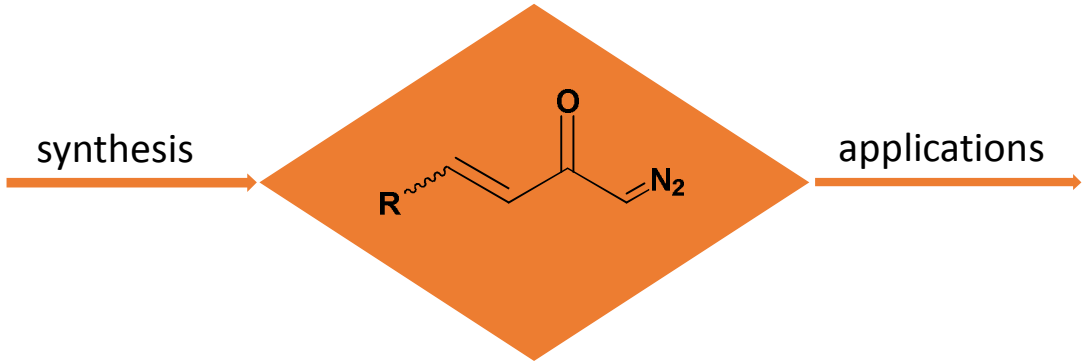
α,β-Unsaturated Diazoketones: Synthesis and Applications in Organic Chemistry



2015. 04. 09
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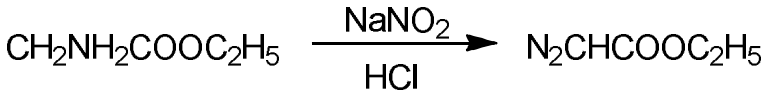
Content

- Introduction and Background
- Preparation of α,β-unsaturated Diazoketones
- Applications of α,β-unsaturated Diazoketones
- Conclusion

α-Diazocarbonyl compound

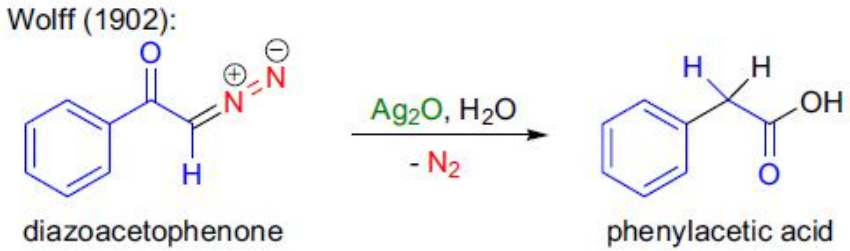
- α-Diazocanbonyl compounds have a long history of useful applications in organic chemistry. They are easily prepared from accessible precursors and can be introduced to undergo a wide variety of chemical transformations under very mild conditions.

- The first reported synthesis of an α-diazocanbonyl compound dates back to the work done by Curtius[1] in 1883.



Curtius, T. Ber. *Dtsch.chem.Ges.* **1883**, 16, 2230

- The Wolff rearrangement[2] -diazocarbonyl compounds were noticed.



Wolff, L. *Justus Liebigs Ann.chenm*. **1902**, 325, 129

α-Diazocarbonyl compound

Two general protocols to prepare diazocarbonyl compound

- The acylation of diazomethane developed by Arndt et al in 1927.

- The important technique of diazo transfer was developed by Regitz

Chart A: Diazomethane Acylation

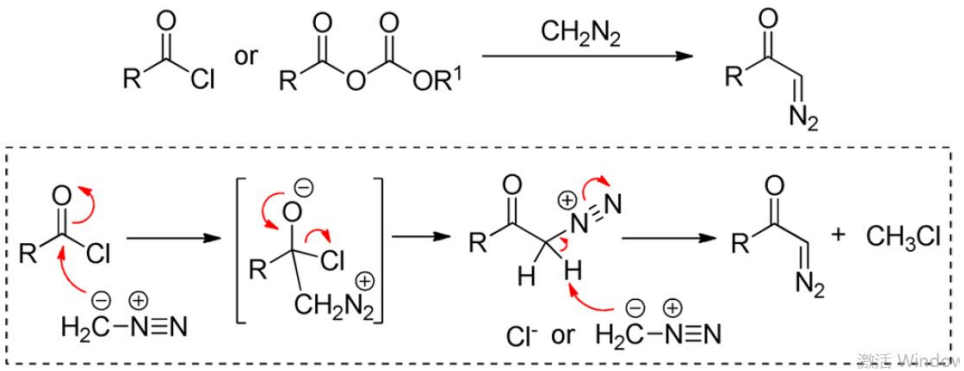
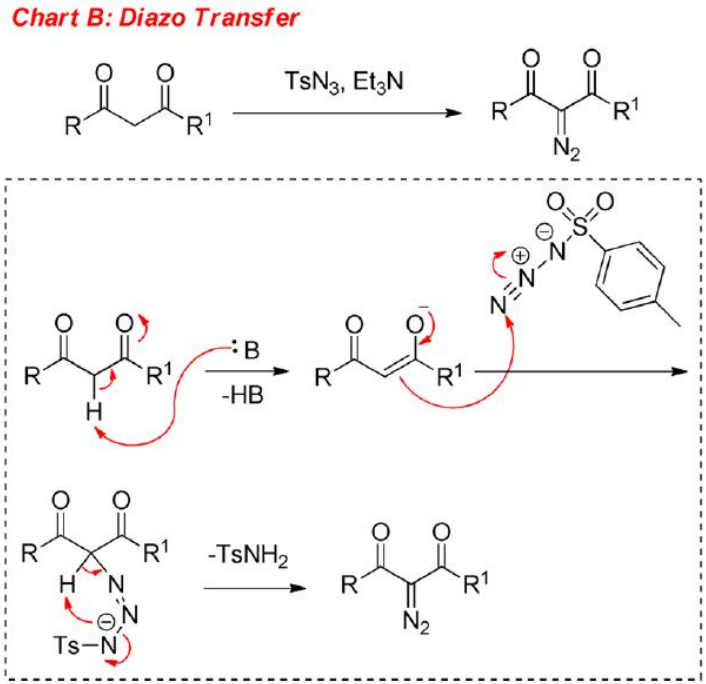


Chart B: Diazo Transfer

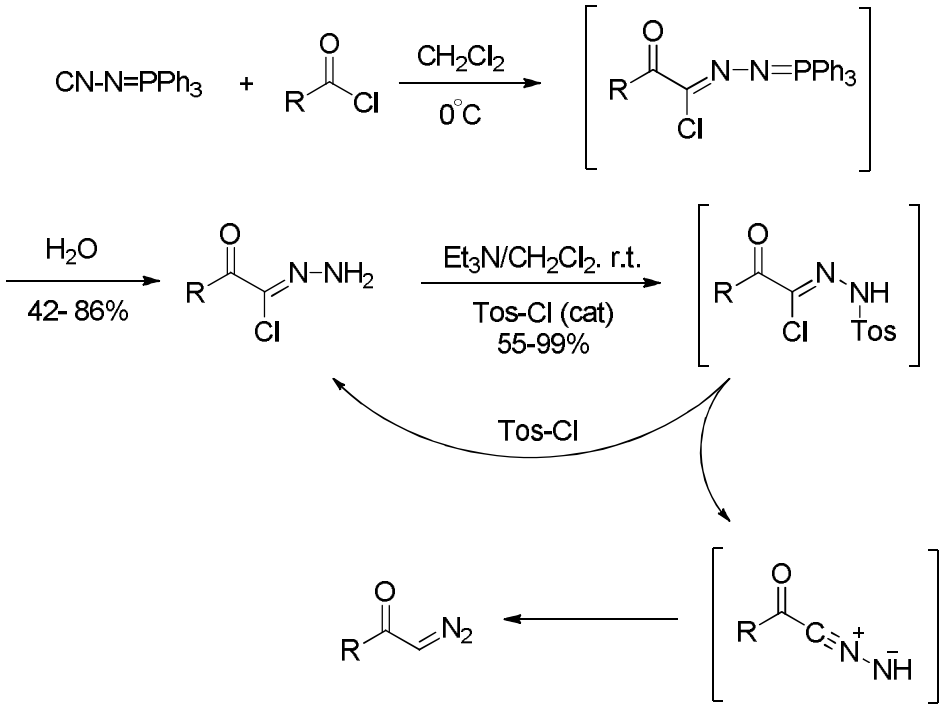


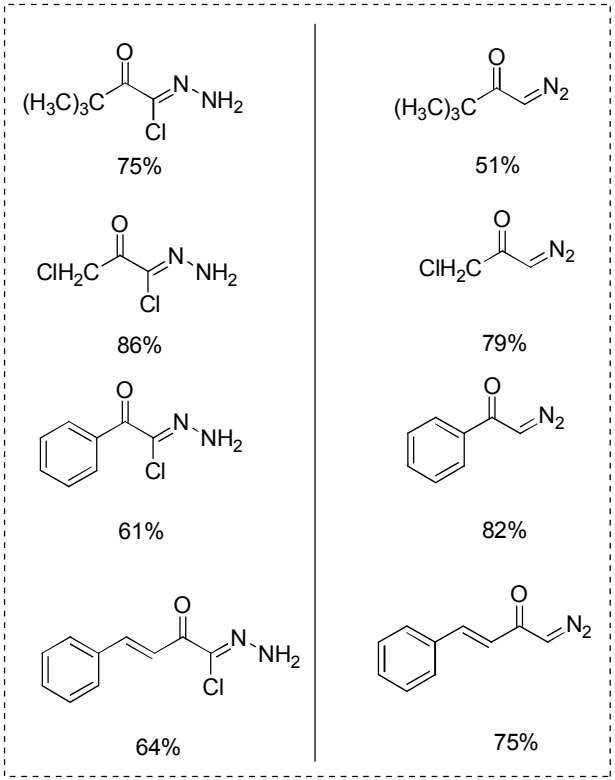
Arndt, F. *Ber. Dtsch. Chem. Ges. B Ser*. **1927**, 60, 1367

Regitz, *M.; Menz, F. Justus Liebigs Ann. Chem.* ***1970****, 739, 174*

α-Diazocarbonyl compound

An interesting and different method to prepare diazoketones done by Aller





Allen, E.; Molina, P.; Lorenzo, A. *Synlett*. **2000** ,526

α-Diazocarbonyl compound

Now many new synthetic methodologies have appeared
Using the α-diazocanbonyl compound(Figure 1).

- Wollf rearrangement
- Cyclopropanation
- Ylide formation
- C-H insertion
- 1,3-Dipolar cycloaddition
- Dimerization

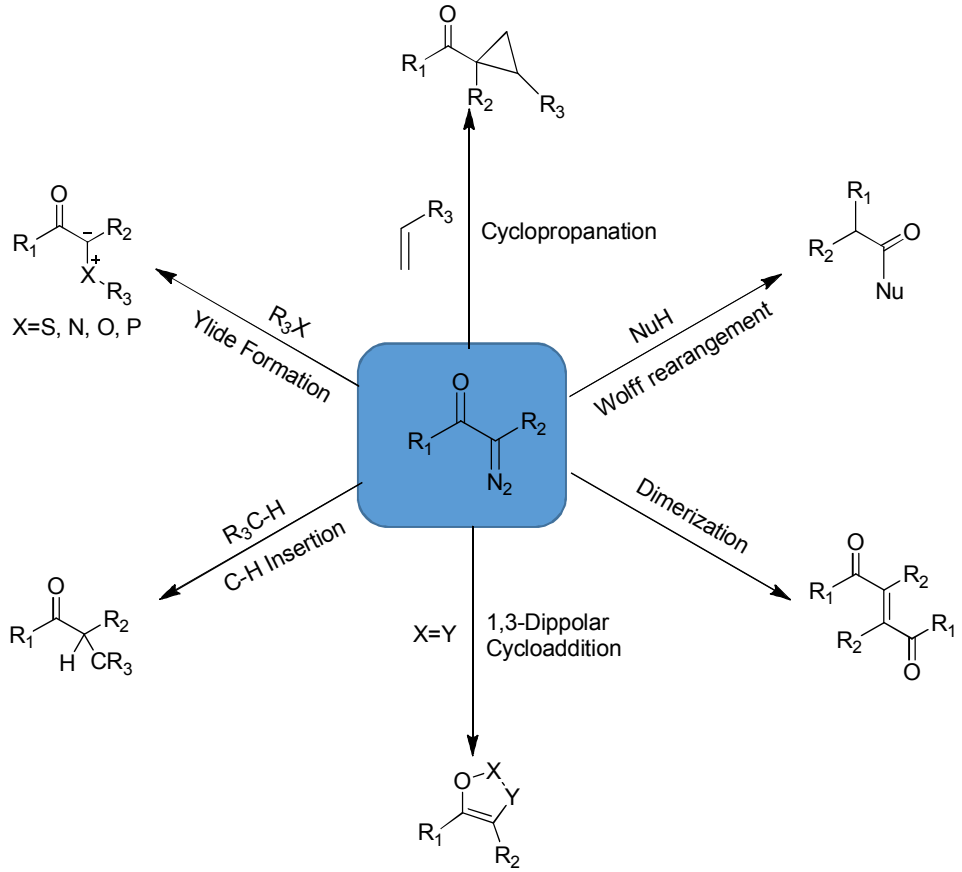


Figure 1

Preparation of α,β-unsaturated Diazoketones

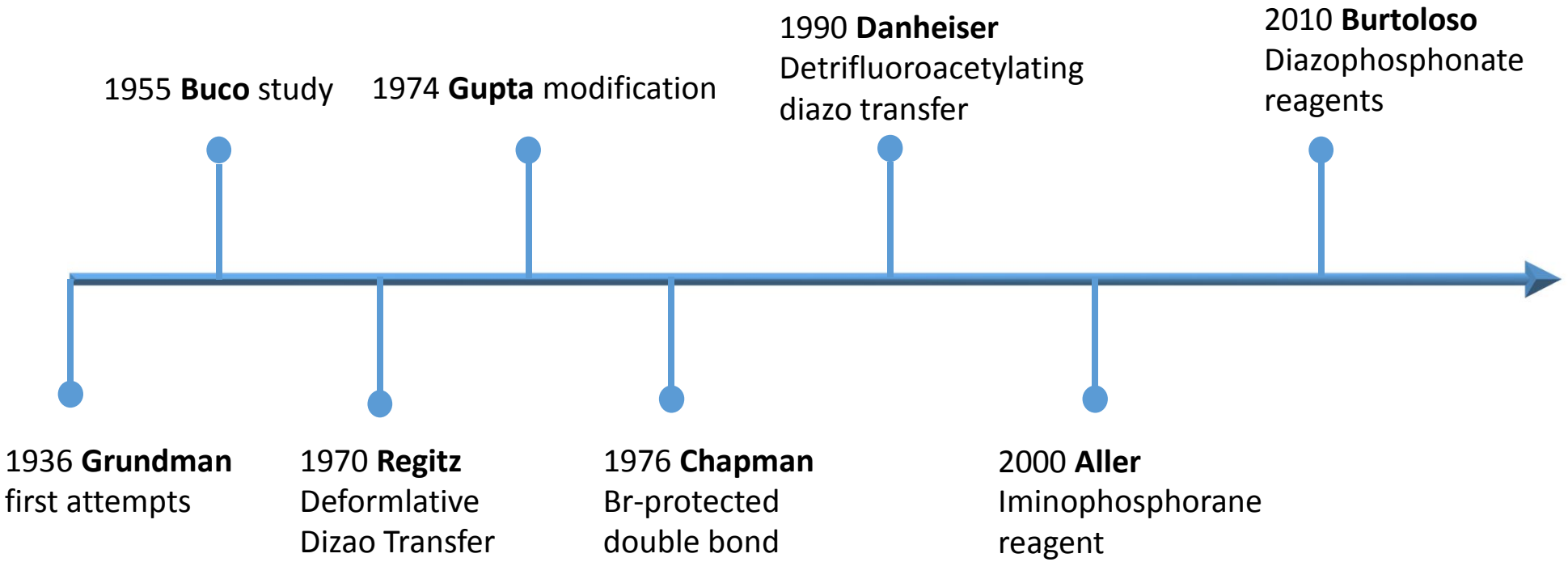
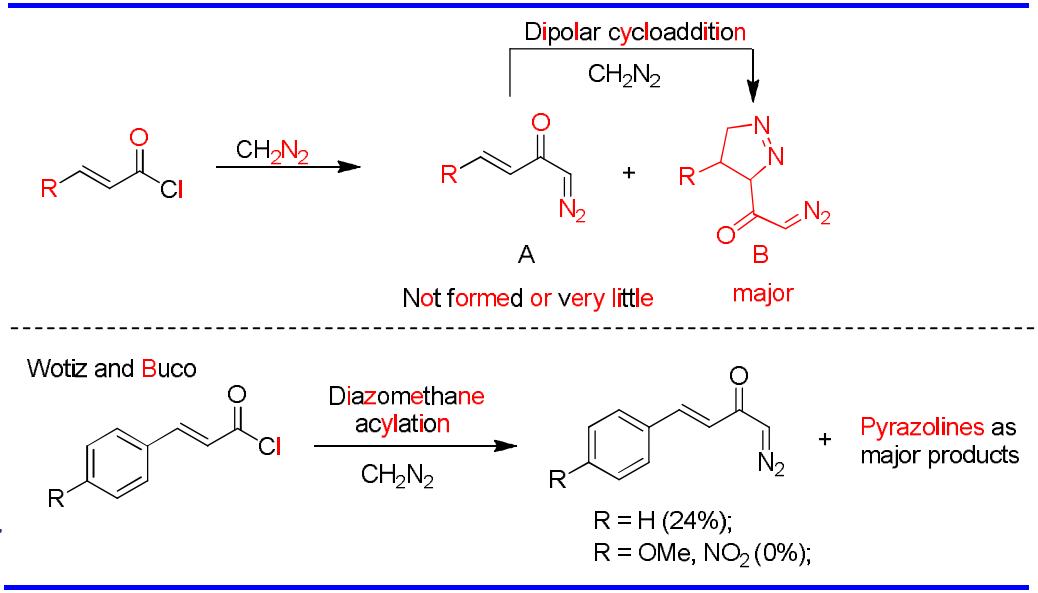


Figure 2. Timeline scale of the methods to prepare α,β-unsaturated α'-diazoketones

Preparation of α,β-unsaturated Diazoketones

Different diazocanbonyl compounds can now be prepared by using the diazomethane acylation and diazo transfer protocols.

Preparation of α,β-unsaturated diazoketones by the diazomethane acylation furnishes poor yields[5](scheme 1).



Scheme 1. Preparation of α,β-unsaturated diazoketones

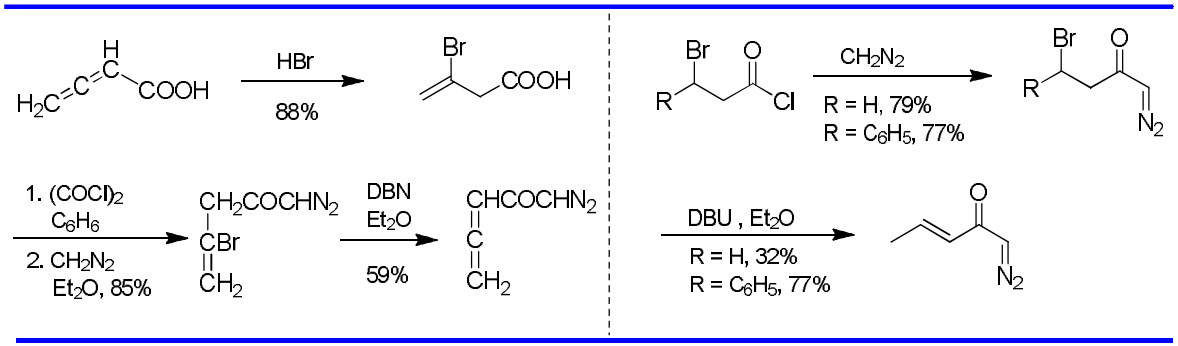
Grundmann, C. *Justus Liebigs Ann. Chem.* ***1936***, 524, 36

Wotiz, J. H.; Buco, S, N. *J. Org. Chem*. **1955**, 20, 210

Preparation of α,β-unsaturated Diazoketones

Several ways to form the unsaturated diazoketone.

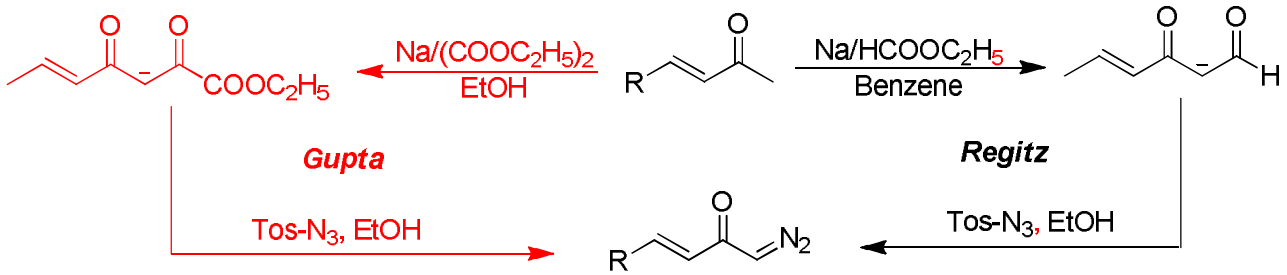
- Br-protected double bond(scheme2[6])



Scheme 2. Synthesis of Unsaturated Diazoketones by Chapman and Rosenquist

Rosenquist, N. R.; Chapman, O, L. *J. Org. Chem*. **1976**, 6.733

- Deformylative dizao transfer(scheme3[7])

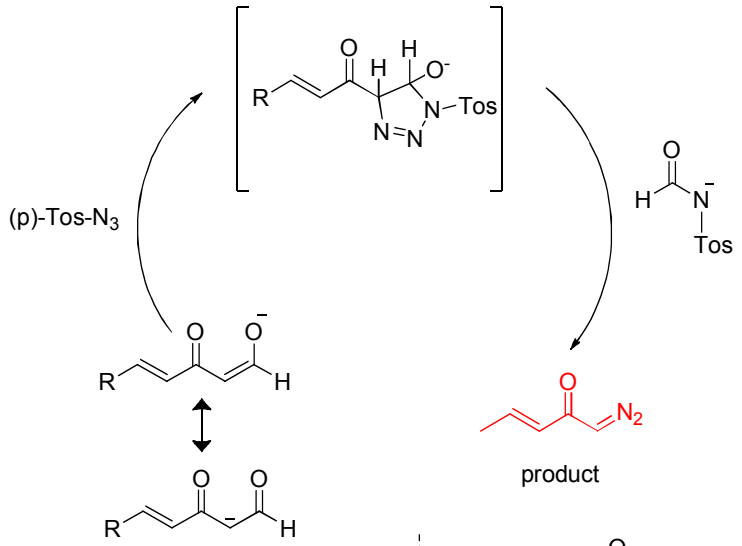


Scheme 2. Synthesis of Unsaturated Diazoketones by Regitz and Gupta

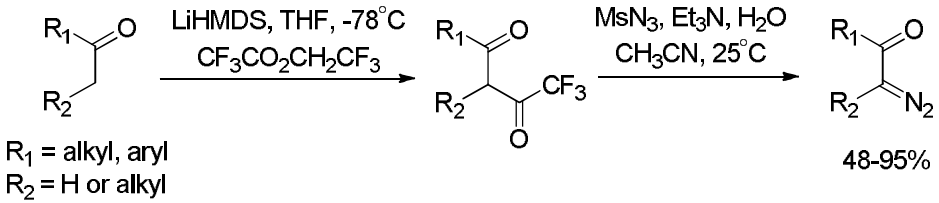
Regitz, M.; Menz, F.; Liedhegener, A. *Justus Liebigs Ann. Chem.* **1970**, 739, 174
Harmon, R. E.; Gupta, S. K. Synthesis. **1974**, 577

Preparation of α,β-unsaturated Diazoketones

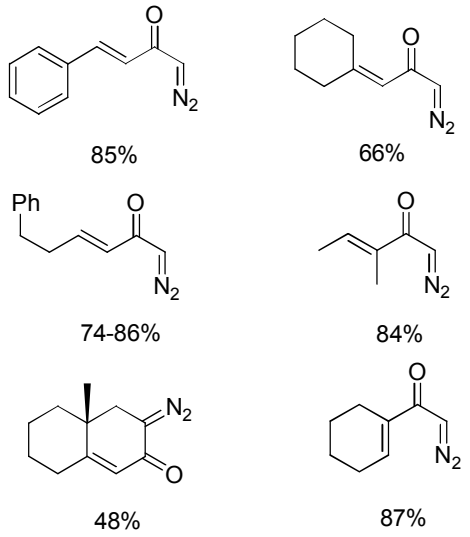
Mechanism:



- Detrifluoroacetylating diazo transfer



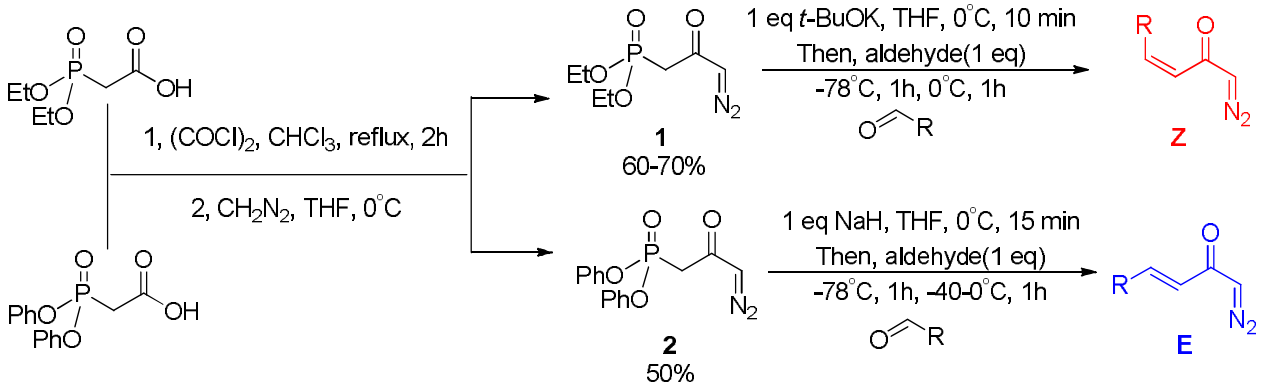
R1 = alkyl, aryl
R2 = H or alkyl



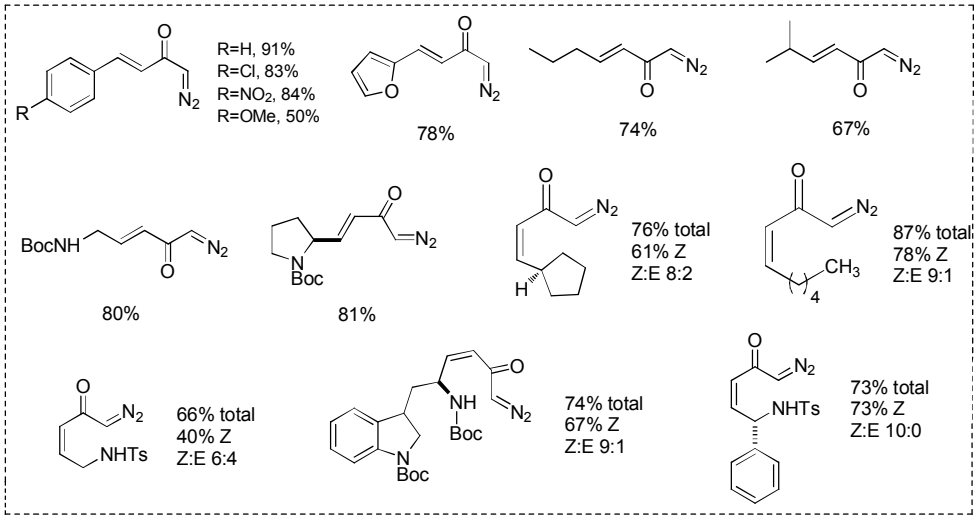
Danheiser, R. L.; Park, S. Z. *J. Org. Chem.* **1990**, 55, 1959

Burtoloso group works

Two types of Horner-Wadsworth-Emmons(HWE) reagents 1 and 2



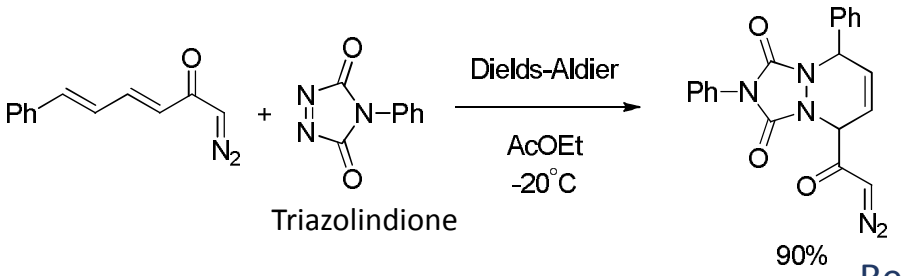
- Complete E selectivity and no epimerization in the γ-position
- High stereoselectivity for reagent 1



Pinho, V. D.; Burtoloso, A. C. B. *J. Org. Chem*. **2011**. 76 289

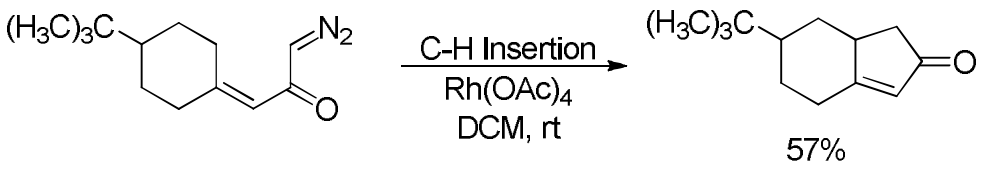
Applications of α,β-unsaturated Diazoketones

First application example of α,β-Unsaturated Diazoketones



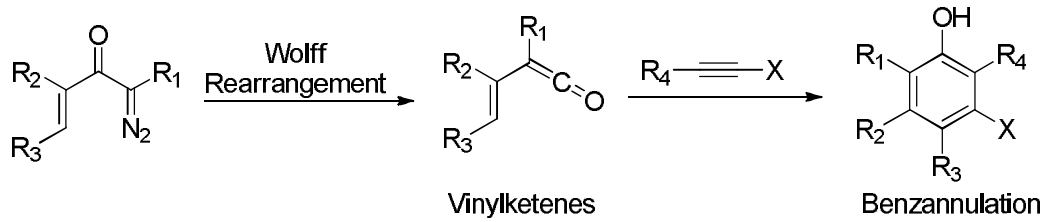
Regtiz, M.; Theis, W. *Tetrahedron Lett*. **1981**, 22, 2535

Cyclopentenone synthesis



Ceccherelli, P.; Wenkert, E. A. *J. Org. Chem.* **1990**, 55, 311

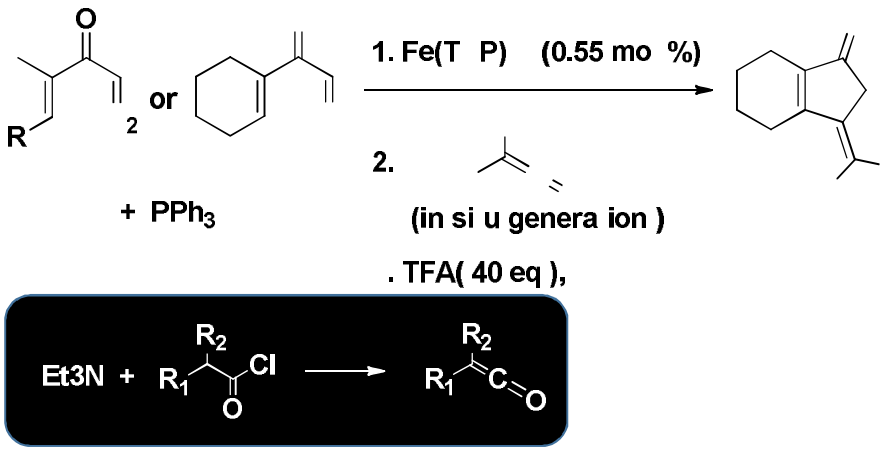
Benzannulation reaction

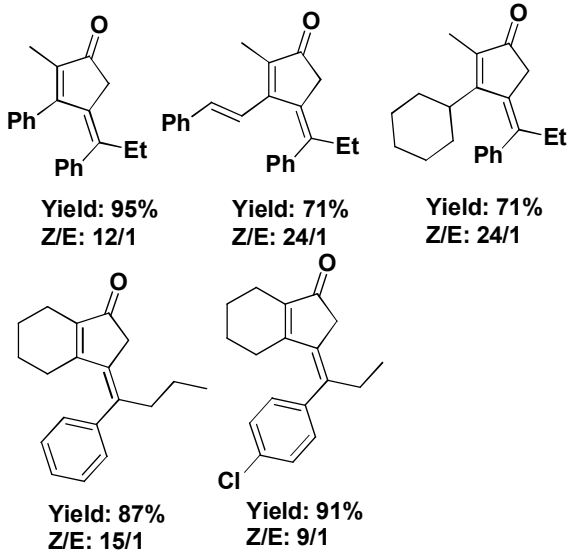


Danheiser, R. L. Miler, R. F. *J . Am. Chem. Soc*. **1990**. 112. 3093

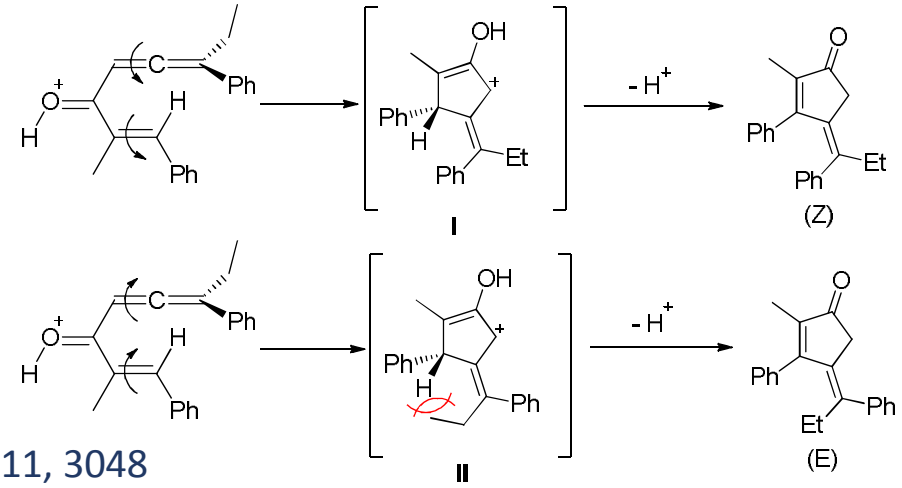
Applications of α,β-unsaturated Diazoketones

Tandem Wittig/Nazarov cyclization





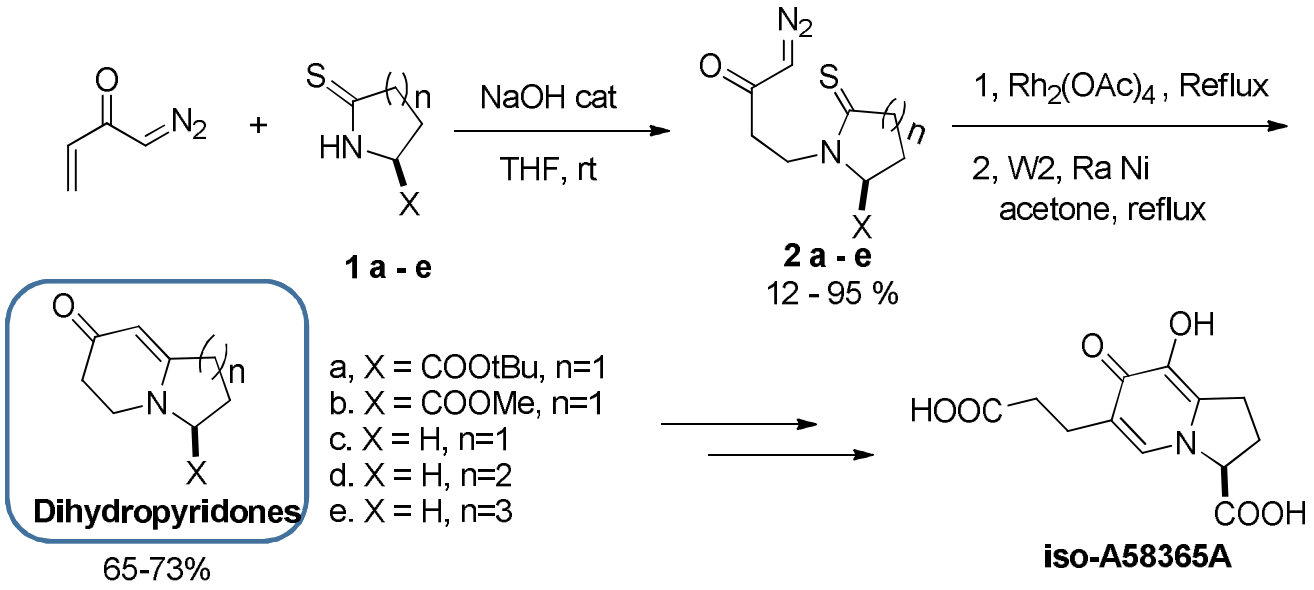
Proposed stererochemical Modle



Cao, P.; Sun, X. L.; Tang, Y. *Org. Lett*. **2009**, 11, 3048

Application used in the synthesis of nitrogen heterocycles

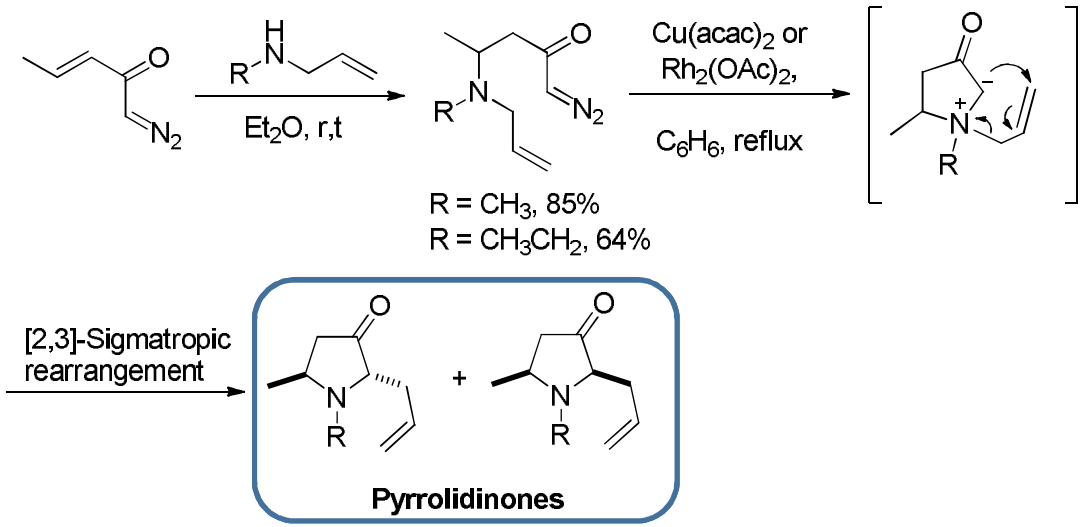
Synthesis of Dihydropyridones



Fang, F. G.; Prato, M. Danishefsky, S. J. *Tetrahedron Lett*. **1989**, 30, 3625

Application used in the synthesis of nitrogen heterocycles

2,5-Disubstituted Pyrrolidinones

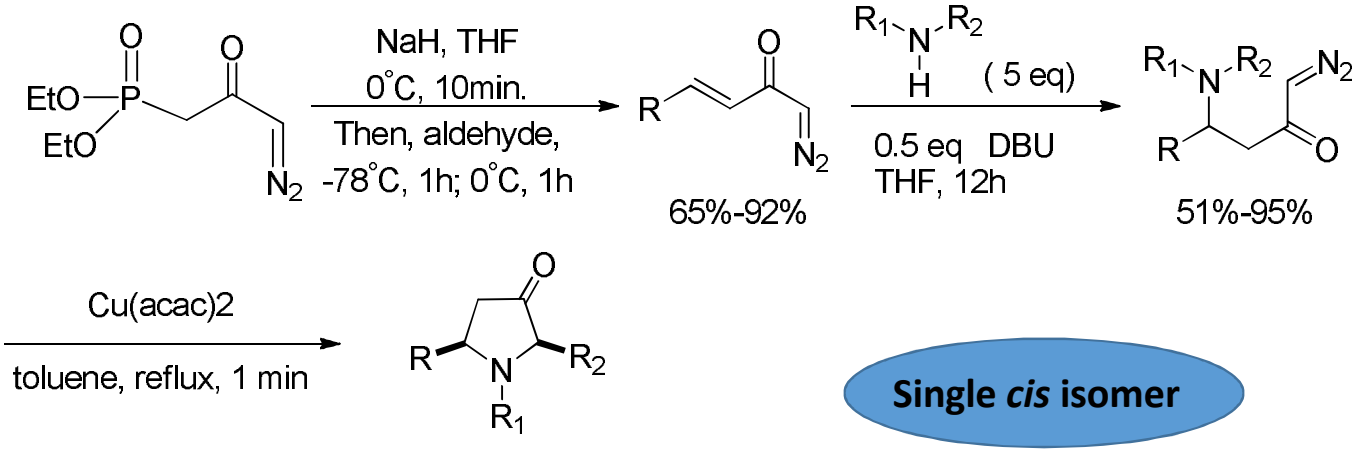


But the Stereoselectivity is not good

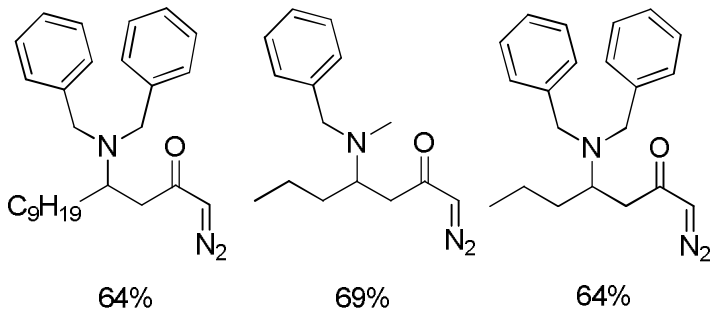
Clark, J. S.; Hodgson, P. B.; Street, L. J. *J. Chem. Soc., Pekin Trans*. 1 **2001**, 3312

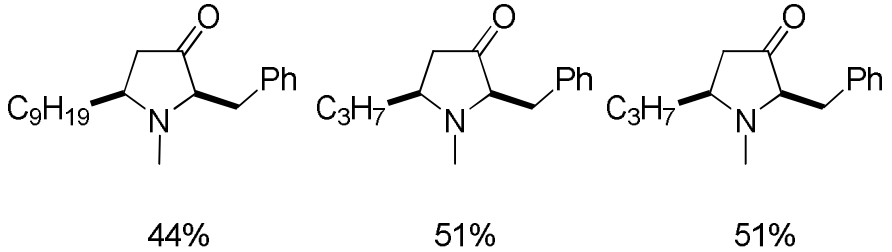
Application used in the synthesis of nitrogen heterocycles

Cis-2,5-Disubstituted Pyrrolidinones



2,5-cis-substituted pyrrolidines

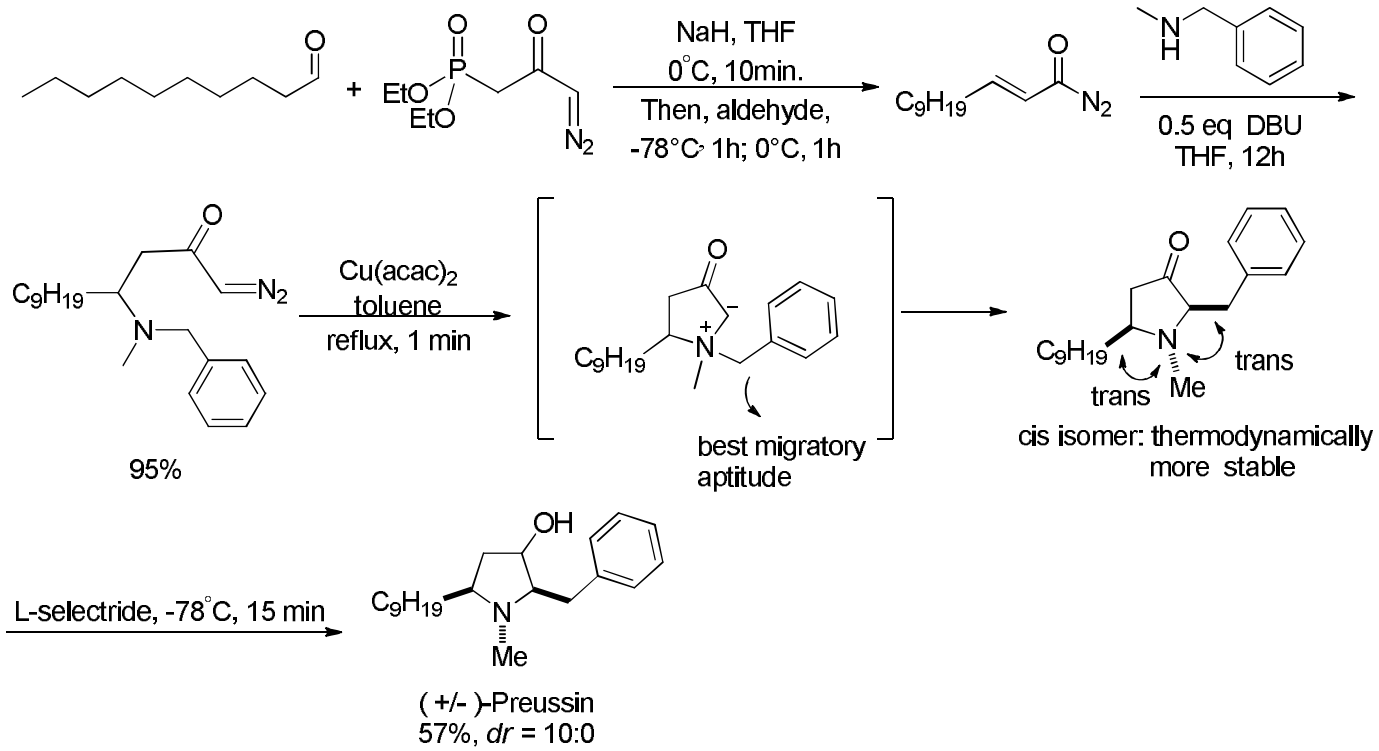




Rossrt, I. G.; Dias, R. M. P.; Burtoloso, A. C .B. *J. Org. Chem*. **2014**, 79, 6748

Application used in the synthesis of nitrogen heterocycles

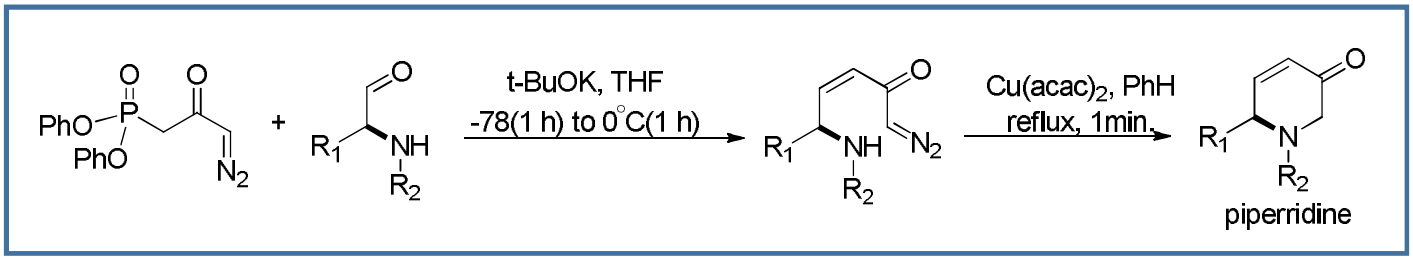
Total synthesis of the alkaloid preussin

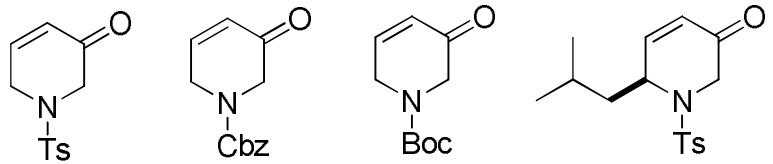


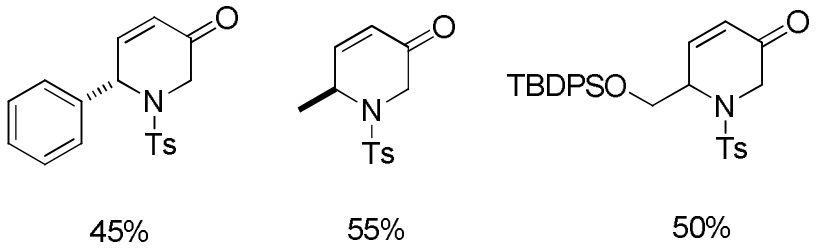
Rossrt, I. G.; Dias, R. M. P.; Burtoloso, A. C .B. *J. Org. Chem*. **2014**, 79, 6748

Application used in the synthesis of nitrogen heterocycles

Synthesis of Dihydropyridin-3-ones







Prepare highly functionlized piperidine in just two steps from Z-unsaturated diazoketones

Rosset, I. G.; Burtoloso, A. C. B. *J. Org.Chem*. **2013**, 76, 9464

Conclusion

- The chemistry of α,β-unsaturated diazokeones has proven to be very promising
- The combination of three important functions(a double bond, a ketone and a diazo) in the same mlolecule makes these compound very useful to synthesis many important moleculaes
- Many transformations still desirve investigation from these substrates