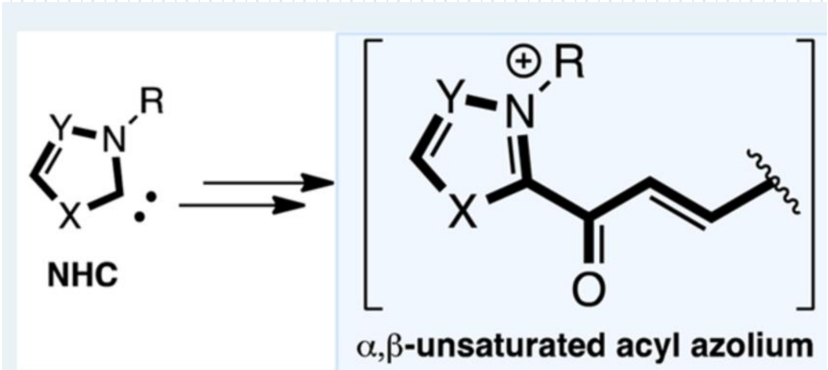
N-Heterocyclic Carbene Catalysis via the α,β-Unsaturated Acyl Azolium



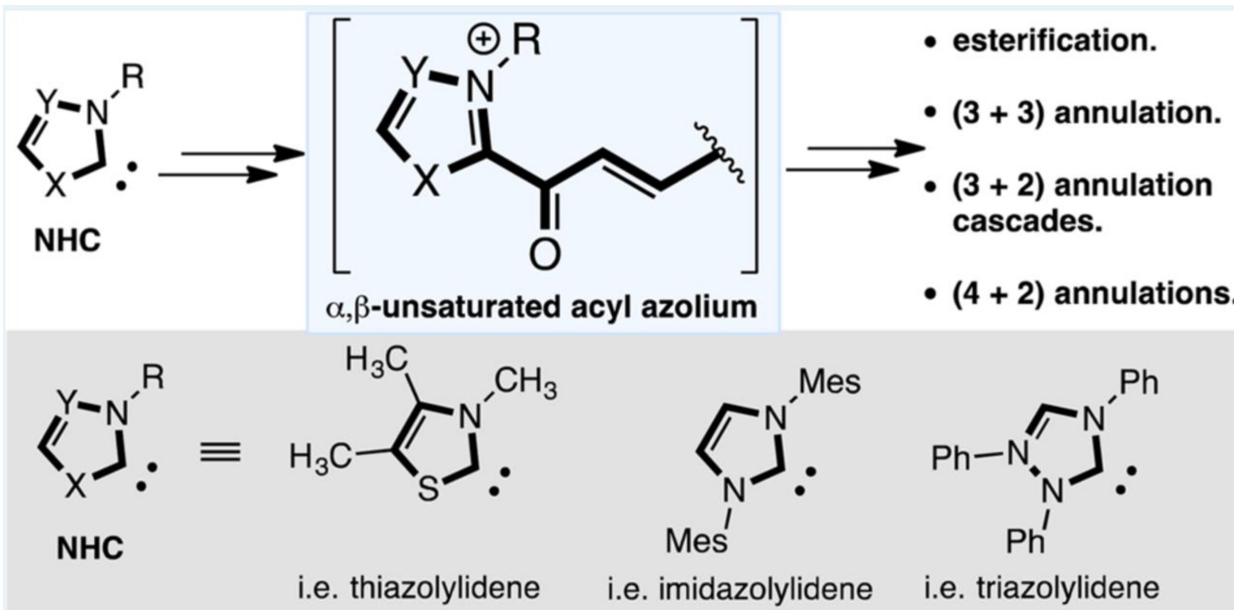
Supervisor: Yong Huang

Reporter: Qian Wang

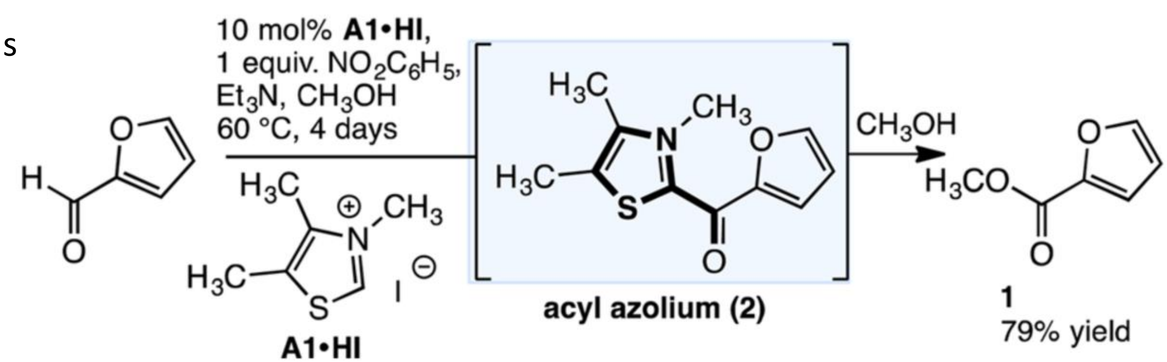
Date: 2017-11-27

Contents

1. Introduction

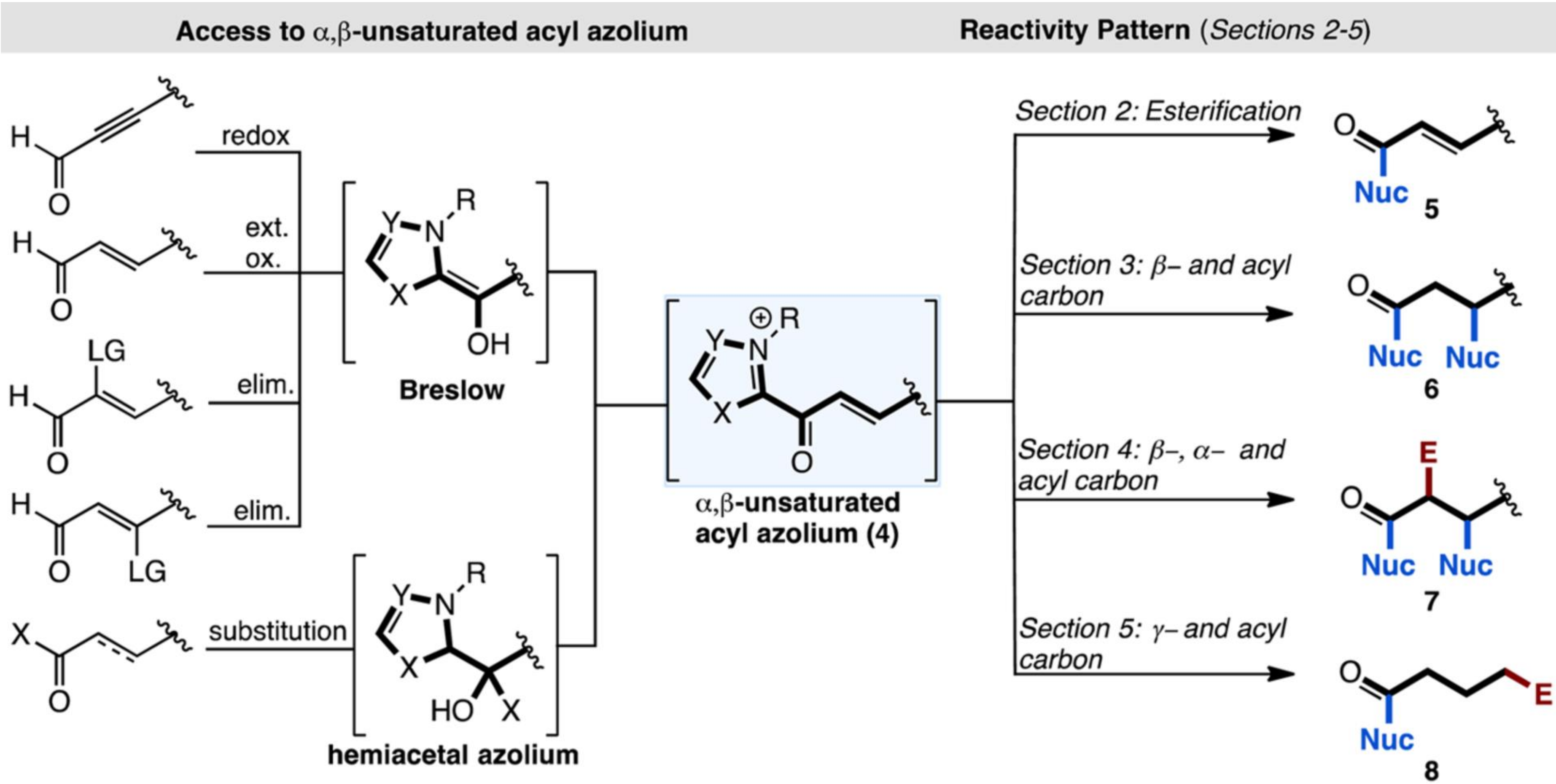


Castells



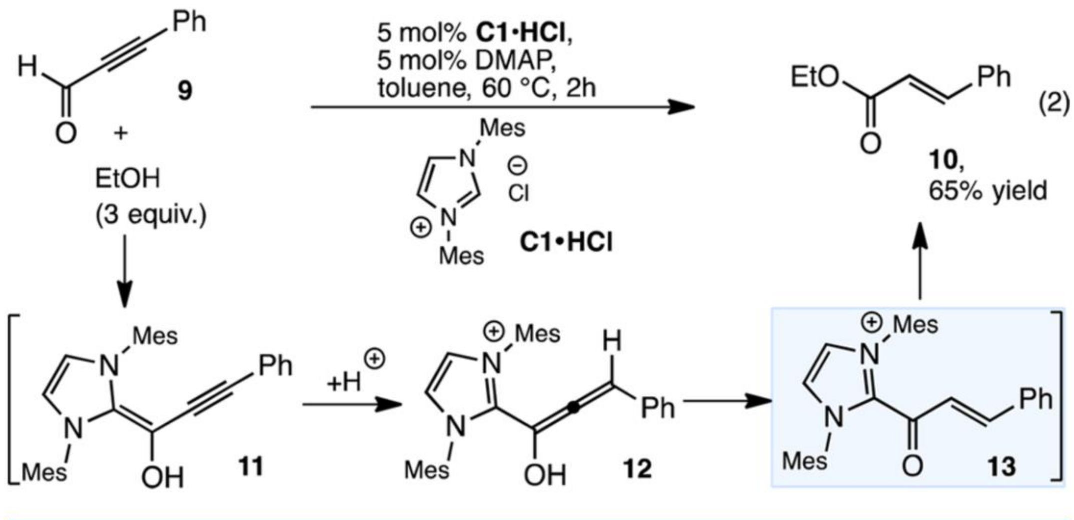
Tetrahedron Lett. **1977**, *18*, 205

1. Introduction

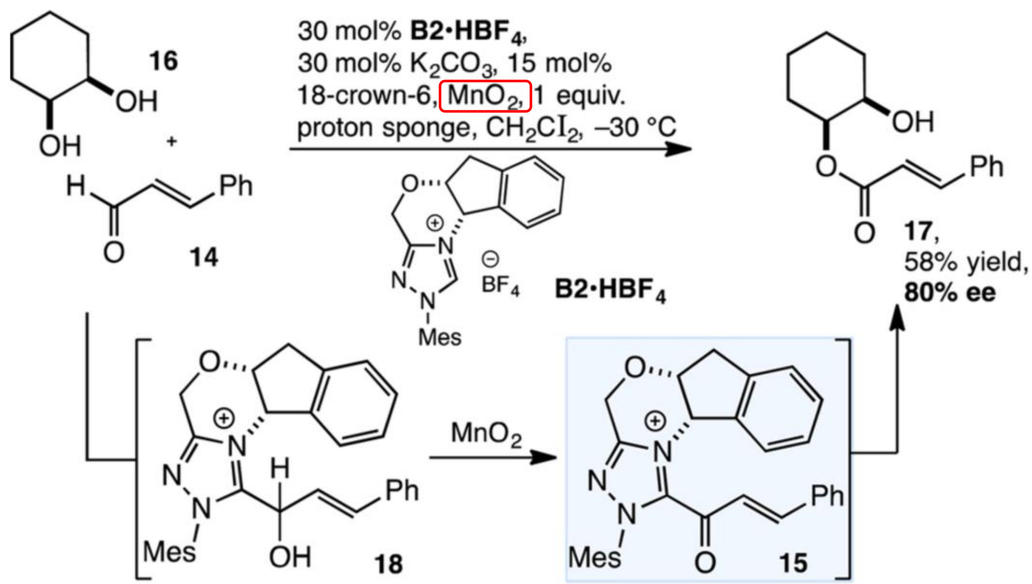


2.1 Esterification of the α,β-unsaturated acyl azolium

Zeitler

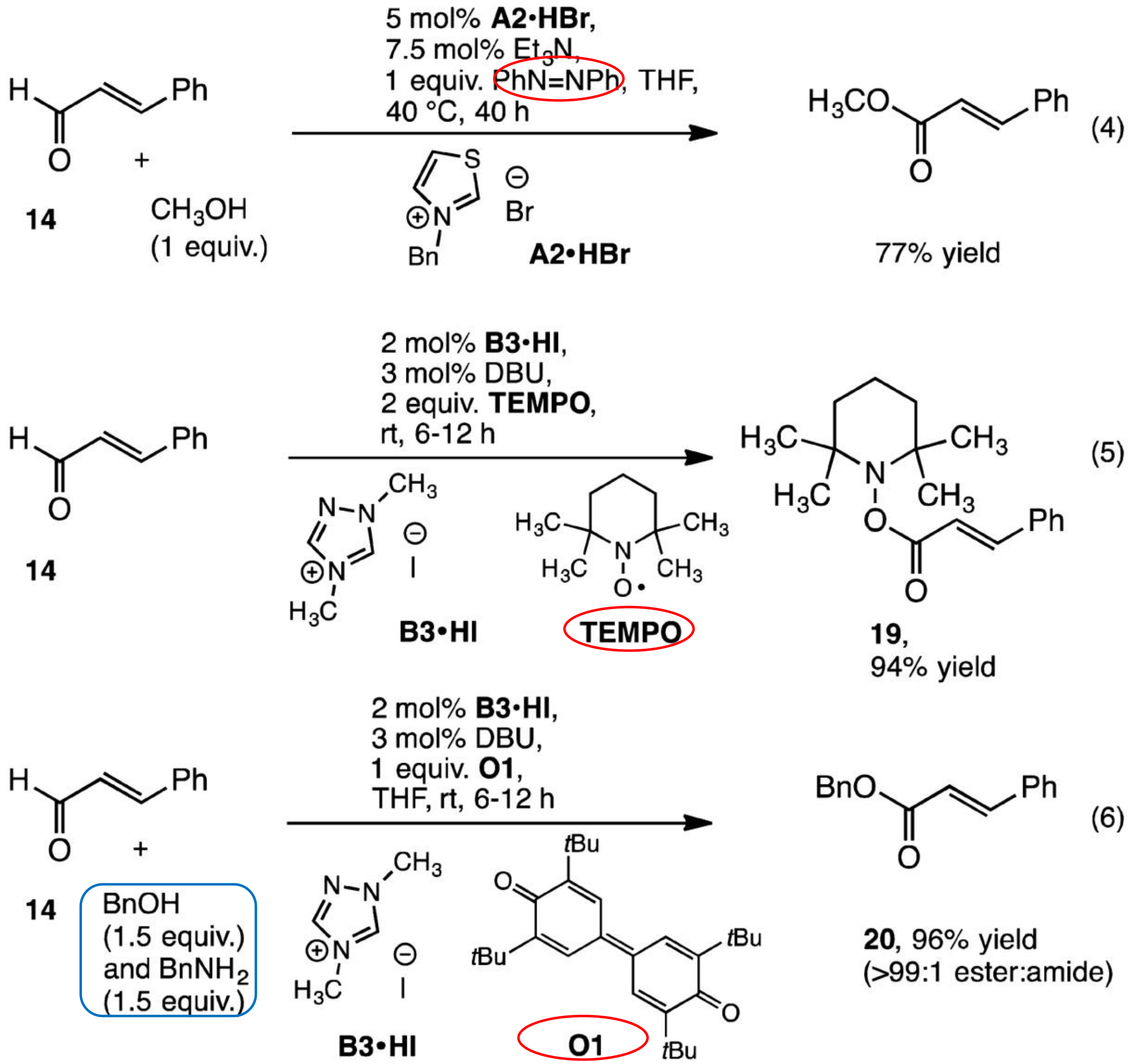


Scheidt



Org. Lett. **2006**, *8*, 637
Org. Lett. **2007**, *9*, 371

2.1 Esterification of the α,β-unsaturated acyl azolium

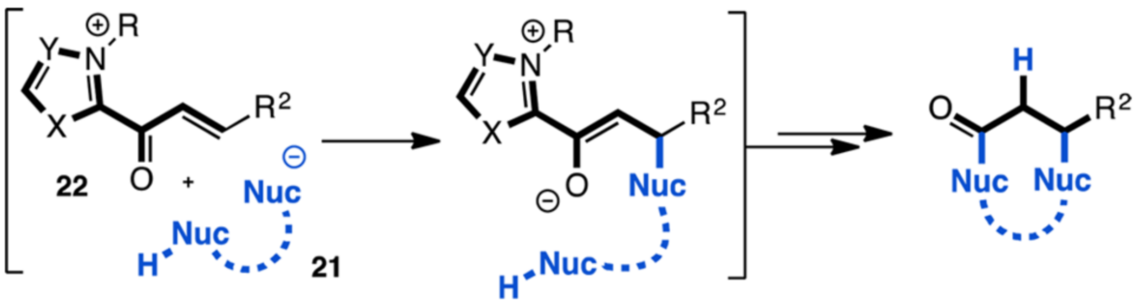


Tetrahedron Lett. **2008**, *49*, 4003
Angew. Chem., Int. Ed. **2008**, *47*, 8727
J. Am. Chem. Soc. **2010**, *132*, 1190

2.2 Cascades involving bond formation at the β- and acyl carbons

2009

Scheme 6. Summary of the Mechanism Described in Section 3



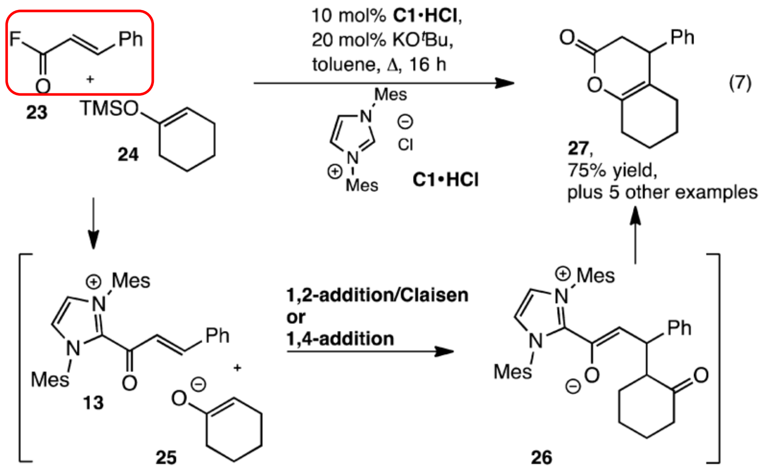
2.2.1 Annulation with enolate bis-nucleophiles

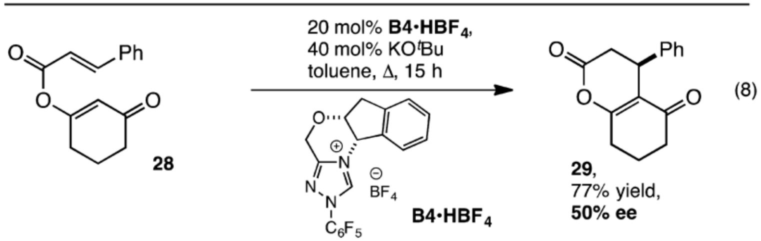
2.2.2 Annulation with enamine bis-nucleophiles

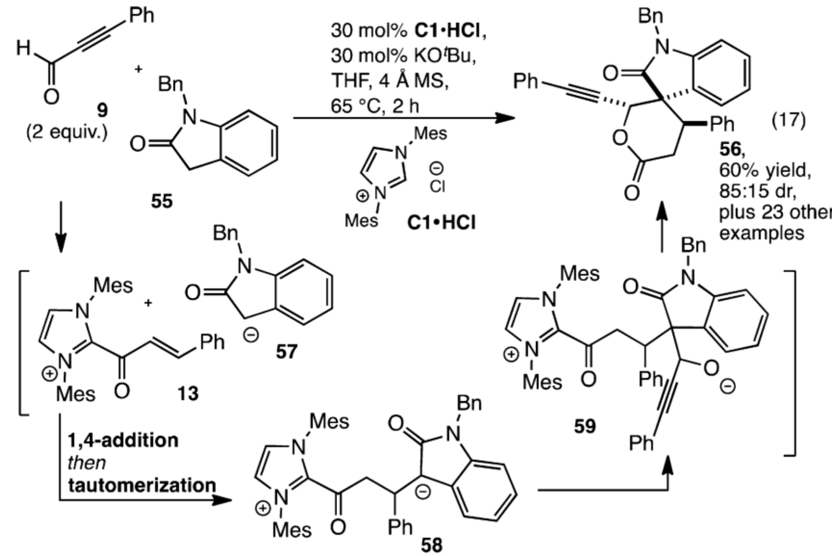
2.2.3 Annulation with other bis-nucleophiles

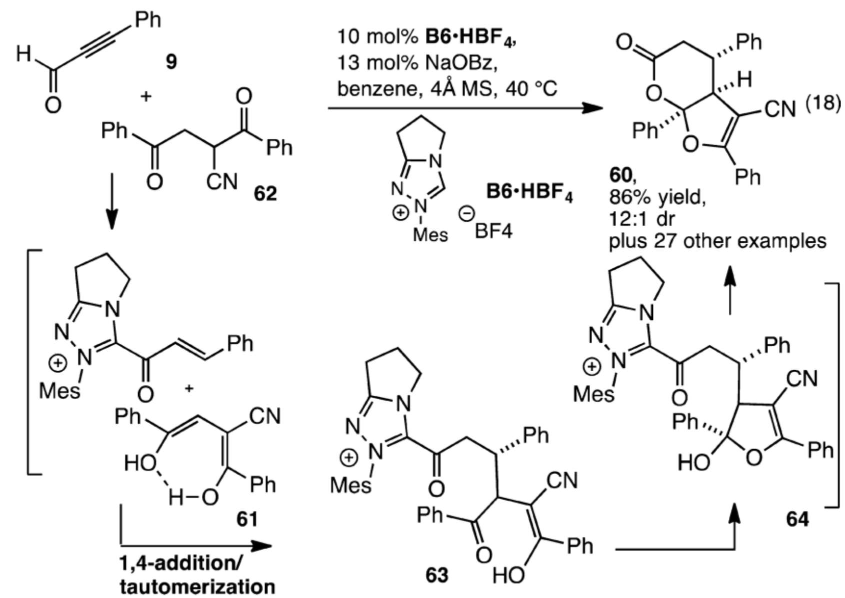
2.2.1 Annulation with enolate bis-nucleophiles

Lupton



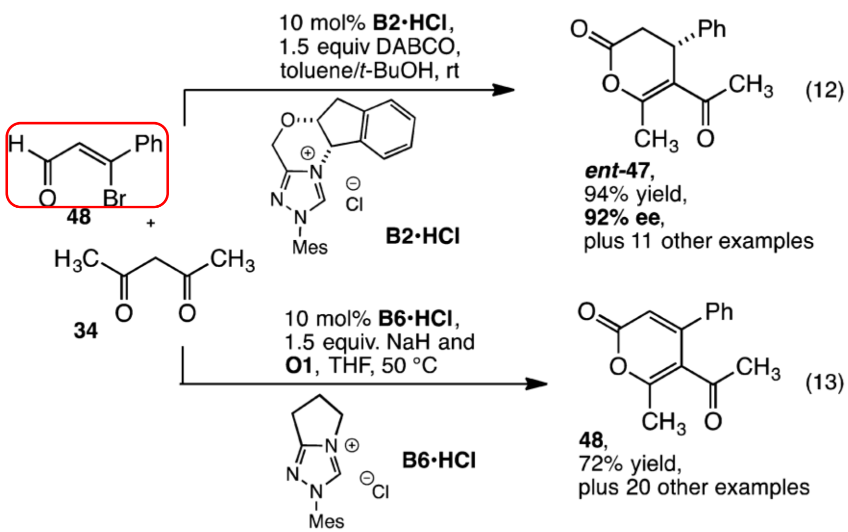






J. Am. Chem. Soc. **2009**, *131*, 14176
Org. Biomol. Chem. **2011**, *9*, 8182
Org. Lett. **2012**, *14*, 1274
Org. Lett. **2012**, *14*, 4906

2.2.1 Annulation with enolate bis-nucleophiles



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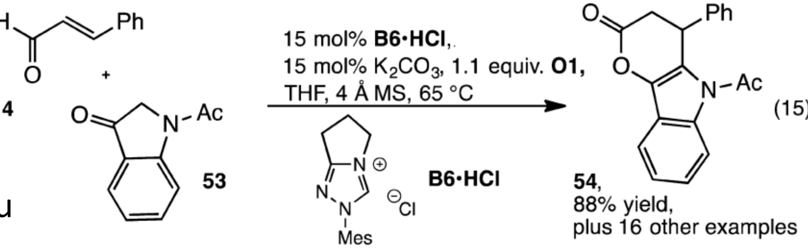
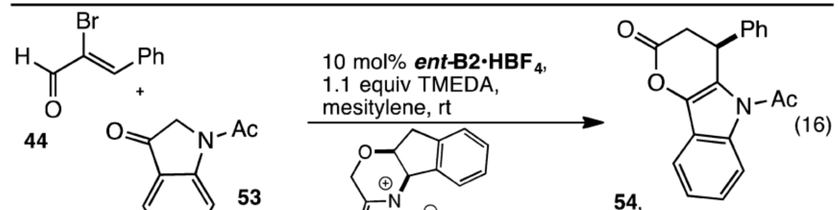
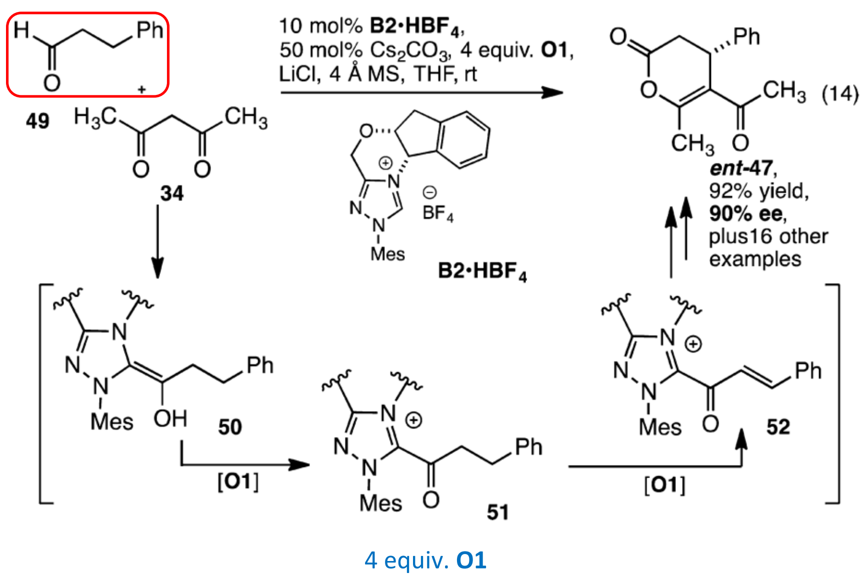


Enders



Chi



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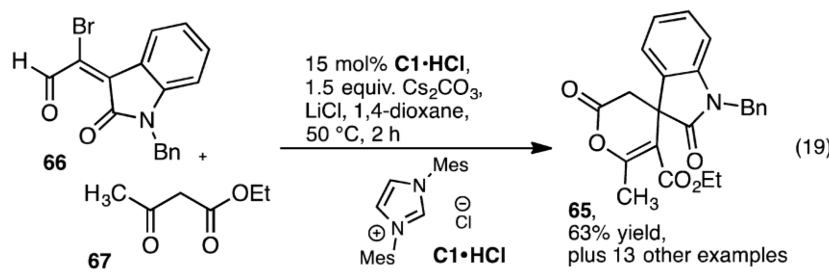
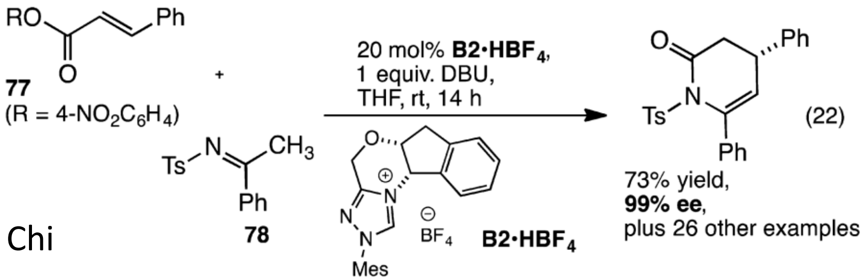


J. Org. Chem. **2013**, *78*, 6223
Chem. Eur. J. **2012**, *18*, 1914
Angew. Chem., Int. Ed. **2013**, *52*, 8588
Adv. Synth. Catal. **2013**, *355*, 321
Chem. Asian J. **2014**, *9*, 1535
Adv. Synth. Catal. **2013**, *355*, 321

2.2.2 Annulation with enamine bis-nucleophiles



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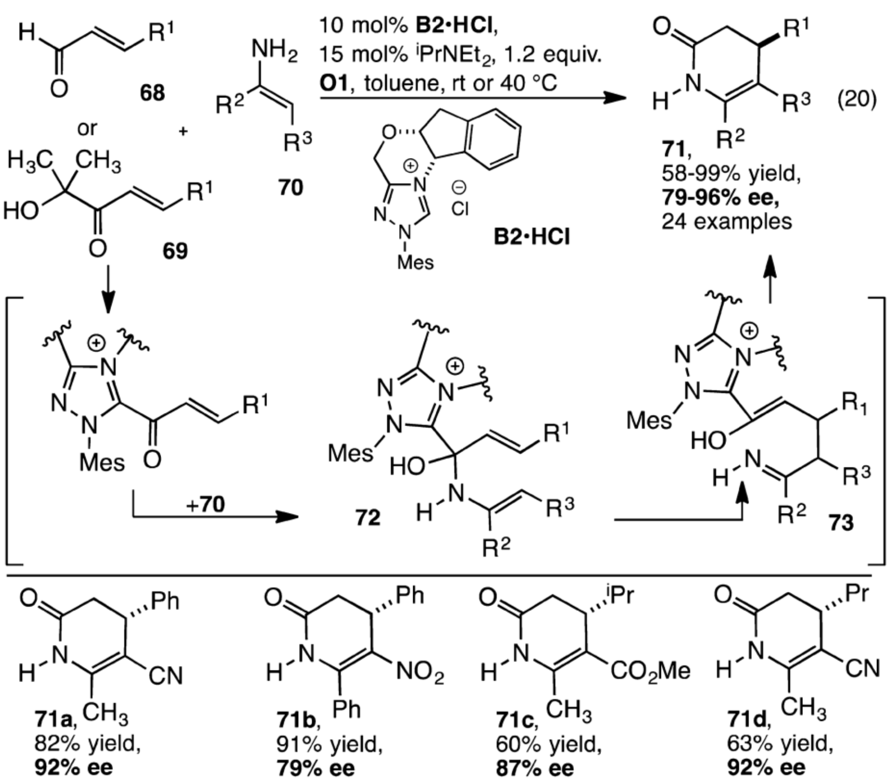
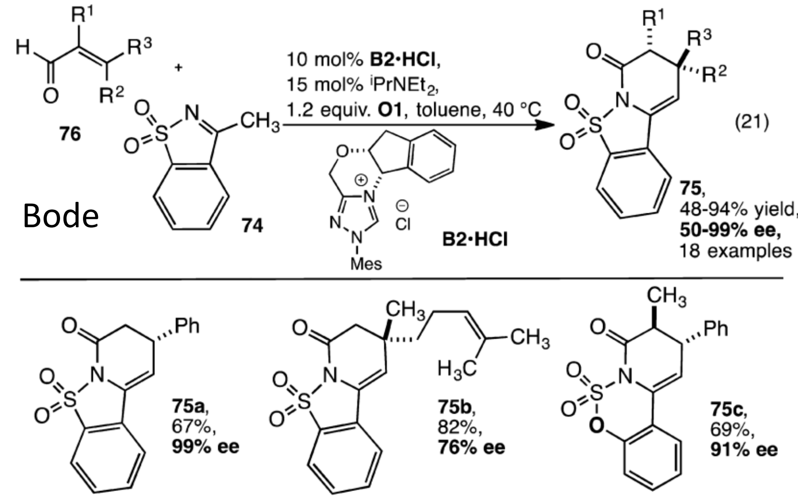


Bode



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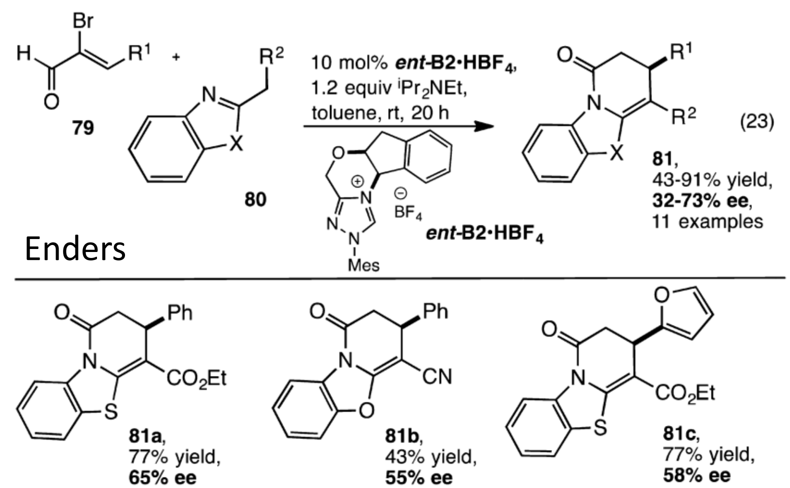


Enders

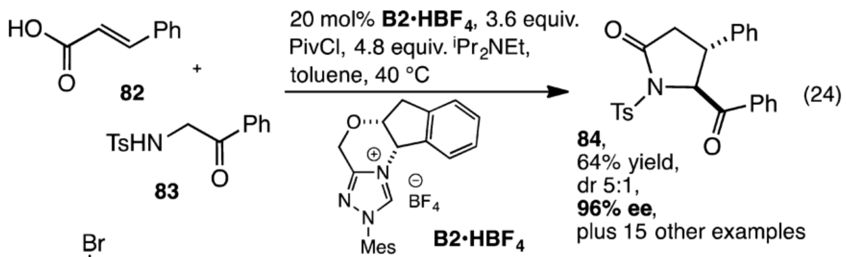
Bode

Angew. Chem., Int. Ed. **2013**, *52*, 8592
Org. Lett. **2011**, *13*, 5378

Angew. Chem., Int. Ed. **2012**, *51*, 9433
Synlett **2015**, *26*, 1465

2.2.3 Annulation with other bis-nucleophiles

Ye



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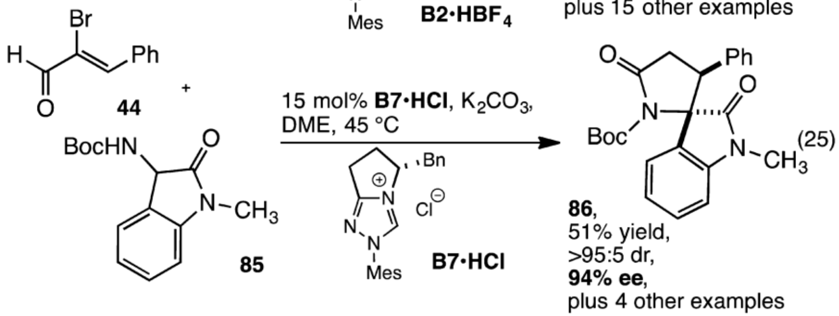

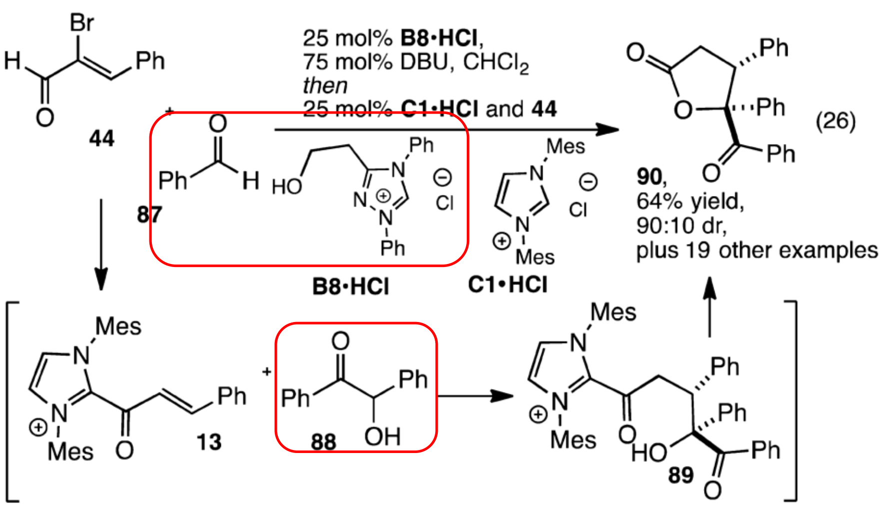

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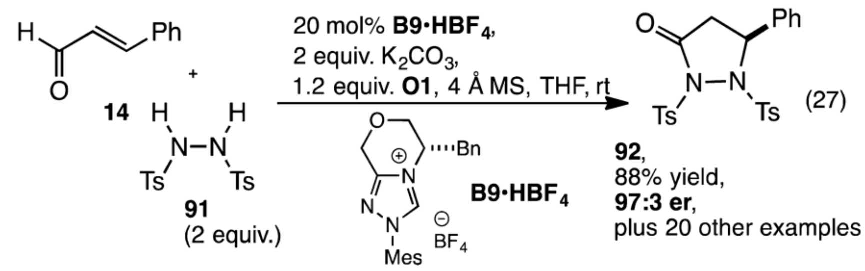
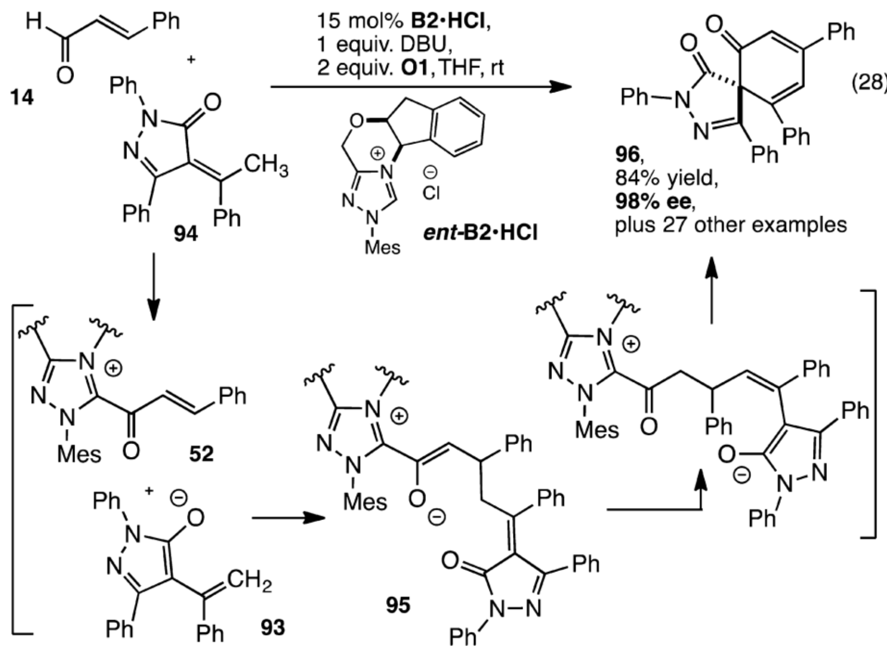


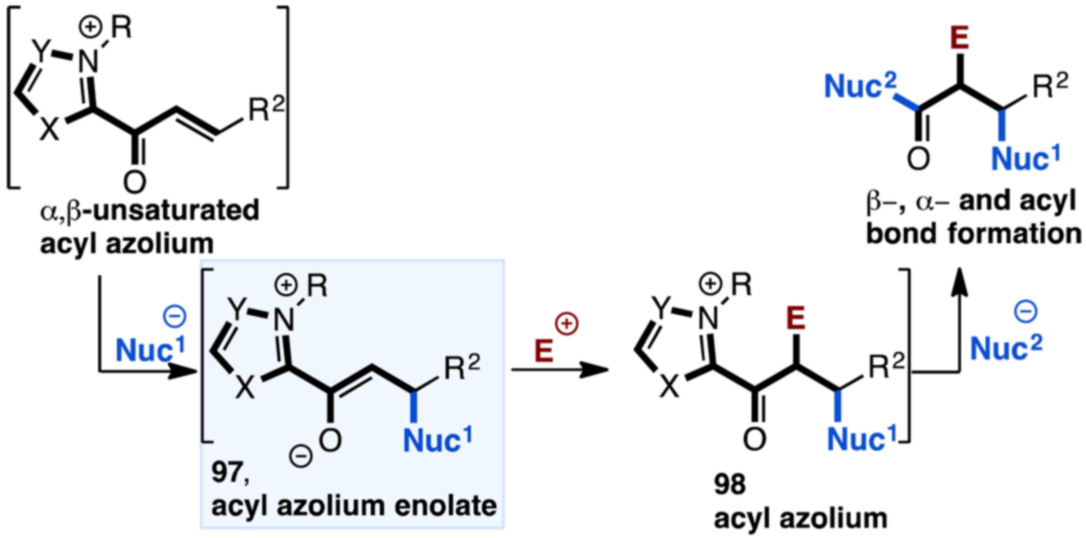


Angew. Chem., Int. Ed. **2014**, *53,* 11611
J. Org. Chem. **2015**, *80*, 11593
RSC Adv. **2015**, *5*, 26972

Angew. Chem., Int. Ed. **2016**, *55*, 12280
Angew. Chem., Int. Ed. **2016**, *55*, 268

2.3 Cascades involving bond formation at the β-, α- and acyl carbons

Scheme 26. Summary of the Mecahnism Described in Section 4



2.3.1 (4+2) Annulation / β-lactonization

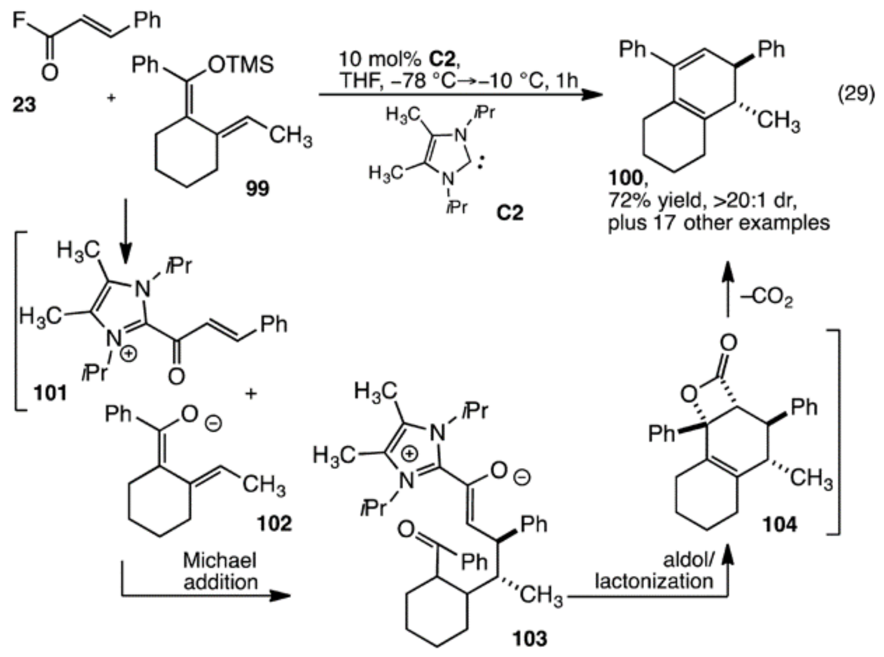
2.3.2 (3+2) Annulation / β-lactonization

2.3.3 (3+2) Annulation / δ-lactonization

2.3.4 Three-component reactions

2.3.1 (4+2) Annulation / β-lactonization

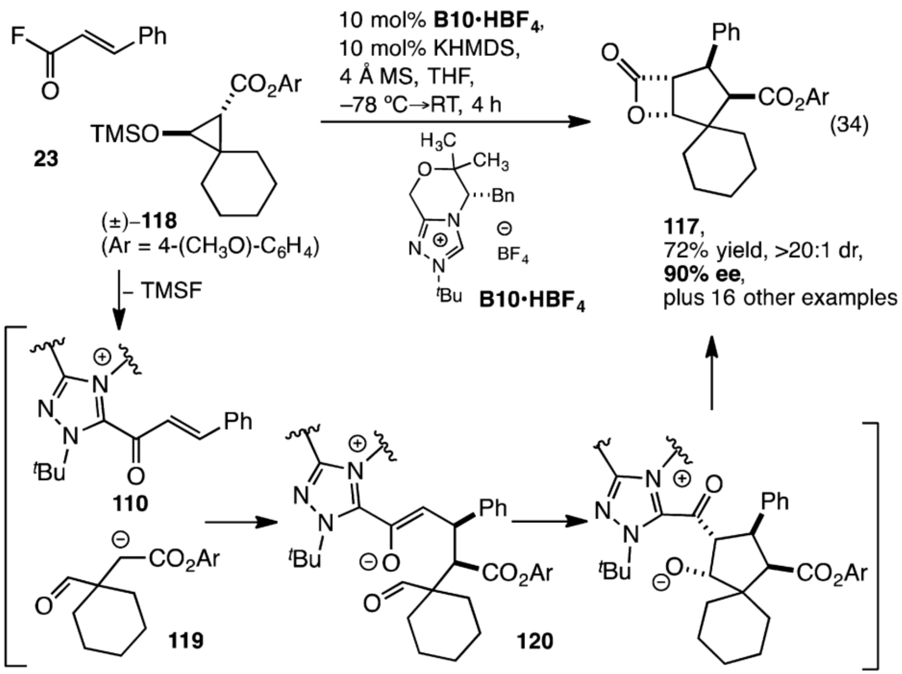
Lupton



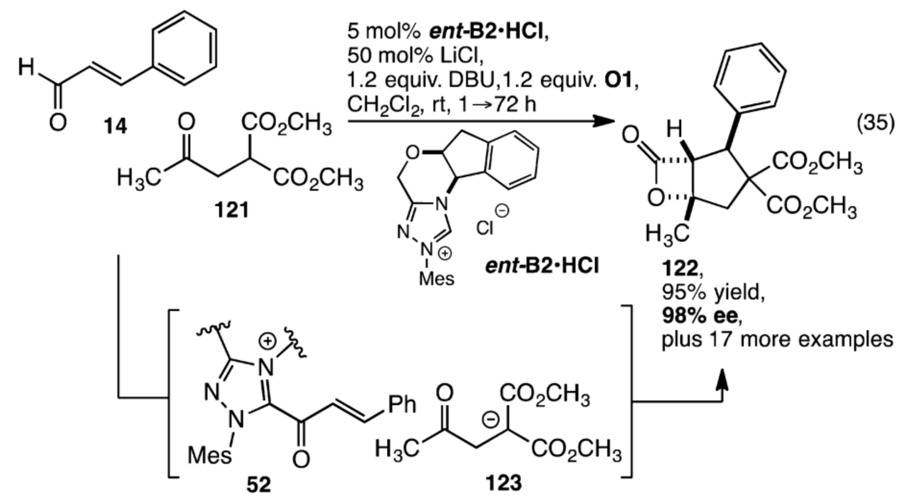
J. Am. Chem. Soc. **2011**, *133*, 4694

2.3.2 (3+2) Annulation / β-lactonization

Lupton



Studer

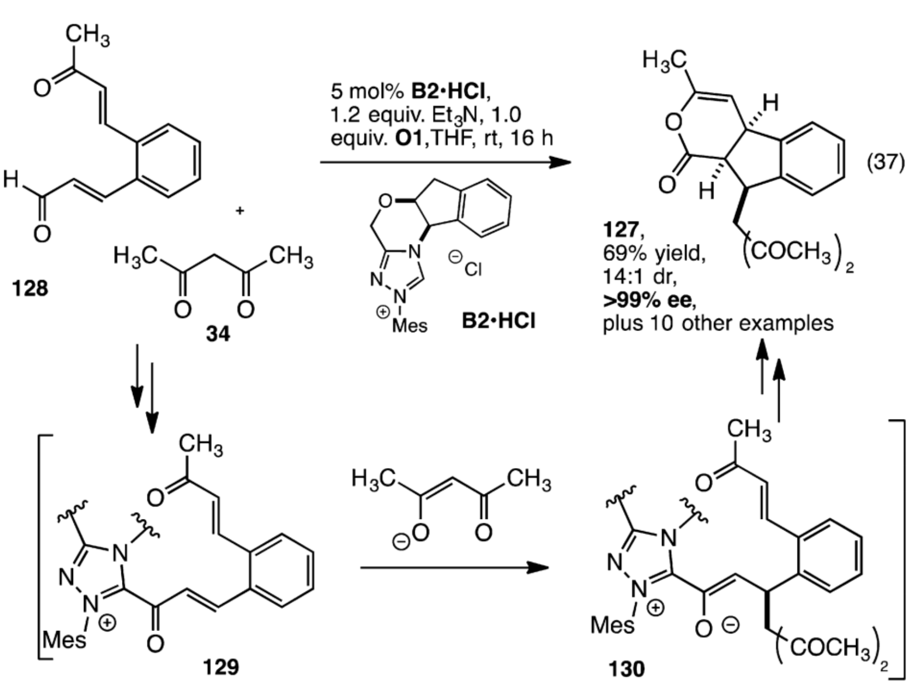


J. Am. Chem. Soc. **2013**, *135*, 58

Angew. Chem., Int. Ed. **2014**, *53*, 9622

2.3.3 (3+2) Annulation / δ-lactonization

Studer



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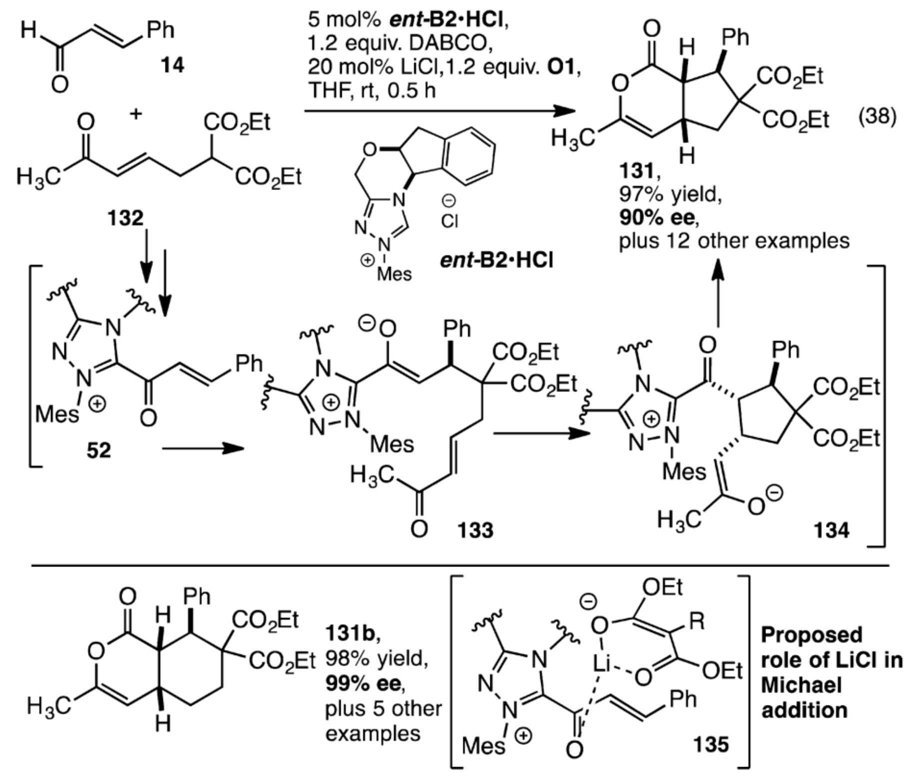
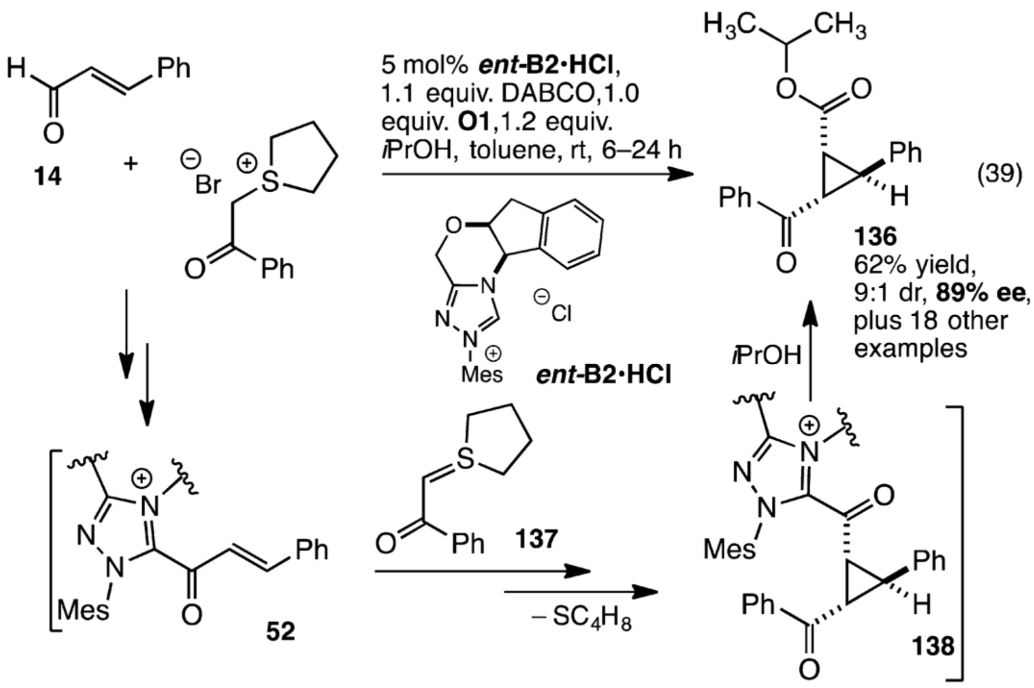


Org. Lett. **2011**, *13*, 4966

Org. Lett. **2015**, *17*, 4940

2.3.4 Three-component reactions

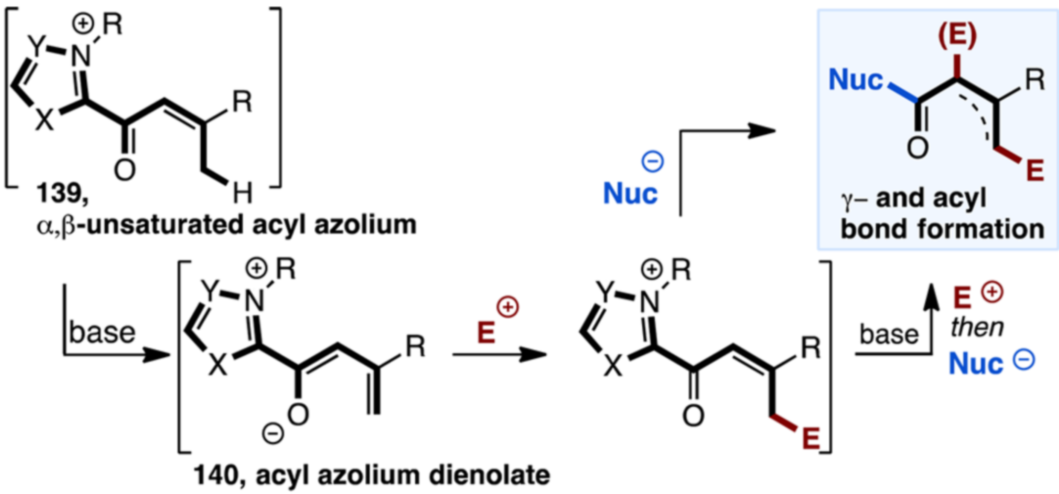
Studer



Chem. Commun. **2012**, *48*, 5190

2.4 Cascades involving bond formation at the γ- and acyl carbons

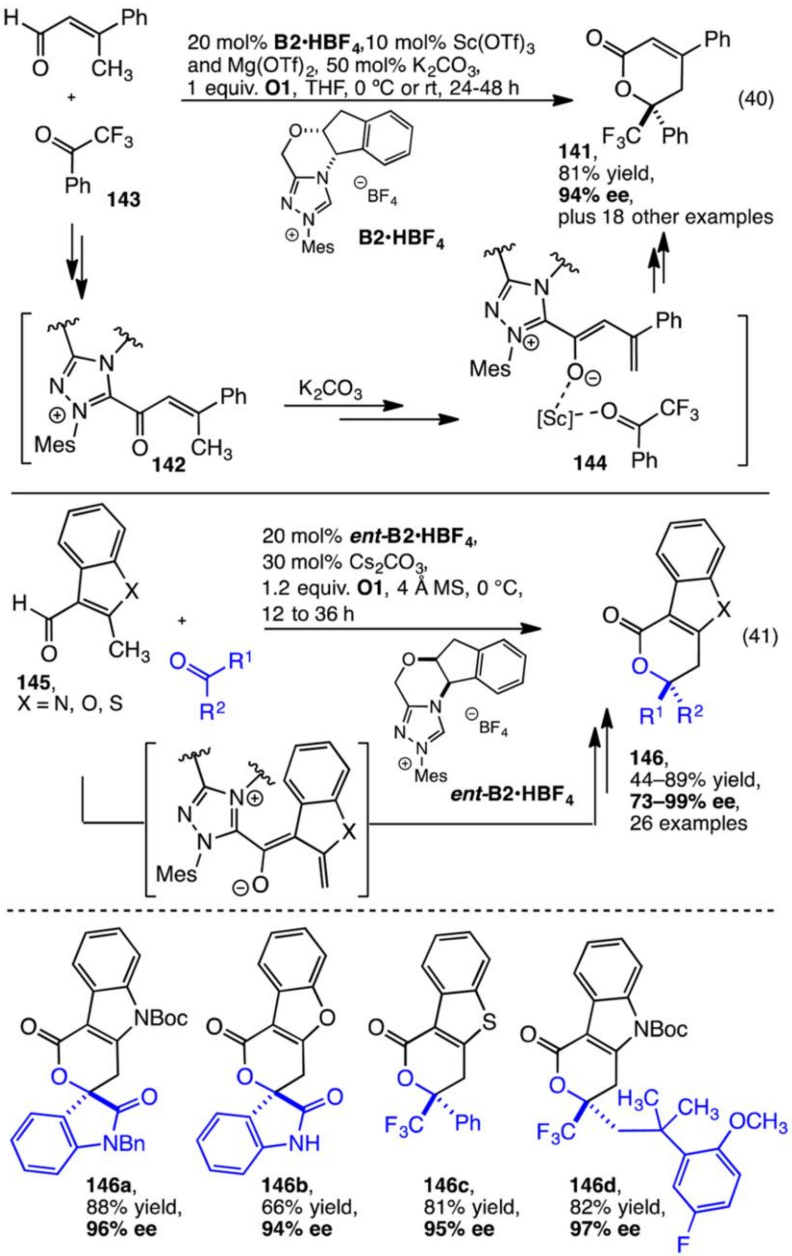
Scheme 35. Summary of the Mechanism Described in Section 5



2.4.1 Annulation with ketones and imines

2.4.2 Annulation with electron-poor olefins

2.4.1 Annulation with ketones and imines



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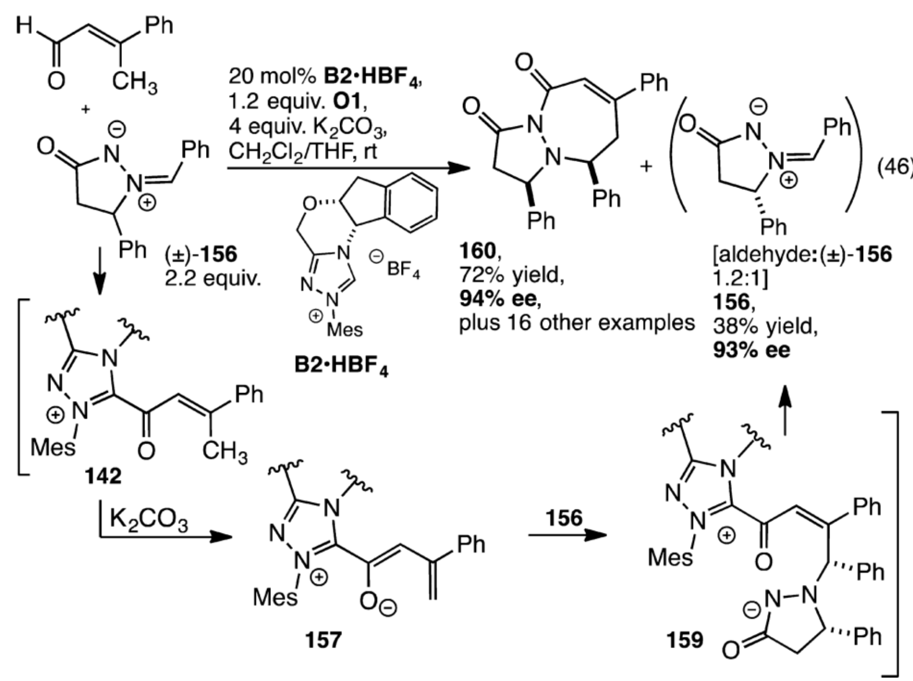
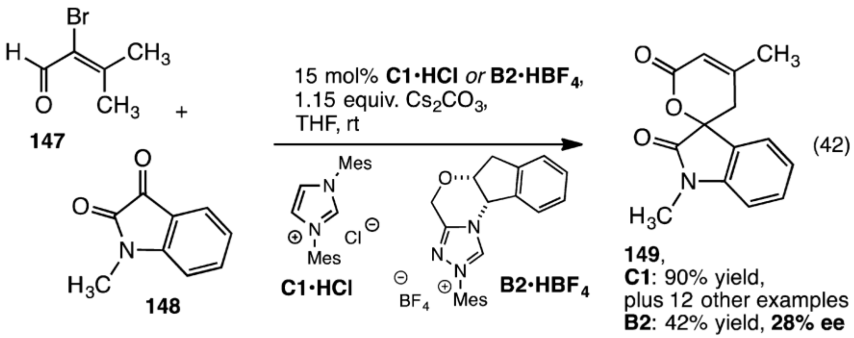


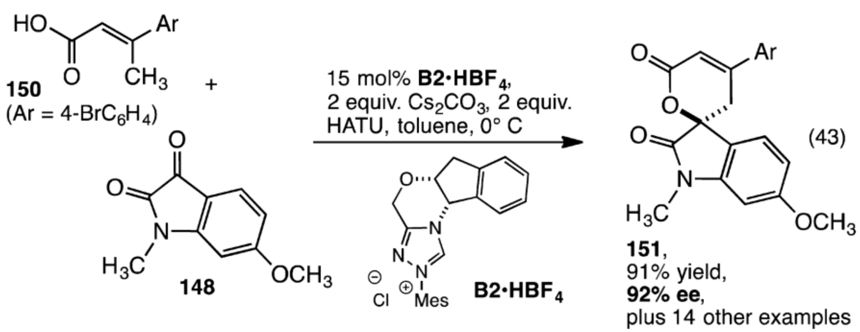
J. Am. Chem. Soc. **2012**, *134*, 8810

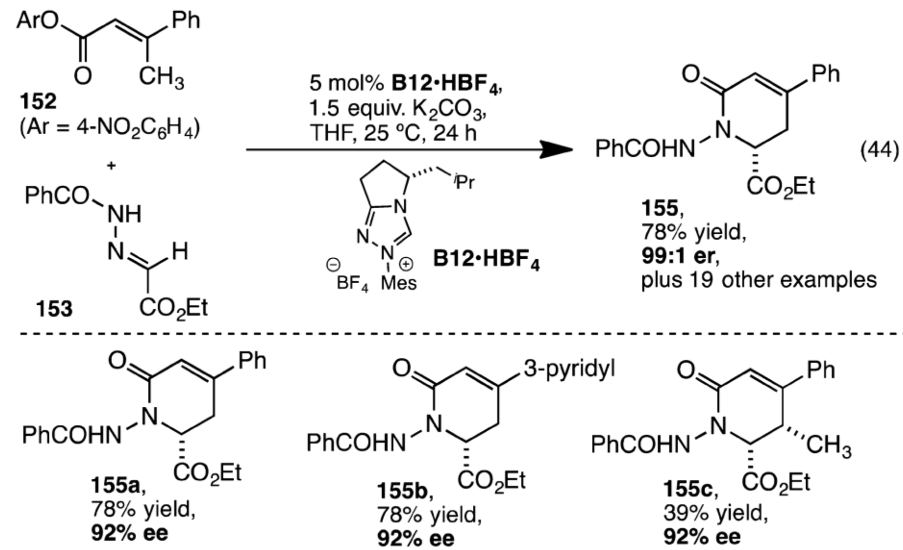
Angew. Chem., Int. Ed. **2013**, *52*, 11134

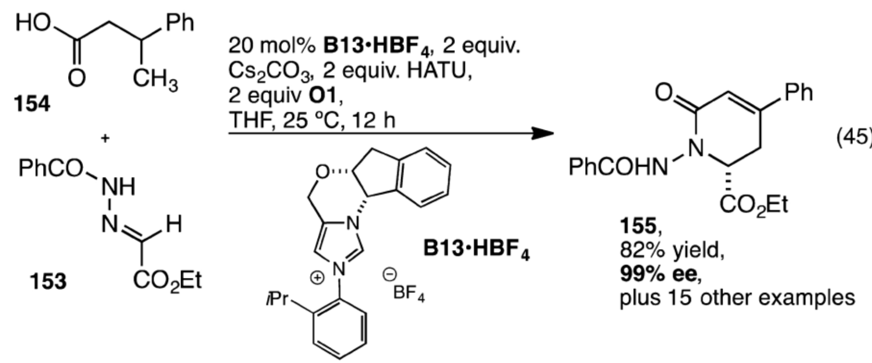
J. Am. Chem. Soc. **2014**, *136*, 1214

2.4.1 Annulation with ketones and imines







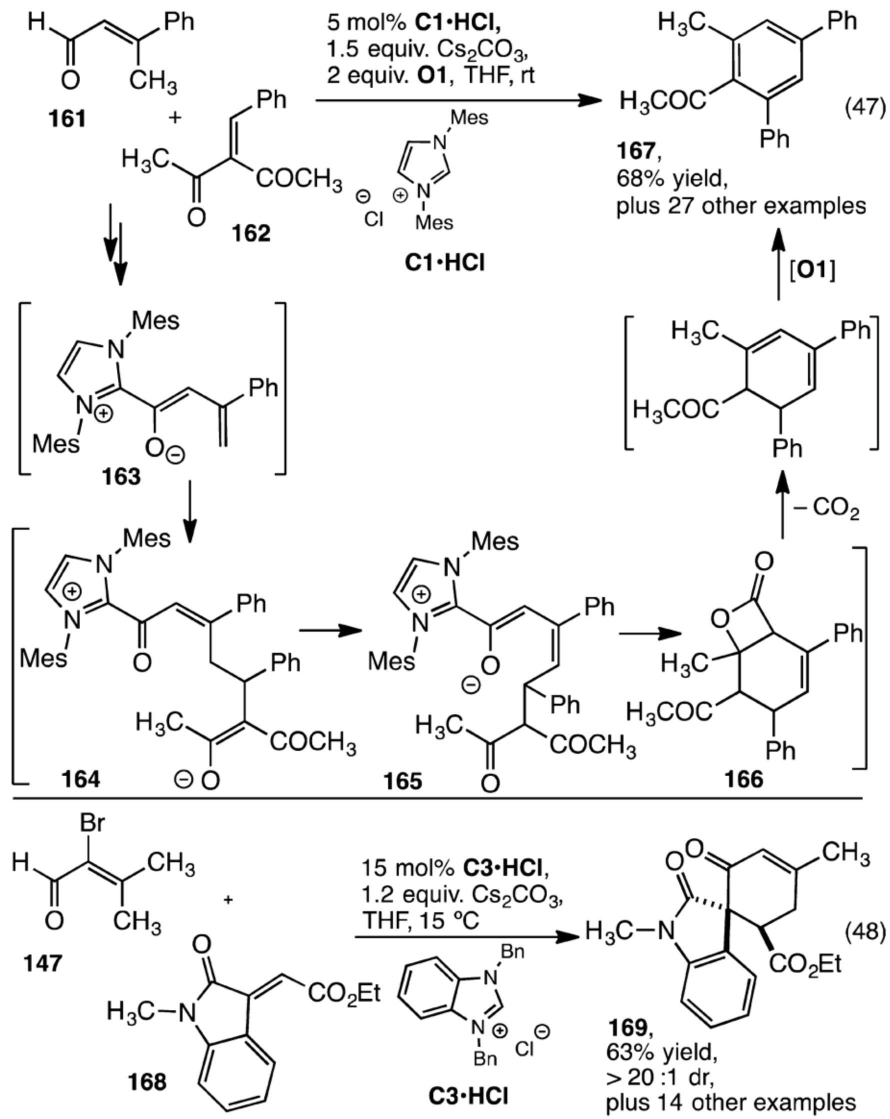


Chem. Eur. J. **2013**, *19*, 456
Org. Biomol. Chem. **2016**, *14*, 1485

Org. Lett. **2013**, *15*, 5028
Org. Lett. **2015**, *17*, 6234

2.4.2 Annulation with electron-poor olefins

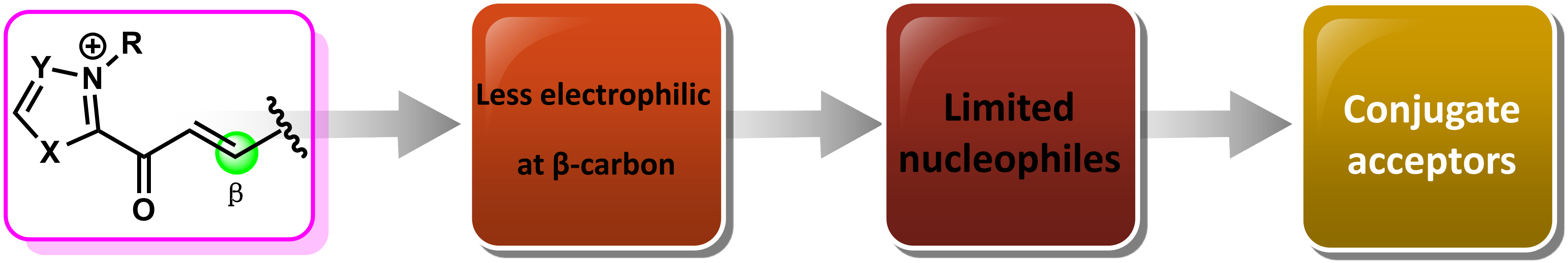
Chi

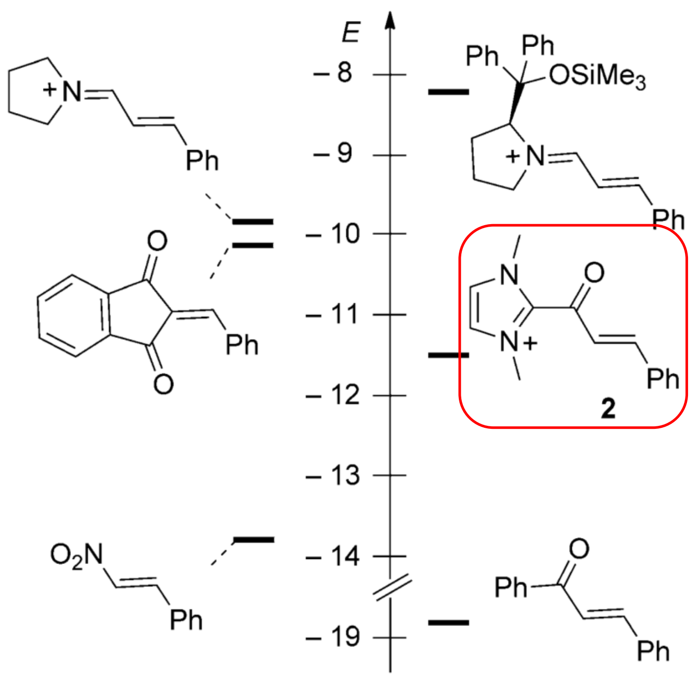


Nat. Commun. **2014**, *5*, 5027

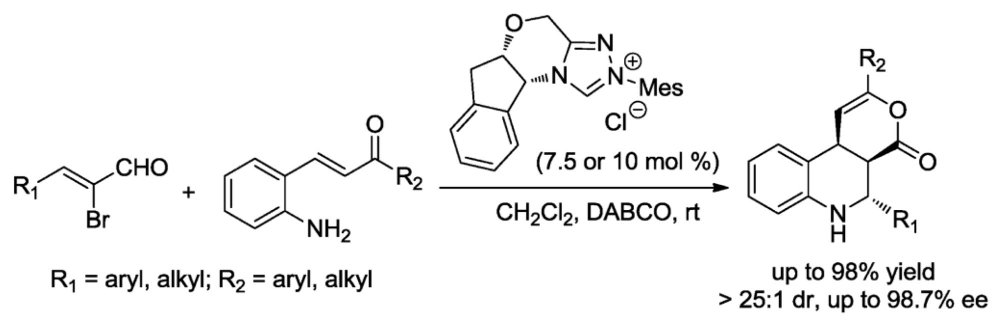
Org. Biomol. Chem. **2015**, *13*, 1829

4. Summary and Outlook

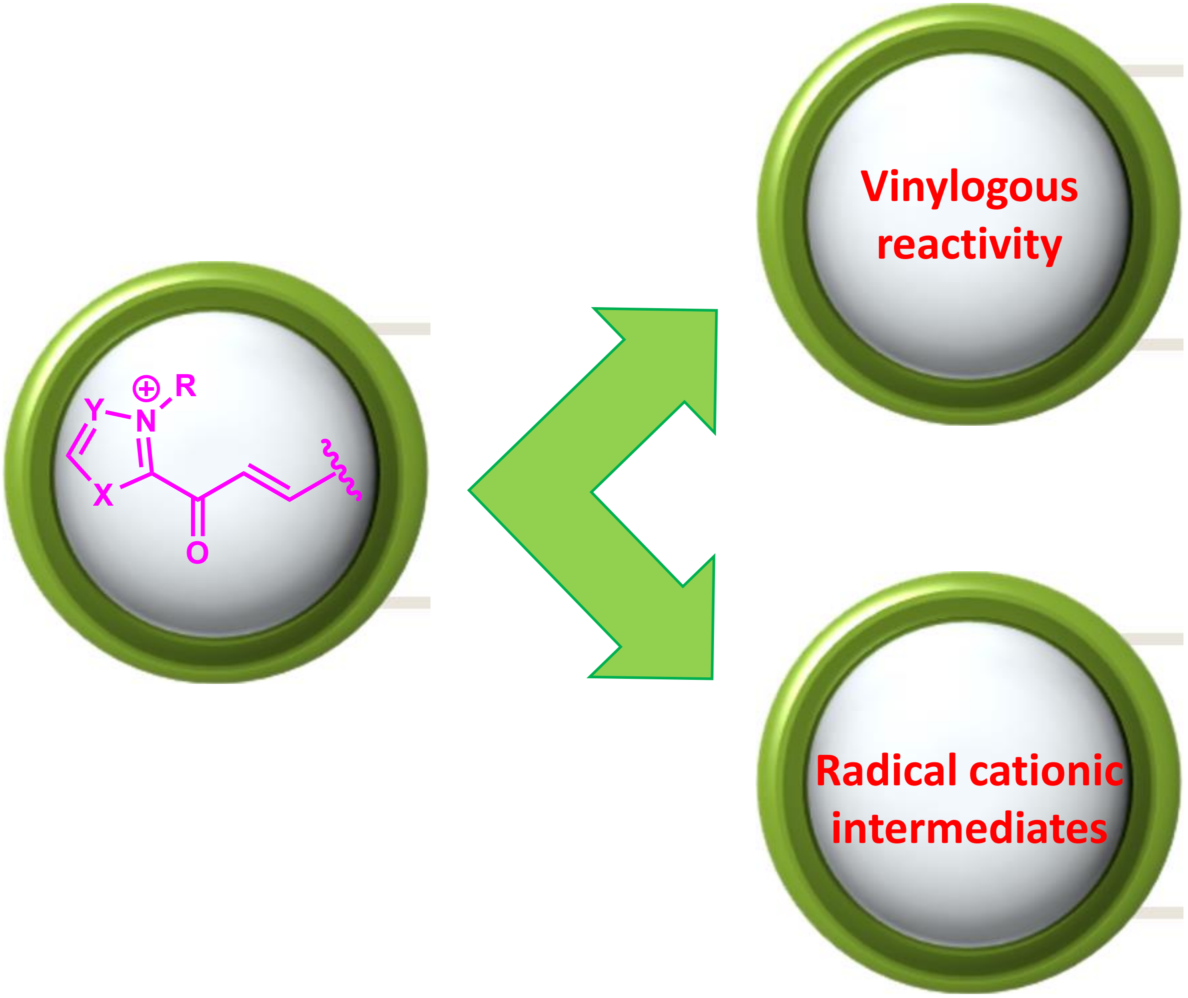




Angew. Chem., Int. Ed. **2012**, *51*, 5234



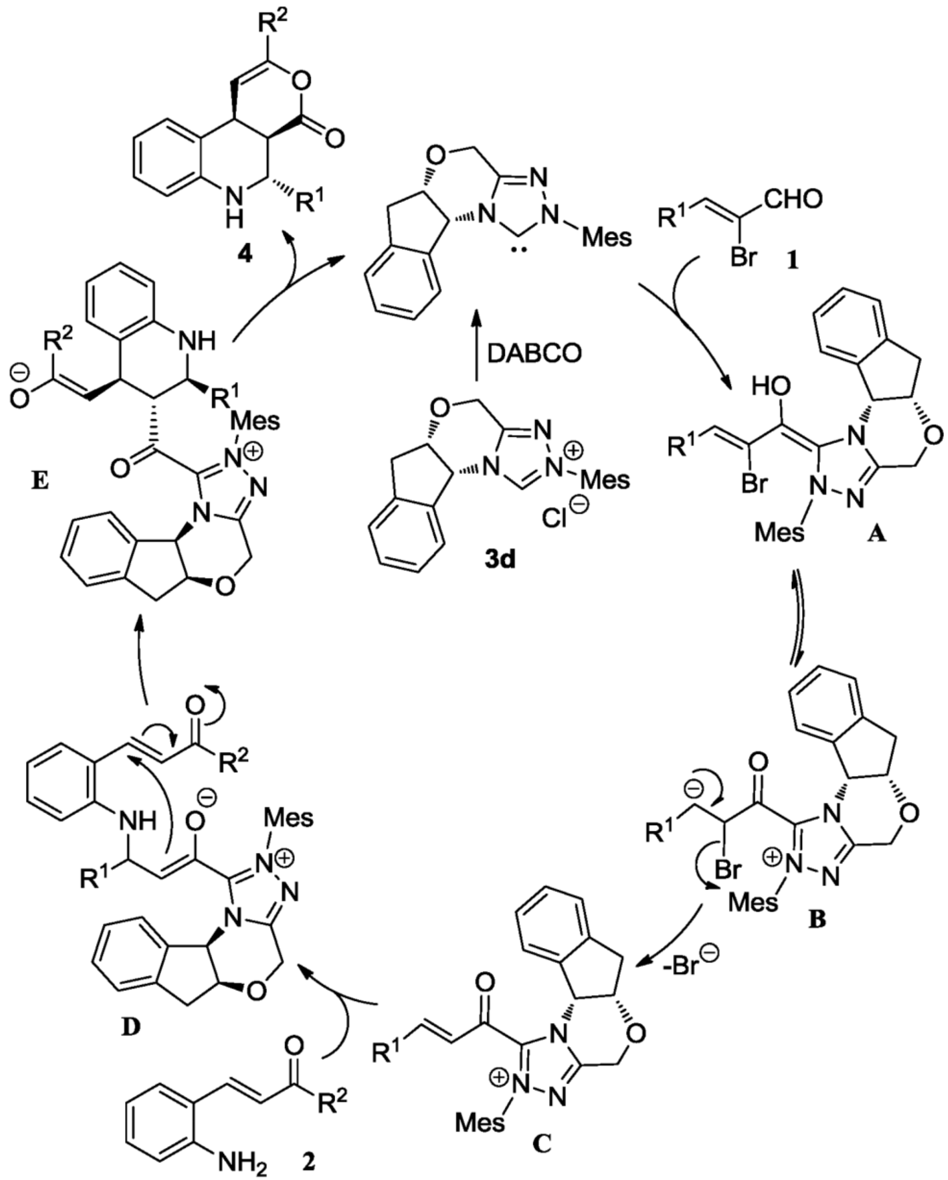
Org. Lett. **2013**, *15*, 4750


Y
N
R
X
O
Vinylogous reactivity
Radical cationic intermediates

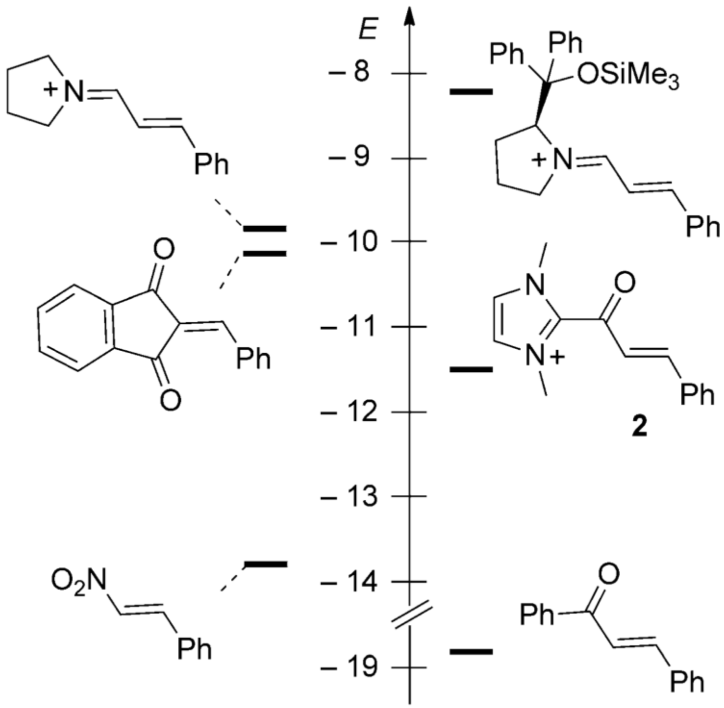
5. Acknowledgement

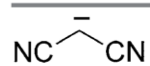
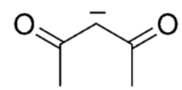
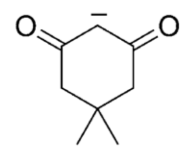
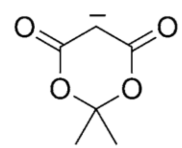
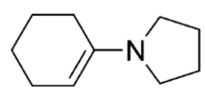
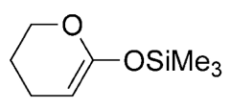
- **Prof. Huang**
- **Mr. Chen**
- **All members here**

Thanks for your attention!

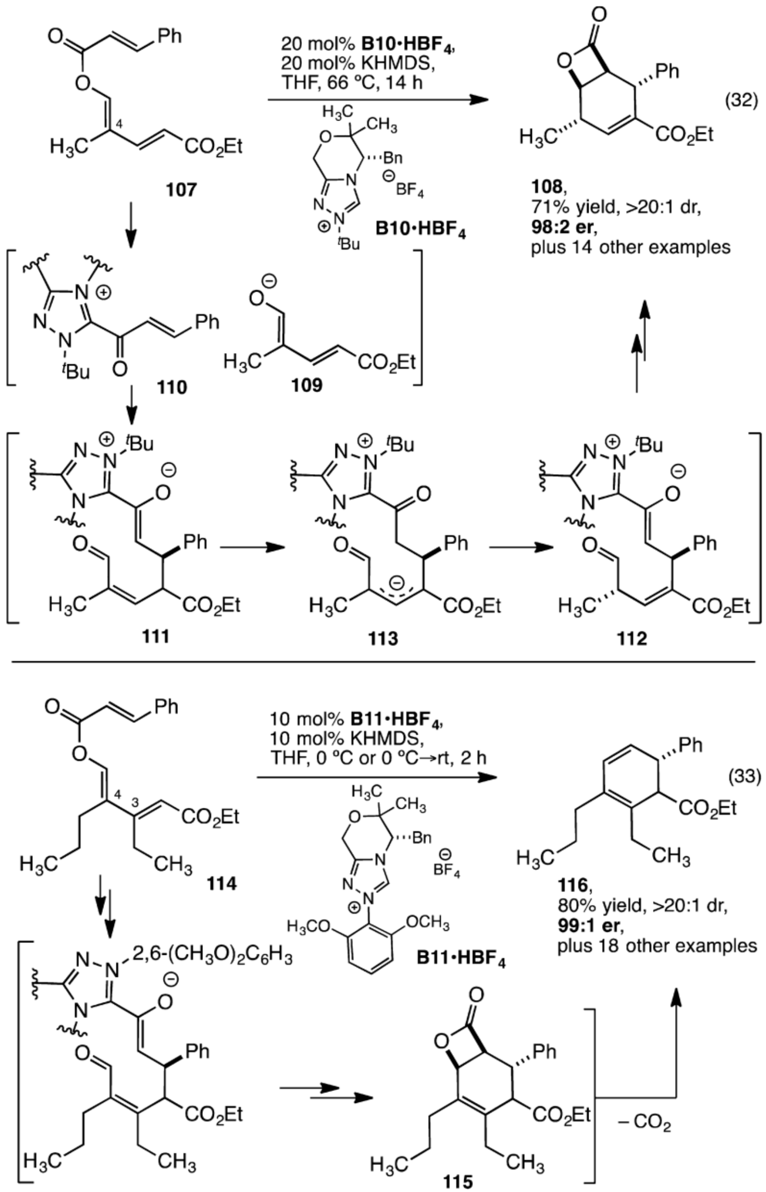


4
1
3d
DABCO
A
B
C
D
E
2
-Br⊖
Cl⊖
Mes
CHO
Br
HO
NH
NH₂
R¹
R²



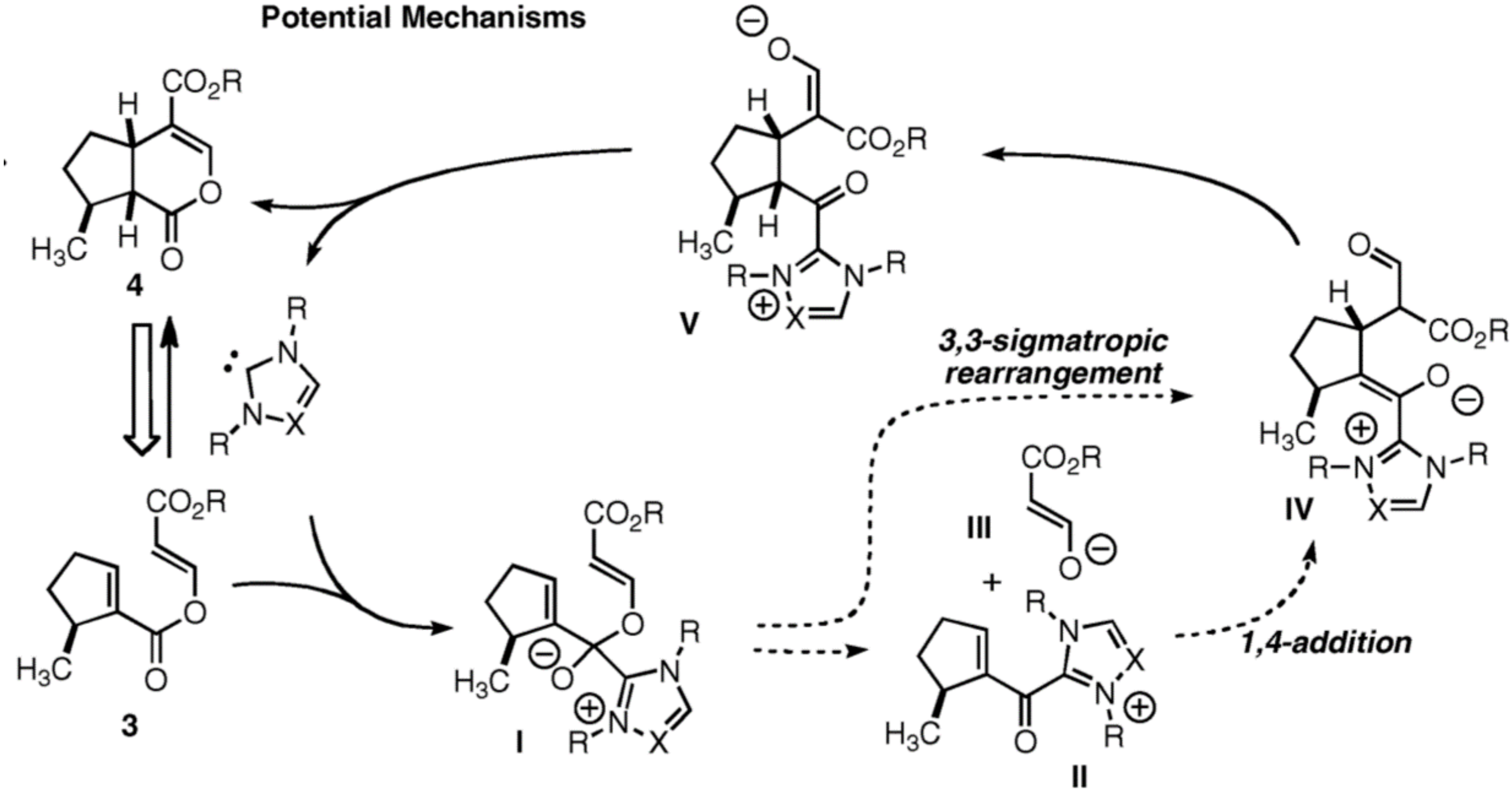
Nucleophile		N/s_N[a]	$k/M^{-1}s^{-1}$
	**4a**	19.36/0.67	2.29×10^{5}[b]
	**4b**	17.64/0.73	5.84×10^{4}[b]
	**4c**	16.27/0.77	9.03×10^{3}[b]
	**4d**	13.91/0.86	2.75×10^{2}[b]
	**5**	16.42/0.70	4.96×10^{2}[c]
	**6**	10.52/0.78	6.19×10^{-2}[c]

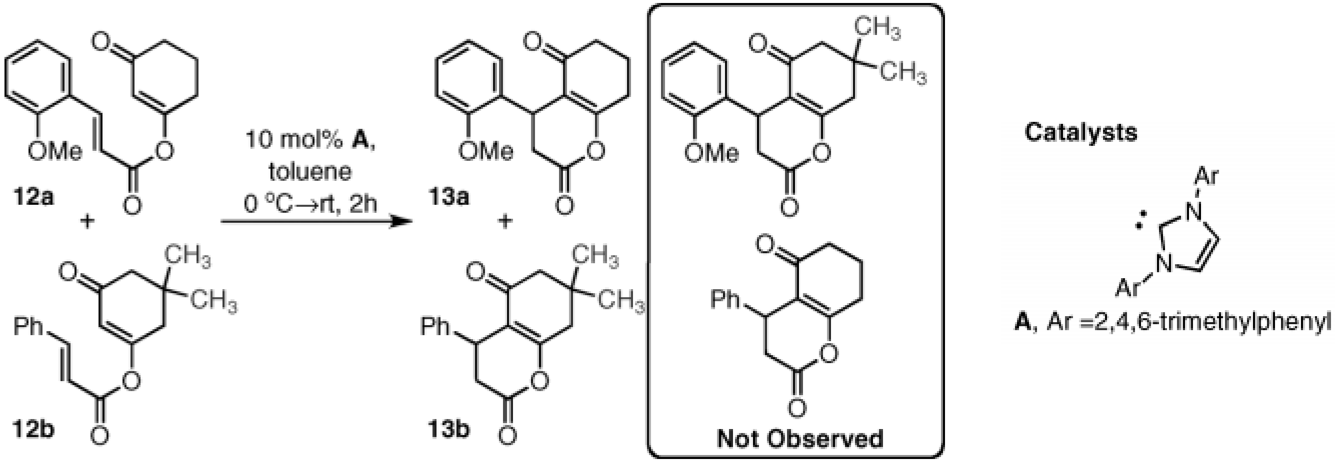
DFT calculations and kinetic experiments

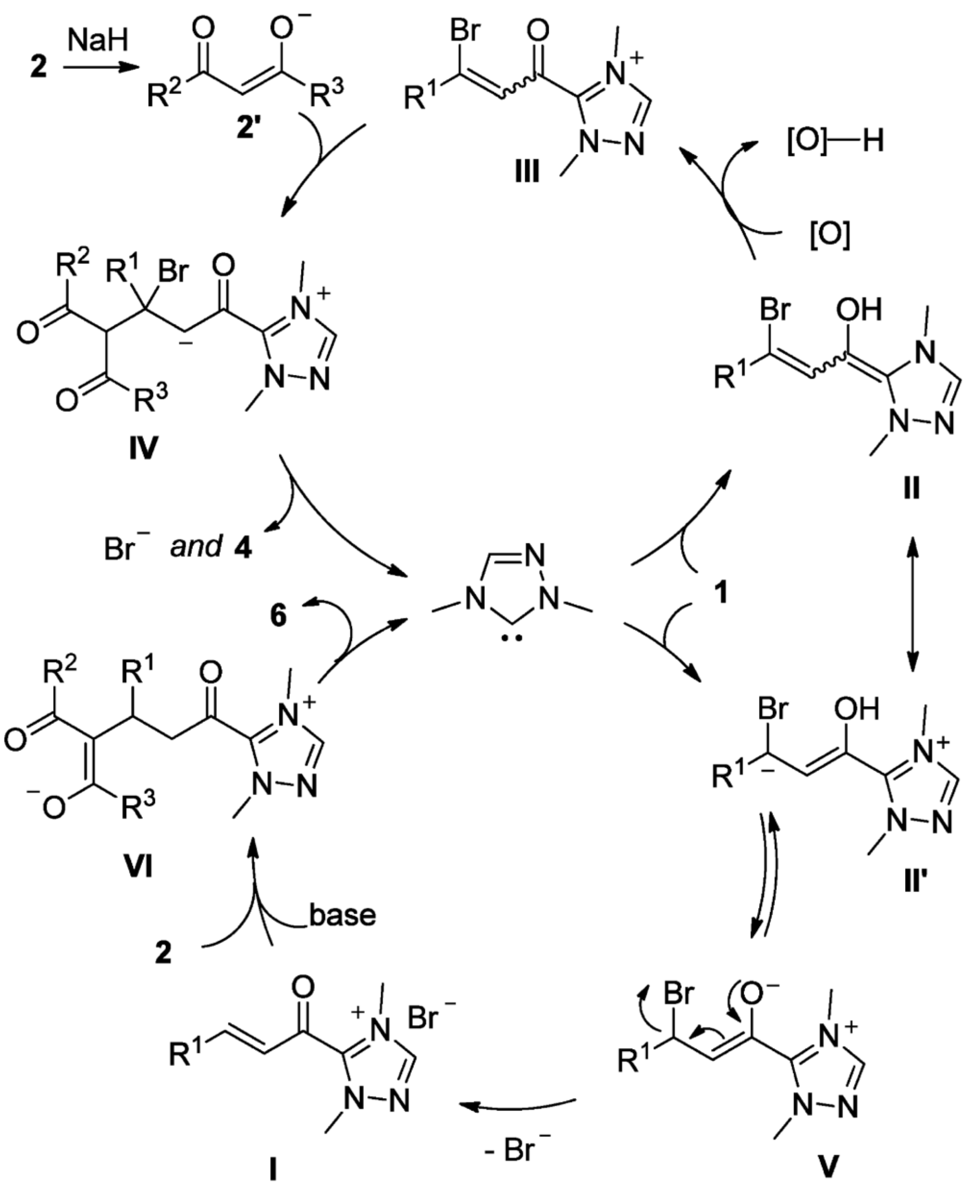


J. Am. Chem. Soc. **2014**, *136*, 14397
Org. Lett. **2015**, *17*, 5332

Potential Mechanisms




OMe
12a
+
Ph
CH3
CH3
12b
10 mol% A,
toluene
0 °C→rt, 2h
13a
+
13b
Not Observed
Catalysts
Ar
N
N
A, Ar =2,4,6-trimethylphenyl


2
NaH
2'
III
[O]—H
[O]
IV
II
Br⁻ and 4
1
6
VI
II'
base
2
I
V
- Br⁻