

Literature Review

N-Heterocyclic Carbene Catalysis and Its Applications in Total Synthesis

Supervisor: Prof. David Zhigang Wang

Reporter: Jing Li

2013-1-9

Content

- ◆ Introduction
- ◆ NHC-Catalyzed Benzoin Condensation
- ◆ NHC-Catalyzed Stetter Reaction
- ◆ NHC-Homoenolate Equivalents
- ◆ Summary

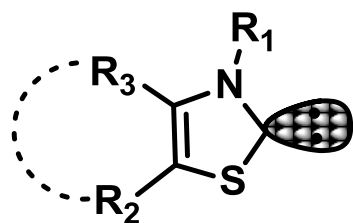
Introduction

1. Carbenes belong to the most investigated reactive species in the field of organic chemistry. As typical structural features, all carbenes are neutral and possess a bivalent carbon atom with an electron sextet.
2. N-heterocyclic carbene (NHC) catalysis has emerged as a powerful method in organocatalysis to fashion new bonds with high levels of stereoselectivity through **Umpolung** as well as normal polarity based transformations.

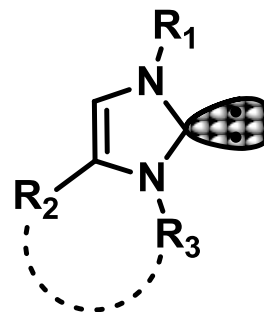
D. Enders.; O. Niemeier.; A. Henseler. *Chem. Rev.* **2007**, *107*, 5606.

Introduction

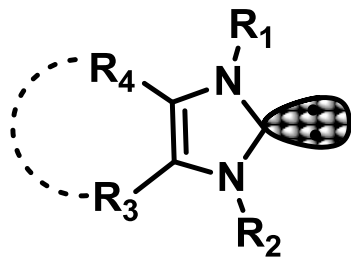
General types of N-heterocyclic carbenes



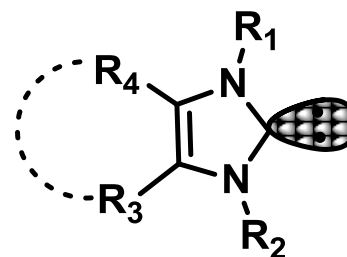
A



B

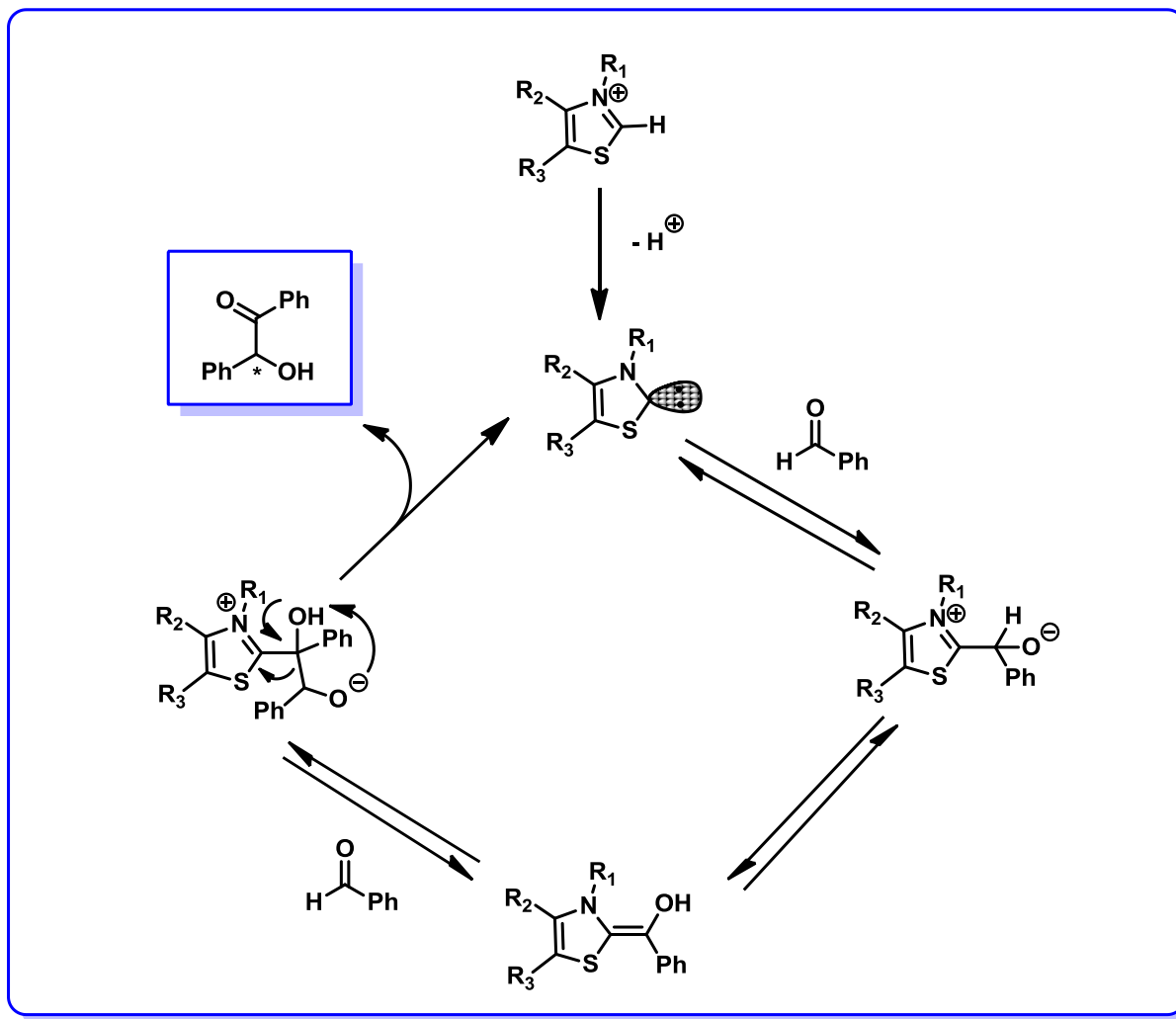


C



D

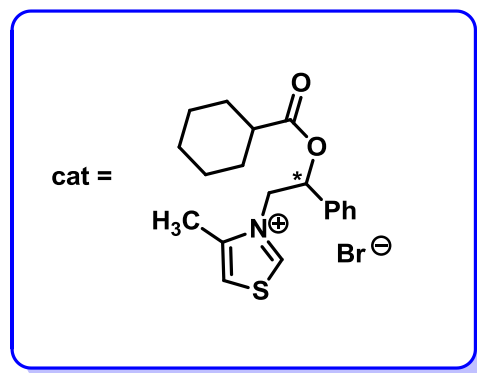
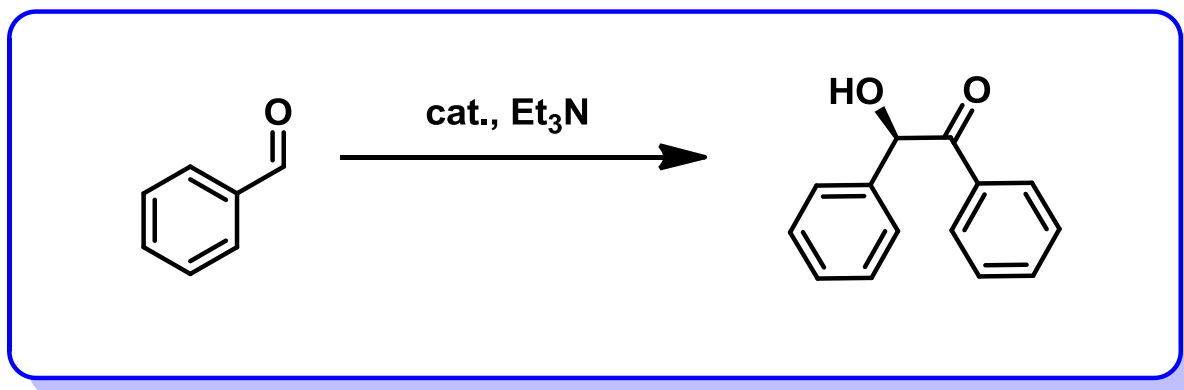
NHC-Catalyzed Benzoin Condensation



R. Breslow. *J. Am. Chem. Soc.* **1958**, 80, 3719.

NHC-Catalyzed Benzoin Condensation

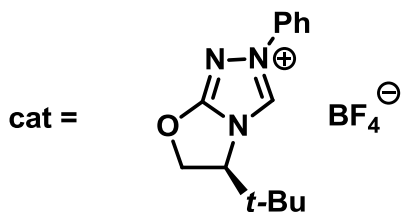
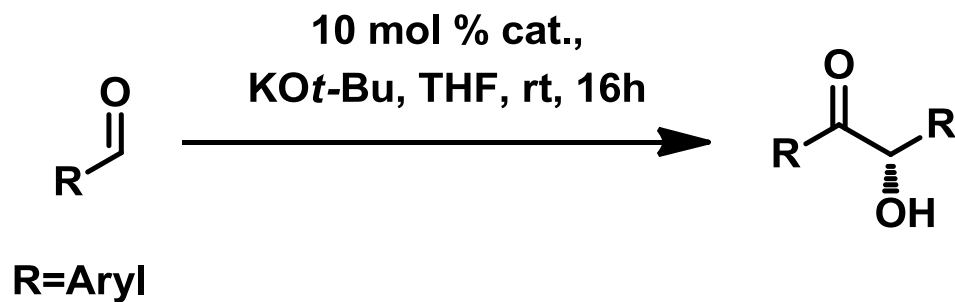
First Asymmetric Benzoin Condensation



ee: 22%

J. Sheehan.; D. H. Hunneman. *J. Am. Chem. Soc.* **1966**, 88, 3666.

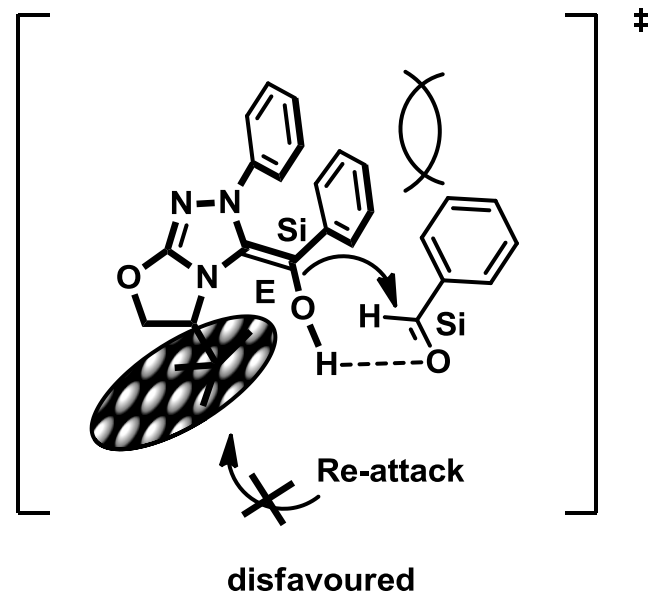
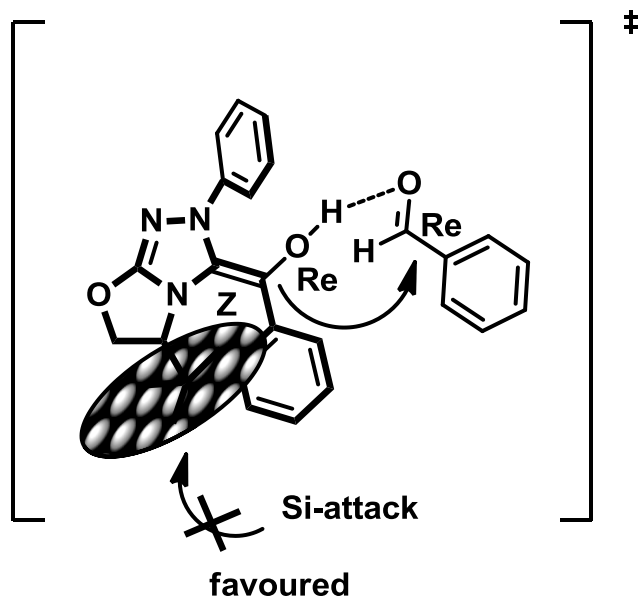
NHC-Catalyzed Benzoin Condensation



ee: 80 - 95%

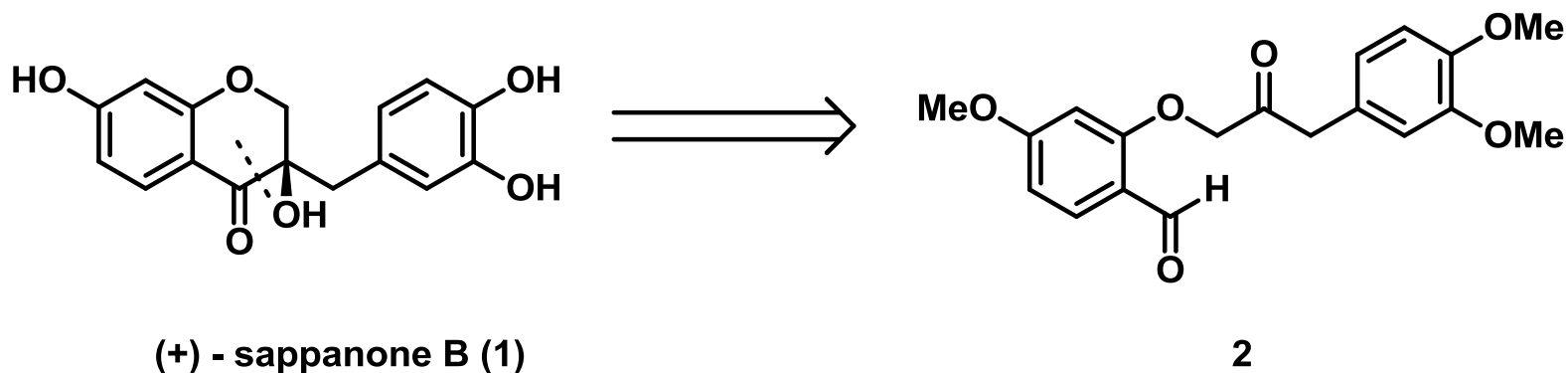
D. Enders.; U. Kallfass. *Angew. Chem., Int. Ed.* **2002**, *41*, 1743.

NHC-Catalyzed Benzoin Condensation



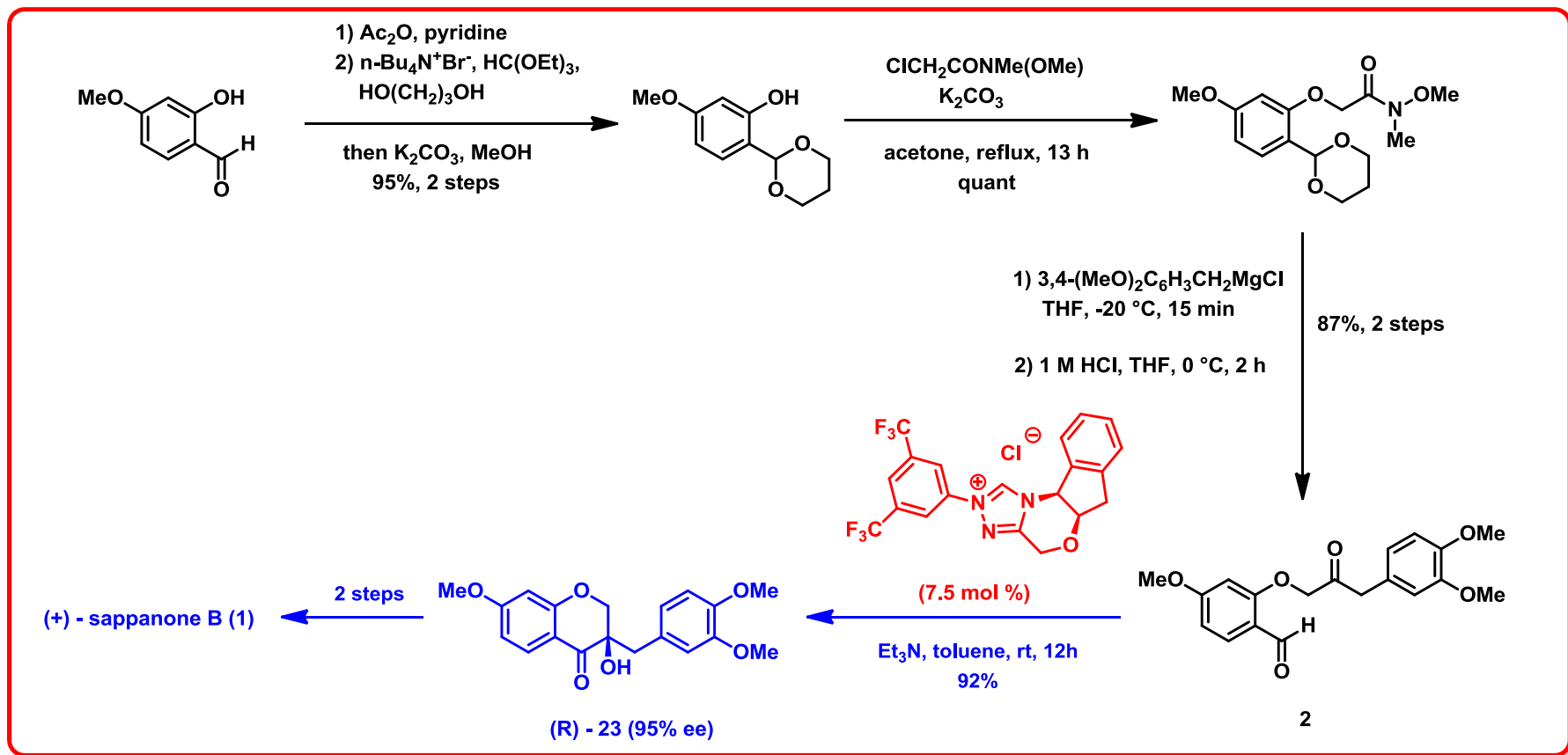
NHC-Catalyzed Benzoin Condensation

Synthesis of (+)-Sappanone B



H. Takikawa.; K. Suzuki. *Org. Lett.* **2007**, *9*, 2713.

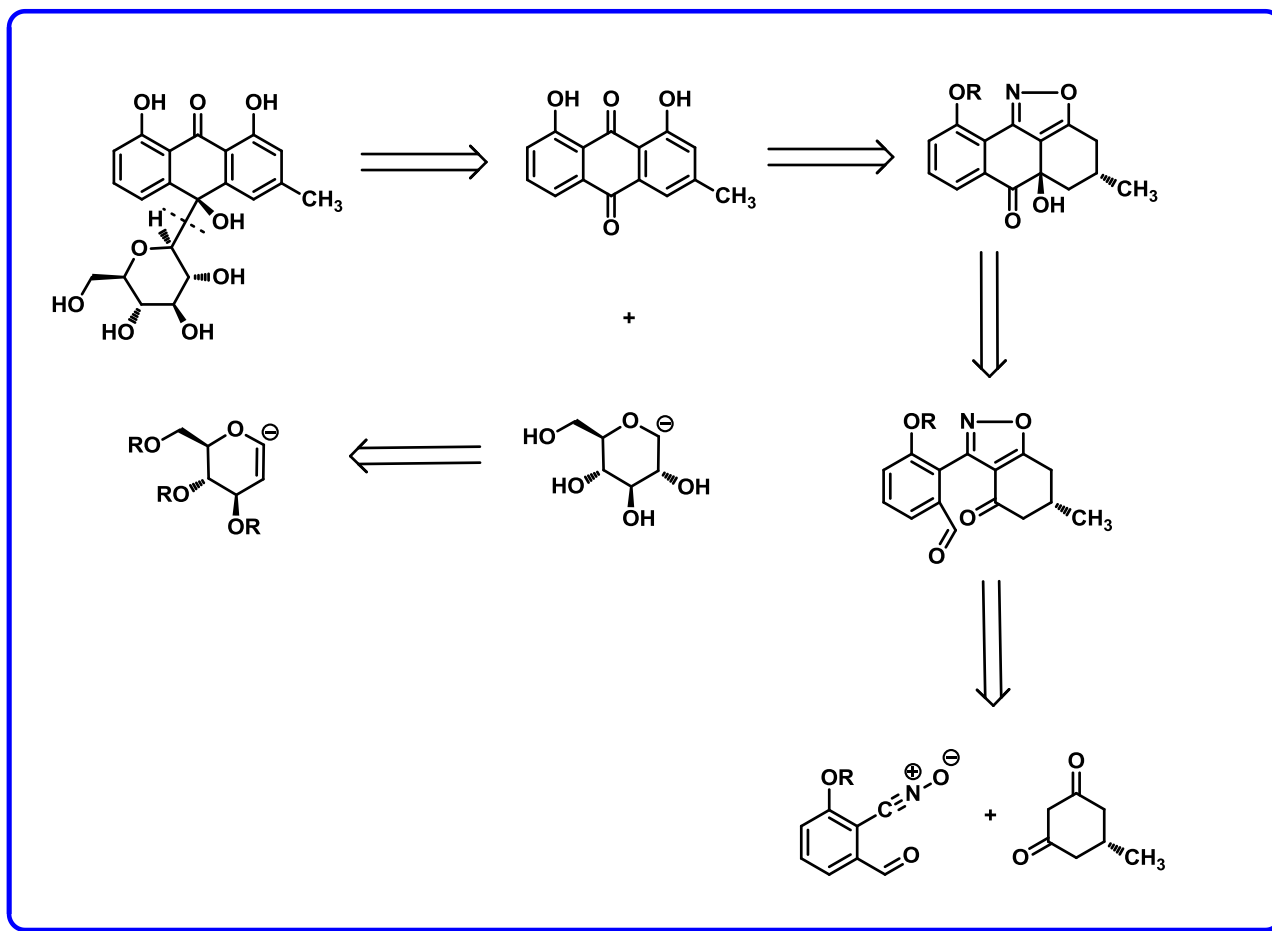
NHC-Catalyzed Benzoin Condensation



H. Takikawa.; K. Suzuki. *Org. Lett.* **2007**, *9*, 2713.

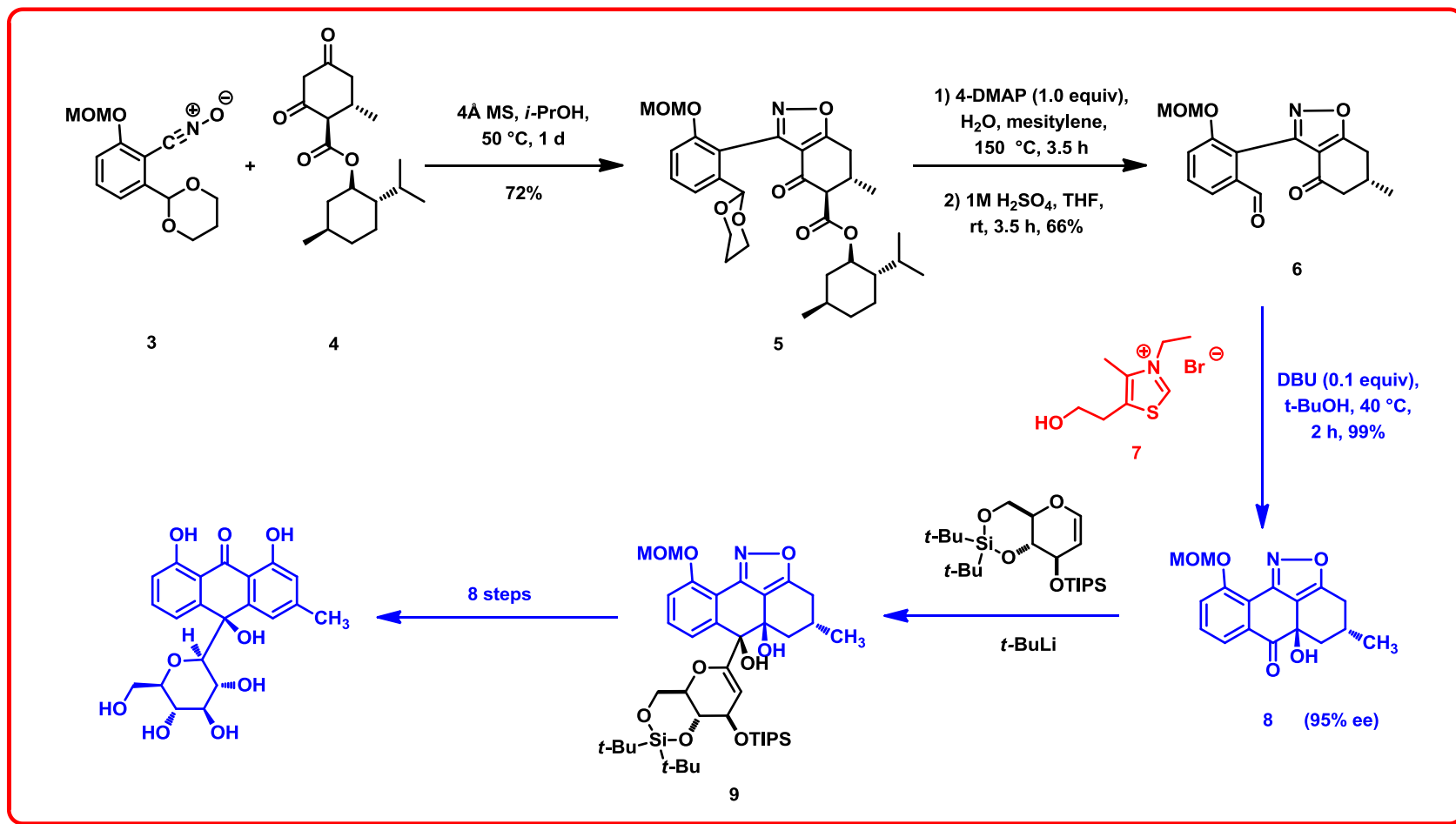
NHC-Catalyzed Benzoin Condensation

Synthesis of (+)-Cassialoin



Y. Koyama.; R. Yamaguchi.; K. Suzuki. *Angew. Chem., Int. Ed.* **2008**, *47*, 1084.

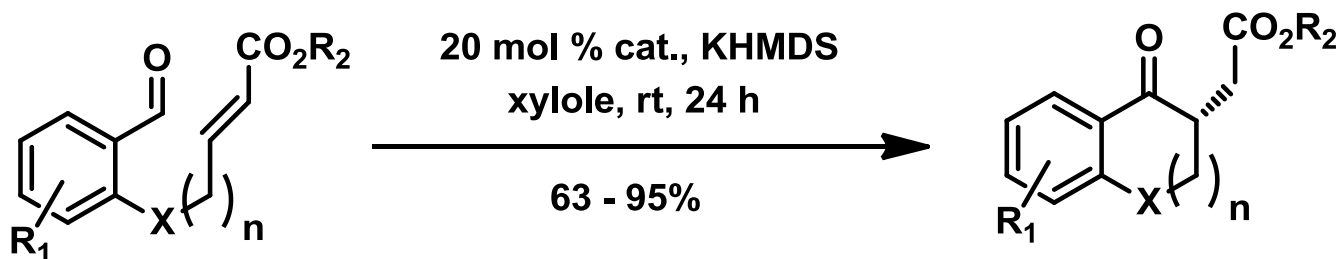
NHC-Catalyzed Benzoin Condensation



Y. Koyama.; R. Yamaguchi.; K. Suzuki. *Angew. Chem., Int. Ed.* **2008**, *47*, 1084.

NHC-Catalyzed Stetter Reaction

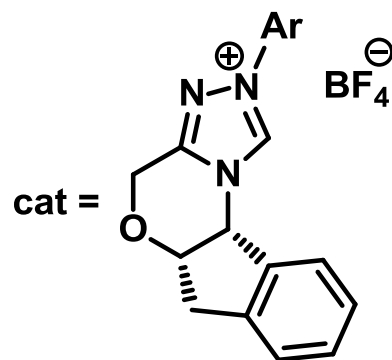
Asymmetric Intramolecular Stetter Reaction



$R_1 = H, 6\text{-Me}, 8\text{-Me}, 8\text{-MeO}$

$R_2 = Me, Et$

$X = O, S, NMe, CH_2$

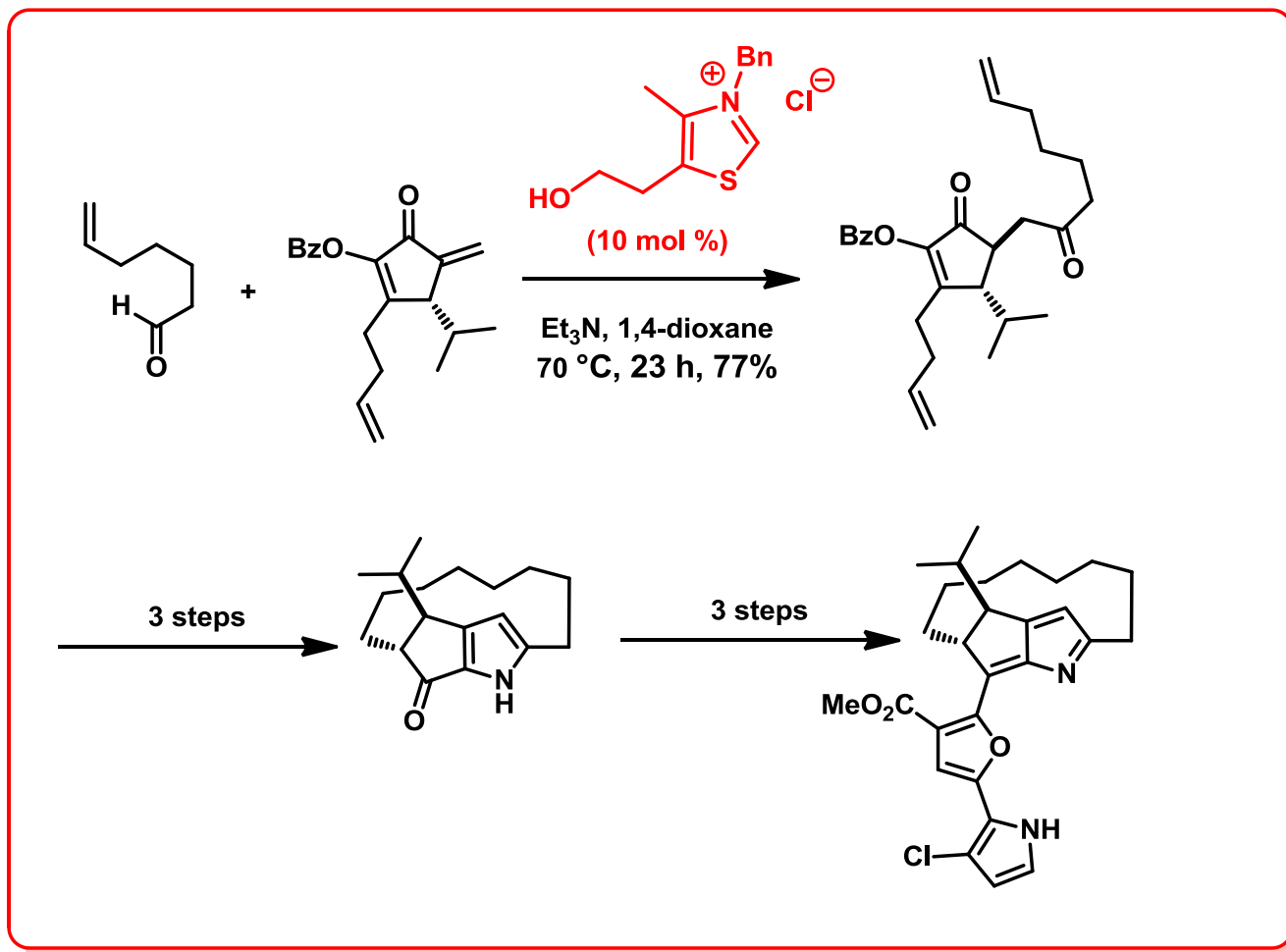


ee: 82 - 97%

M. S. Kerr.; J. Read de Alaniz.; T. Rovis. *J. Am Chem. Soc.* **2002**, *124*, 10298.

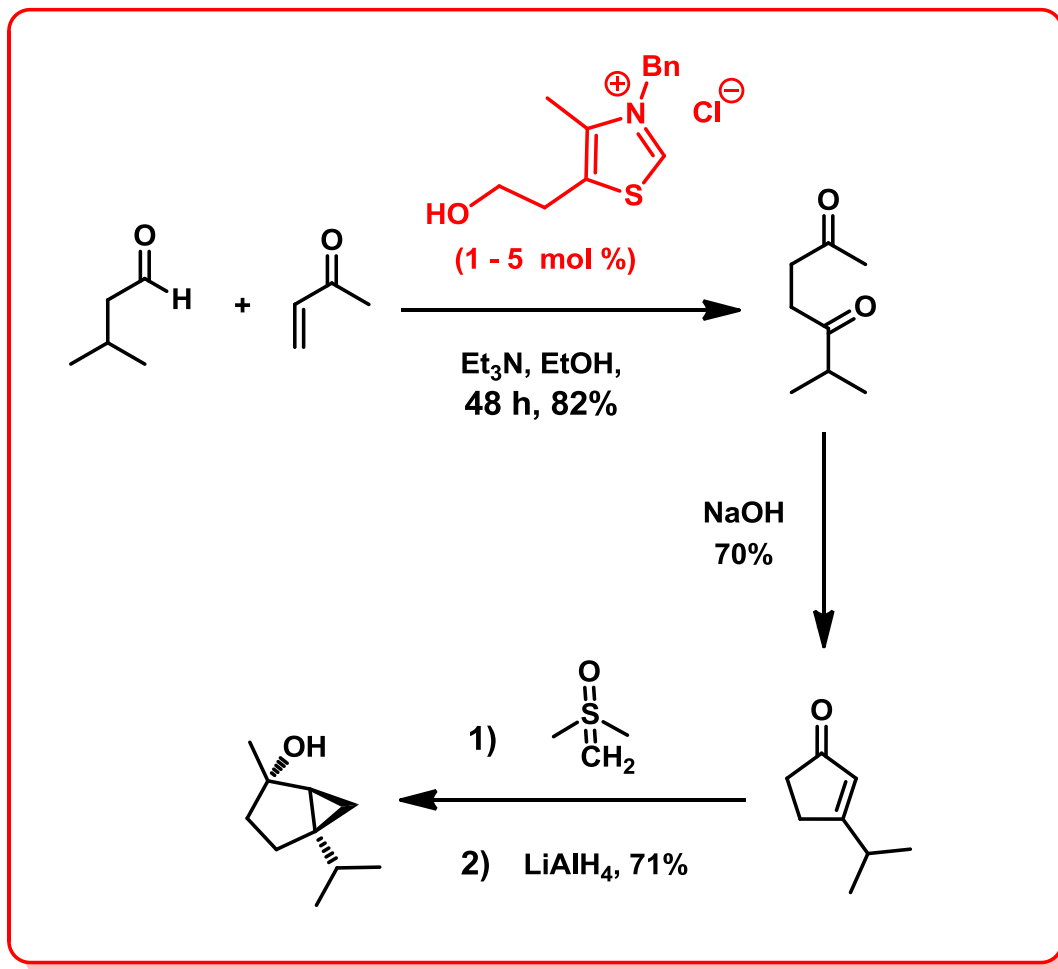
NHC-Catalyzed Stetter Reaction

Synthesis of Roseophilin



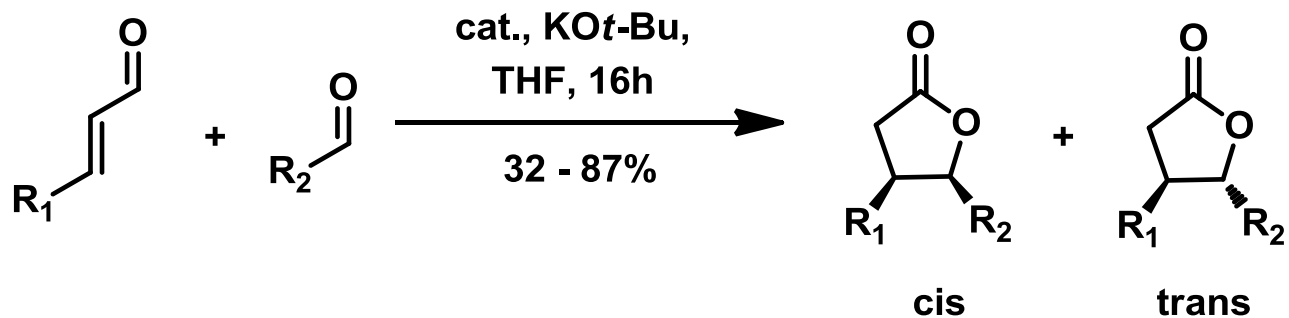
NHC-Catalyzed Stetter Reaction

Synthesis of (\pm)-trans-sabinene hydrate



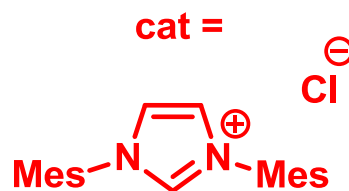
C. C. Galopin. *Tetrahedron Lett.* **2001**, 42, 5589.

NHC-Homoenolate Equivalents



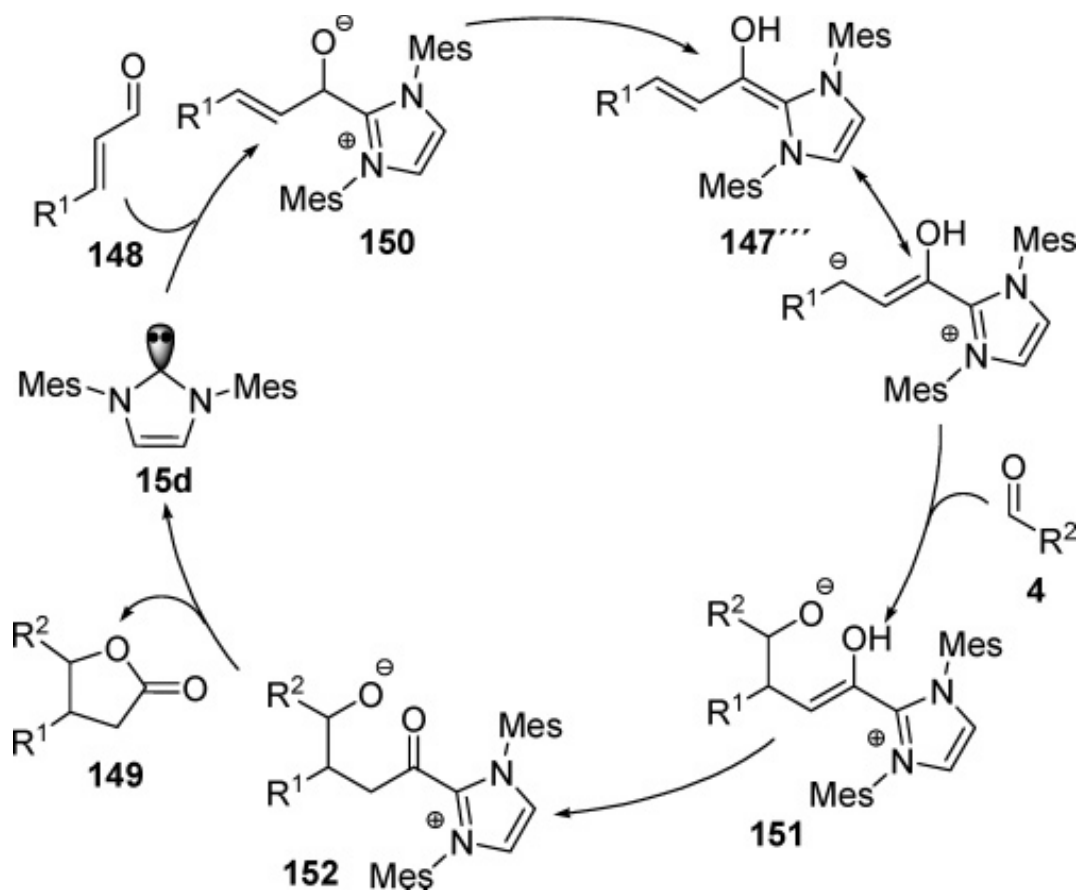
$R_1 = p\text{-Cl-Ph}, p\text{-Br-Ph}, p\text{-CO}_2\text{Me-Ph},$
 $p\text{-F-Ph}, m\text{-F-Ph}, m\text{-Cl-Ph},$
 $m\text{-Br-Ph}$

$R_2 = \text{Ph}$



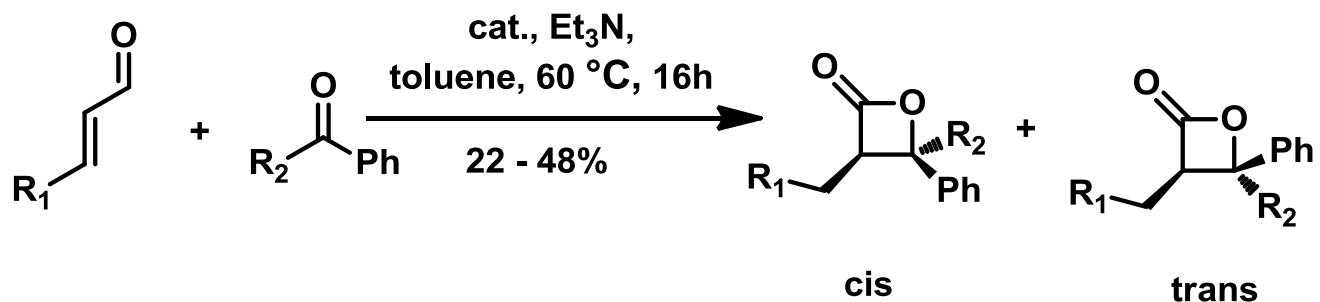
cis / trans = 4 / 1

NHC-Homoenolate Equivalents

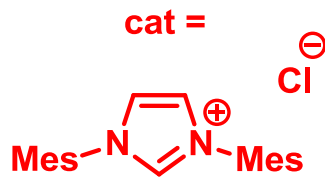


C. Burstein.; F. Glorius. *Angew. Chem., Int. Ed.* **2004**, *43*, 6205.

NHC-Homoenolate Equivalents

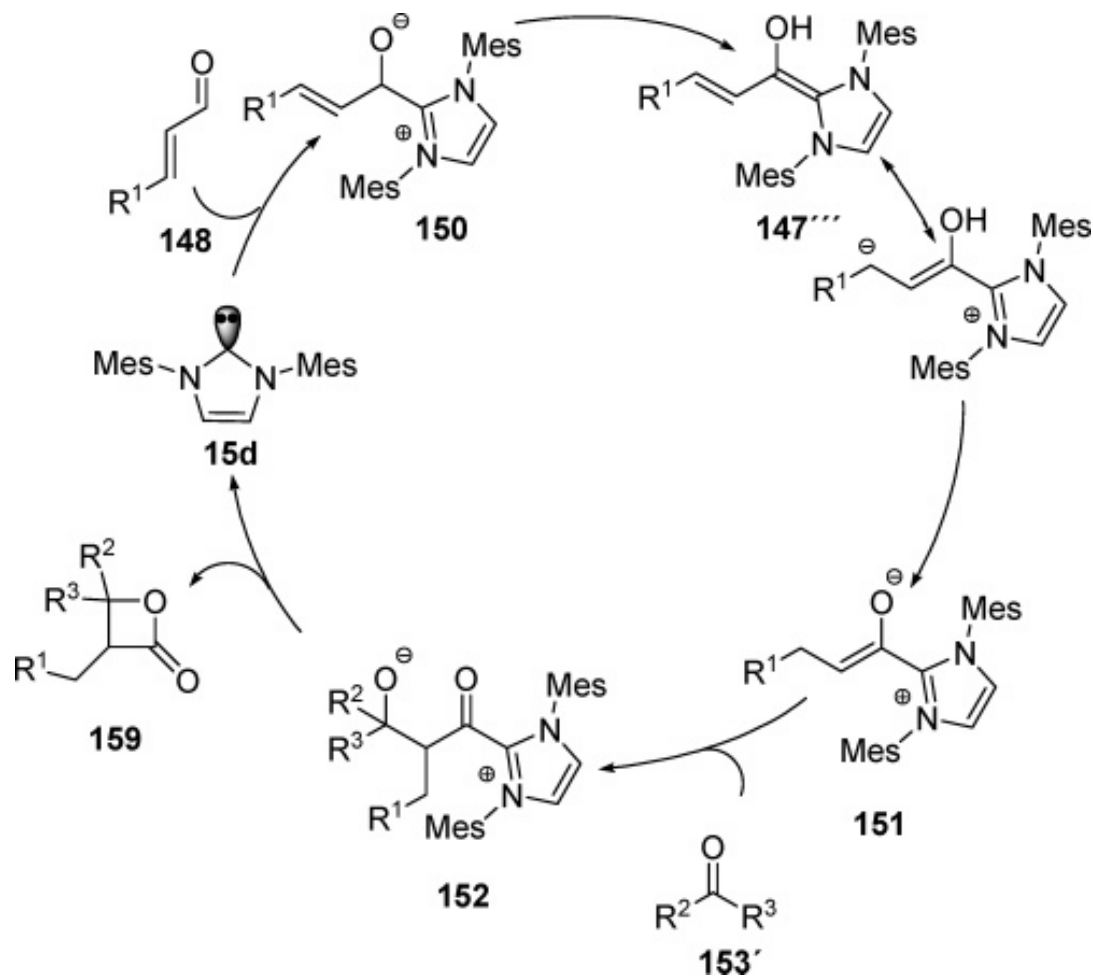


$\text{R}_1 = \text{Me, Pr, } i\text{-Pr, Ph}$
 $\text{R}_2 = \text{CF}_3, \text{CO}_2\text{Me}$



cis / trans = 1 / 1 - 7 / 3

NHC-Homoenolate Equivalents



M. He.; J. W. Bode. *Org. Lett.* **2005**, *7*, 3131.

Summary

1. Carbene catalysis is a rapidly expanding field that has greatly added to the arsenal of efficient and stereoselective bond-forming reactions over the last decade.
2. The further exploration of NHC catalysis will undoubtedly fuel the continued discovery of new methods and reactions, with future subsequent applications in total synthesis.

J. Izquierdo.; G. E. Hutson.; D. T. Cohen.; K. A. Scheidt.
Angew. Chem., Int. Ed. **2012**, *51*, 11686.

THANK YOU!