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Thiourea Catalyst Development

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Thiourea Catalyst Development

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CELEBRATING SCHOLARSHIP AND CREATIVITY DAY

APRIL 23RD, 2020

Catalysis

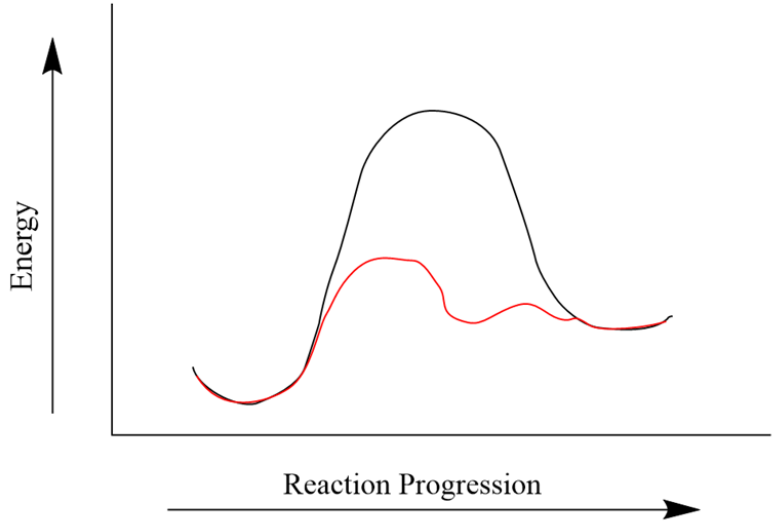
Provides an alternate pathway to reduce the activation energy

Catalyst temporarily binds to the reactants

- Does not chemically change

A few types of catalysts:

- Enzymes
- Metals
- Organic molecules



Black: regular reaction

Red: catalyzed reaction

Organocatalysis

Use of low molecular weight organic molecules to accelerate chemical reactions

Alternative to the heavily-studied metal- and enzyme-catalysts.[1]

Advantages[2]:

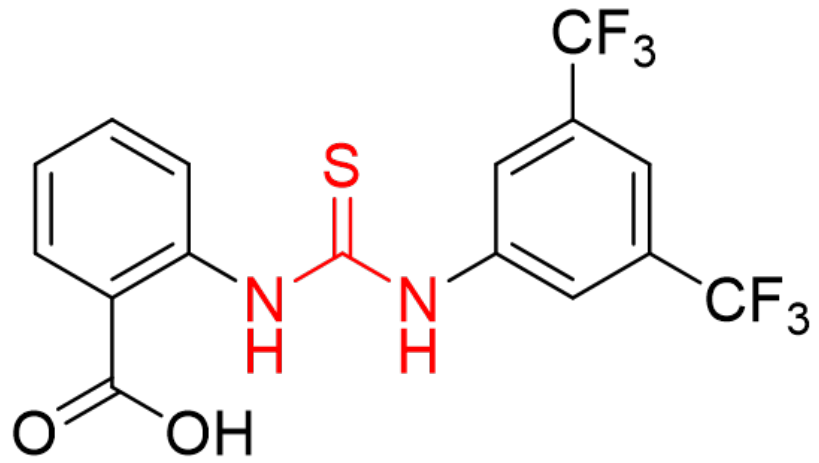
- low catalyst loading
- mild reaction conditions
- green chemistry characteristics
- high selectivity and efficiency
- low cost materials

1. Atodiresei, I. *ACS Catalysis,* **2015**
2. Seayad, J, *Organic Biomolecular Chemistry,* **2005**

Thiourea Organocatalyst

Noncovalent interactions
- Hydrogen bonding

Dual activation
- Nucleophile and Electrophile



Red: Thiourea functional group

Why use thiourea molecules?

ADVANTAGES

Low catalyst loading[3]

Mild reaction conditions[4]

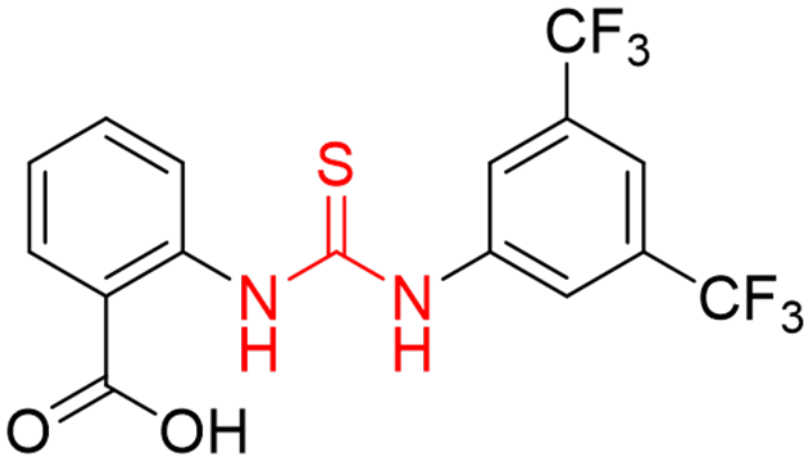
Stereoselectivity[5]

Low cost materials

APPLICATIONS

Pharmaceutical drug syntheses

Materials science syntheses



Red: Thiourea functional group

3. Giacalone, F, *Chemical Society Reviews* **2012**
4. Kiesewetter, M. K. *Macromolecules* **2010**
5. Jiang, X, *Organic Letters,* **2009**

Many Variations

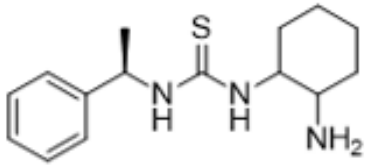
Two previously studied molecules shown on the right

Jiang – Michael addition[5]

Supady – Diels-Alder[6]

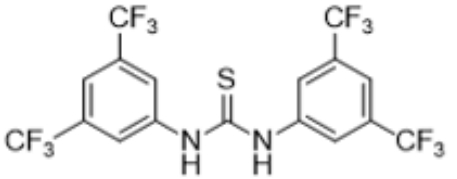
Carbon-carbon bond forming reactions

1



Jiang, X, et. al

2



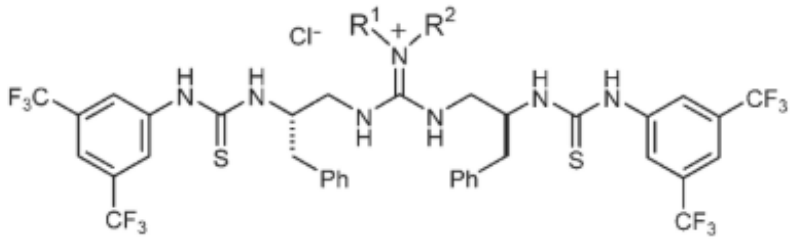
Supady, X, et. al

5. Jiang, X, *Organic Letters,* **2009**
6. Supady, A, *Organic Letters*, **2017**

Thiourea Catalyzes a Henry Reaction

Sohtome et. al, synthesized a guanidine-thiourea bifunctional organocatalyst[7]

Organocatalyst variations synthesized by Sohotome:



1a : $R^1 = C_4H_9$, $R^2 = H$
1b : $R^1 = C_4H_9$, $R^2 = C_4H_9$
1c : $R^1 = R^2 = (CH_2)_4$
1d : $R^1 = C_8H_{17}$, $R^2 = H$
1e : $R^1 = C_{18}H_{37}$, $R^2 = H$
1f : $R^1 = 3, 5\text{-}(CF_3)_2\text{-}C_6H_4$, $R^2 = H$
1g : $R^1 = 3, 5\text{-}(OMe)_2\text{-}C_6H_4$, $R^2 = H$

7. Sohotome, Y, *Adv. Synth. Catal.* **2005**

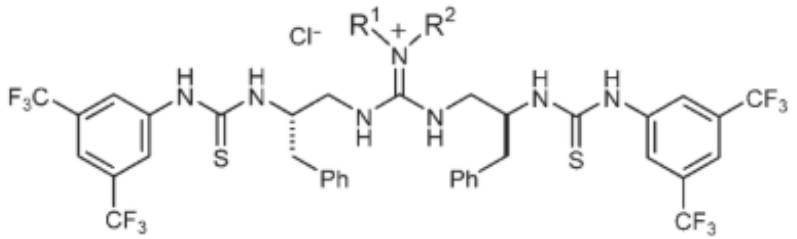
Thiourea Catalyzes a Henry Reaction

Sohtome et. al, synthesized a guanidine-thiourea bifunctional organocatalyst[7]

Studied it in a Henry, or nitroaldol reaction

Inspired a direction for our research

Organocatalyst variations synthesized by Sohotome:



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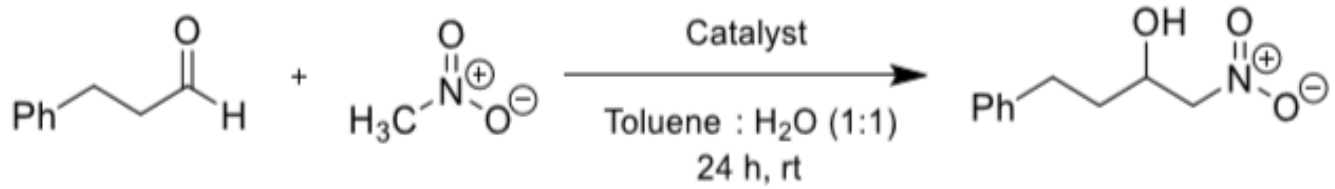
Henry (nitroaldol) reaction:

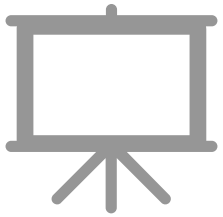


7. Sohotome, Y, *Adv. Synth. Catal.* **2005**

How do the functional groups present on a thiourea catalyst, as well as the shape and size of the molecule, affect its effectiveness as a catalyst?

Experiment Idea

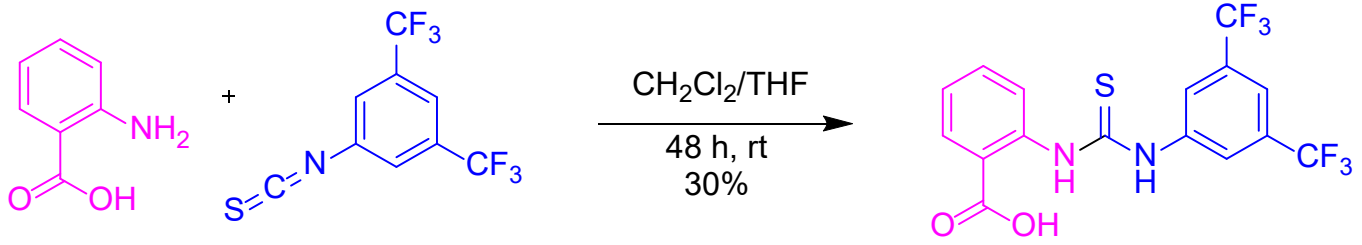
1. Synthesize novel thiourea molecules with varying functional groups



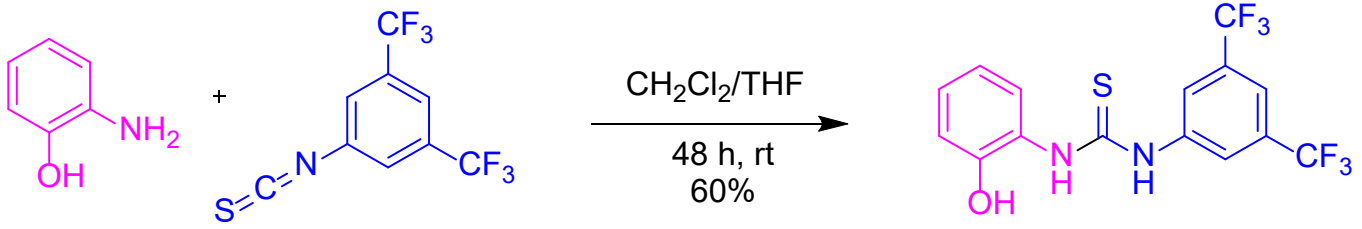
2. Screen them in a Henry reaction

3. Test how well the molecules promote the reaction

Synthesis of Novel Organic Molecules

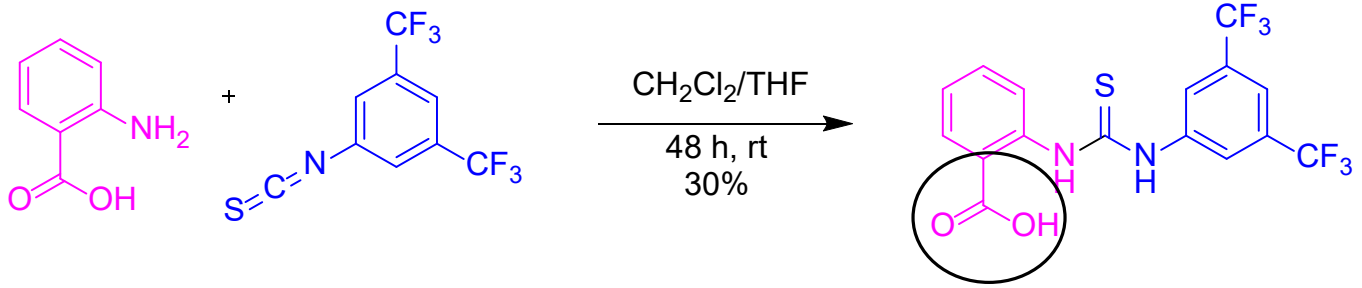


- ***ortho*-acid**

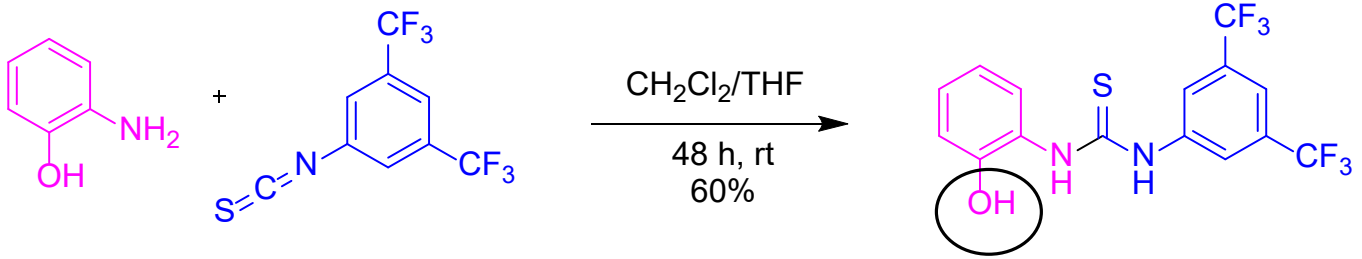


- ***ortho*-phenol**

Synthesis of Novel Organic Molecules

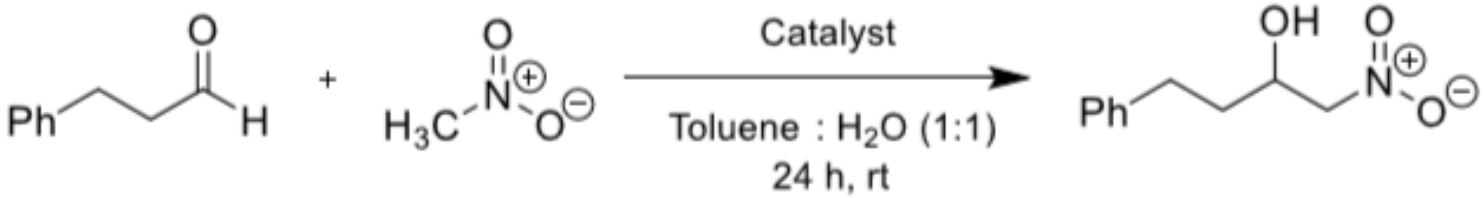


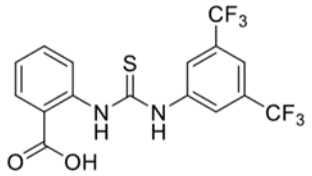
- ***ortho*-acid**



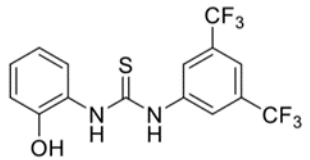
- ***ortho*-phenol**

Catalytic Screening in the Henry Reaction

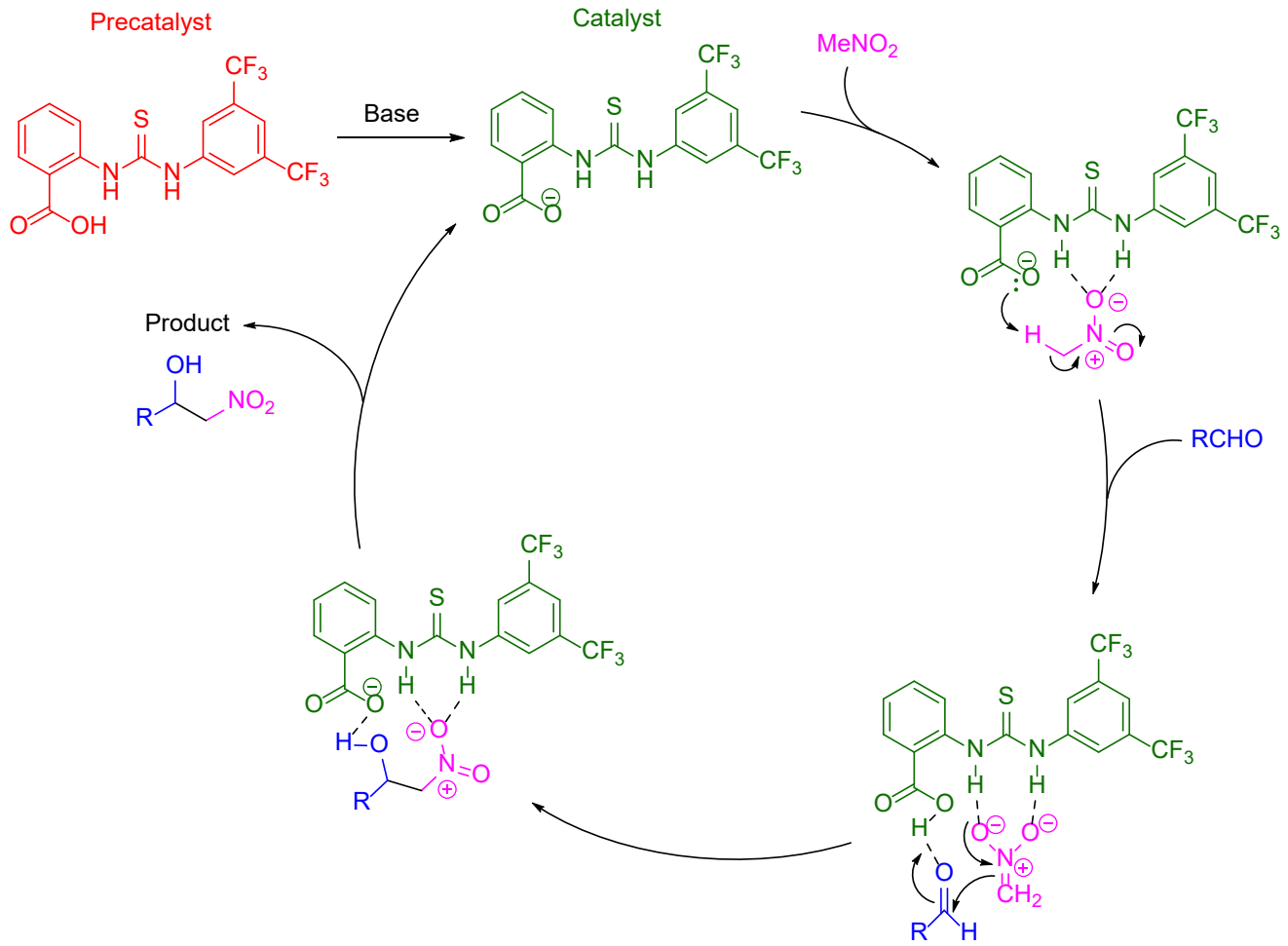




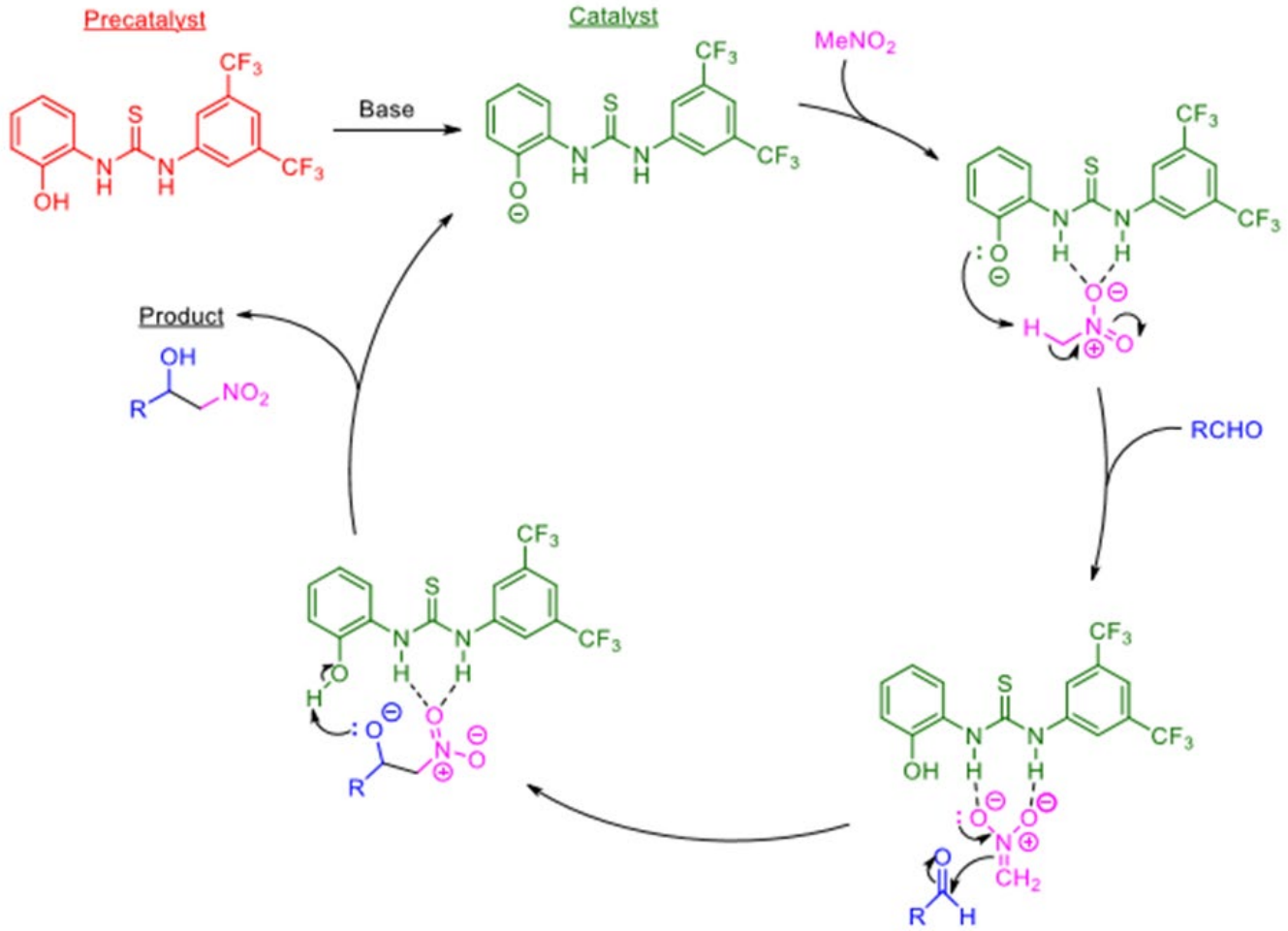
- ***ortho*-acid**



- ***ortho*-phenol**

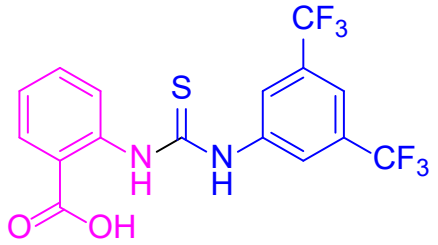


o-acid Proposed Catalytic Cycle

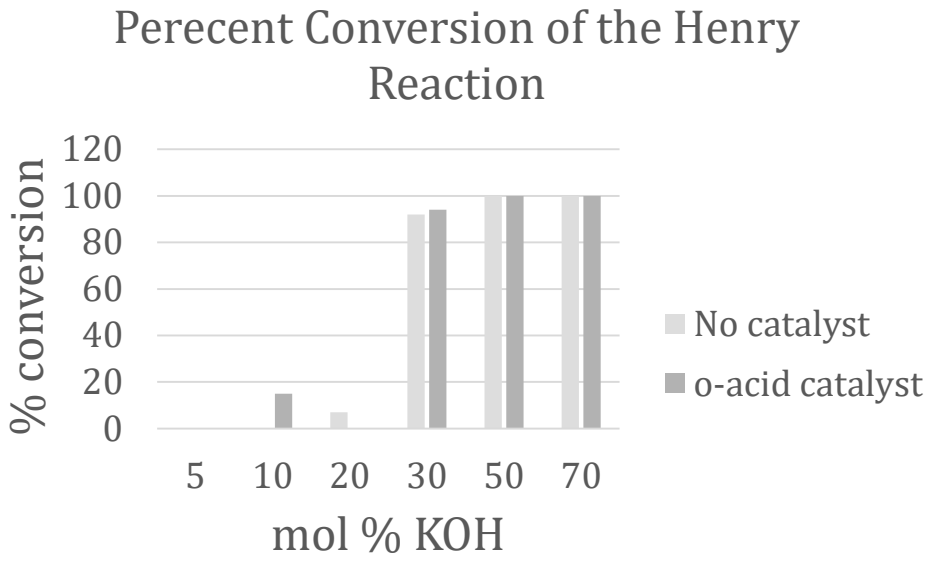


o-phenol Proposed Catalytic Cycle

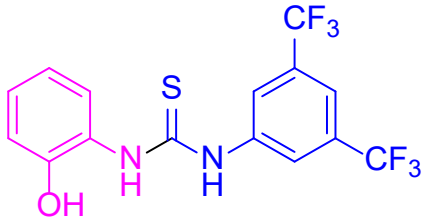
Screening Results: *o*-acid thiourea



mol % KOH (per aldehyde)	% conv. no catalyst	% conv. 10 mol % o-acid catalyst
5	0	0
10	0	15
20	7	In progress
30	92	94
50	Quant.	Quant.
70	Quant.	Quant.



Screening Results: *o*-phenol thiourea



mol % KOH (per aldehyde)	% conv. no catalyst	% conv. 10 mol % o-phenol catalyst
5	0	0
10	0	0
20	7	In progress
30	92	In progress
50	Quant.	In progress

This experiment is still in progress.

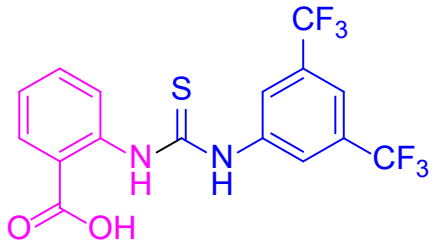
Conclusion

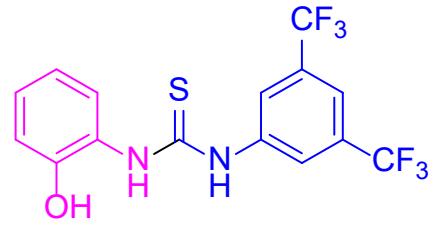
Henry reaction works with only base

- Catalyst optimizes balance of efficiency, safety, environment

Collect more data to finish the tables

- Determine which functional group produces a higher yield





Future Work

Finish gathering data on the current catalysts

Try other reactions:

- Diels-Alder
- Michael Addition

Synthesize different thiourea molecules

- Larger
- Mimic an enzyme active site

Acknowledgments

Thank you to the CSB/SJU Undergraduate Research Program for financial support. Thank you to the National Science Foundation for funding the FoCuS scholarship that brought me to CSB. Thank you to the Montana State University NSF-REU Program for the support and learning opportunities. Thank you to my research advisors Dr. Thomas Nicholas Jones, Dr. Mary Cloninger, and Dr. Kate Graham for guidance. Thank you to all my previous research partners Augie, Kenzie, and Brad and to Abby and Ellen for taking over the project for a while. Thank you to my professors, family, and friends for the support during my undergraduate career at the College of Saint Benedict.

UNDERGRADUATE RESEARCH PROGRAM
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Thank you!

PLEASE EMAIL ME WITH ANY QUESTIONS YOU MAY HAVE.

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