Literature Report 2

Cobalt-Catalyzed Enantiospecific Dynamic Kinetic Cross-Electrophile Vinylation of Allylic Alcohols with Vinyl Triflates

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Checker: Xiang Li

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Ma, W.-Y.; Han, G.-Y.; Liu, X.-Y.; **Shu, X.-Z.** *J. Am. Chem. Soc.* **2021**, *143*, 15930

CV of Prof. Xingzhong Shu (舒兴中)

Research Interests:

- Silicone Chemistry
- Asymmetric Catalysis
- Reductive Coupling Reaction

Education:

- **2001-2005** B.S., Shaoxing University
- **2005-2010** Ph.D., Lanzhou University
- **2010-2012** Postdoc., University of Wisconsin-Madison
- **2012-2015** Postdoc., University of California-Berkeley
- **2015-Now** Professor, Lanzhou University

Contents

Introduction

= alkyl, aryl; X = halide, OR, NR_2; [M] = metal or metalloid

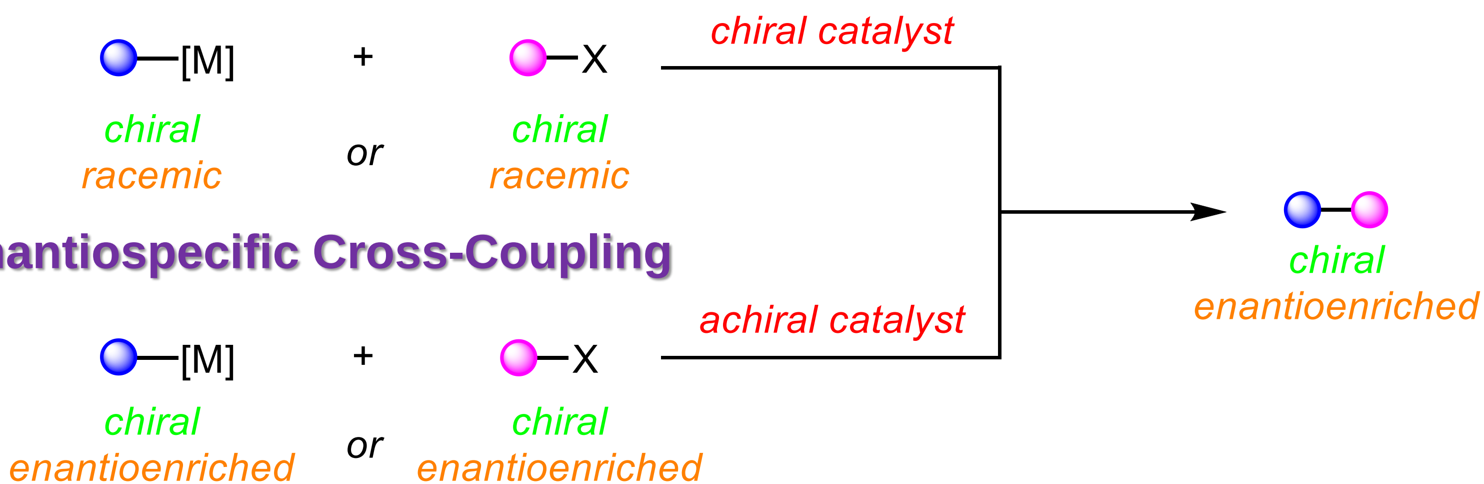
C-C Formation

- **Enantioselective Cross-Coupling**
- **Enantiospecific Cross-Coupling**

Introduction

= alkyl, aryl; X = halide, OR, NR_2; [M] = metal or metalloid

Enantioselective Cross-Coupling



Enantiospecific Cross-Coupling

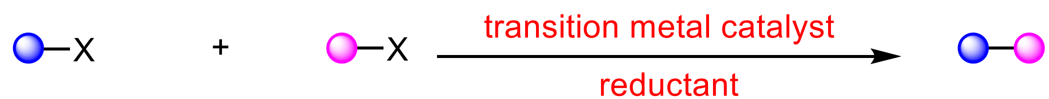
Introduction

The Ways of Cross-Coupling Reactions

1. Traditional Cross-Coupling

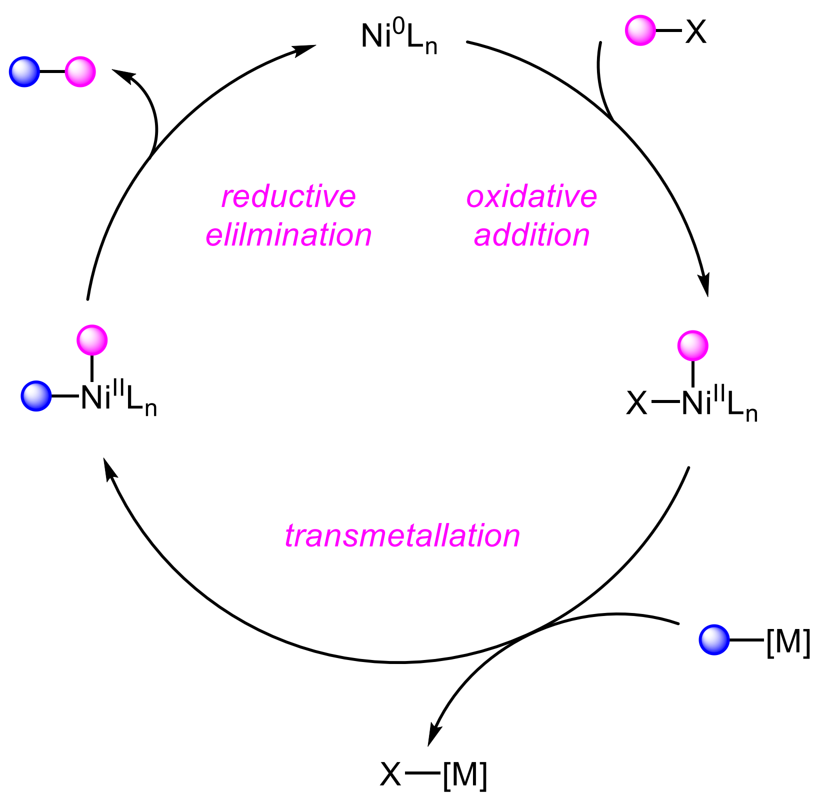
= alkyl, aryl; X = halide, OR, NR_2; M = metal or metalloid

2. Cross-Eletrophile Coupling



Introduction

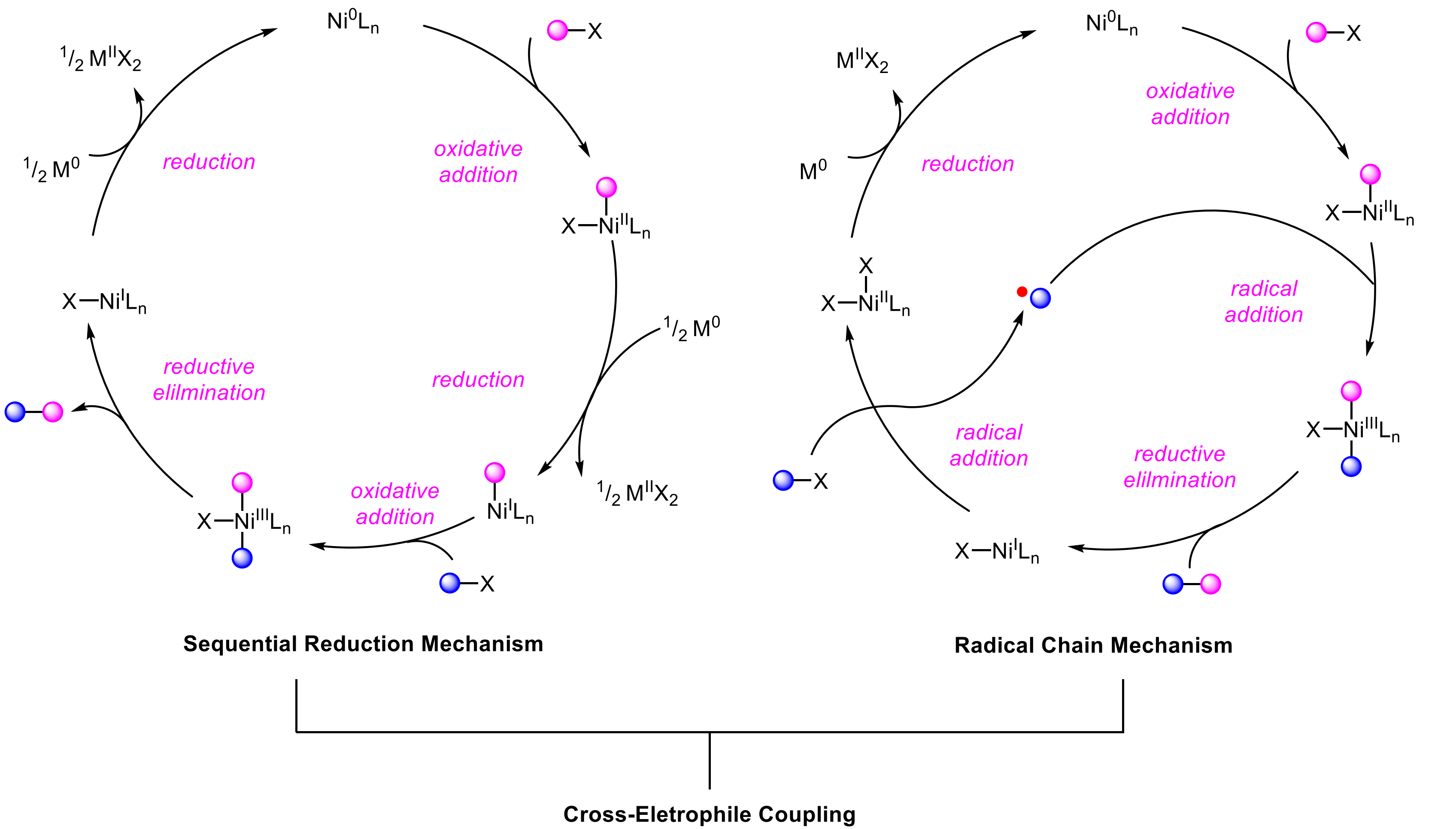
The Mechanism of Traditional Cross-Coupling Reactions



Traditional Cross-Coupling

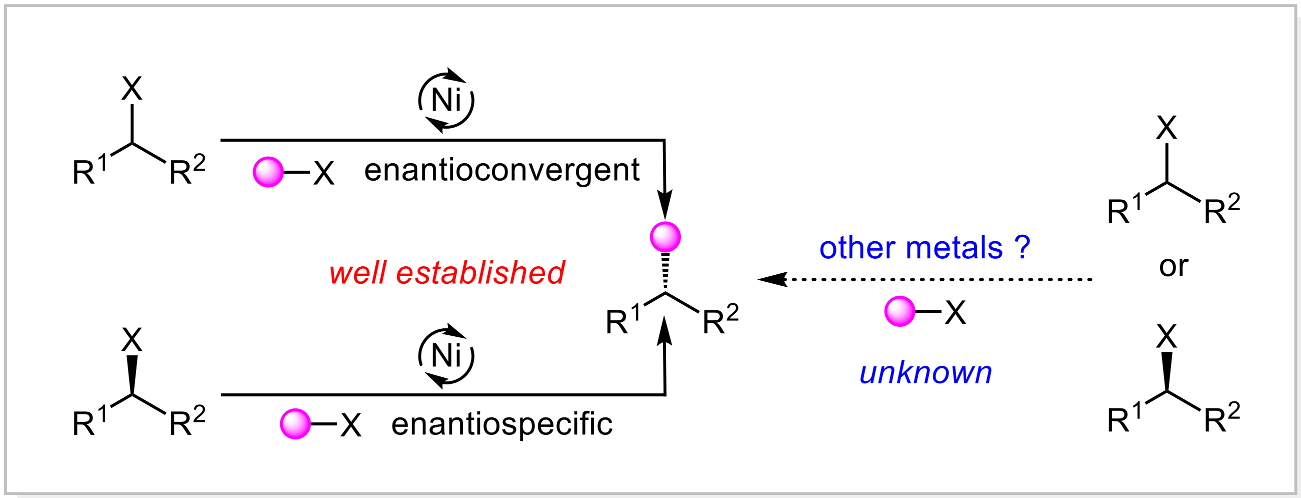
Introduction

The Mechanism of Cross-Electrophile Coupling Reactions



Introduction

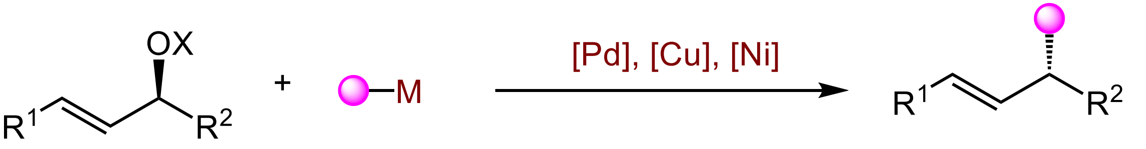
Asymmetric Cross-Electrophile Couplings by Transition-Metal Catalysis



Introduction

Enantiospecific C-Functionalization of Allylic Electrophiles

Enantiospecific Allylic C-Functionalization Reactions (State-of-the-Art)

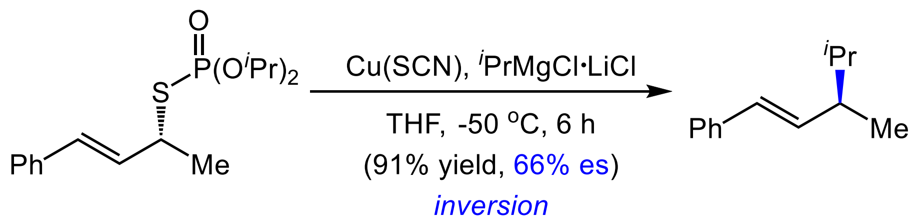


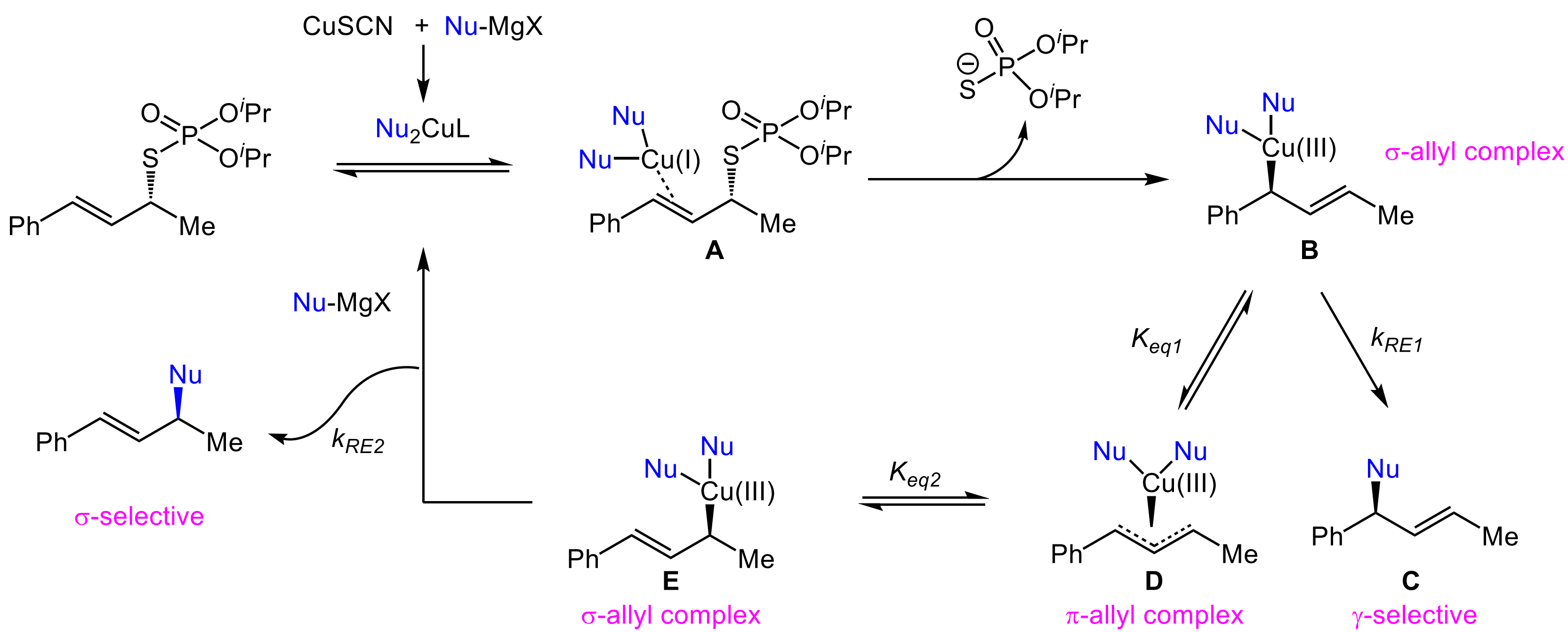
State-of-the-Art

● Reaction:	√ Arylation and Alkylation	× Vinylation
● Reactant:	√ R-M (M = B, Mg, Zn...)	× R-X

Introduction

Cu-Catalyzed Enantiospecific Allylic Substitutions

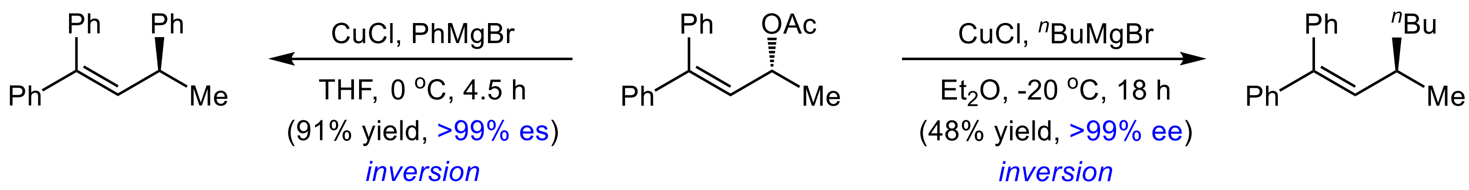




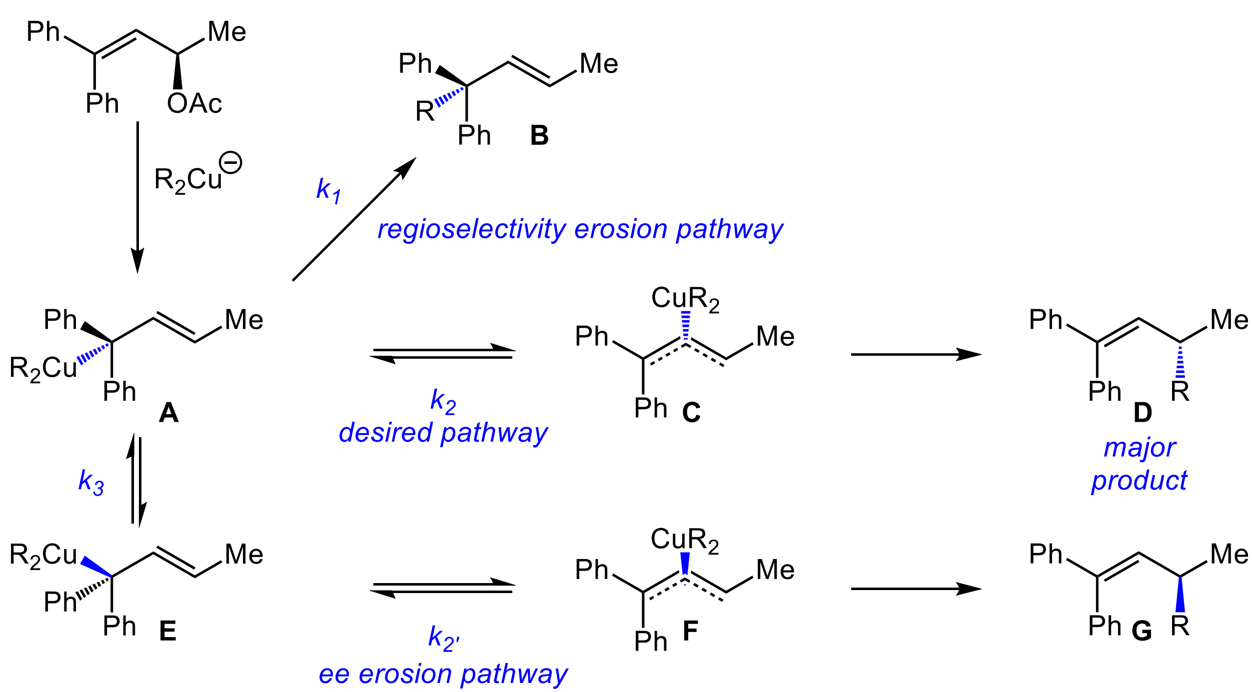
Wu, J. *J. Am. Chem. Soc.* **2011**, *133*, 9119

Introduction

Cu-Catalyzed Enantiospecific Allylic Substitutions



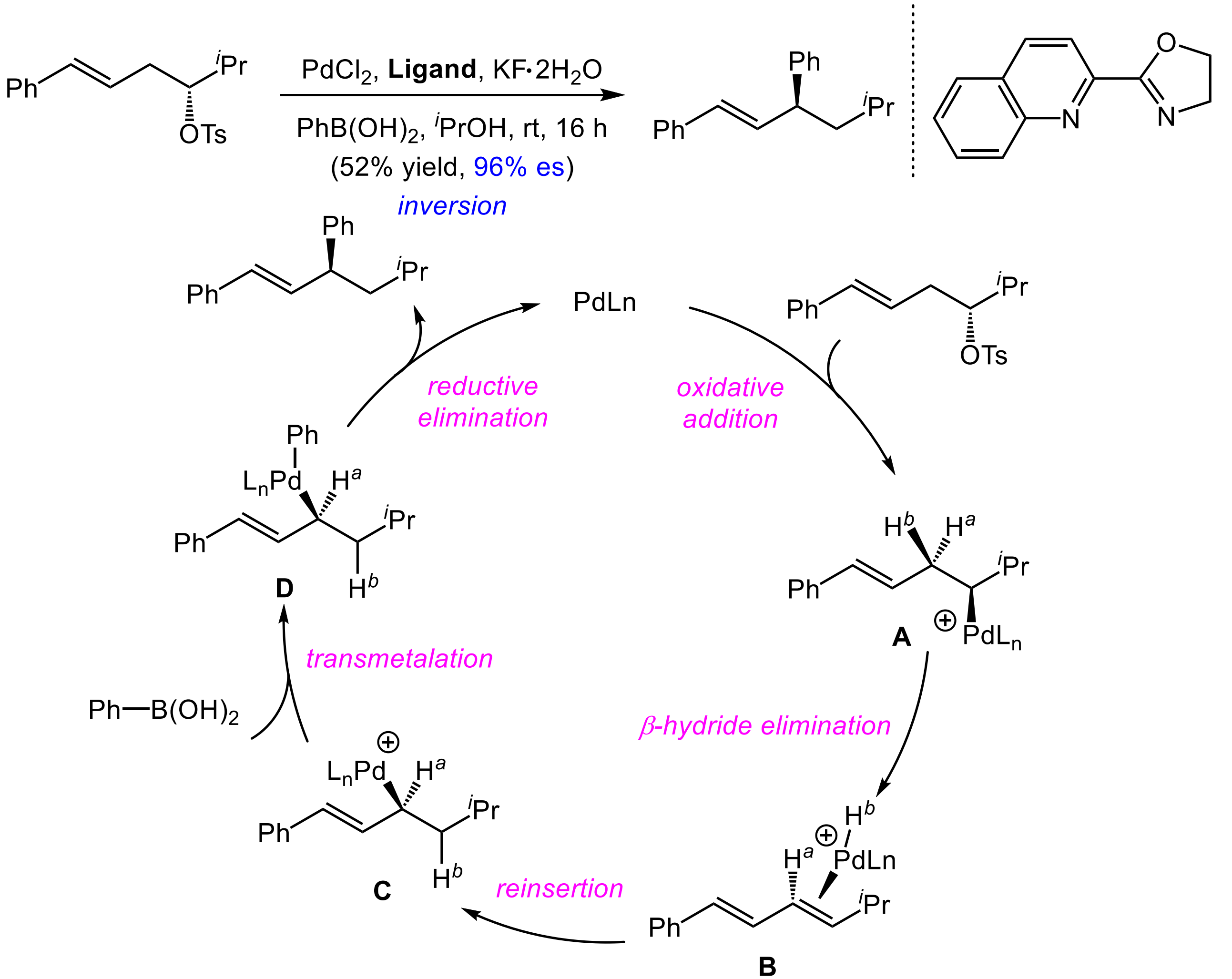
Mechanism giving rise to α-selectivity



Reisman, S. E. *Chem. Rev.* **2015**, *115*, 9587

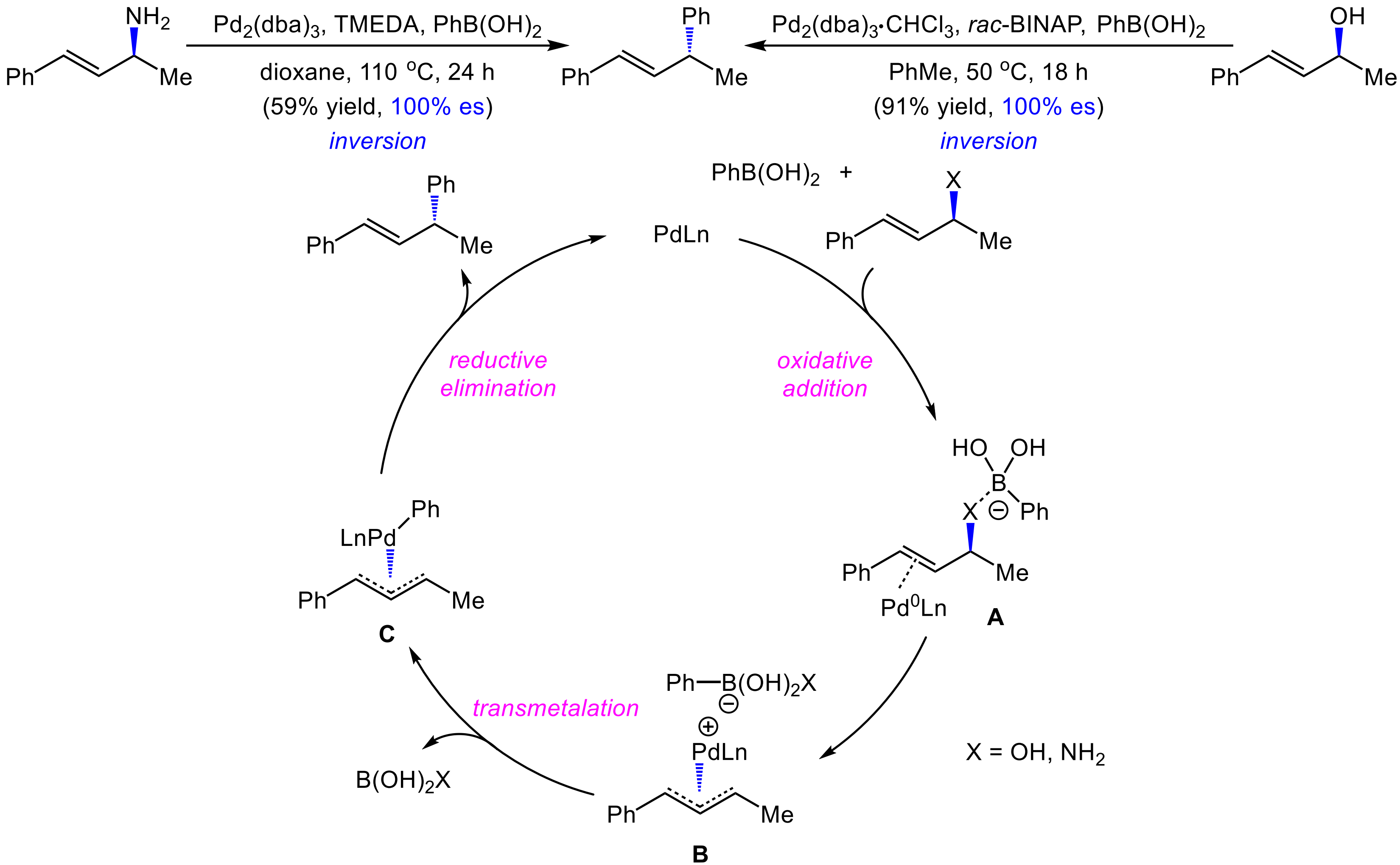
Introduction

Pd-Catalyzed Enantiospecific Allylic Substitutions



Introduction

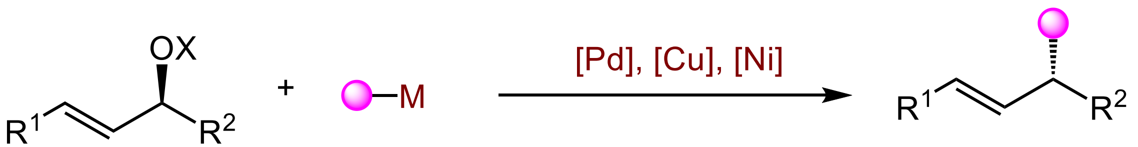
Pd-Catalyzed Enantiospecific Allylic Substitutions



Introduction

Enantiospecific C-Functionalization of Allylic Electrophiles

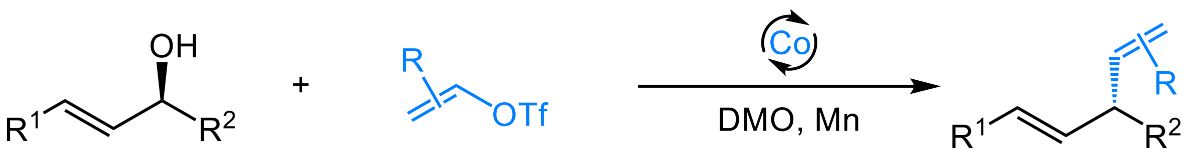
a. Enantiospecific Allylic C-Functionalization Reactions (State-of-the-Art)



State-of-the-Art

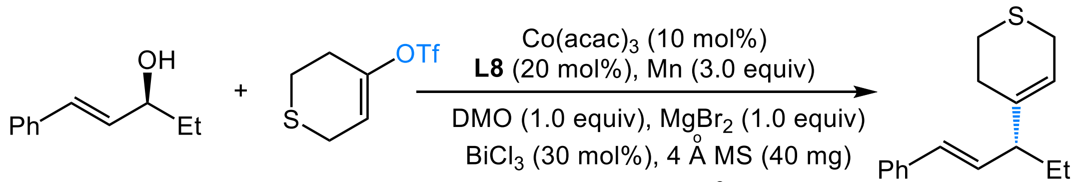
- Reaction: √ Arylation and Alkylation × Vinylation
- Reactant: √ R-M (M = B, Mg, Zn...) × R-X

b. Cross-Electrophile Allylic Vinylation Reactions (This Work)

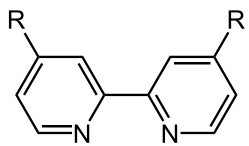


up to >99% ee, >99% es

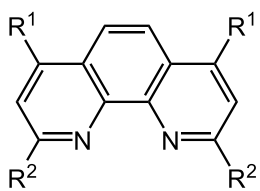
Optimization of the Reaction Conditions



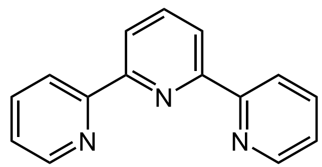
1a **2a** **3a**



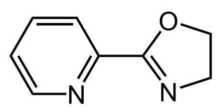
L1, R = H
5% yield, **65**% ee, **68**% es
L2, R = ^{t}Bu
3% yield, **51**% ee, **53**% es



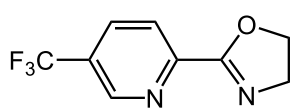
L3, R^1 = H, R^2 = H
4% yield, **13**% ee, **14**% es
L4, R^1 = Ph, R^2 = H
5% yield, **16**% ee, **17**% es
L5, R^1 = H, R^2 = CH_3
0% yield



L6, trace



L7, **18**% yield
87% ee, **91**% es

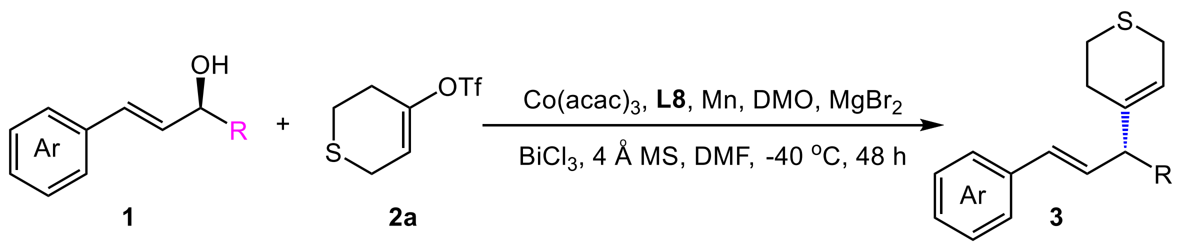


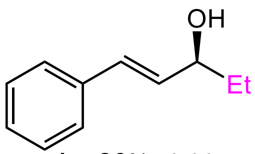
L8, **87**% yield
96% ee, **99**% es

entry	change of conditions	yield (%)	ee/es[b]
1	none	87(80)	98/>99
2	$CoCl_2$	62	96/99
3	$CoBr_2$	75	92/95
4	No 4Å MS	25	95/98
5	No $MgBr_2$	40	95/98
6	No $BiCl_3$	18	92/95
7	Zn Stead of Mn	21	90/93
8	At 0 °C	61	83/86
9	No Co, Mn, or DMO	0	-

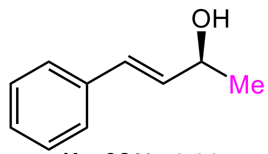
[b]The ee values were determined by chiral HPLC analyses; es = ee(product)/ ee(starting material).

Scope of the Reaction with Allylic Alcohols

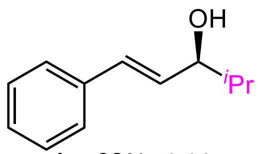




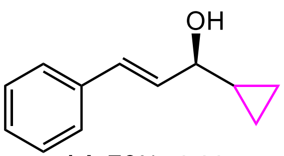
1a, **86**% yield
96% ee, **97**% es



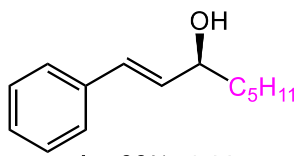
1b, **68**% yield
96% ee, **97**% es



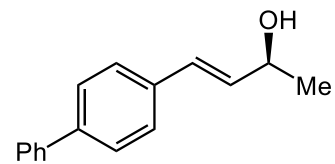
1c, **68**% yield
95% ee, **97**% es



1d, **76**% yield
96% ee, **98**% es

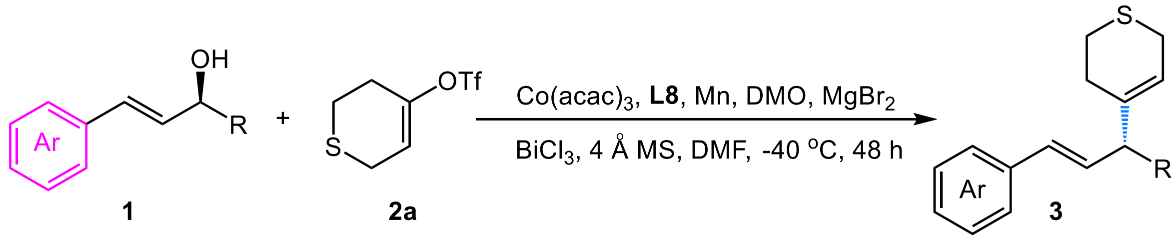


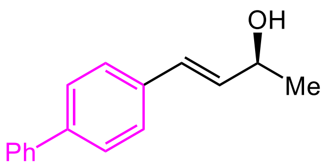
1e, 66% yield
95% ee, **99**% es



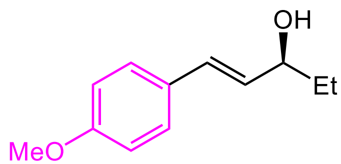
1f, 87% yield
93% ee, >**99**% es

Scope of the Reaction with Allylic Alcohols

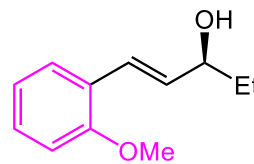




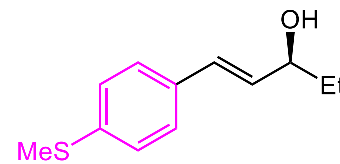
1f, 87% yield
93% ee, >**99**% es



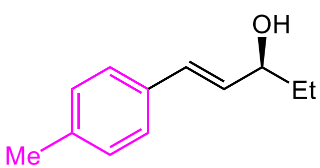
1g, 72% yield
97% ee, **99**% es



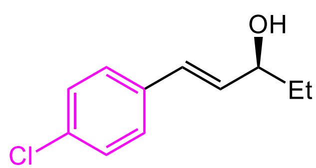
1h, 57% yield
>99% ee, >**99**% es



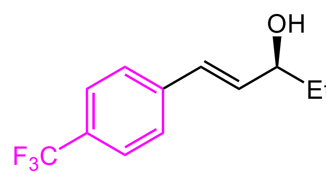
1i, 77% yield
96% ee, **98**% es



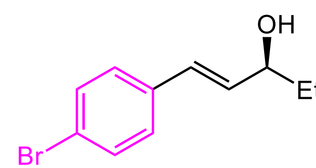
1j, 74% yield
>99% ee, >**99**% es



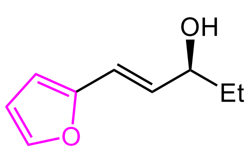
1k, 70% yield
91% ee, **93**% es



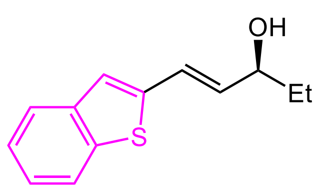
1l, 61% yield
95% ee, **97**% es



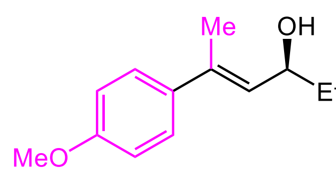
1m, 60% yield
96% ee, **98**% es



1n, 60% yield
95% ee, **99**% es

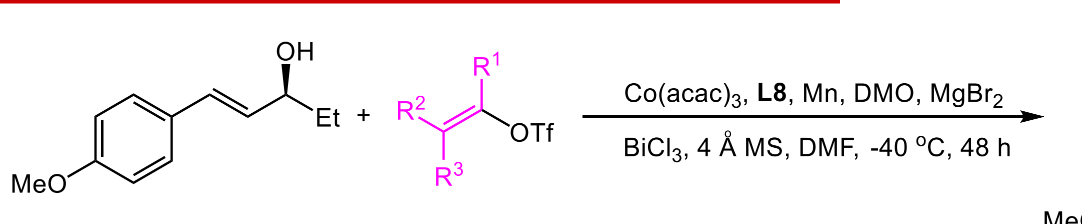


1o, 55% yield
93% ee, **97**% es

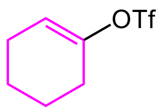


1p, 75% yield
82% ee, **95**% es

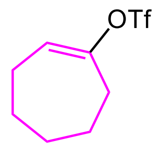
Scope of the Reaction with Vinyl Triflates



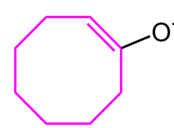
1g **2** **3**



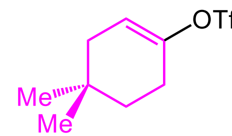
2b, **61**% yield
95% ee, **97**% es



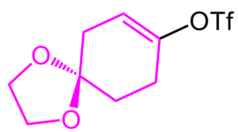
2c, **74**% yield
95% ee, **97**% es



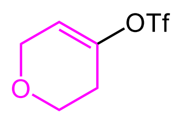
2d, **56**% yield
94% ee, **96**% es



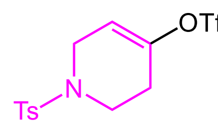
2e, **57**% yield
96% ee, **98**% es



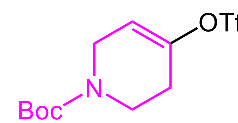
2f, 52% yield
96% ee, **98**% es



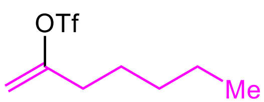
2g, 61% yield
96% ee, **98**% es



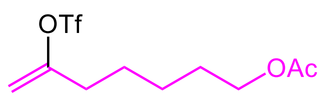
2h, 85% yield
96% ee, **98**% es



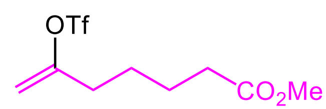
2i, 78% yield
94% ee, **96**% es



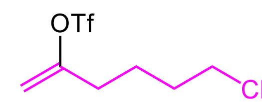
2j, 58% yield
96% ee, **98**% es



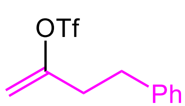
2k, 42% yield
97% ee, **99**% es



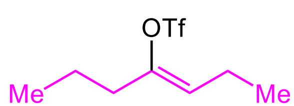
2l, 57% yield
95% ee, **97**% es



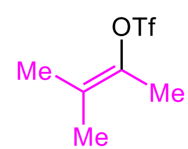
2m, 60% yield
93% ee, **95**% es



2n, 67% yield
94% ee, **96**% es

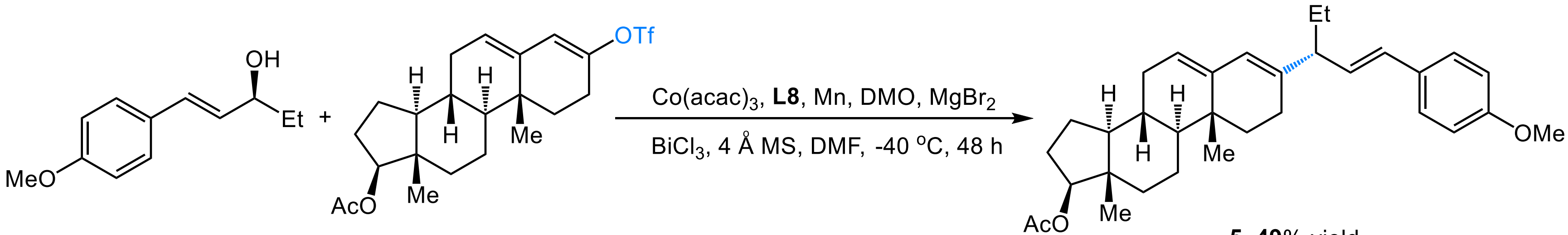


2o, 55% yield
94% ee, **96**% es

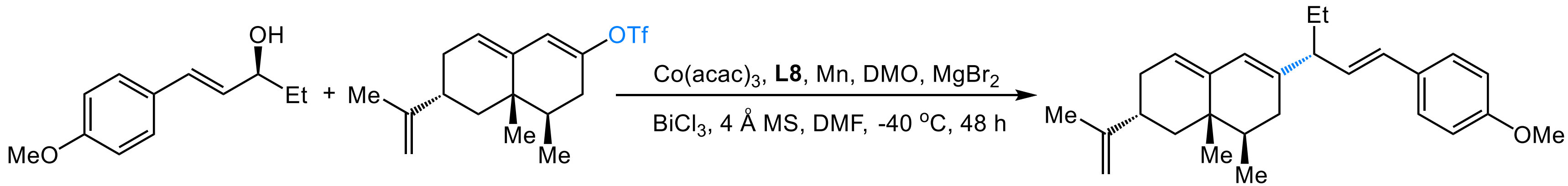


2p, 52% yield
93% ee, **95**% es

Modification of Biologically Active Molecules

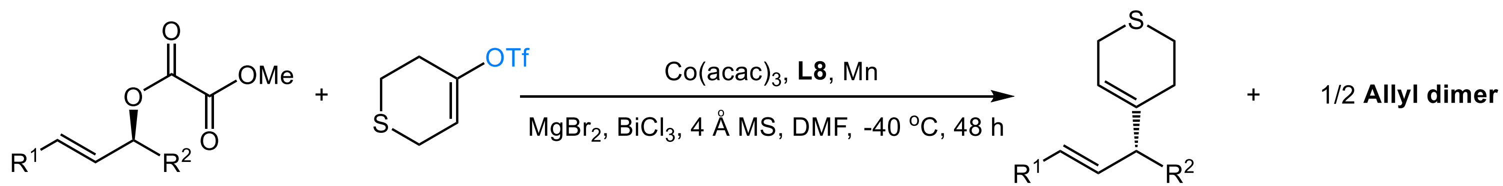


1g **4** (from Testosterone) **5**, **49**% yield, **90**% de, **92%** ds



1g **6** (from (+)-Nootkatone) **7**, **57**% yield, **95**% de, **97%** ds

Reactions of Oxalates



oxalate 8 **2a** **3** **9**

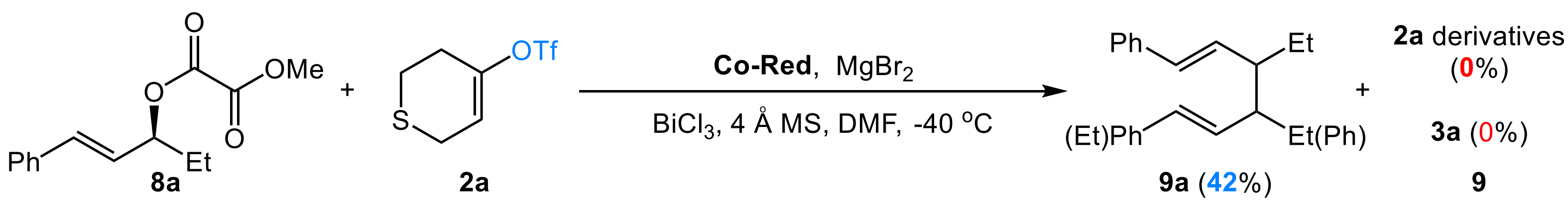
8a (R^1 = Ph, R^2 = Et) **3a** 17% yield, 96% ee, 98% es **9a** 70% yield

8b (R^1 = 4-MeOPh, R^2 = Et) **3b** 31% yield, 96% ee, 98% es **9b** 42% yield

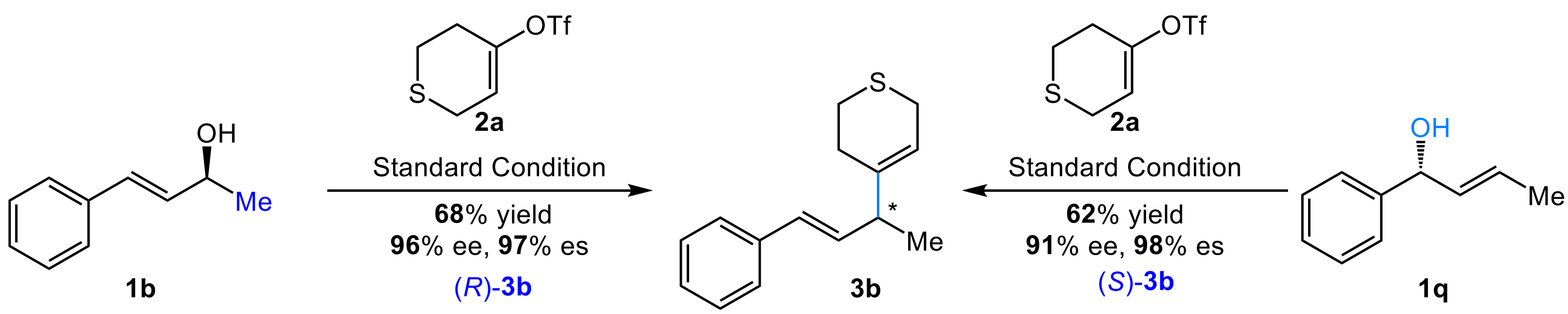
8c (R^1 = Ph, R^2 = cyclopropanyl) **3c** 28% yield, 96% ee, 98% es **9c** 44% yield

Mechanistic Investigation

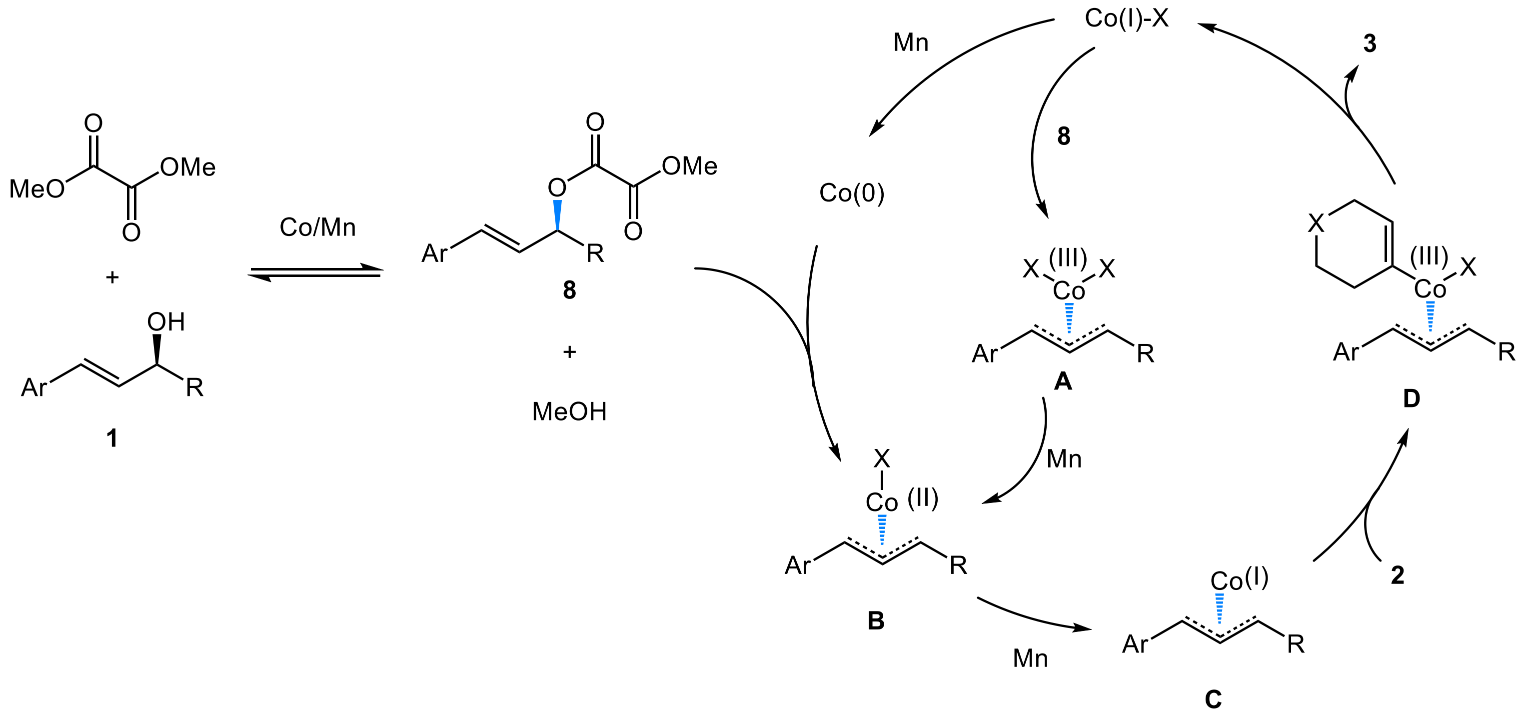
a. The Reactivity of Allyl Oxalate and Vinyl Triflates toward Low-valent Co Species



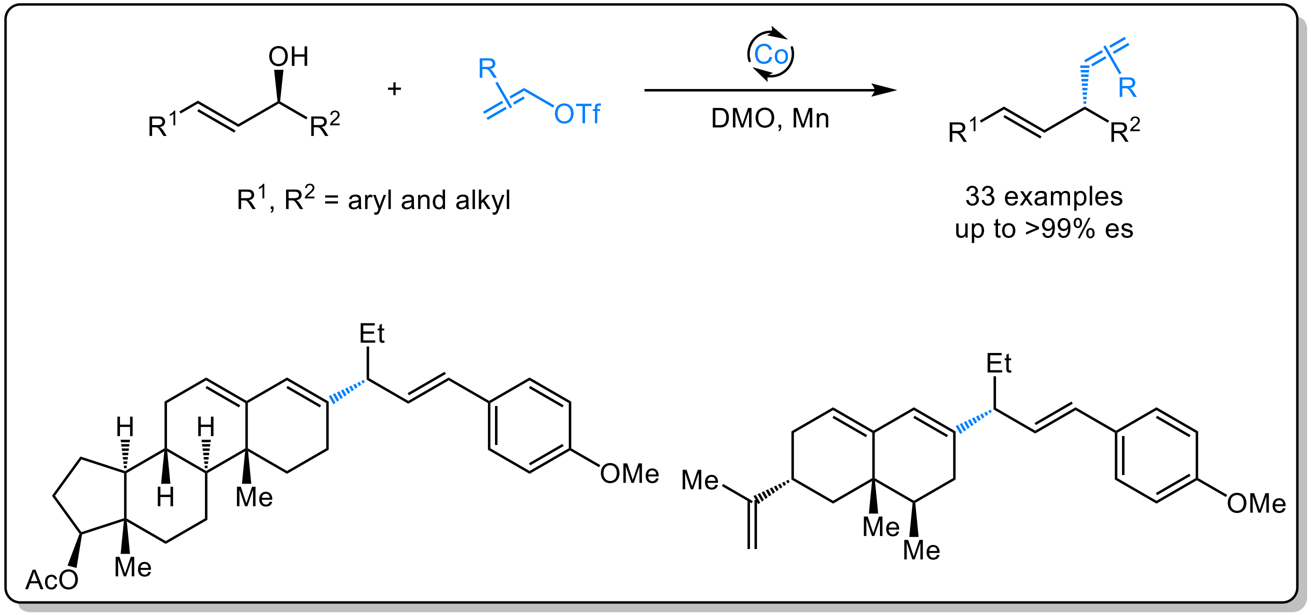
b. Experiments to Probe η^3-π Allyl Intermediates



Proposed Mechanism



Summary



- A **Co-catalyzed Enantiospecific Vinylation Reaction;**
- **The Higher Enantiospecificity of Coalt than Nickel;**
- **An Complementary and Efficient Approach to Form Chiral 1,4-Dienes;**
- **Saving Steps and Improving the Chemoselectivity of the Cross-product.**

The First Paragraph

Writing Strategies

The Importance of Asymmetric Cross-Couplings by Transition-Metal Catalysis

↓

The Progress of Enantioconvergent Cross-Electrophile Couplings by Transition-Metal Catalysis

↓

The Limitations of Enantiospecific Cross-Electrophile Couplings by Transition-Metal Catalysis

The First Paragraph

Asymmetric cross-couplings catalyzed by transition metals provide a revolutionary way of producing chiral molecules. Recent studies in this field have focused on the couplings of electrophiles to form C−C bonds. This method avoids the handling of sensitive organometallic reagents and is orthogonal to classic cross-couplings. Since the pioneering work of the Reisman and Weix groups, major progress has been achieved on enantio-convergent cross-electrophile reactions. The enantiospecific variants were developed by the Jarvo group, and this approach enabled facile access to enantioenriched cyclic compounds by coupling of intramolecular chiral electrophiles. However, to date, all of these reactions have used nickel complexes. The unique properties of other transition metals may offer opportunities for solving problems that are not easily addressed by nickel, but this potential remains to be explored.

The Last Paragraph

Writing Strategies

The Summary of This Work

↓

The Features of This Work

↓

The Prospects of This Work

The Last Paragraph

In conclusion, we have reported a cobalt-catalyzed enantiospecific vinylation reaction of allylic alcohols by dynamic kinetic cross-electrophile coupling. The use of cobalt enables the reaction to proceed with high enantiospecificity, which has failed to be realized by nickel. The method harnesses the ease of access of enantioenriched allylic alcohols, and it offers an approach to chiral 1,4-dienes that is complementary to those from established methods. The dynamic kinetic approach described here not only saves steps but also provides a way to improve the chemoselectivity of the cross-product. Further expansion of the scope of cobalt-catalyzed asymmetric cross-electrophile coupling and the use of the dynamic kinetic method are ongoing in our laboratory.

Representative Examples

1. In this context, the enantiospecific reactions **harness the ease of** preparation of highly enantioenriched secondary allylic alcohols and avoid the requirement for chiral ligands. (**易于做某事**)

2. To provide insight into whether the allyl oxalate or vinyl triflate reacts with cobalt first, the low-valent cobalt species Co-Red was prepared. (**去深入了解……**)

3. This reactivity **is opposite to** that observed for nickel catalysis, and it may account for the good selectivity for the cross-products under cobalt catalysis **in comparison to** that for nickel. (**与……相反；与……对比**)

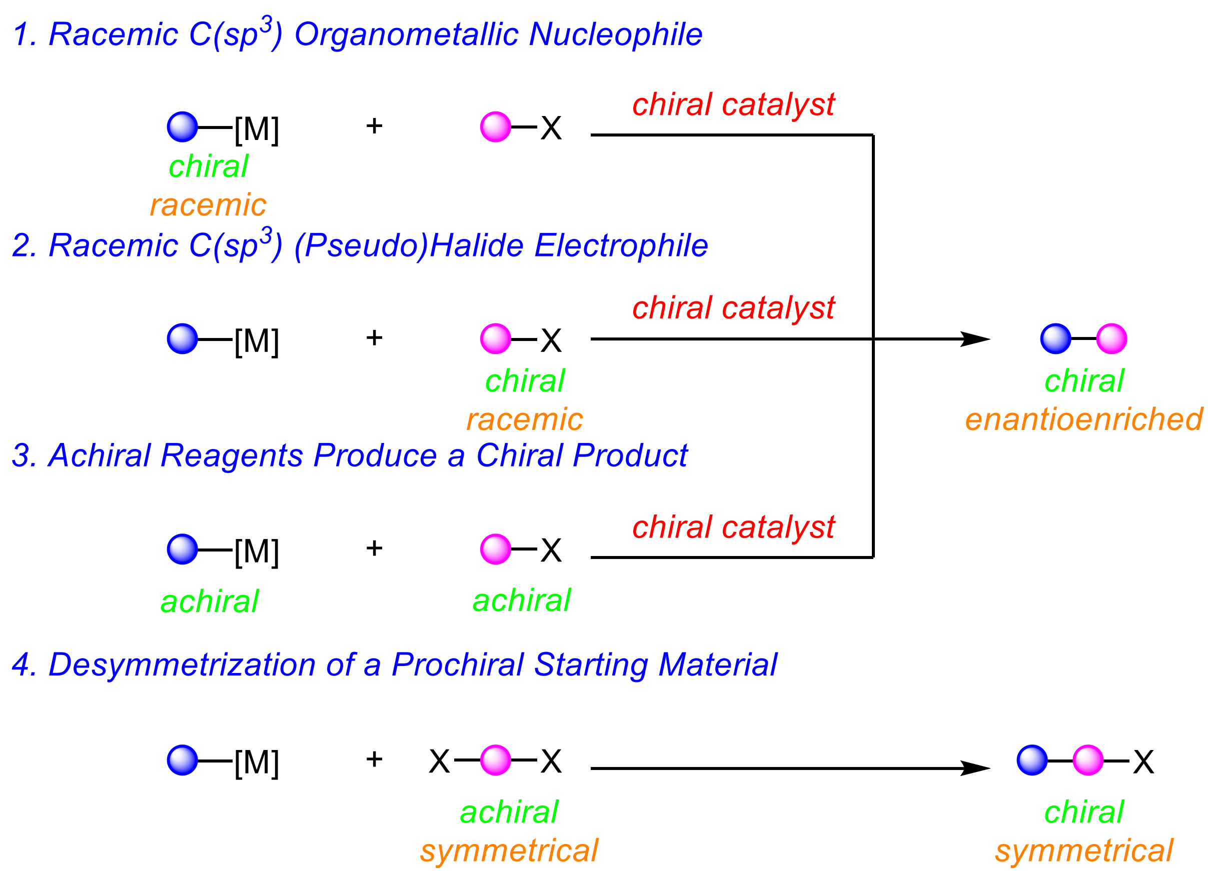
Acknowledgement

Thanks for your attention!

Introduction

Enantioselective Cross-Coupling

Enantioselective Cross-Coupling



Introduction

Enantiospecific Cross-Coupling