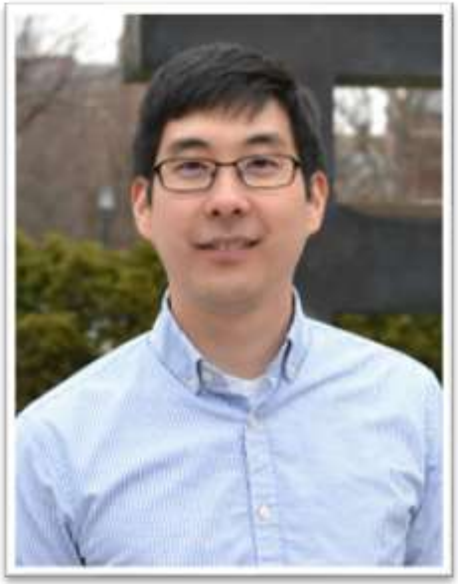
Literature Report 10

Catalytic Asymmetric Ring-Opening Reactions of Unstrained Heterocycles Using Cobalt Vinylidenes

Reporter: Han Wang
Checker: Shan-shan Xun
Date: 2023.12.11

Kanale, V. V.; Uyeda, C.* *Angew. Chem. Int. Ed.* **2023**, *62*, e202309681.

CV of Dr. Christopher Uyeda



Background:

- **2001-2005** B.S., Columbia University
- **2005-2011** Ph.D., Harvard University
- **2011-2013** Postdoc., Caltech (Jonas Peters)
- **2013-2019** Assistant Prof., Purdue University
- **2019-2022** Associate Prof., Purdue University
- **2022-now** Professor, Purdue University

Research:

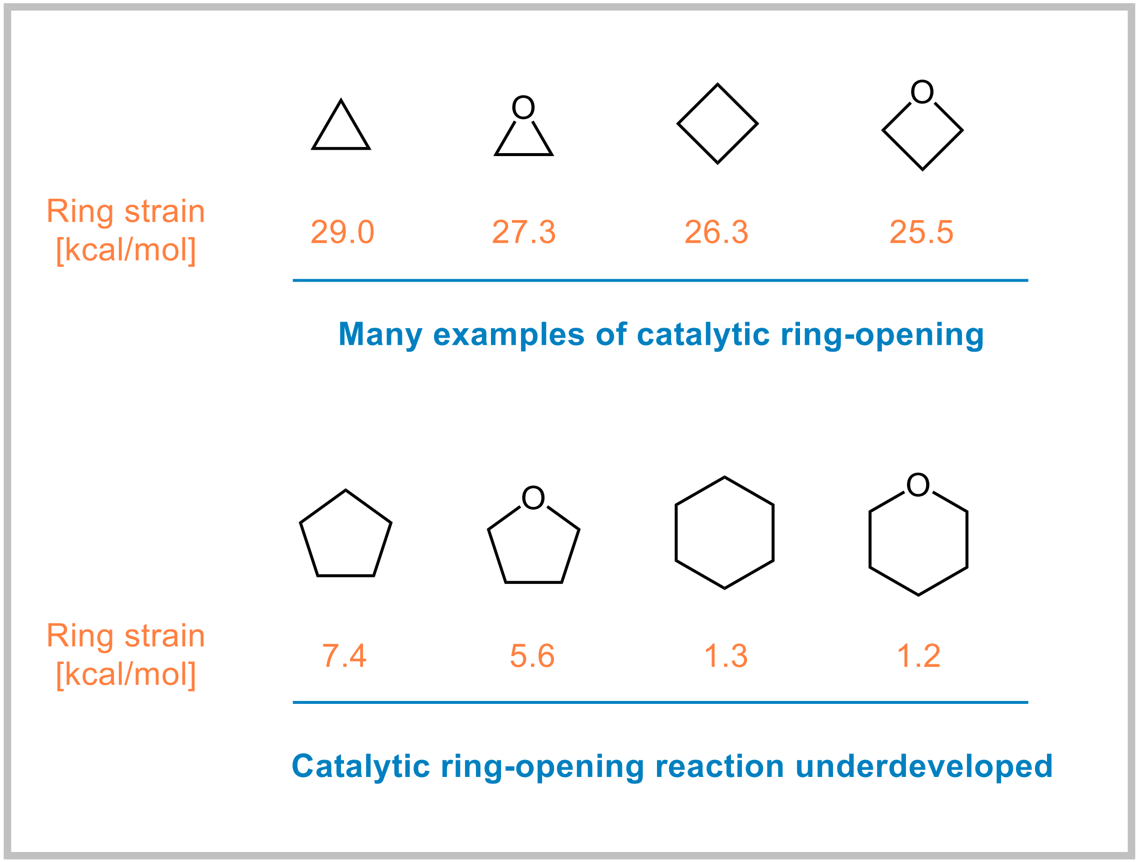
✓ **Design and study of catalysts**

✓ **Development of catalytic carbene transfer reactions**

✓ **Synthesis of conjugated materials containing N=N linkages**

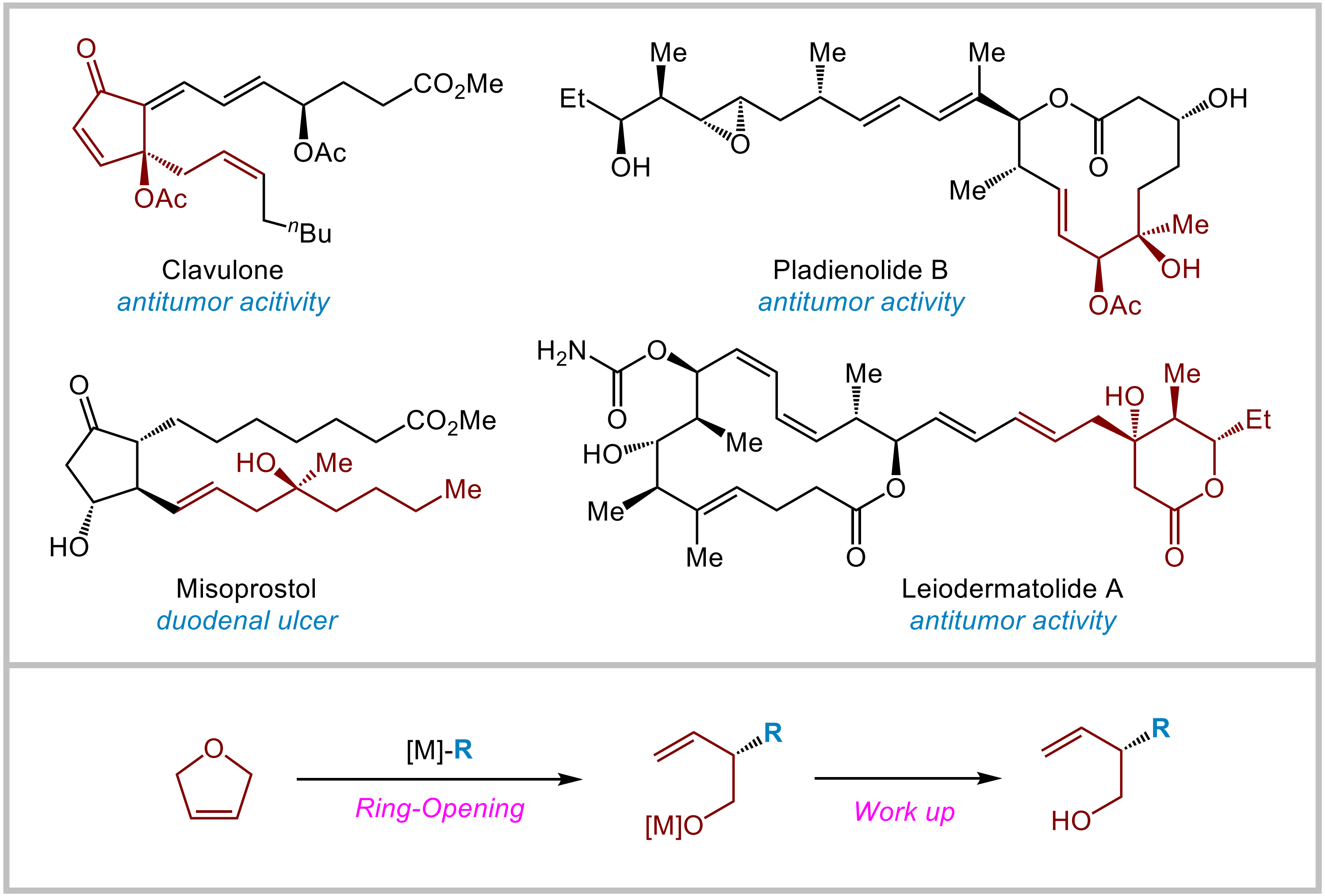
Contents

Introduction



Cramer, N. *et al. Chem. Rev.* **2015**, *115*, 9410.

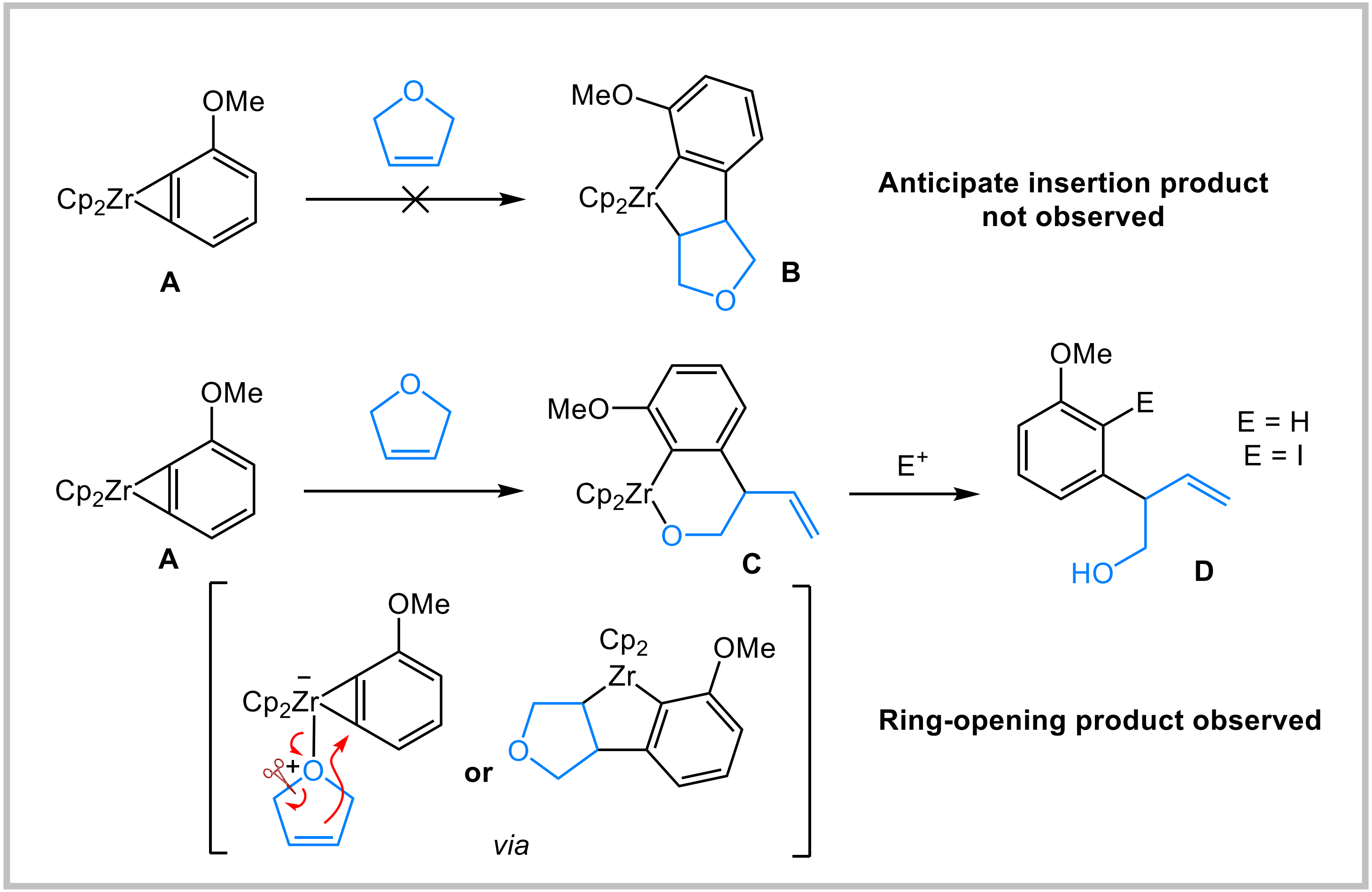
Introduction



Gao, S; Yao, H.-Q. *et al. Angew. Chem. Int. Ed.* **2023**, *62*, e202311540.

Introduction

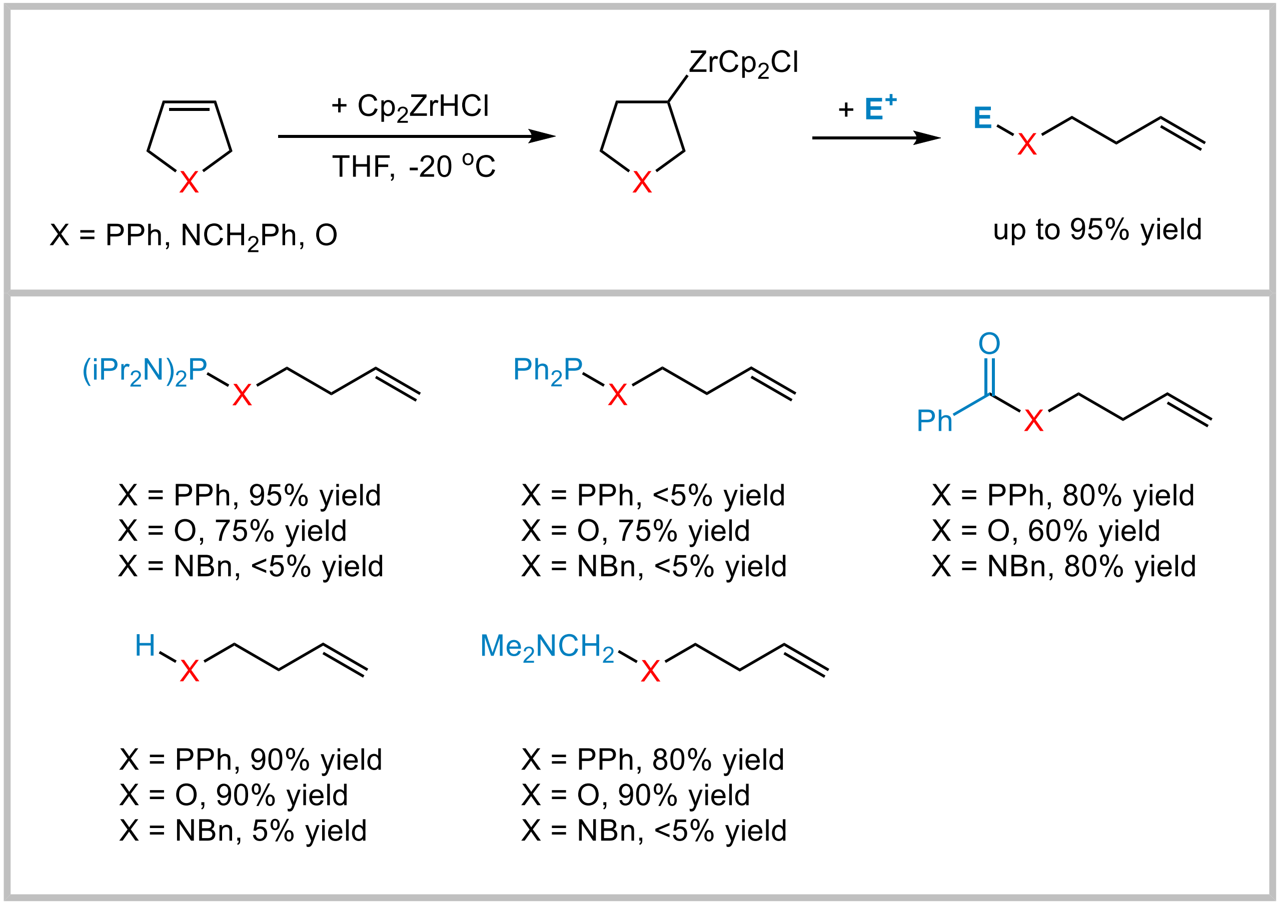
Zr Species Induced Ring-opening



Buchwald, S. L. *et al. Organometallics* **1991**, *10*, 363.

Introduction

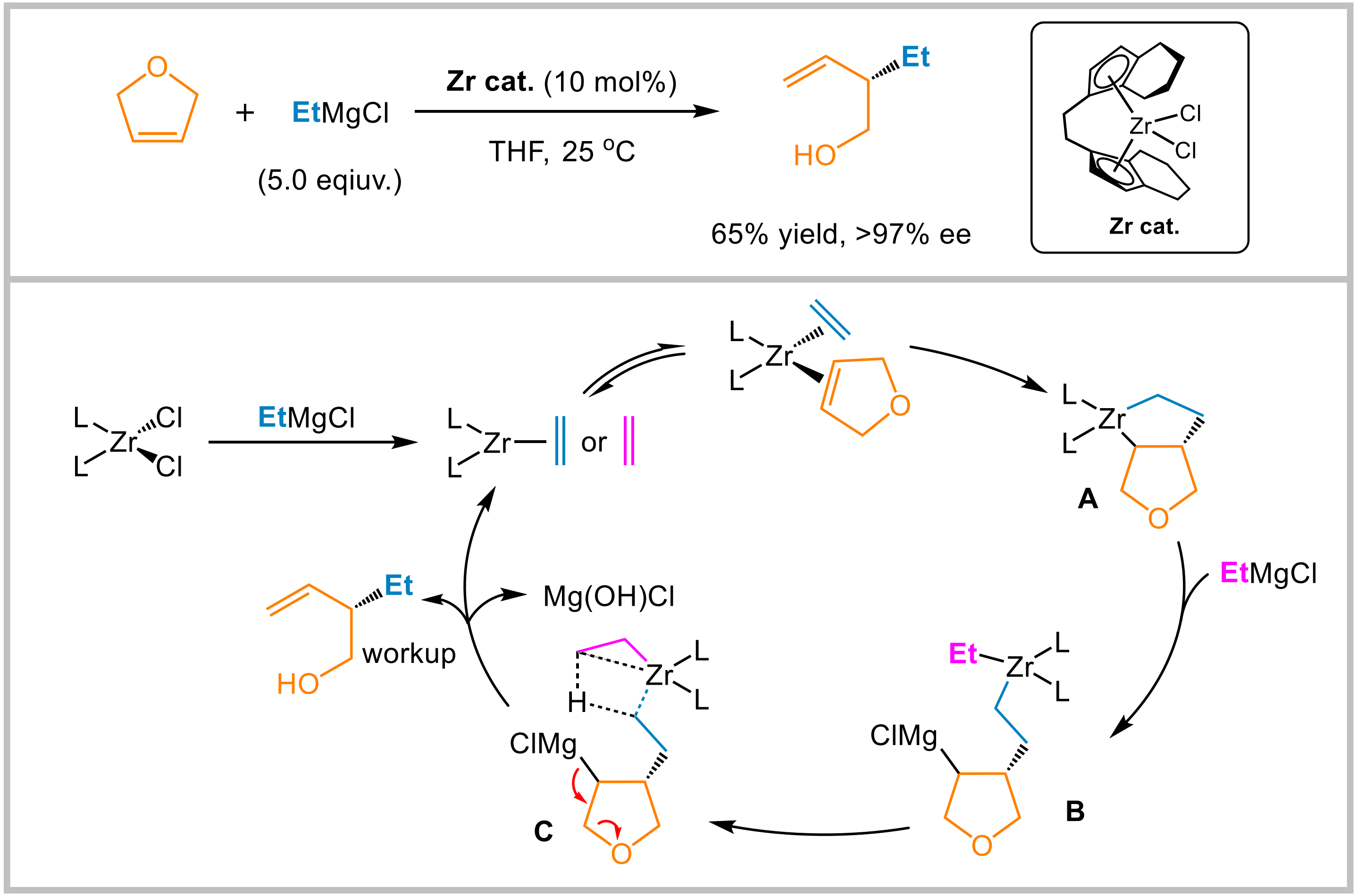
Zr Species Induced Ring-opening



Pietrusiewicz, M. *et al. Organometallics* **1994**, *13*, 5166.
Skowronska, A. *et al. Organometallics* **1996**, *15*, 1208.

Introduction

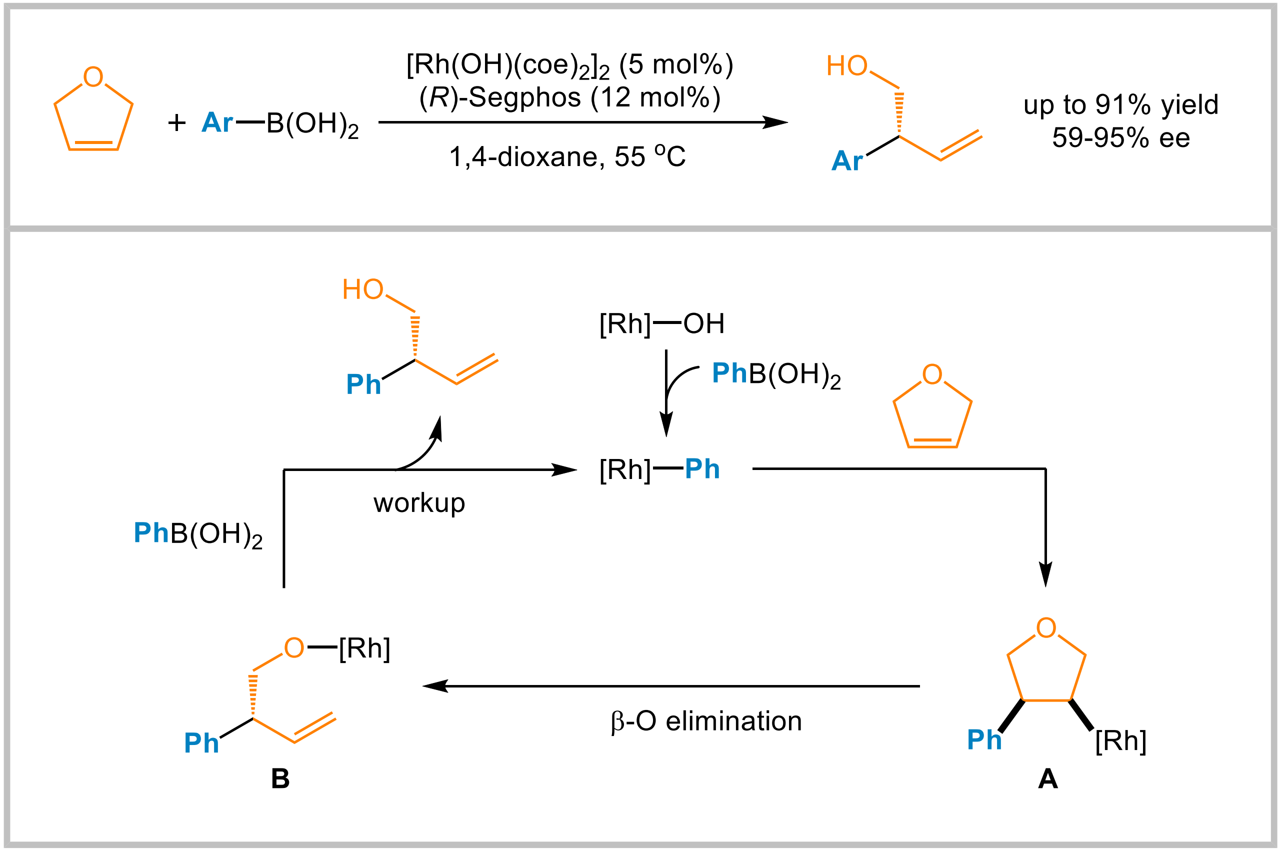
Zr-catalyzed Ring-opening



Hoveyda, A. H. *et al. J. Am. Chem. Soc.* **1993**, *115*, 6997.

Introduction

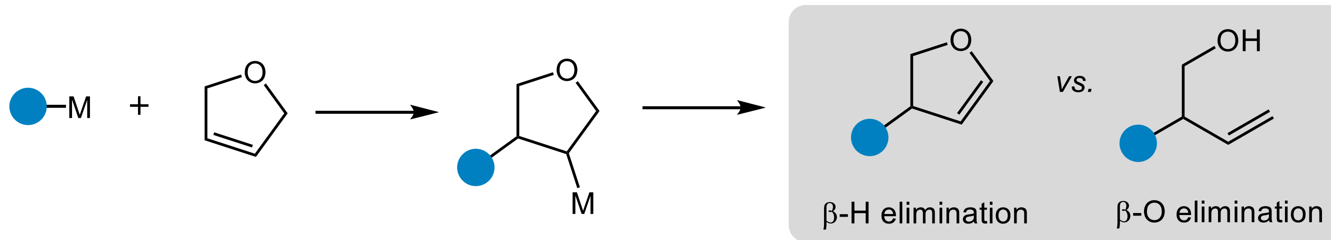
Rh-catalyzed Addition of Aryl Boronic Acid



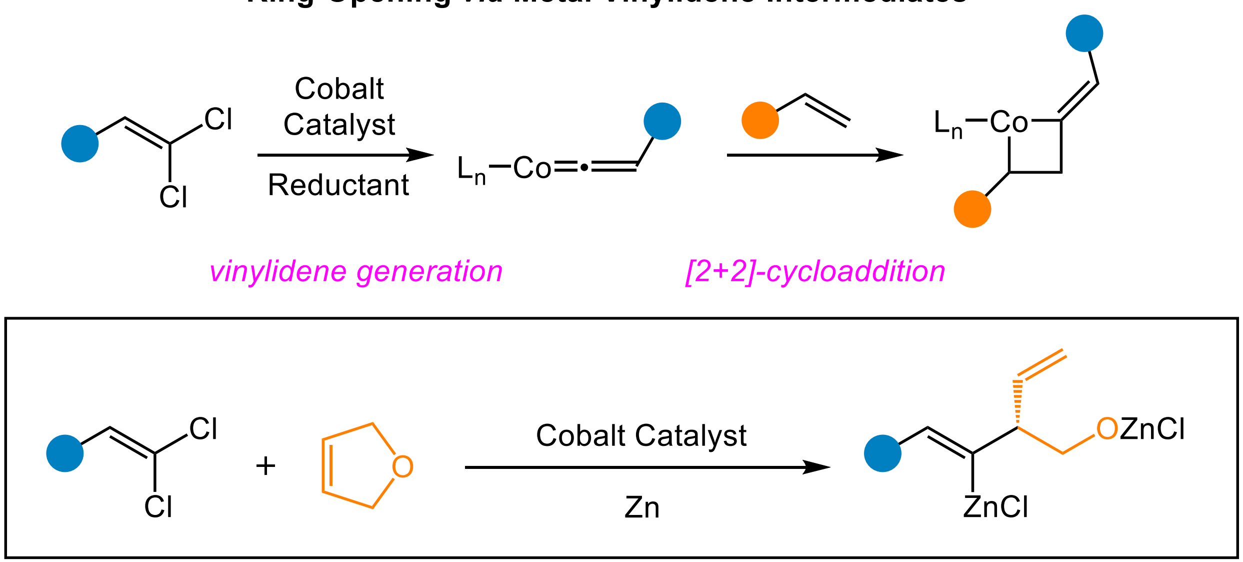
Hayashi, T.; Dou, X.-W. *et al. ACS Catal.* **2020**, *10*, 2958.

Prospect

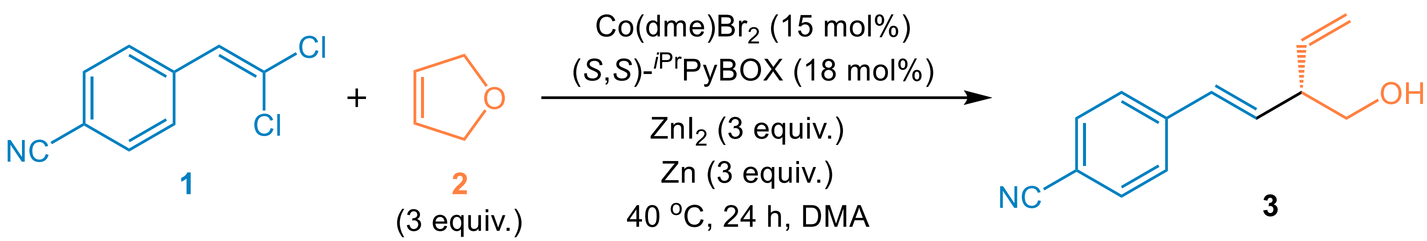
Challenge: Controlling the Selectivity of β-H *vs.* β-O Elimination



Ring-Opening *via* Metal Vinylidene Intermediates



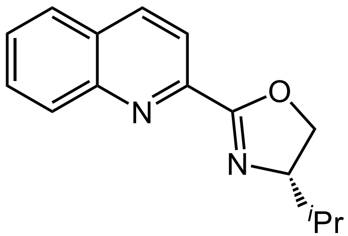
Optimization of Reaction Parameters



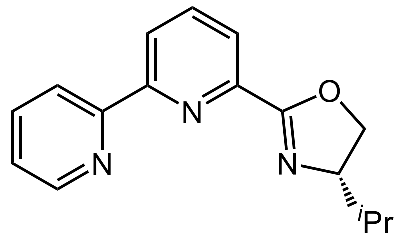
Entry[a]	Changes from Standard Conditions[b]	Yield [%]	*E:Z*	Ee [%]
1	None	80	20:1	96
2	No Co(dme)Br$_2$	0	-	-
3	No ligand **4**	0	-	-
4	2 equiv. of **2**	62	20:1	94
5	Without ZnI$_2$	41	20:1	92
6	ZnCl$_2$ instead of ZnI$_2$	60	20:1	94
7	Cp$_2$Co instead of Zn, without ZnI$_2$	0	-	-
8	Cp$_2$Co instead of Zn, with ZnI$_2$	50	20:1	91

[a] Yields and *E:Z* ratios of **3** were determined by ^{1}H NMR, using 1,3,5-trimethoxylbenzene as an internal standard. [b] Reaction conditions: **1** (0.1 mmol), **2** (3 equiv.), Zn (3 equiv.), ZnI$_2$ (3 equiv.), Co(dme)Br$_2$ (0.15 equiv.), (*S*,*S*)-$^{i\text{Pr}}$Pybox (0.18 equiv.), DMA (0.75 mL), 40 °C, 24 h.

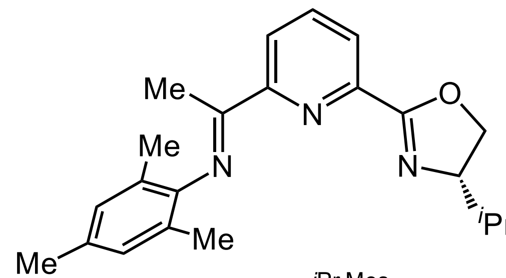
Optimization of Reaction Parameters



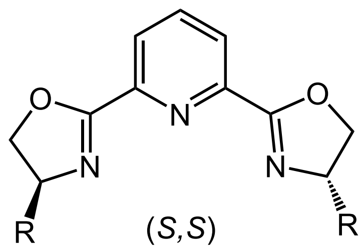
5 (*S*)-^{iPr}Quinox
11% yield, 20:1 *E:Z,* 25% ee



6 (*S*)-^{iPr}Bipyox
78% yield, 20:1 *E:Z,* 30% ee



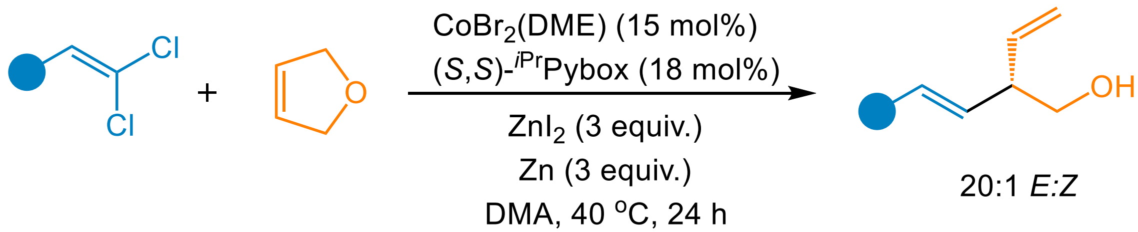
7 (*S*)-^{iPr,Mes}OIP
61% yield, 11:1 *E:Z,* 94% ee

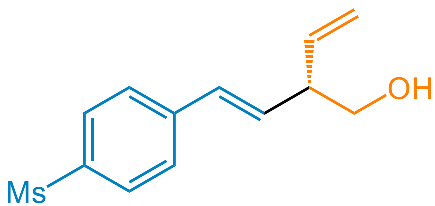


4 R = ^{i}Pr 80% yield, 20:1 *E:Z*, 96% ee
8 R = ^{i}Bu 70% yield, 20:1 *E:Z*, 82% ee
9 R = ^{t}Bu 37% yield, 20:1 *E:Z*, 81% ee

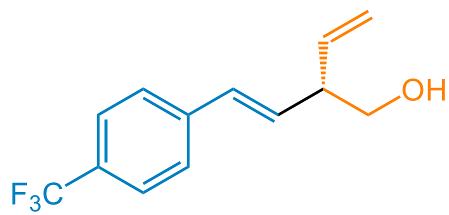
Reaction conditions: **1** (0.1 mmol), **2** (3 equiv.), Zn (3 equiv.), ZnI_2 (3 equiv.), $Co(dme)Br_2$ (0.15 equiv.), ligand (0.18 equiv.), DMA (0.75 mL), 40 ^{o}C, 24 h.

Scope of Substrates

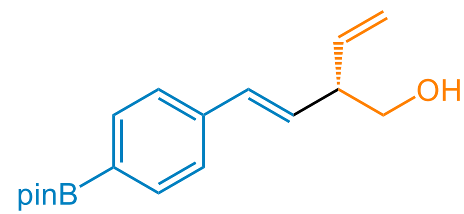




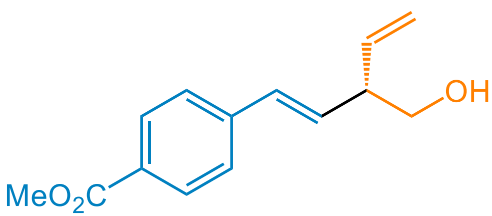
10
76% yield, 95% ee



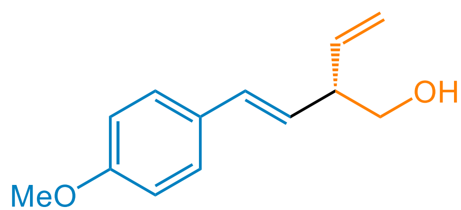
11
73% yield, 96% ee



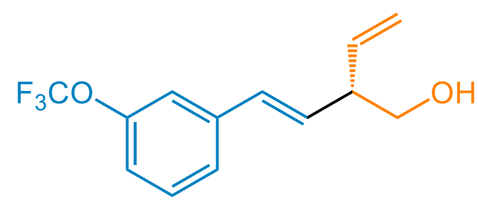
12
66% yield, 95% ee



13
54% yield, 95% ee

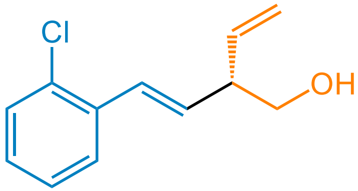


14
56% yield, 94% ee

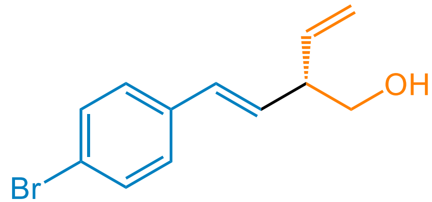


15
72% yield, 94% ee

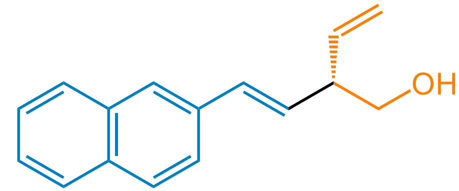
Scope of Substrates



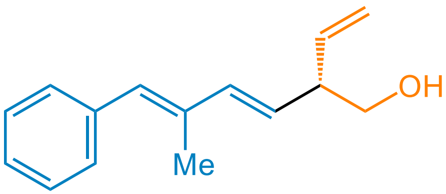
16
72% yield, 96% ee



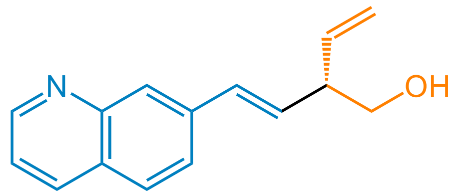
17
54% yield, 95% ee



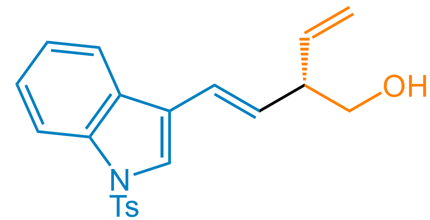
18
66% yield, 95% ee



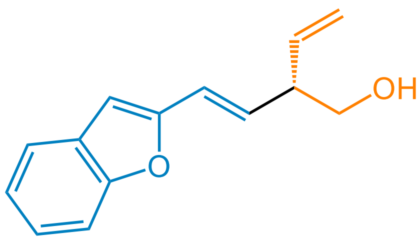
19
53% yield, 4:1 *E:Z*, 95% ee



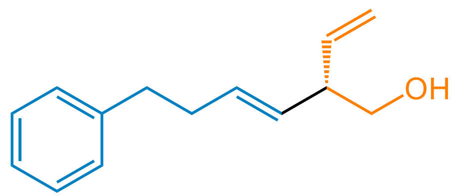
20
59% yield, 93% ee



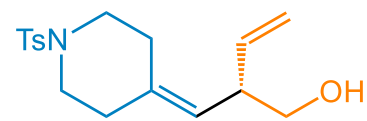
21
60% yield, 92% ee



22
46% yield, 88% ee

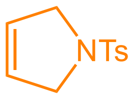


23
31% yield, 3:1 *E:Z*, 92% ee

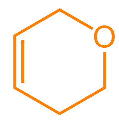


24
32% yield, 99% ee

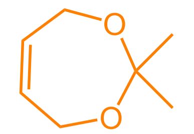
Scope of Substrates



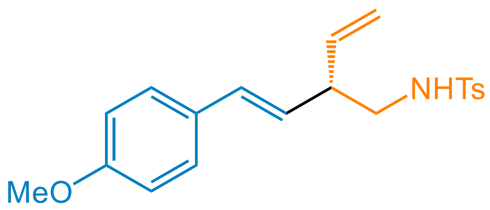
25



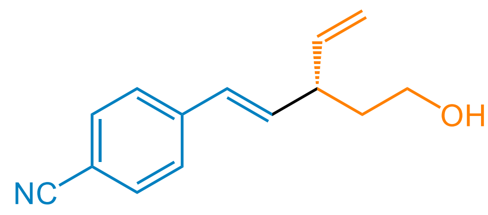
27



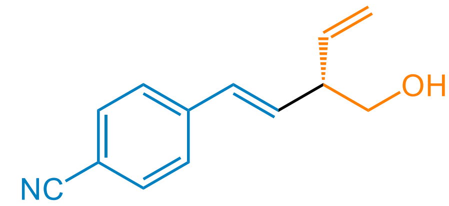
29



26[a][b]
55% yield, 97% ee



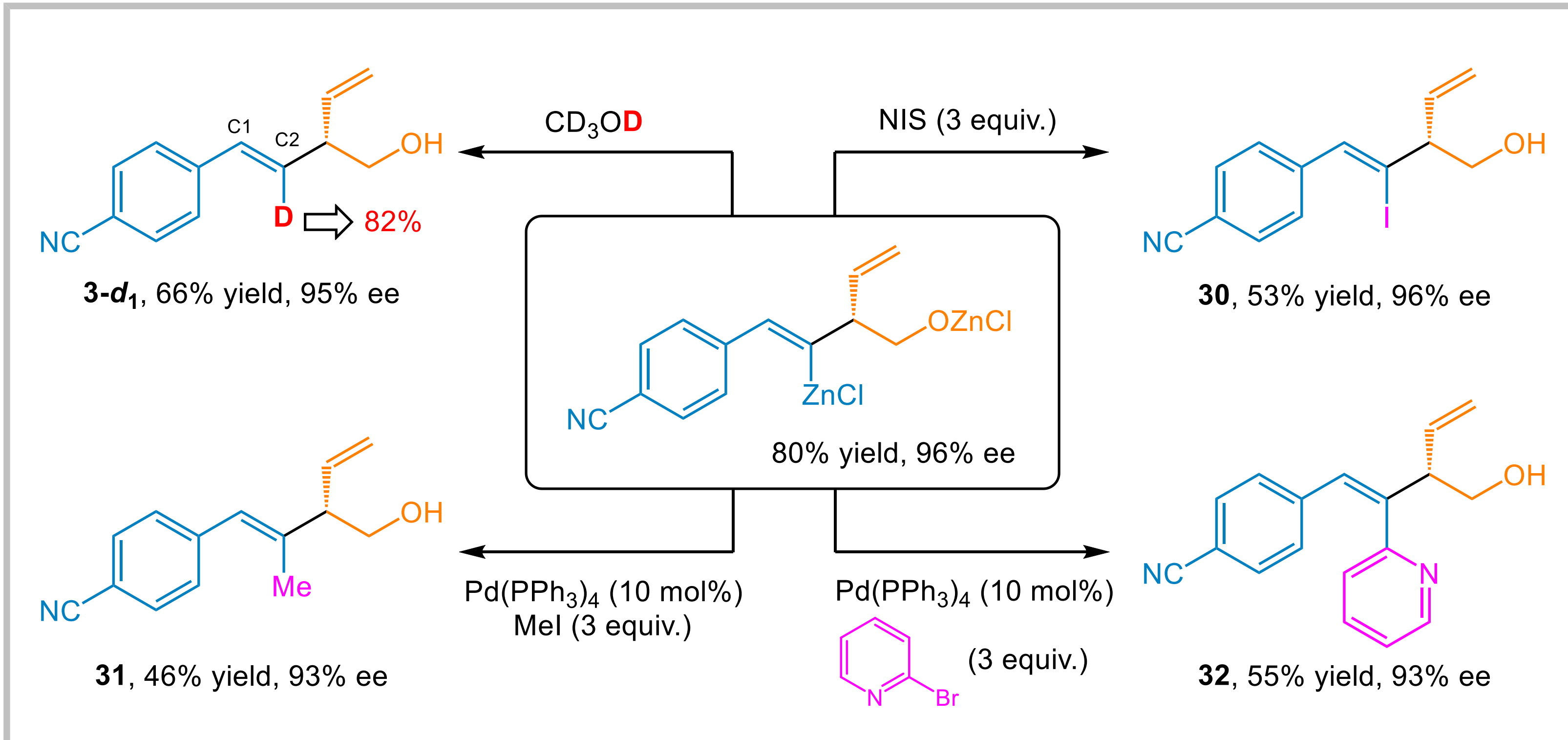
28[b]
20% yield, 97% ee



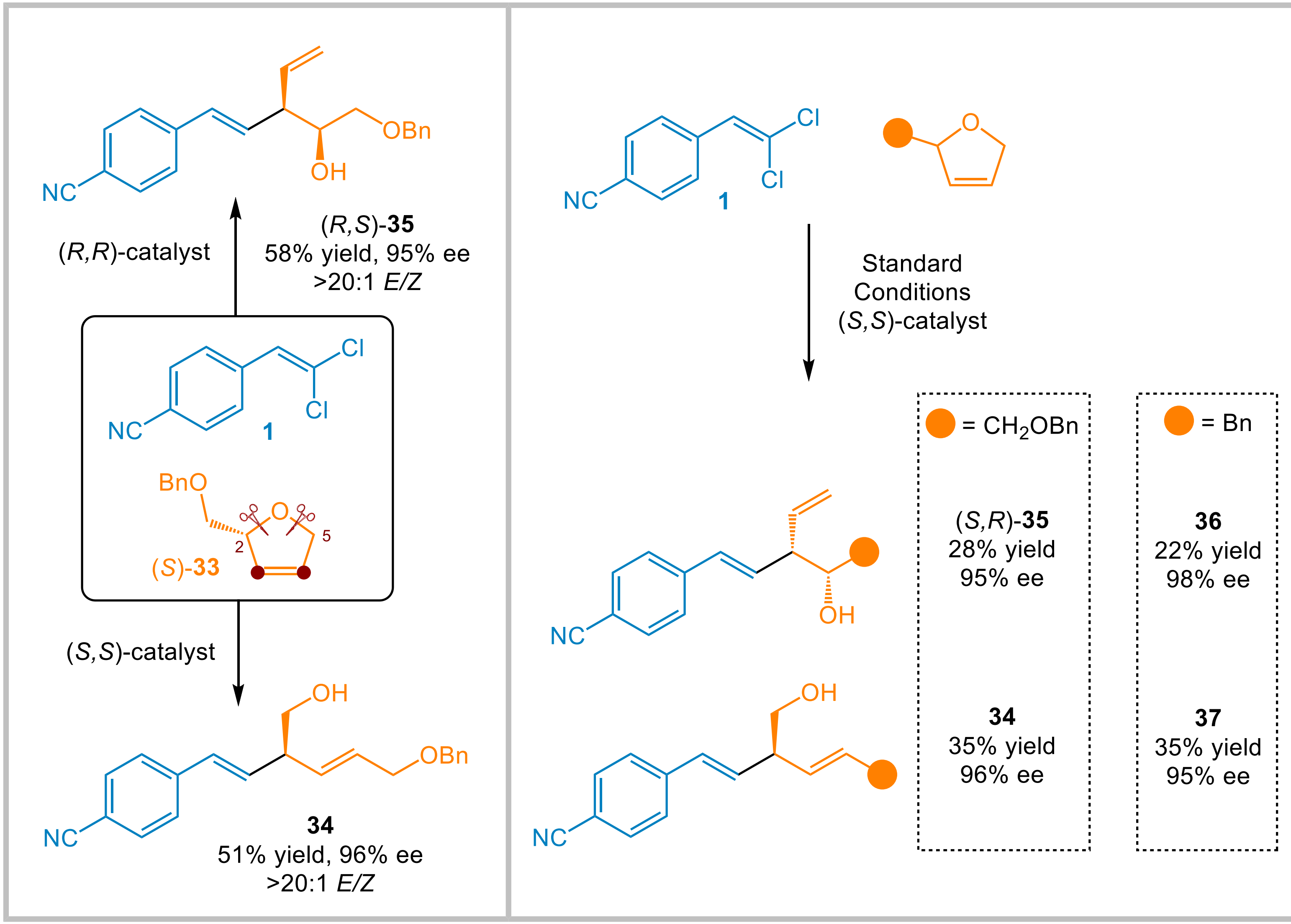
3
28% yield, 99% ee

[a] Co(dme)Br_2 (20 mol%), ligand **4** (24 mol%). [b] $ZnCl_2$ (5 equiv.) instead of ZnI_2

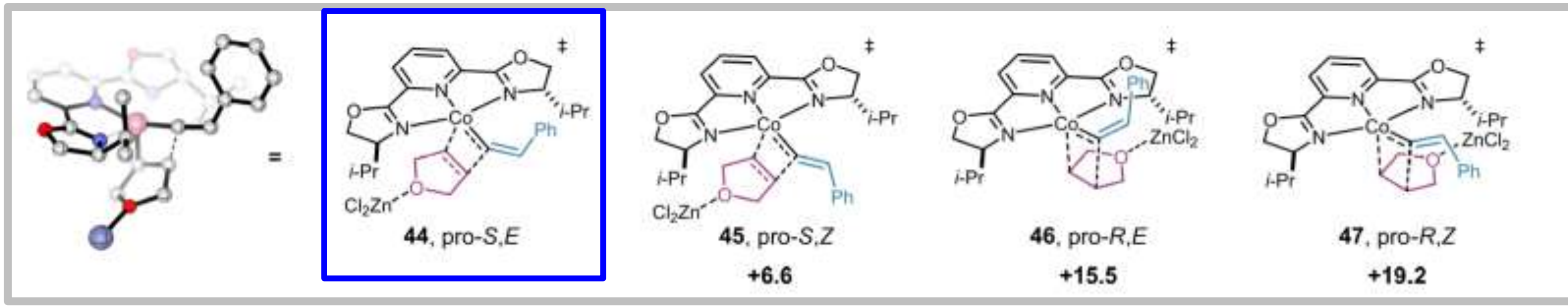
Organozinc Functionalization

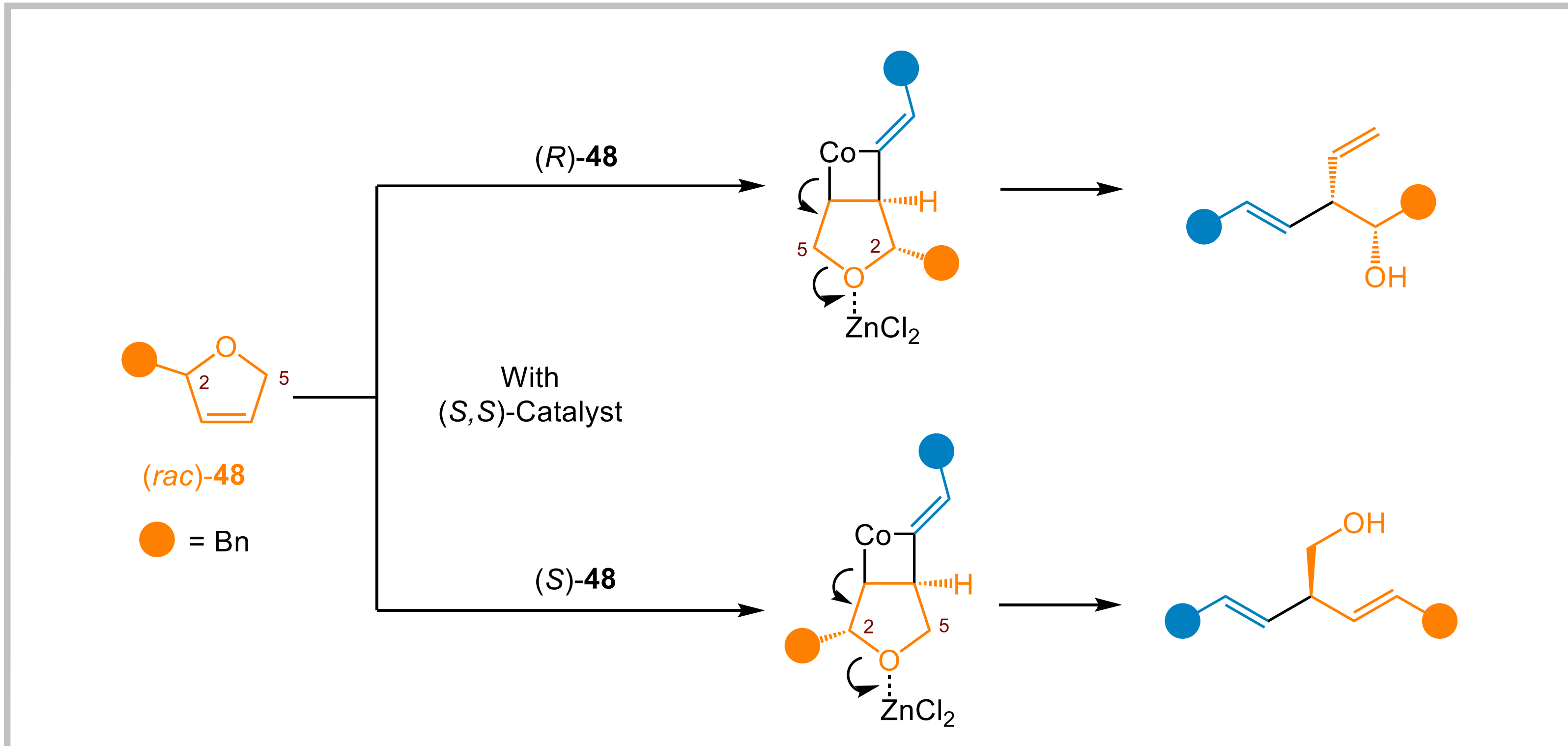


Regiodivergent Ring-Opening

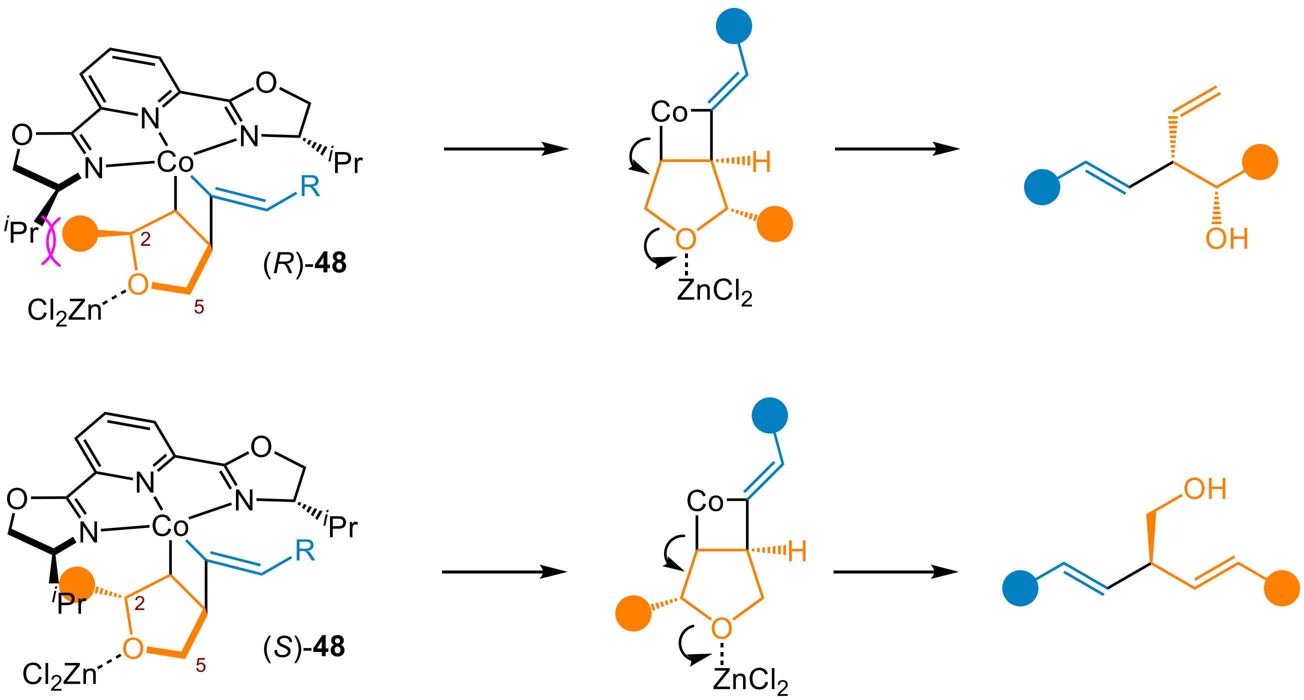


Regiodivergent Ring-Opening

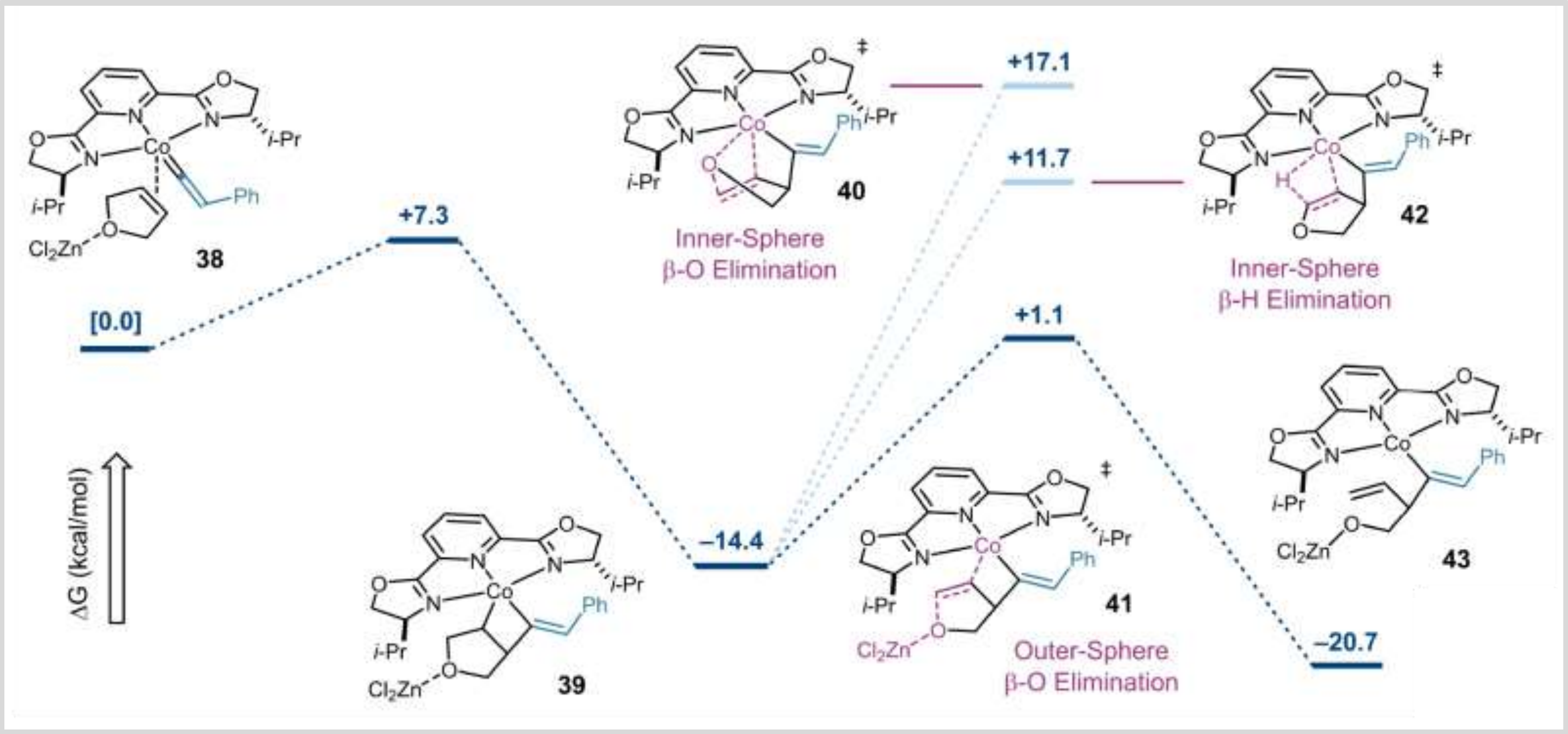




Regiodivergent Ring-Opening

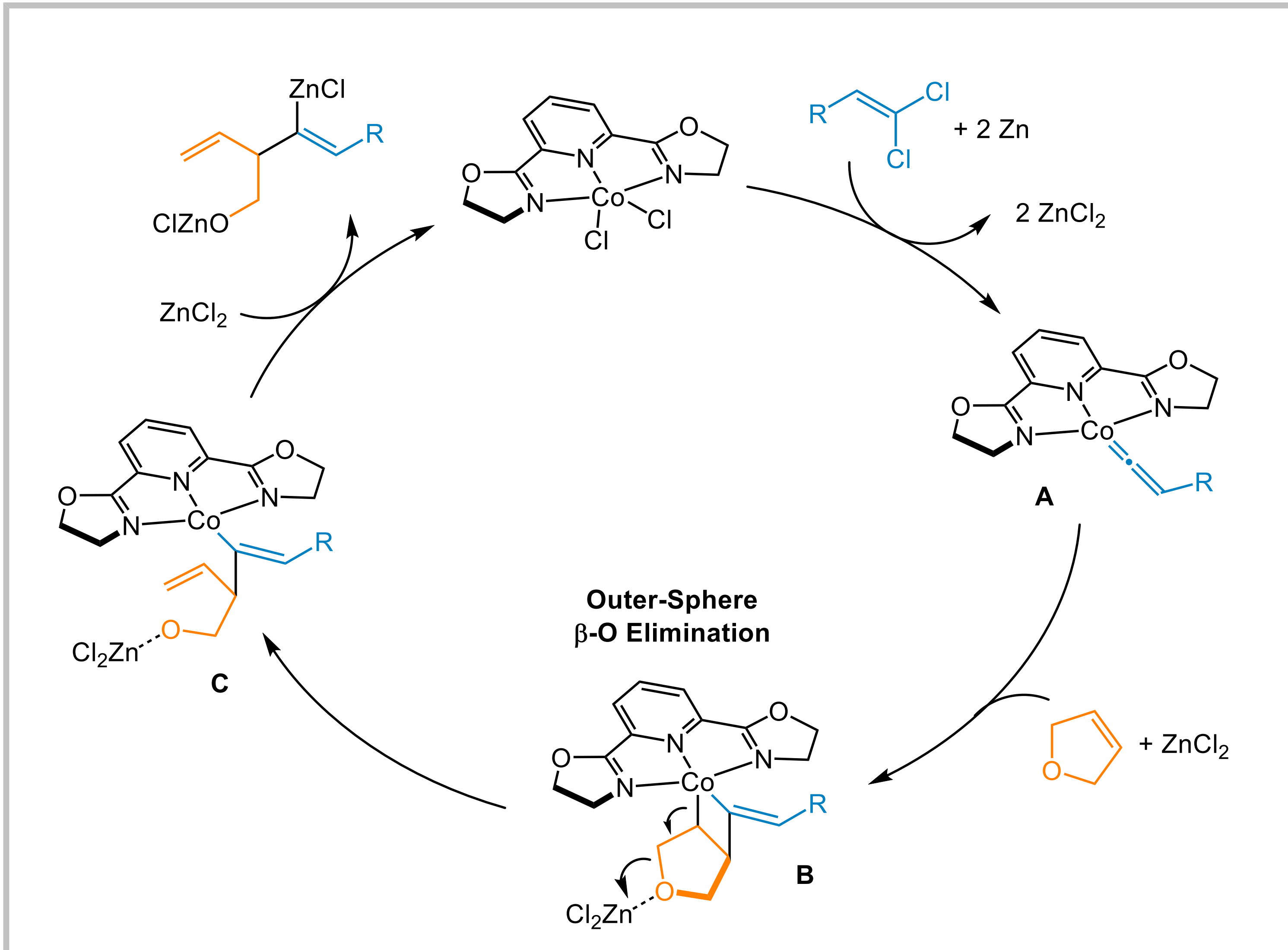


DFT Calculation

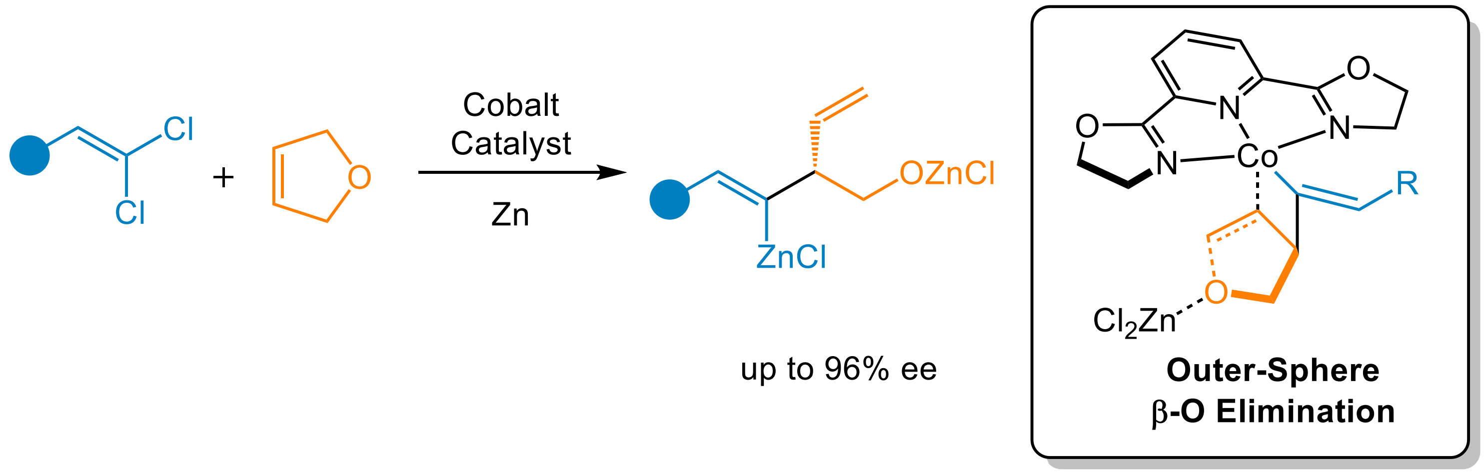


外球β-O消除具有更低的过渡态能量

Proposed Mechanism



Summary



- A viable mechanism to carry out ring-opening reactions of unstrained five-membered heterocycles;
- A cooperative bimetallic outer-sphere β-O elimination;
- 18 Examples, easy to functionalization, up to 99% ee.

Writing Strategy

➢ Introduction

The challenge of unstrained ring-opening reaction

↓

Current research of unstrained ring-opening reactions

- ♣ Strained three-membered heterocycles, such as epoxides and aziridines, are common synthetic intermediates that participate in a broad range of ring-opening reactions. Extending such processes to larger unstrained rings would provide access to useful alternative bond constructions. However, few examples are known due to the comparative lack of thermodynamic driving force. Additionally, three-membered rings feature bent σ-bonding orbitals that allow them to engage more readily with transition metal catalysts.
- ♣ In the absence of these distorted bonds, C-X activation becomes more challenging. There are isolated cases where substrates such as 2,5-dihydrofuran can undergo catalytic ring-opening. However, most of these reactions rely on oxophilic Zr species to induce β-O elimination, with the one notable exception of a Rh-catalyzed addition of aryl boronic acids. For other catalytic additions to 2,5-dihydrofuran, competing β-H elimination is the favored pathway.

Writing Strategy

➢ The Last Paragraph

Summary of the work

↓

Challenges and strategies

↓

Prospect

- ♣ In summary, β-X elimination processes provide a viable mechanism to carry out ring-opening reactions of unstrained five-membered heterocycles.
- ♣ However, β-H elimination is a competing pathway that must be avoided. Here, we show that this selectivity challenge can be addressed using reaction pathways available to cobalt vinylidene species. Addition of a cobalt vinylidene to 2,5-dihydrofuran generates a metallacyclo-butane. The structural rigidity of this intermediate suppresses inner-sphere syn β-elimination mechanisms. Instead, a cooperative bimetallic outer-sphere β-O elimi-nation takes place in which a zinc Lewis acid assists in ionization of the leaving group.
- ♣ Ongoing efforts are directed at exploiting the unique properties of metal vinylidene [2+2]-cycloadducts in other coupling reactions.

Representative Examples

- The excess 2,5-dihydrofuan remains intact at the end of the reaction. Thus, recovery of the excess reaction partner is possible in cases where it is precious…..adding additional Zn(II) salts improves the yield, presumably by aiding in the transmetallation step. (Intact 完整的，表达回收剩余底物； aid in 援助)
- Quinoline, indole, and benzofuran heterocycles can be present in the substrate without deleterious effect. (deleterious 有害的，表达对底物有负面影响)
- Rather, the constrained geometry of the metallabicyclic intermediate suppresses all inner-sphere pathways, allowing outer-sphere β-elimination pathways to predominate. (predominate 占主导地位，表达主要反应路径)

Acknowledgement

Thanks
for your attention