SYNTHESIS OF ENAMINONES UTILIZING COPPER CATALYSTS

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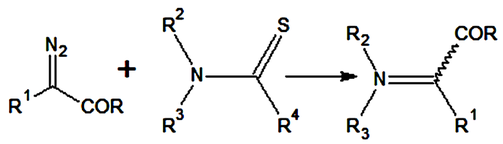
Introduction

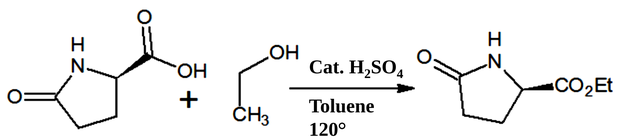
The synthesis of enaminones is of particular interest in organic chemistry as enaminones are good synthetic intermediates that are widely used in the development of pharmaceuticals. Enaminones function well as synthetic intermediates due to their function as both nucleophiles and electrophiles. The goal of our research is to develop a more general and efficient method for their synthesis. The synthetic reaction of enaminones begins from diazo and thioamide reactants as shown in the scheme below.

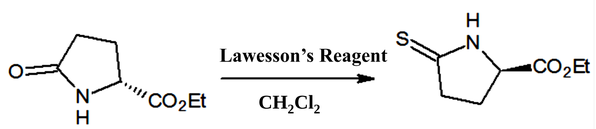


- Three different diazo compounds; a ketoester, diketone, and a diester have been chosen
- Two thioamides chosen: main thioamide for catalyst screening and second thioamide for enaminone formation.
- The goal is to identify the best overall catalysts from the catalyst screening results and the formation of three different enaminones.

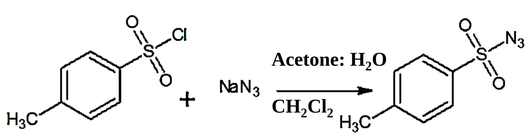
Materials and Methods

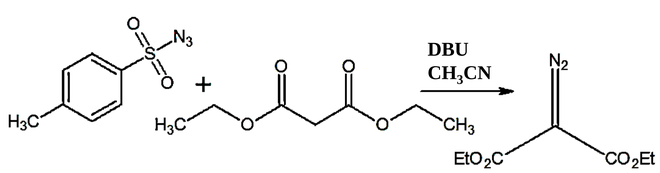
Thioamide Formation



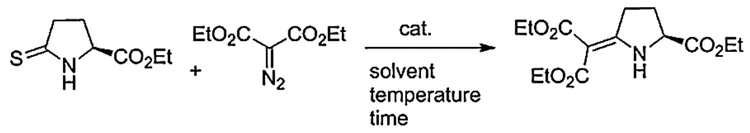


Diazo Formation





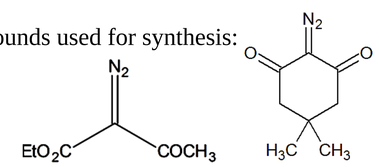
Results



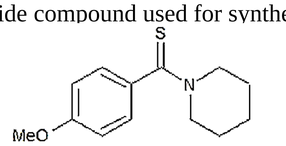
Catalyst	Solvent	Temperature	Time
$CuSO_4 \cdot 5H_2O$	Dichloromethane	50°C	20 hours
$Cu(OTf)_2$	Benzene	90°C	< 18hours
CuTc	Benzene	90°C	< 18hours
CuOTf	Toluene	90°C	21 hours
CuI	Dichlorobenzene	50°C	< 26 hours

Summary

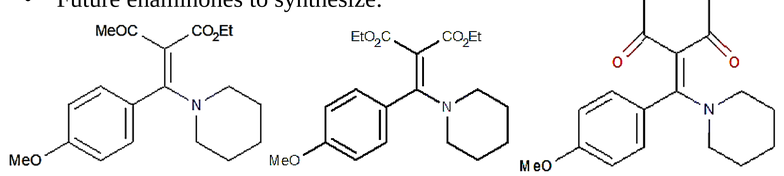
- Two step synthesis of Thioamide and Diazo starting materials
- Copper (II) Sulfate Hydrate at 50° C has been the best catalyst screened
- Copper (I) Thiopene Carboxylate at 90°C has been efficient in formation of enaminones.
- Further Diazo compounds used for synthesis:



- Further Thioamide compound used for synthesis:



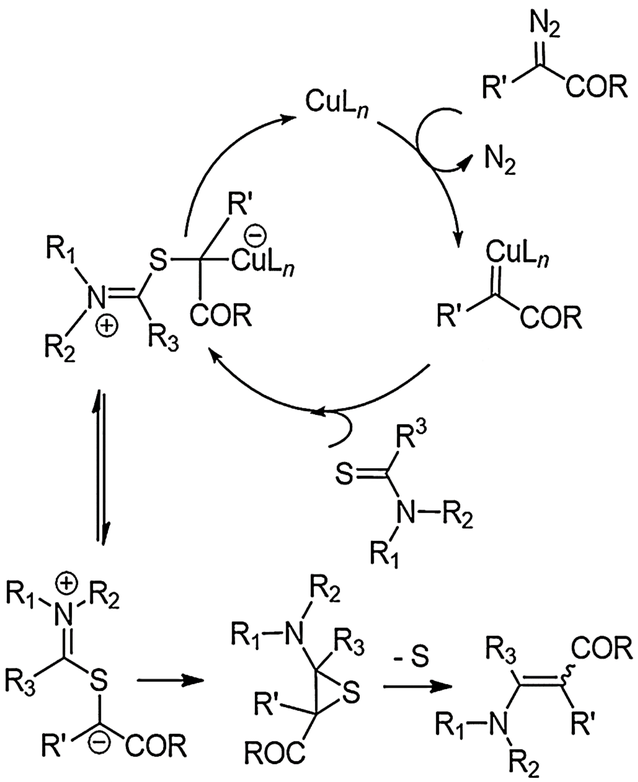
- Future enaminones to synthesize:



Conclusions

1. Copper (II) Sulfate Hydrate at 50° C has been best catalyst screened
2. Copper (I) Thiopene Carboxylate and Copper (II) triflate have been efficient in the formation of enaminones at 90° C.

Proposed Mechanism



"Ruthenium catalyzed synthesis of enaminones", N. D. Koduri, H. Scott, B. Hileman, J. D. Cox, M. Coffin, L. Glicksberg and S. R. Hussaini, *Org. Lett.*, **2012**, 14, 440–443.

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References

Ruthenium catalyzed synthesis of enaminones", N. D. Koduri, H. Scott, B. Hileman, J. D. Cox, M. Coffin, L. Glicksberg and S. R. Hussaini, *Org. Lett.*, **2012**, 14, 440–443.