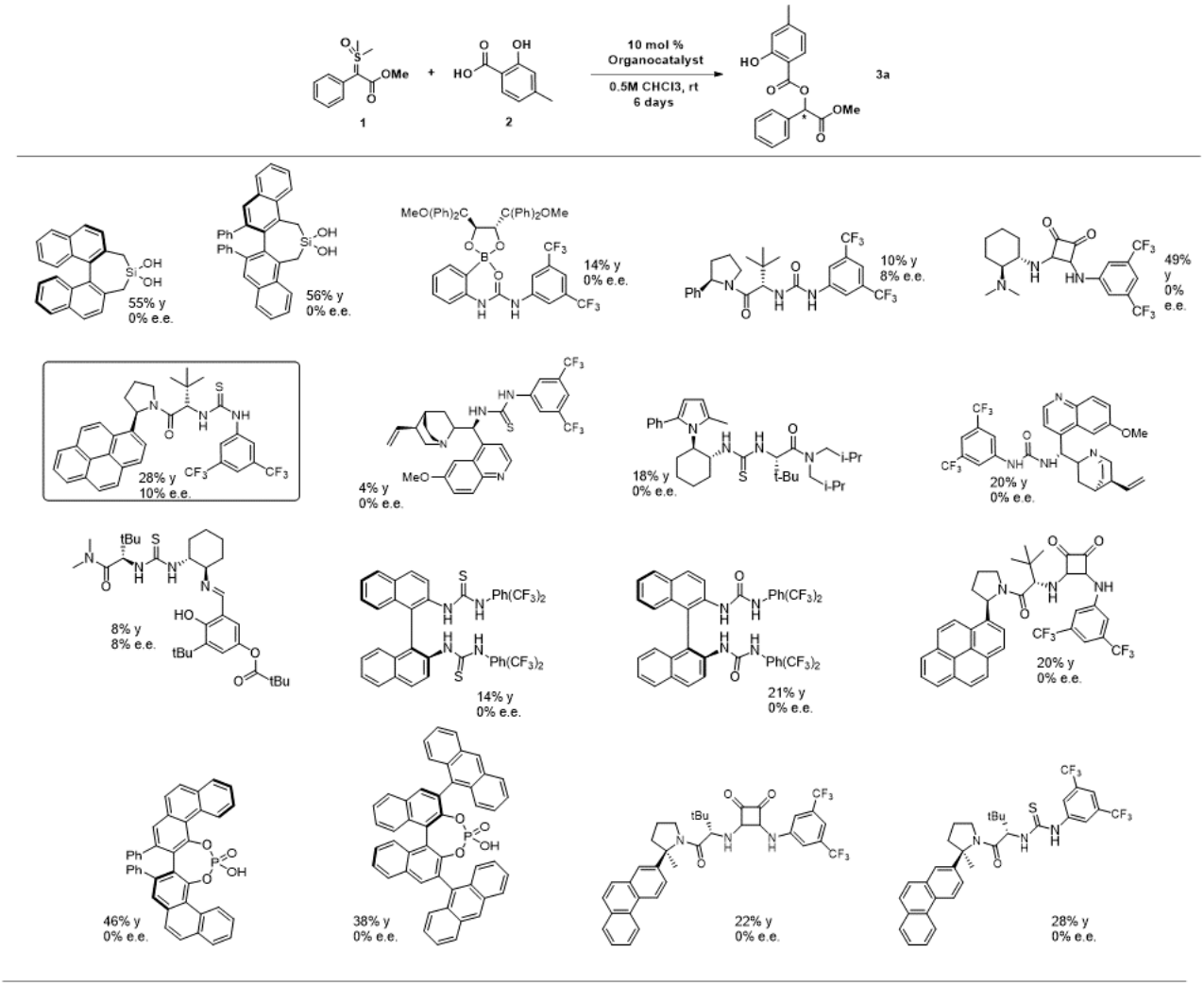


Figure 8: Sulfoxonium ylide and aryl thiol substrate scope. [10]

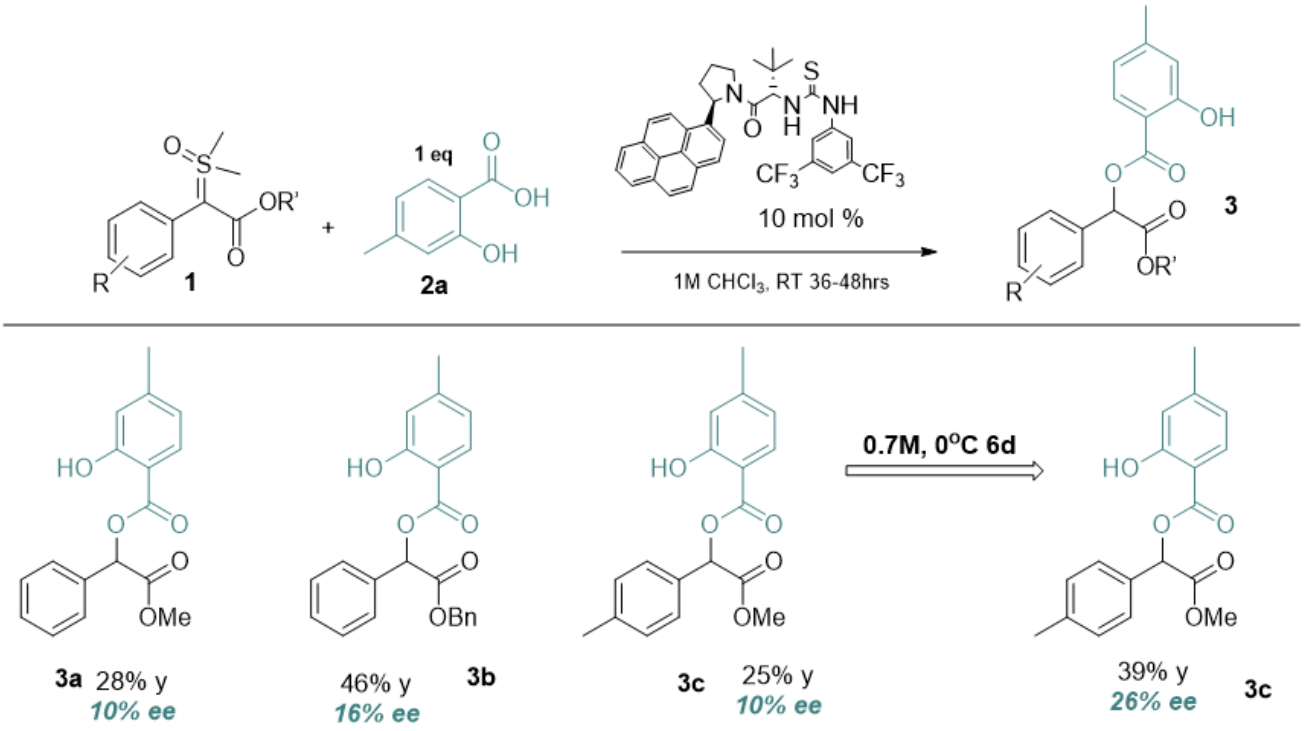
Table 1*:* Organocatalysts screening for the enantioselective O-H insertion with unsubstituted sulfoxonium ylide.



Ylide Screen O-H Insertions:

Taking the pyrene thiourea catalyst and the 2-hydroxy-4-methylbenzoic acid **(2a)** we furthered the optimization by conducting a screen of three ylides which were synthesized in the lab. Testing these other ylides, seen in Table 2, we found that the *p*-methyl phenyl sulfoxonium ylide **3c** gave *20% ee*, as opposed to *10% ee* from the unsubstituted ylide **3a**, at room temperature. When the same reaction with the *p*-methyl phenyl ylide was cooled to 3°C and reacted for six days, we were able to achieve *26% ee*. The benzyl ylide **3b** had the largest yield of 46% but saw a decrease in *ee* of 10% when compared to **3c**.

Table 2: Testing various ylides with 2OH, 4Me benzoic acid and pyrene thiourea catalyst.

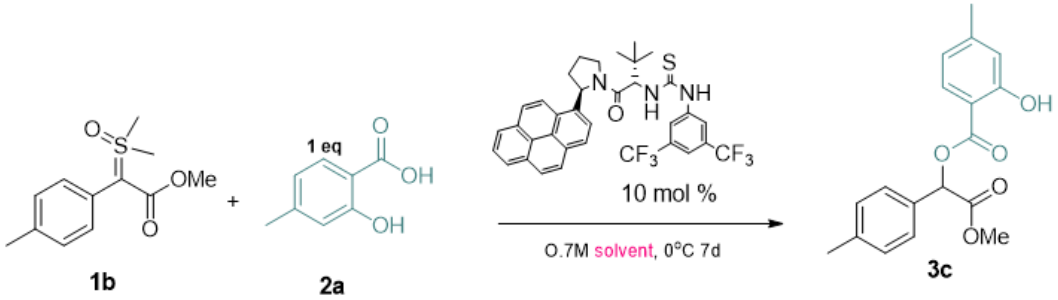


When optimized conditions, were applied to other ylides racemically, we found that the reaction successfully worked for twelve other sulfoxonium ylides, opening the door to a massive amount of insertion possibilities.

Solvent Screen O-H Insertions:

With the combined optimized conditions to synthesize **3c**, a solvent screen at 0°C eluded that tert-butyl methyl ether (TBME) produced the highest enantioselectivity (54% *ee*) but had a considerably low yield of 7%. When **3c** was synthesized under the same conditions but this time reacting at room temperature, we observed an increased yield, but unfortunately the enantioselectivity decreased by 9%. Compared to the other seven solvents, TBME at room temperature still afforded the highest *ee*, only to be closely followed by ethanol at 40% *ee*. We decided to continue our optimization studies with the solvent and temperature that gave the best *ee* and yield together (TBME at room temperature), hoping to increase the enantioselectivity upon further optimization studies.

Table 3: Solvent screen with optimized conditions.

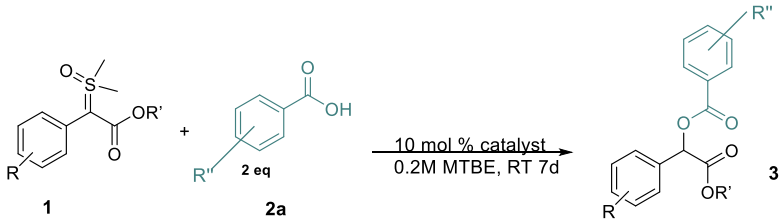


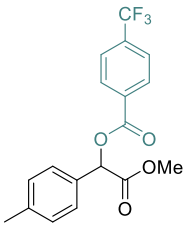
SOLVENT	TIME	YIELD	EE
DCM	5d	18%	Racemic
$CHCl_3$	6d	39%	26%
Et_2O	5d	5%	40%
TBME	**6d**	**7%**	**54%**
Toluene	5d	37%	26%
THF	6d	11%	22%
ClBn	6d	17%	26%
o-Xylene	6d	18%	28%

We had previously characterized a great deal of racemates, so at this point we were ready to begin testing a variety of benzoic acids and ylides with the predetermined conditions of 0.2M TBME, RT for 6-7 days**.** With these conditions, we were able to perform several chiral reactions using a combination of ylides and benzoic acids, refer to Table 4, but ultimately due to the

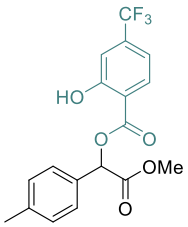
supply chain, progress was halted because of the inability to obtain the starting material needed for the pyrene thiourea catalyst. Following this, we continued an expansive racemic substrate scope, in toluene at 60-80^{o}C, which included electron donating and withdrawing substituents. Once these racemic substrates can be paired with the optimized conditions, the project will have a large scope of enantioselective products to draw conclusions from. All racemic compounds are displayed in Table 5 and the characterizations can be found in *Chapter 3* in the event that another student works to complete this project later.

Table 4: Chiral substrates with respective *ee* that were synthesized and characterized.

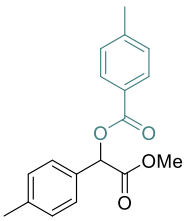




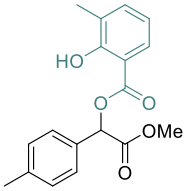
3x: 29% y
14% ee



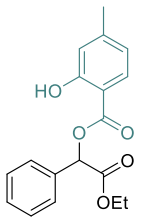
3y: 32% y
0% ee



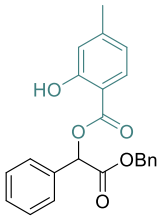
3z: 40% y
24% ee



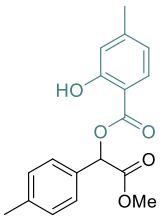
3aa: 53% y
28% ee



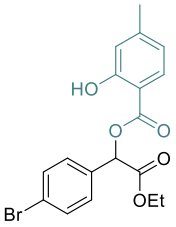
3ab: 27% y
30 % ee



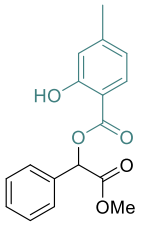
3ac:: 12% y
38% ee



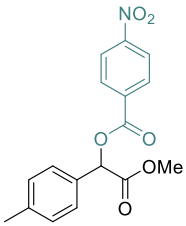
3c: 35% y
40% ee



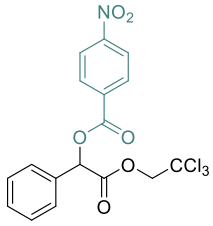
3ad: 21% y
24% ee



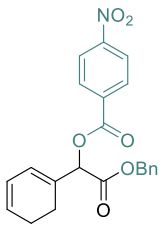
3a: 14% y
30% ee



3ae: 25% y
32% ee

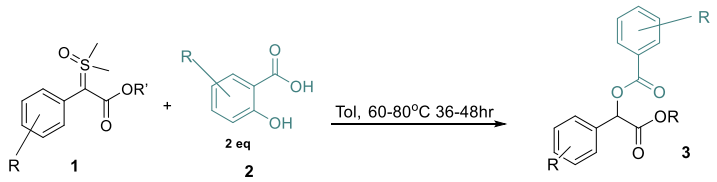


3af: 38% y
24% ee

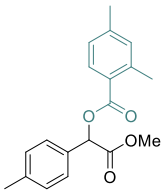


3ag: 10% y
26% ee

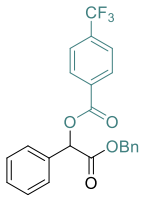
Table 5: Racemic substrates synthesized and characterized.



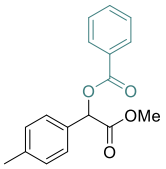
1 2 3



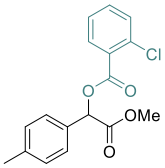
3b: 53% y



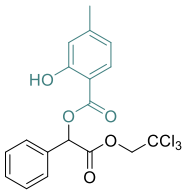
3d: 74% y



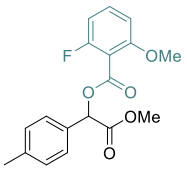
3e: 51% y



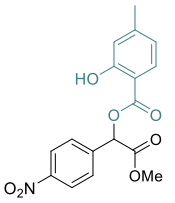
3f: 48% y



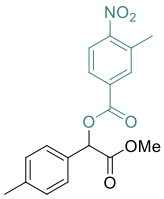
3g: 33% y



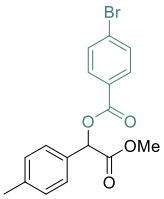
3h: 53% y



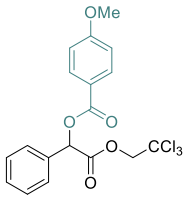
3i: 20% y



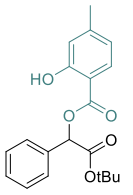
3j: 90% y



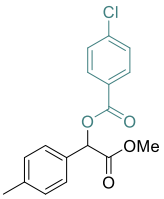
3k: 67% y



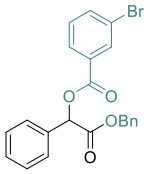
3l: 48% y



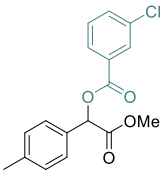
3m: 15% y



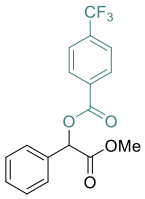
3n: 85% y



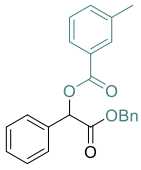
3o: 50% y



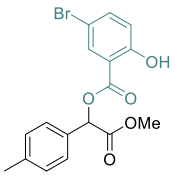
3p: 73% y



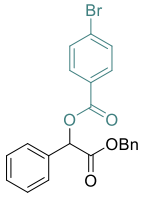
3q: 57% y



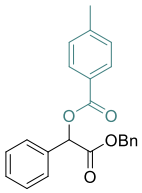
3r: 88% y



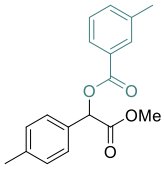
3s: 30% y



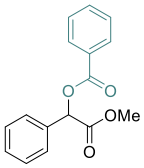
3t: 62% y



3u: 65% y



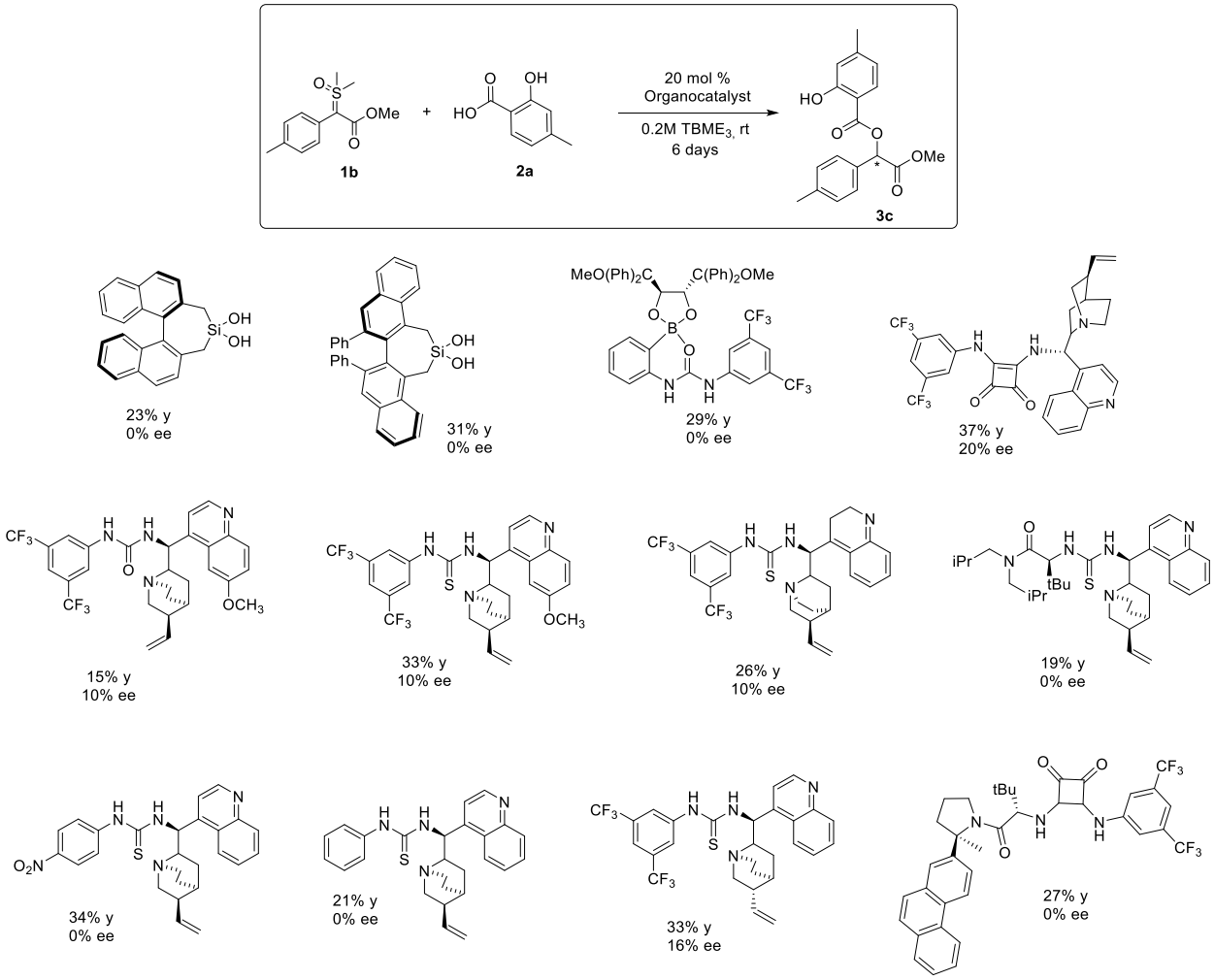
3v: 85% y



3w: 29% y

Therefore, we wondered if the catalysts in the solvents we found to have worked better in the solvent screen would produce higher *ee* when compared to the chloroform. This led us to do another catalyst screen in TBME at room temperature. Unfortunately, doing so did not give us a higher *% ee* when compared to the success with achieved with our optimized conditions (*47% ee*).

Table 6*:* Organocatalyst screening for the enantioselective O-H insertion with the *p*-methyl sulfoxonium ylide.



Summary and Future Work:

Due to the unforeseen circumstances described above and the current status, there is still potential for this project. Fortunately, the work that has been done up until this point has provided us with a well-rounded catalyst that has shown enantioselectivity of 40% *ee*. Therefor

going forward, the next part of the project would be to use the characterizations of the racemic compounds and synthesize them chirally to determine the enantioselectivity of them. Although there were only twelve compounds, we were able to optimize chirally, we were able to draw upon some conclusions and hypothesize what ylide and benzoic acid combinations will afford the highest enantioselectivity. When the electron withdrawing group CF_3 was in the *para* position, the resulting products (**3x** & **3y**) afforded low enantioselectivity, but when the electron withdrawing group NO_2 was in the same position, the resulting products (**3ae**, **3af**, & **3ag**) afforded moderate yields and *ee*. When the hydroxy (OH) electron withdrawing group was in the *ortho* position, aside from when combined with CF_3 (**3y**), the resulting products (**3a** & **3aa**-**3ad**) showed moderate to high enantioselectivity ranging from 24% - 40%.

The *p*-methyl sulfoxonium ylide was best with the 2OH, 4Me benzoic acid (**3c**) where the 40% *ee* was achieved but was racemic when the methyl group was replaced with a trifluoromethyl group. The benzyl ylide **3ac** and **3ag** had slight ee in the two reactions but both yields were only around 10%. Since the chiral scope was limited, it cannot be concluded the effects of the substituents on the ylides in respect to *ee*.

Chapter 2: Quinolones

2.1 Nitrogen Heterocycles:

Nitrogen heterocycles have gained increased attention in life science studies which has been attributed to their comprehensive pharmacological activities, contribution to the development of hundreds of organic synthesizes, and the fact that their backbones are constituents of bioactive molecules.[11-12] Additionally, N-heterocyclic compounds are electron rich and can readily accept or donate a proton and easily establish weak interactions with other molecules, such as hydrogen bonding, dipole-dipole, and van der Waals. These interactions illude to the high solubility of the compounds, which markets these skeletons extremely valuable to drug research and design because they allow high affinity binding with a variety of receptors and enzymes in bioactive targets. [12]

Nitrogen containing heterocycles can range from three membered to eight membered aromatic or non-aromatic heterocycles. These analogs make up more than 75% of FDA approved drugs, which is unsurprising due to the characteristics described above.[12] Figure 9 details some examples of heterocyclic nitrogen-containing drugs, biologically active compounds, and structures found in nature. [4]

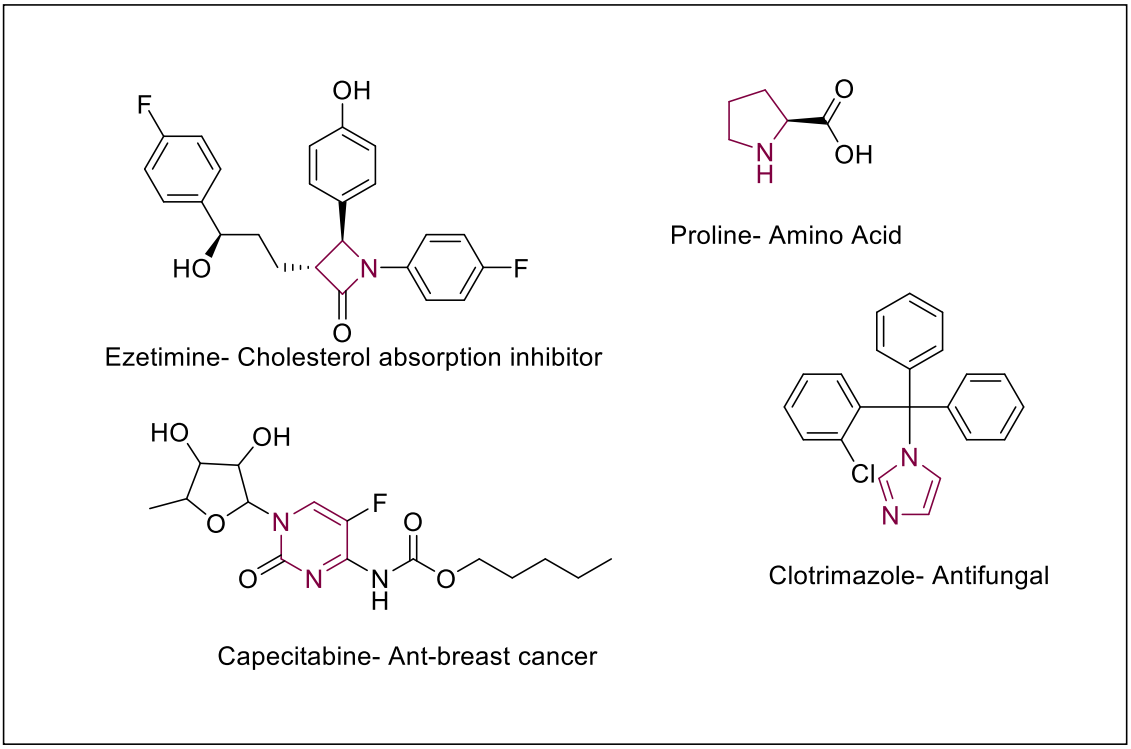


Figure 9: Examples of heterocyclic nitrogen-containing drugs, biologically active compounds, and structures found in nature. [4]

2.2 Quinolones:

Quinoline and quinolone backbones are seen extensively in the pharmaceutical industry as well as in nature, where their structures are typically seen as subunits for more complex compounds. In essence, the quinolone backbone is a quinoline, as seen in Figure 10. Both compounds can easily be tautomerized to the hydroxyl product. These products and their derivatives have been shown to possess antimalarial, antibiotic, antitubercular, antiproliferative, antiprotozoal, antihypertensive, and anti-HIV biological activities.[12] Some examples of those such compounds are referenced in Figure 11.

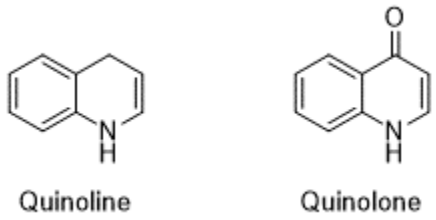


Figure 10: Difference between quinolone and quinoline.

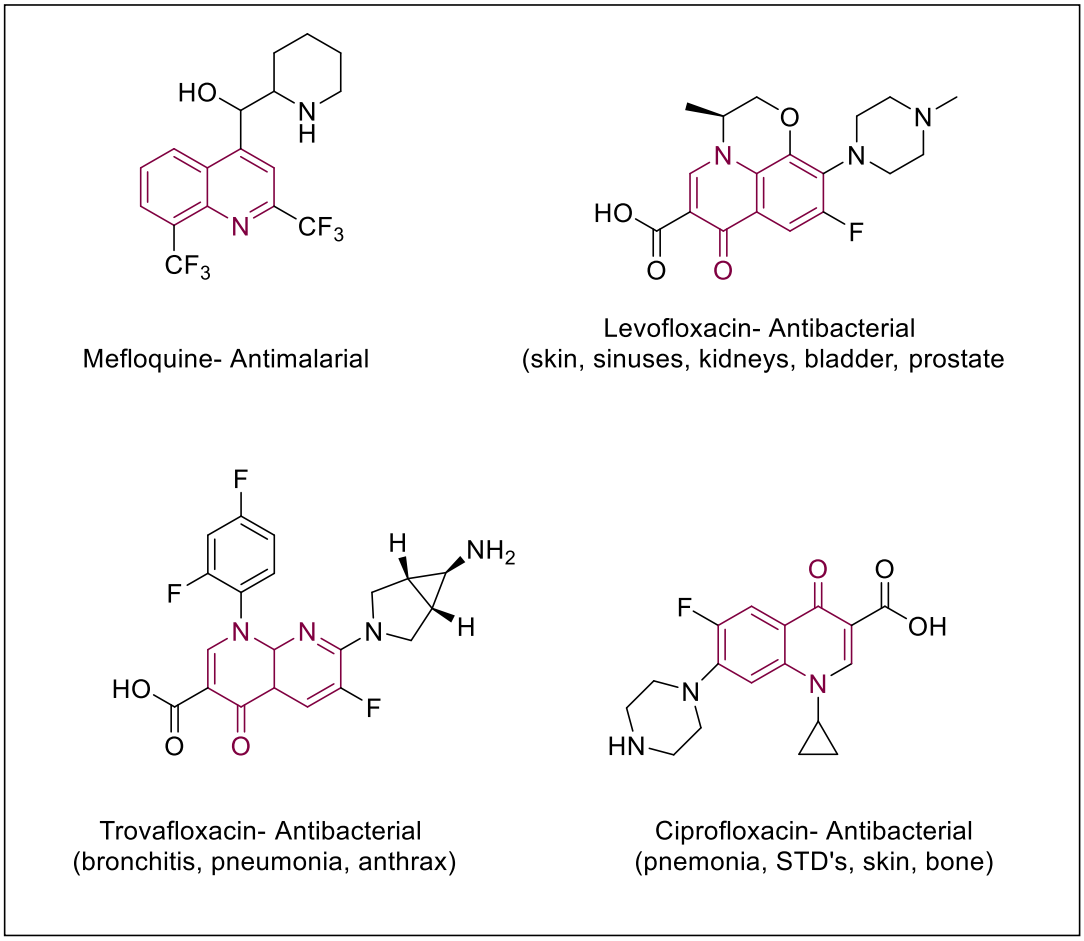


Figure 11: Biological compounds with quinolone backbone.

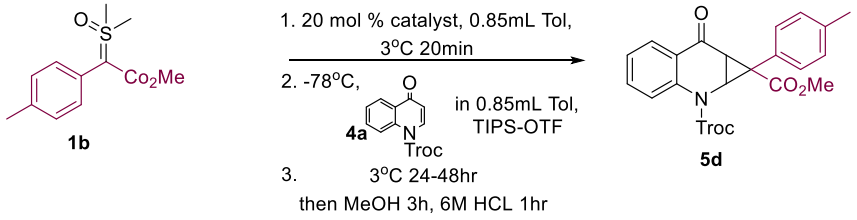
The quinolone structure can go through a diverse range of treatments to be altered, one being ring expansion via a cyclopropanation. At the time this report was written, there are no known reactions of quinolone cyclopropanation with sulfoxonium ylides. The scope of this work is on the characterization of cyclopropanations of quinolones. Upon further reaction, the cyclopropanation has been shown to result in a 7-membered ring expansion. Although, no research was done to examine the enantioselectivity of these compounds, only of the cyclopropanation reactions. It is because of the time constraints with this project that led us to the decision to discontinue the investigation of catalytic sources, leaving the characterization for a new member of the group to further conduct a catalyst screen and reoptimize the conditions to find which is the most appropriate.

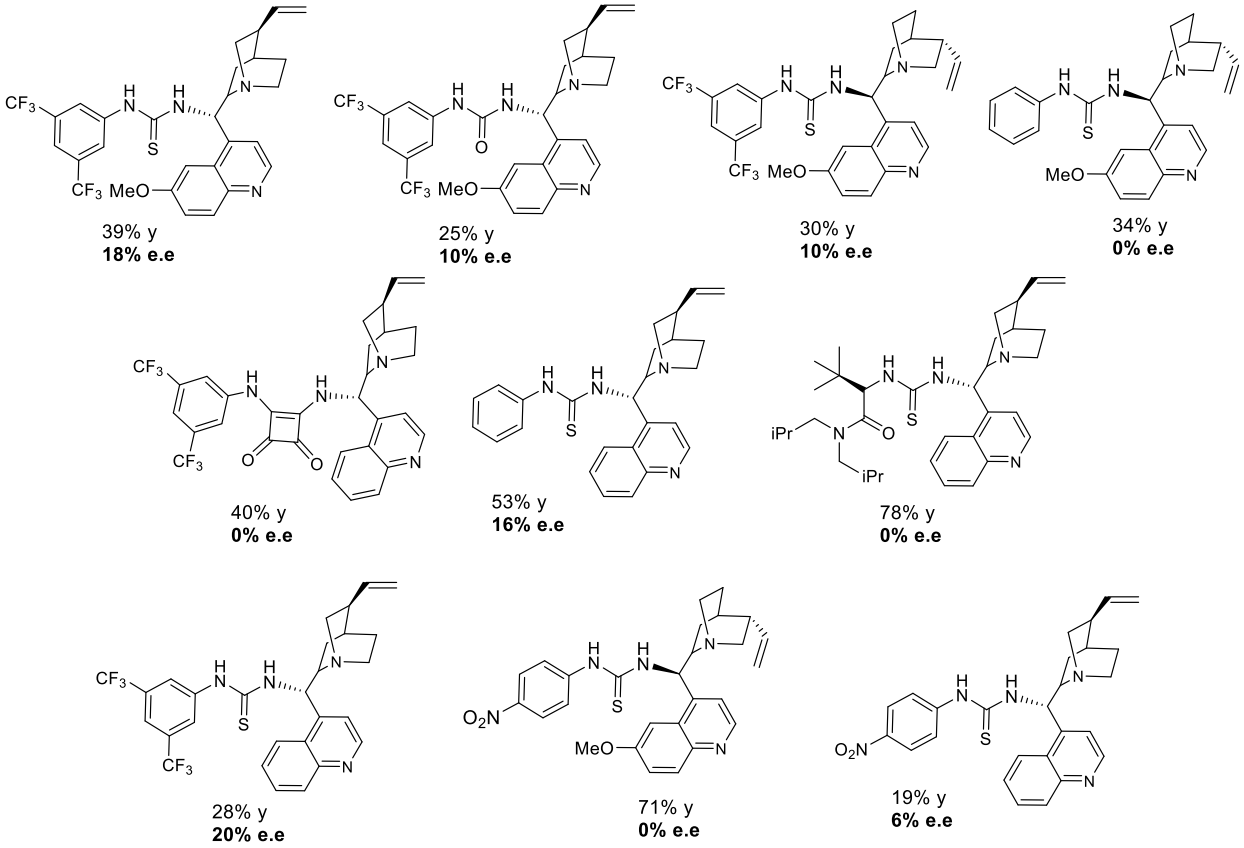
2.3 Experimental:

Quinolone Catalyst Screen:

After confirming via ^{1}H NMR spectroscopy and HPLC that a troc-protected quinolone formed a cycloproponated product racemically, we began a catalyst screen looking for *ee* produced by one or more catalysts. Though most of the screened catalysts had under 10% *ee*, we saw that a $(CF_3)_2$ thio-cinchronidine and thio-quinidine both gave about 20% *ee* unoptimized.

Table 7: Organocatalyst screening for the enantioselective cycloproponation with the *p*-methyl sulfoxonium ylide and troc protected quinolone.





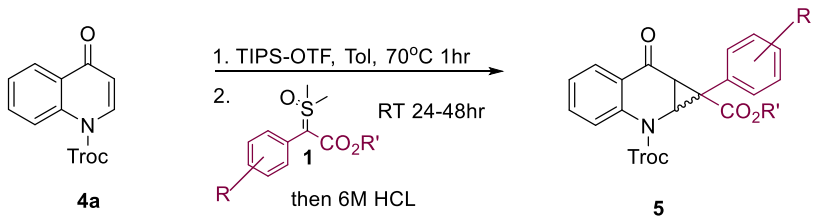
Looking to further explore the reactivity patterns of these quinolones, we began investigating the possible coordination with metals and catalysts to produce enantiomeric excess. As this is novel research, we needed to explore possible order of operations as well as different combinations of catalysts and lewis acids. This screen can be found in the *Supporting Information.* Unfortunately, after a significant number of reactions with various metals, catalysts, quinolones, and ylides at different temperatures, we were unable to conclude on a mechanism that produced higher enantiomeric excess than that of the initial catalyst screen. The table of

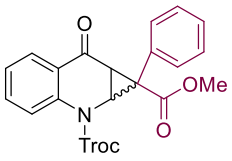
different order of operations, catalysts, and metals that were used can be found in the Supporting Information section of this paper.

Racemic Substrates:

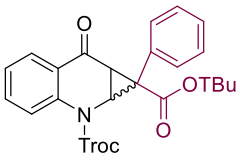
All sulfoxonium ylides available to be synthesized were tested to see if they formed the predicted cycloproponated products and eight of them did, as seen in Table 8. The cycloproponated products whose results were inconclusive involved a *p*-NO_2 phenyl, CCl_3 ester, and *o*-Cl ylide.

Table 8: Racemic substrates synthesized with the troc protected quinolone and a variety of sulfoxonium ylides.

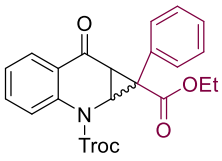




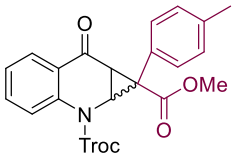
5a: 58%y



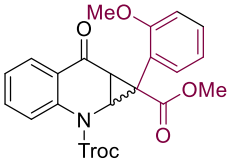
5b: 53% y



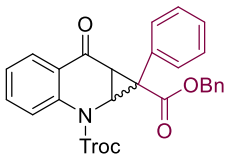
5c: 58% y



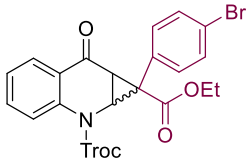
5d: 63% y



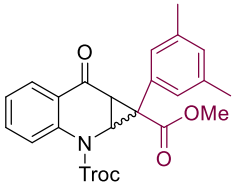
5e: 53% y



5f: 36% y



5g: 30 % y



5h: 55% y

2.4 Summary and Future Work:

A significant start to this novel research has been completed by the characterization of eight new racemic compounds. Included in this characterization is ^{1}H NMR, ^{13}C NMR, and IR

for four of the products and just the RF value for the other four. The remainder of the data which was not finalized by the time of this paper's submission can be found in a forthcoming paper written by Alexandria Leveille and myself. All the compounds that are synthesized and characterized thus far are single diastereomers, aside from the ones used in the catalyst screening and for continuation of this project an effective catalyst will need to be determined so that the reactions can be characterized based on their enantioselectivity as well. Based on the original catalyst screening, the reactions seem to favor thiol-based catalysts, particularly ones with two CF_3 groups on a phenyl ring, as the highest *ee* recognized was with the $(CF_3)_2$-phenyl thiol cinchronadine and $(CF_3)_2$-phenyl thiol quinidine.

We were fortunate enough to be able to test a variety of ylides with the troc protected quinolone but going forward a wider substrate scope could be established by testing other substituted troc protected quinolones as well as other protected quinolones. Four other protecting groups on the quinolone were tested (Me, Co_2Me, OBn, & Boc) and we were unable to isolate a product spot and we hypothesize that these other protecting groups are not as acidic as the troc and do not effectively protect the nitrogen from being involved in side reactions.

Additionally, as seen with the Chromenome project, there is potential for the cycloproponated products to continue reacting and undergo a seven membered ring expansion. This theory was tested with the unsubstituted ylide **1a** and the product was isolated in low yield. Since the yield was low, there was not enough product to conduct any further characterizations aside from a crude NMR to conclude it was the product. Although that data is not present in this publication, it is mentioned because it illudes to the wide scope of other reactions and chemical synthesis that are possible with the cycloproponated products. Ideally, a catalyst which could produce enantioselectivity with the ring expanded products will be discovered, as this is an area that we did not investigate.

Chapter 3: Experimental Procedures and Characterizations

The Supporting Information can be found in the attached document.

Acknowledgements and References

The completion of this project would have not been possible without the help and support from Anita Mattson and her group members as well as the Worcester Polytechnic Institutes Chemistry department. A special thanks to Alexandria Leveille who took on the role of mentoring me four years ago. This project and my success in the lab would not have been possible without Allie's guidance and support.

1. Burtoloso, A.C.B., Dias, R.M.P. and Leonarczyk, I.A. Sulfoxonium and Sulfonium Ylides as Diazocarbonyl Equivalents in Metal-Catalyzed Insertion Reactions. *Eur. J. Org. Chem.*, **2013**: 5005-5016. https://doi.org/10.1002/ejoc.201300581
2. Couch, E.D., Auvil, T.J. and Mattson, A.E. Urea-Induced Acid Amplification: A New Approach for Metal-Free Insertion Chemistry. *Chem. Eur. J*. **2014**, *20:* 8283-8287. https://doi.org/10.1002/chem.201403283
3. Zhu SF, Zhou QL. Transition-metal-catalyzed enantioselective heteroatom-hydrogen bond insertion reactions. Accounts of Chemical Research. **2012**, *45(8):*1365-1377. DOI: 10.1021/ar300051u. PMID: 22651217
4. Campos, K. R.; Coleman, P. J.; Alvarez, J. C.; Dreher, S. D.; Garbaccio, R. M.; Terrett, N. K.; Tillyer, R. D.; Truppo, M. D.; Parmee, E. R. The Importance of Synthetic Chemistry in the Pharmaceutical Industry. *Science* **2019**, *363* (6424), eaat0805. https://doi.org/10.1126/science.aat0805.
5. Tan, F., Liu, X., Hao, X., Tang, Y., Lin, L., & Feng, X. Asymmetric Catalytic Insertion of α-Diazo Carbonyl Compounds into O–H Bonds of Carboxylic Acids. *ACS Catalysis* **2016**, *6*, 6930-6934.
6. Kerru, N.; Gummidi, L.; Maddila, S.; Gangu, K.K.; Jonnalagadda, S.B. A Review on Recent Advances in Nitrogen-Containing Molecules and Their Biological Applications. *Molecules* **2020**, *25*, 1909. https://doi.org/10.3390/molecules25081909
7. Vermeeren, P., Hamlin, T. A., Bickelhaupt, F. M., & Fernández, I. Bifunctional Hydrogen Bond Donor-Catalyzed Diels-Alder Reactions: Origin of Stereoselectivity and Rate Enhancement. *Chemistry (Weinheim an der Bergstrasse, Germany)* **2021**, *27*(16), 5180–5190. https://doi.org/10.1002/chem.202004496
8. Kerru, N., Gummidi, L., Maddila, S., Gangu, K. K., & Jonnalagadda, S. B. A Review on Recent Advances in Nitrogen-Containing Molecules and Their Biological

Applications. *Molecules (Basel, Switzerland)* **2020**, *25*(8), 1909. https://doi.org/10.3390/molecules25081909

9. Ramakrishna, K, Jayarani, A, Koothradan, FF, Sivasankar, C. An efficient method to prepare sulfoxonium ylides and their reactivity studies using copper powder and Sc(III) as catalysts: Molecular and electronic structure analysis. *Appl Organomet Chem*. **2020**; 34:5748. https://doi.org/10.1002/aoc.5748
10. P. B. Momo, A. N. Leveille, E. H. E. Farrar, M. N. Grayson, A. E. Mattson, A. C. B. Burtoloso, *Angew. Chem. Int. Ed.* **2020**, *59*, 15554.anie.202007001.pdf (Transition Metal Catalyzed Insertion Reactions with Donor/Donor Carbenes)
11. Shintani, R., Yamagami, T., Kimura, T., & Hayashi, T. Asymmetric synthesis of 2-aryl-2,3-dihydro-4-quinolones by rhodium-catalyzed 1,4-addition of arylzinc reagents in the presence of chlorotrimethylsilane. *Organic letters* **2005**, *7*(23), 5317–5319. https://doi.org/10.1021/ol052257d
12. Auvil, T.J., Schafer, A.G. and Mattson, A.E. Design Strategies for Enhanced Hydrogen-Bond Donor Catalysts. *Eur. J. Org. Chem*., **2014**: 2633-2646. https://doi.org/10.1002/ejoc.201400035