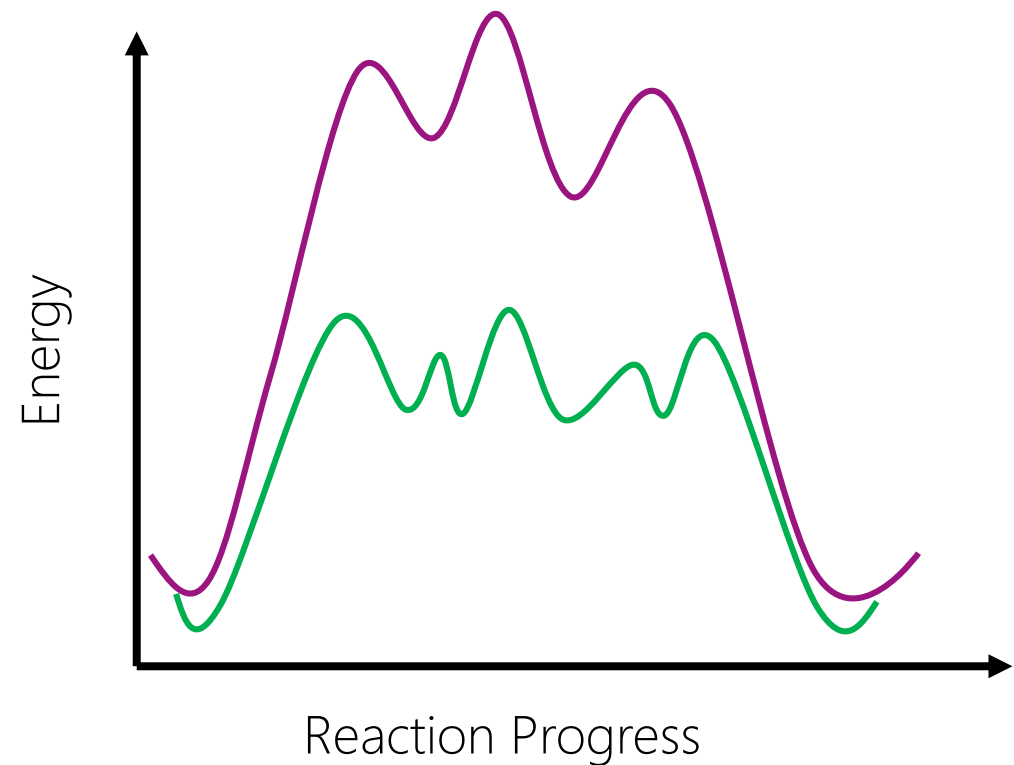


Development of Anthranilic Acid Based Thiourea Catalysts

Augie Witkowski
Jones & Graham

What is a catalyst?

- a recyclable compound that increases the rate of the reaction
- Use a different reaction pathway to lower overall energy



Organocatalysis

Use of low molecular weight compounds for catalysis

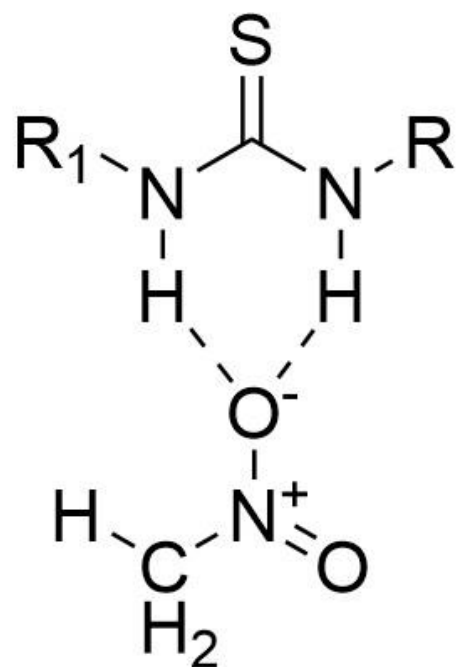
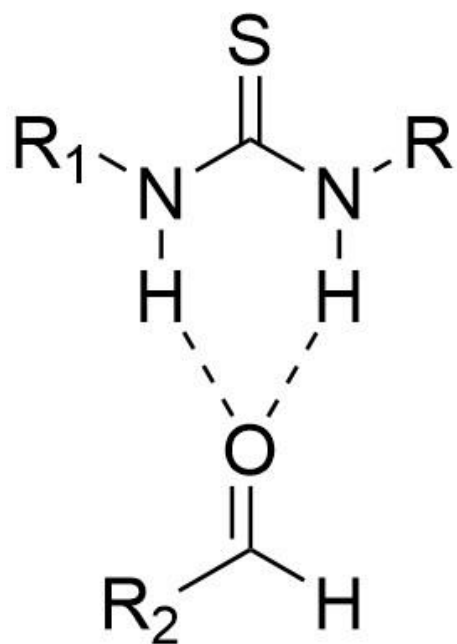
ADVANTAGES

- Can replace toxic and expensive metal catalysts
- Mild reaction conditions
- Does not require covalent activation

DISADVANTAGES

- High catalyst loading needed
- Potentially difficult separation

Thiourea Activation

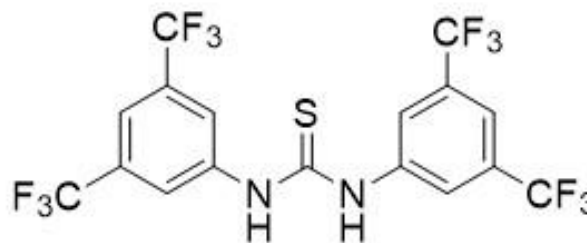
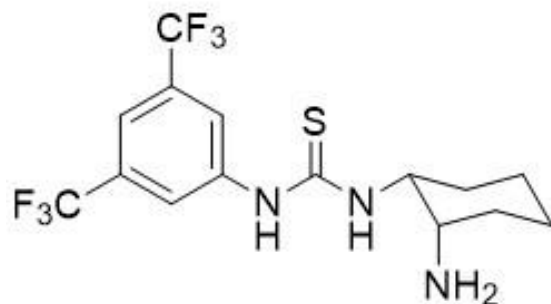
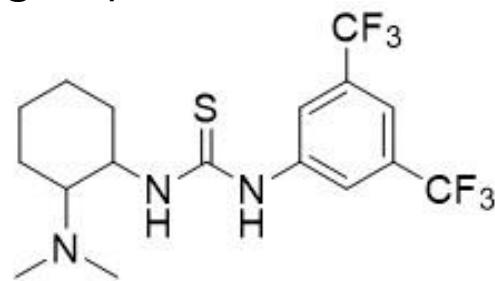


- Mild conditions
- Hydrogen bonding activation
- Nucleophilic and electrophilic activation

Prior Catalyst Structures

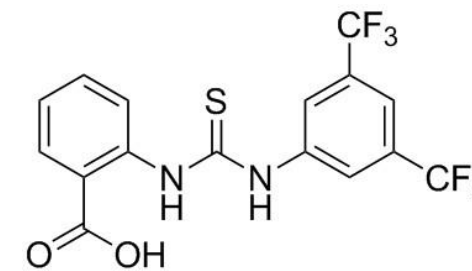
Common structural motifs:

- Electron withdrawing groups
- Bifunctional
- Basic amine groups

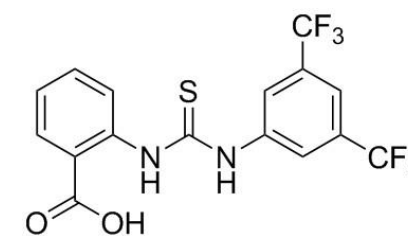
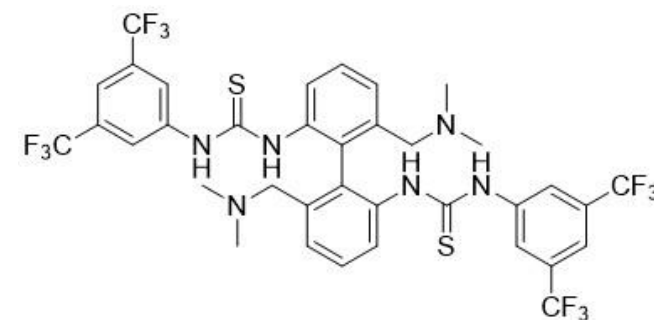
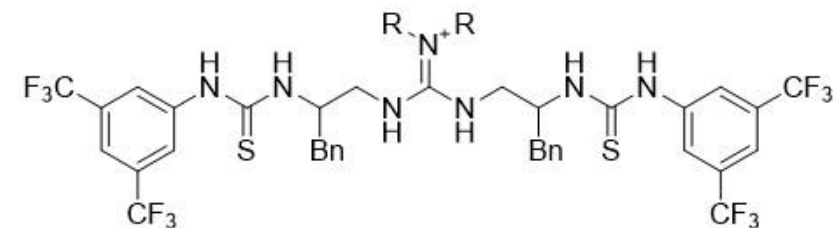
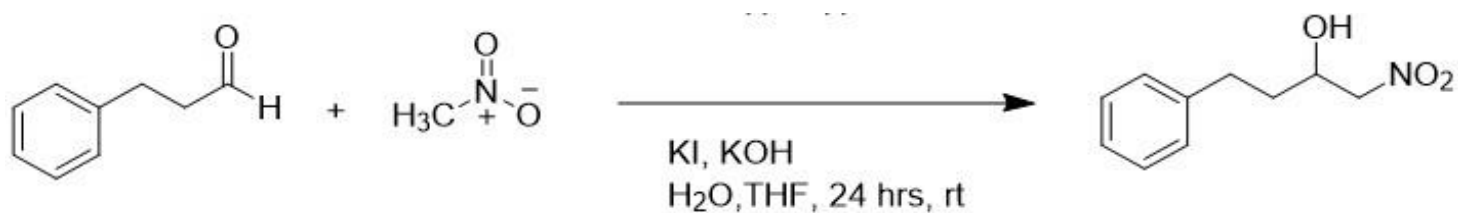
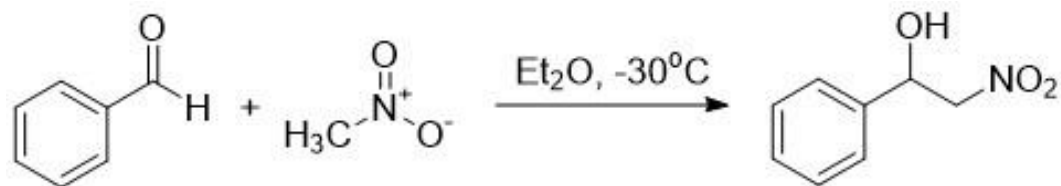
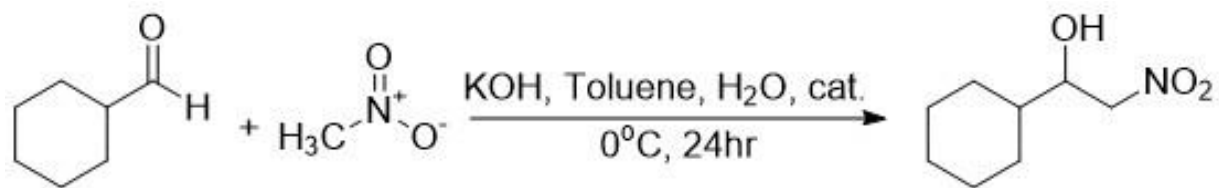


Our catalyst:

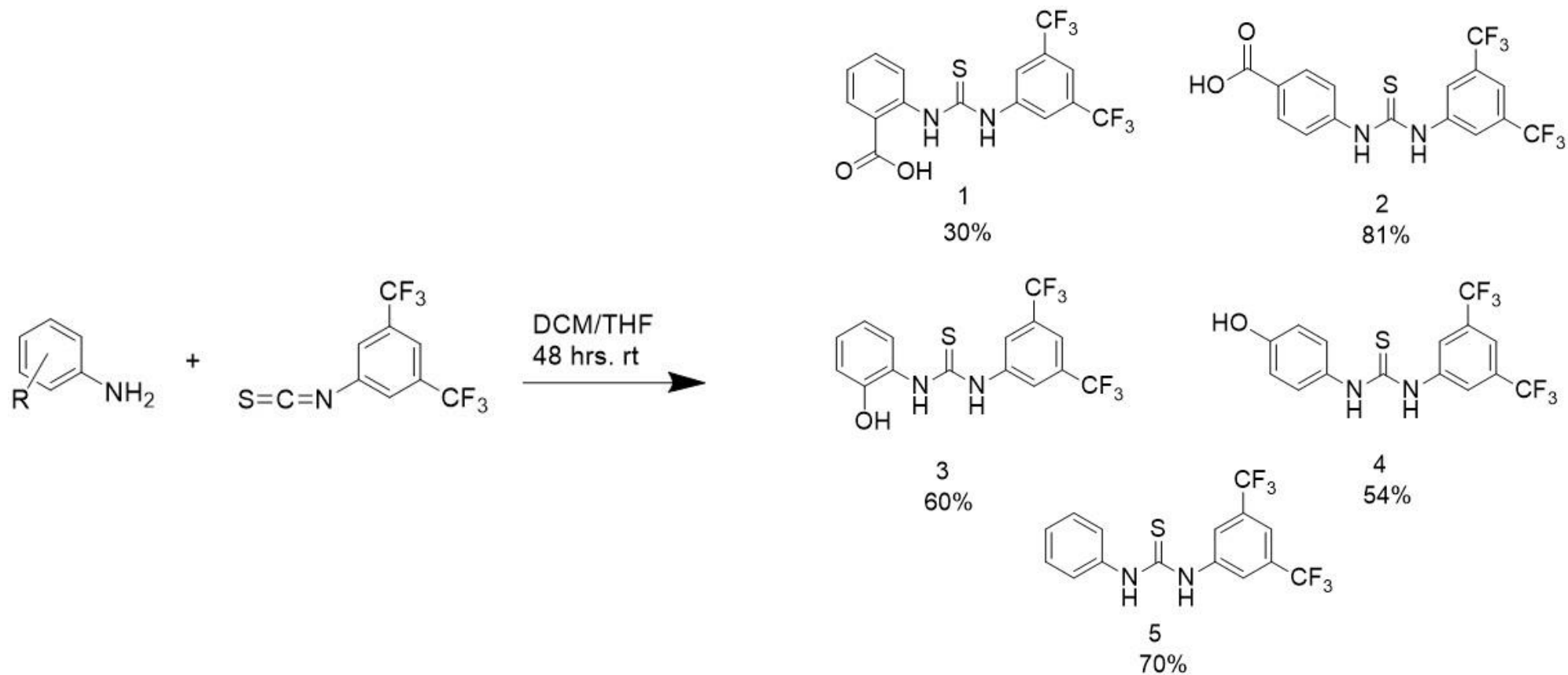
- Electron withdrawing groups
- Bifunctional
- Carboxylic acid group



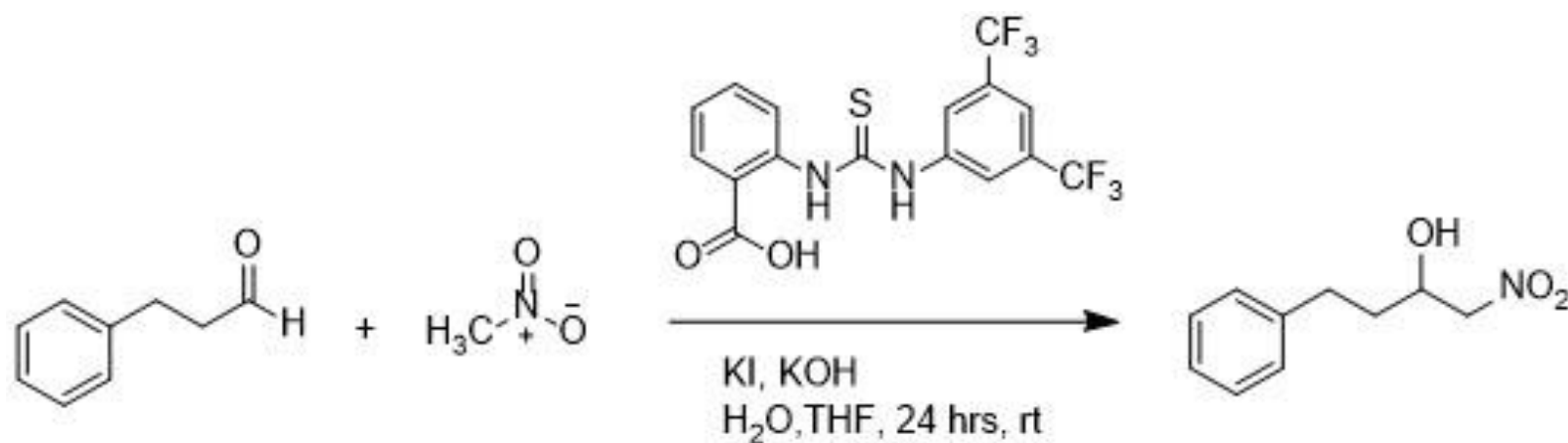
Previously Catalyzed Reactions



Synthesis of Catalysts

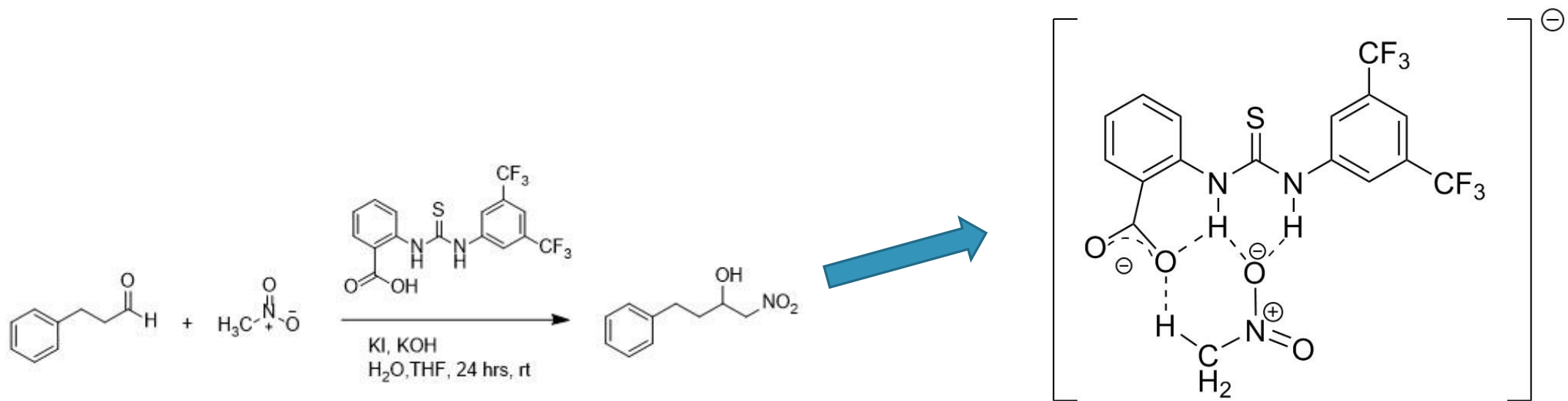


Screening of Anthranilic Acid Catalyst



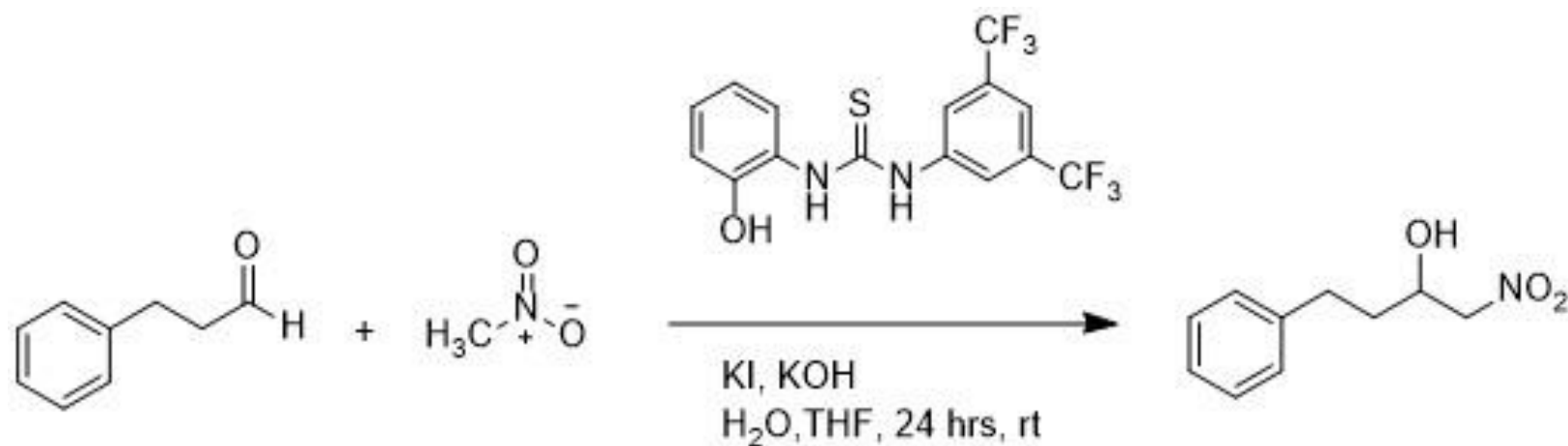
Average Percent Conversion with 5 mmol KI/KOH: 83%
Catalyst loading: 10% mol

How the Catalyst Works



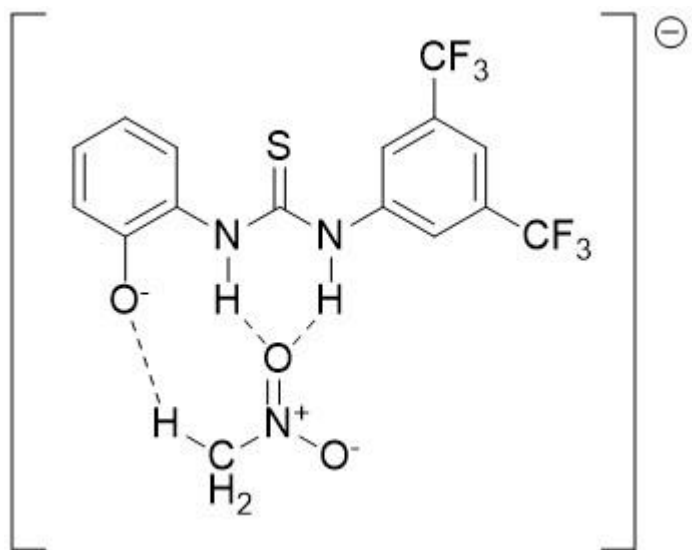
Proposed ring-like
stabilized transition state.

Screening of o-phenol catalyst

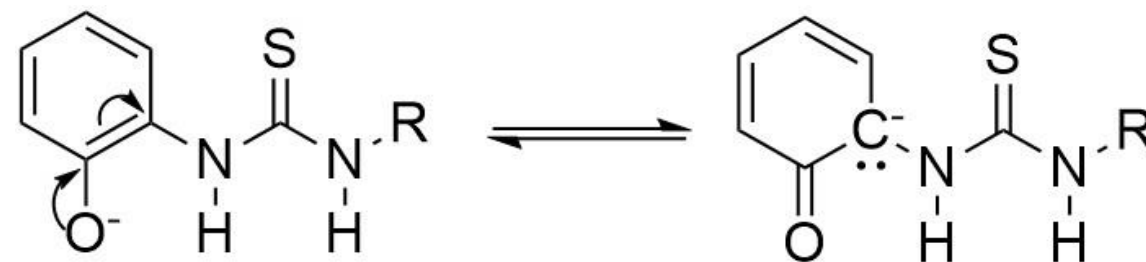


Percent Conversion with 5 mmol KI/KOH: 34%
Catalyst Loading: 10 mol %

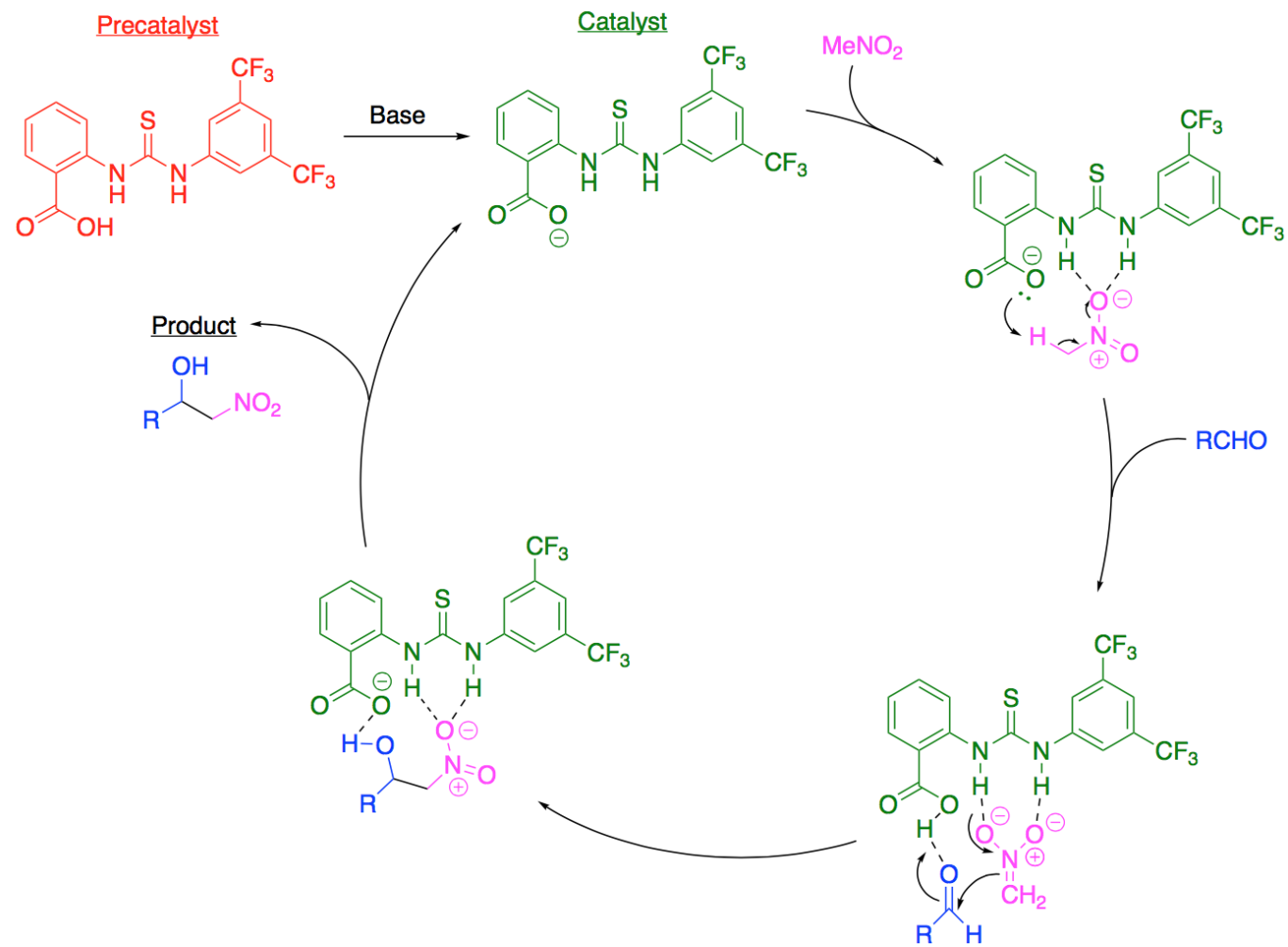
Variability in Yield



-Proposed transition state stabilization similar to the ortho-carboxylic acid catalyst

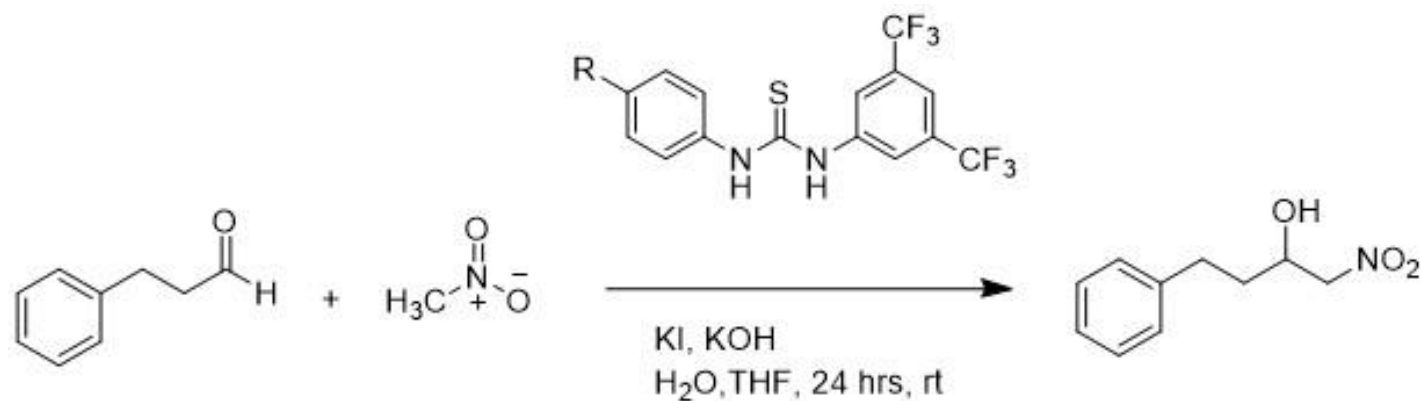


-Resonance structure increases the pKa of the donating hydrogens



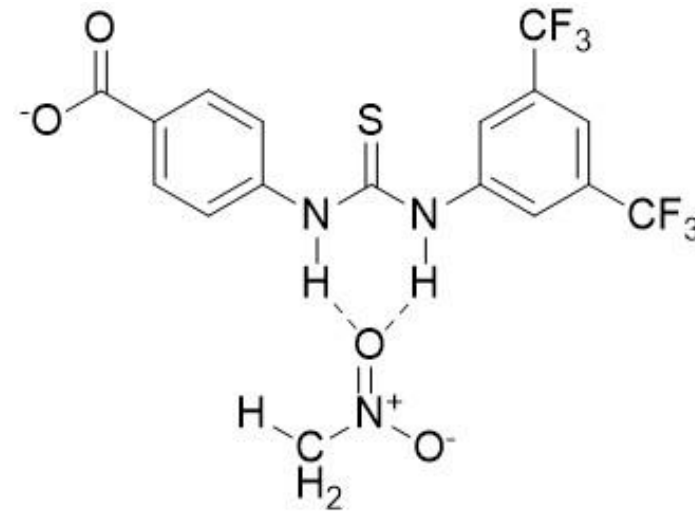
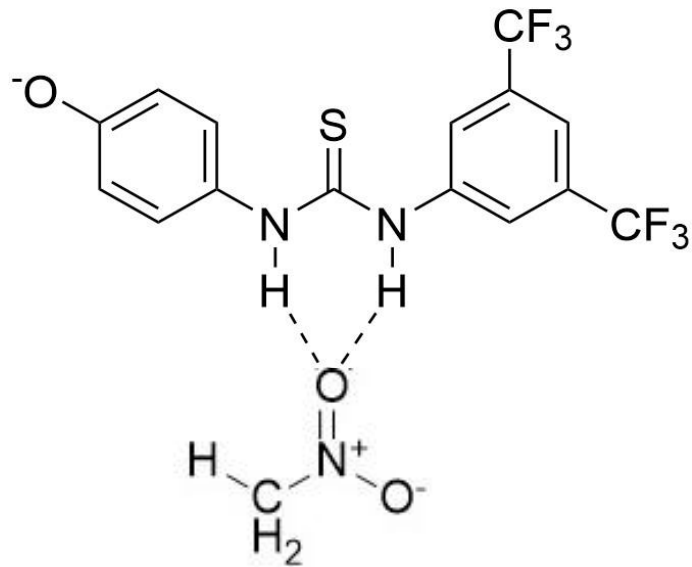
Proposed Catalytic Cycle

Yields in Control Reactions

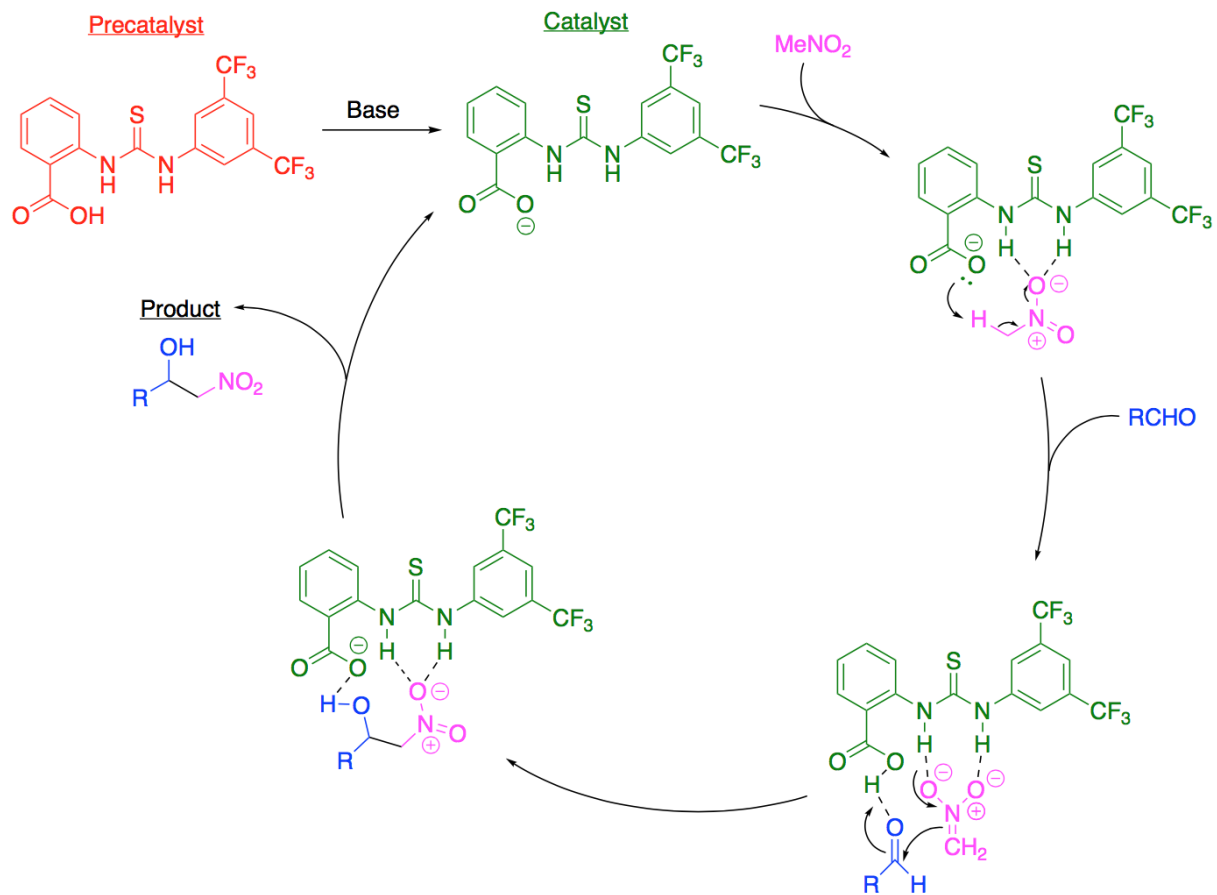


R	5 mmol KI/KOH
COOH	53%
OH	11%
H	72%
No catalyst	42%

Less Effective Activation



- Loss of transition state stabilization
- Multiple intermolecular interactions needed for deprotonation

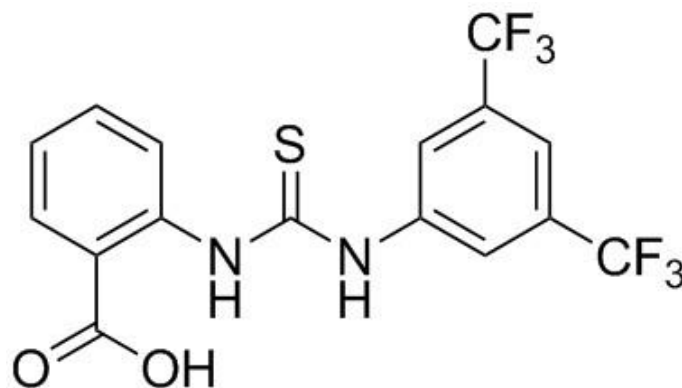


Conclusions

- Product conversion is increased with presence of anthranilic acid catalyst
- Ortho positioning of carboxylate and hydroxyl groups is necessary for catalytic activity
- Para positioned groups force reaction to depend on unfavored intermolecular forces

Future Work

- Determine isolated yields from the Henry Reaction
- Expand the substrate scope of the catalysts
- Screen the anthranilic acid catalyst in new reactions



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FoCuS Program

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