Literature Report V

Cobalt-Catalyzed Enantioselective Hydroamination of Arylalkenes with Secondary Amines

Reporter: Hao Tang
Checker: Yu-Qing Bai
Date: 2022-12-07

Miao, H.; Guan, M.; Xiong, T.; Zhang,G.; Zhang, Q.
Angew. Chem. Int. Ed. **2022**, e202213913

CV of Prof. Qian Zhang

Education and Employment:

- **1989–1993** B.S., North East Normal University
- **1993–1996** M.S., North East Normal University
- **1996–1999** Teaching assistant, North East Normal University
- **2000–2003** Ph.D., CIAC
- **2003–2004** Visiting scholar, University of Sydney
- **2004–Now** Professor, North East Normal University

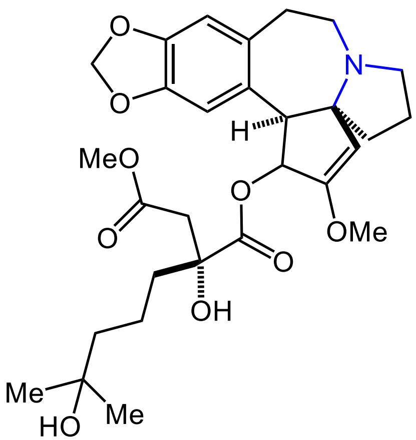
Prof. Qian Zhang

Research Interest:

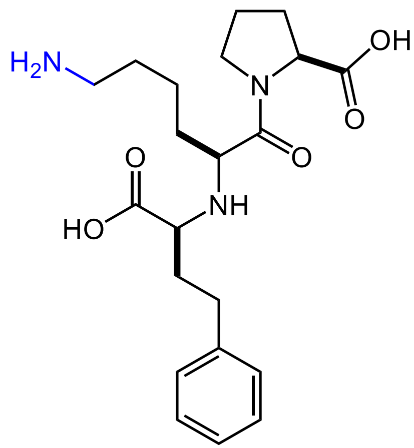
- New Method of Efficient and Highly Selective C-N Bond Construction.

Contents

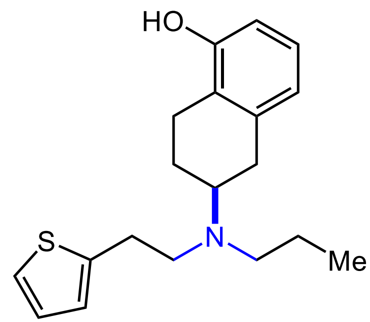
Introduction



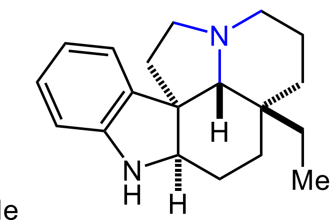
omacetaxine
acute myeloid leukaemia



lisinopril
ACE inhibitor



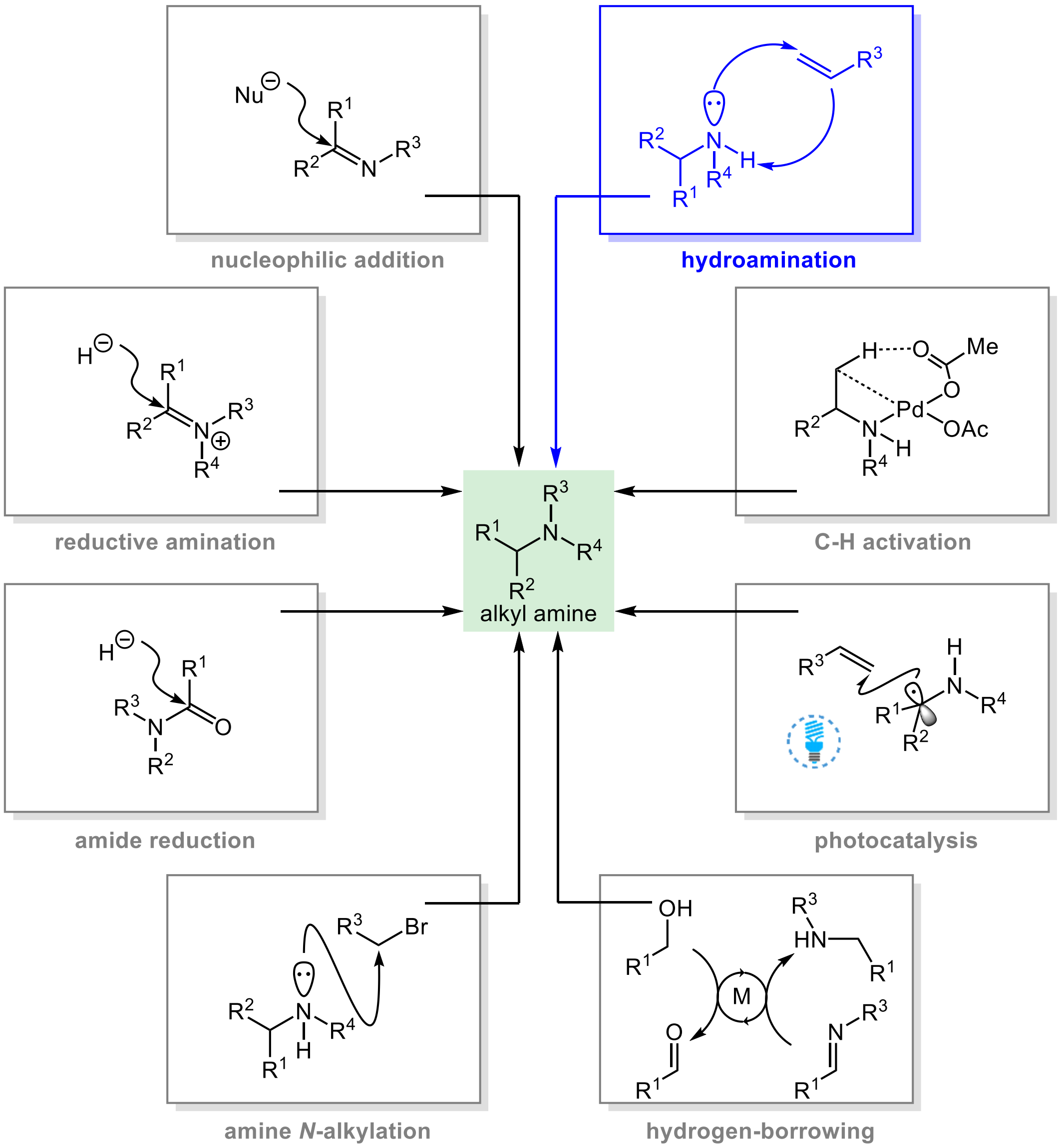
neupro
muscular skeletal disorder



aspidospermidine
common motif in natural products

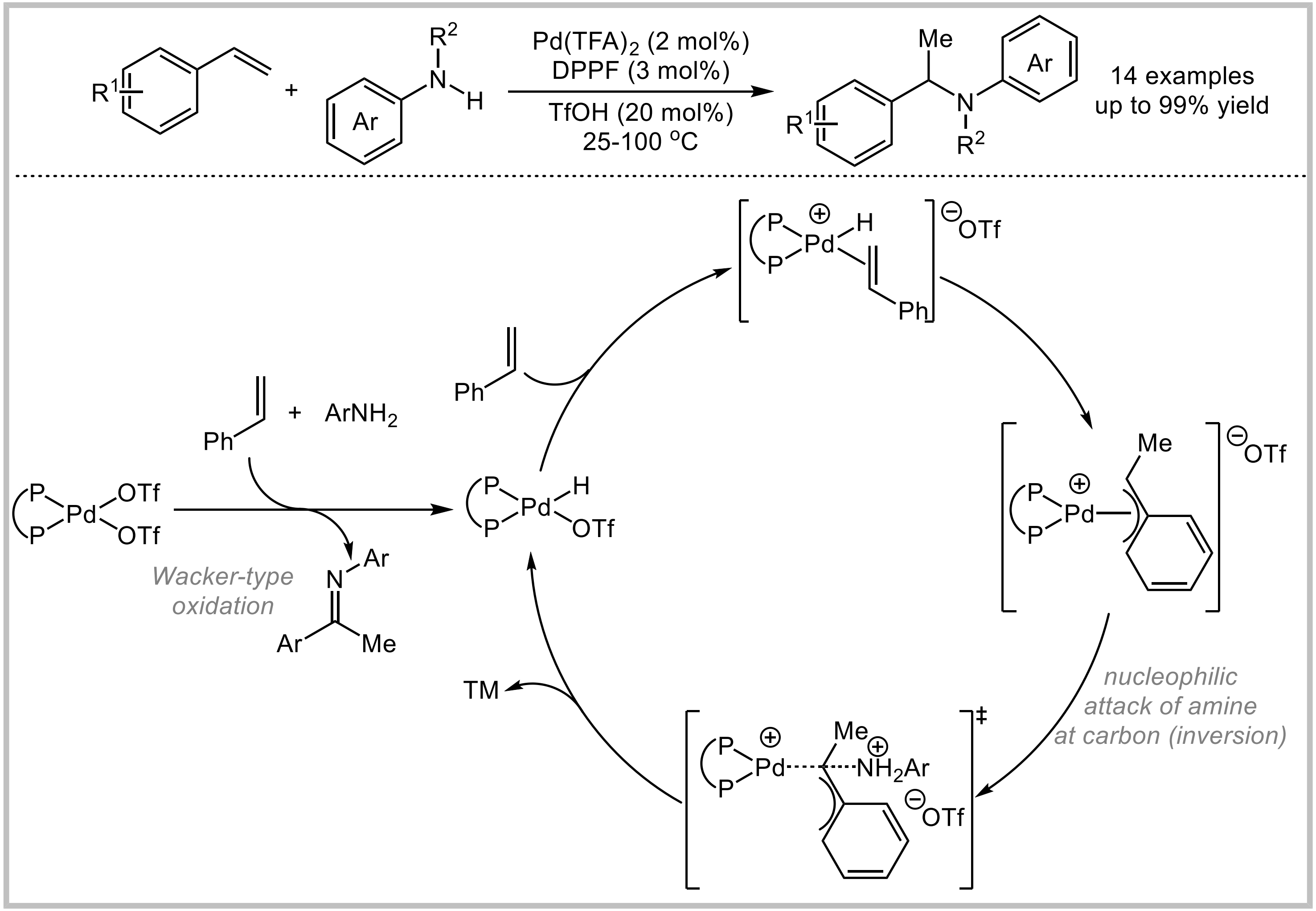
Trowbridge, A.; Walton, S. M.; Gaunt, M. J. *Chem. Rev.* **2020**, *120,* 2613

Introduction



Introduction

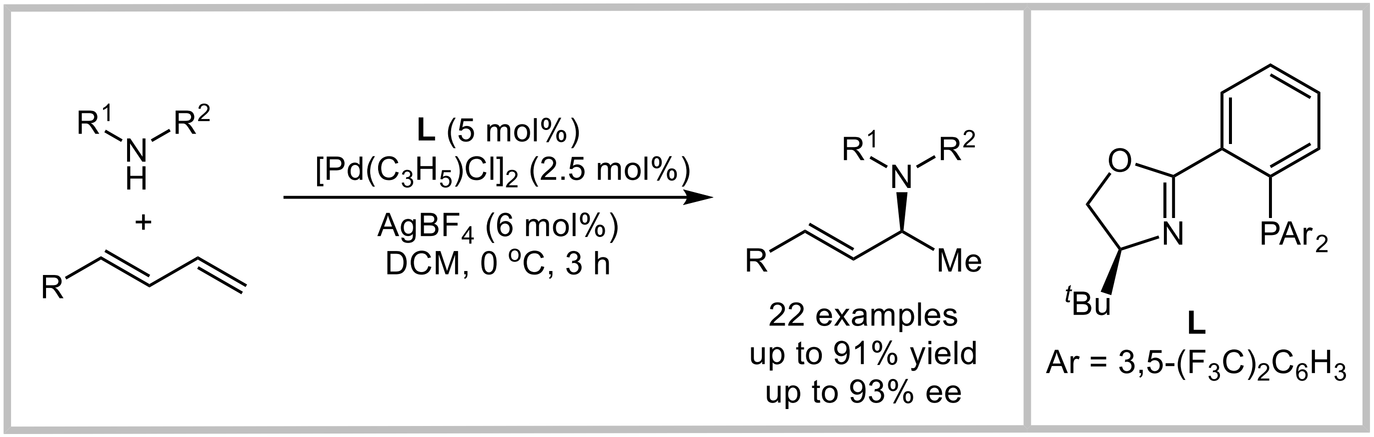
Palladium-Catalyzed Hydroamination



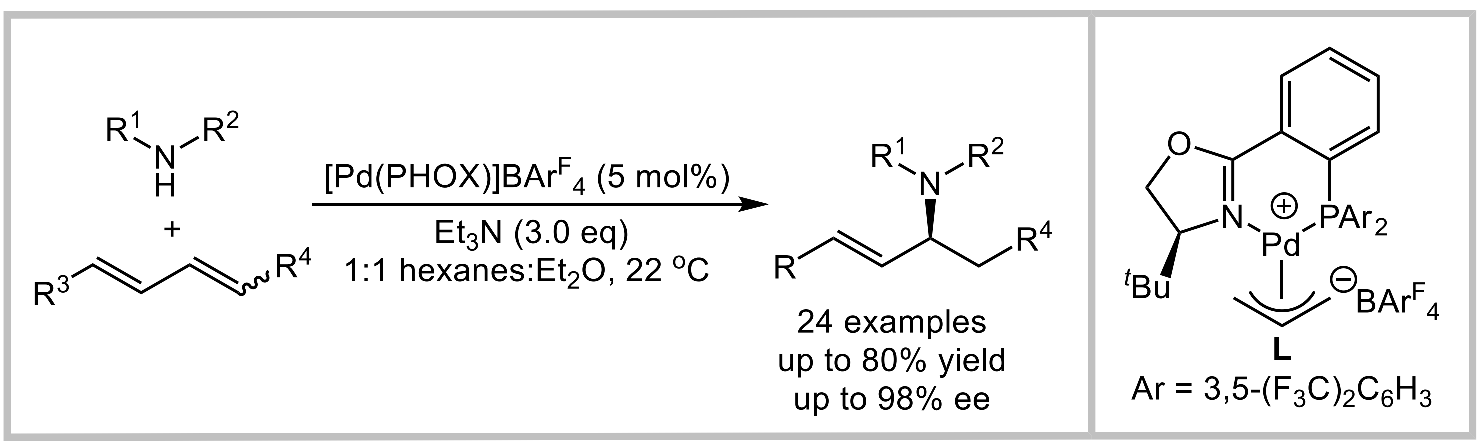
Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2000**, *122*, 9546

Introduction

Palladium-Catalyzed Hydroamination



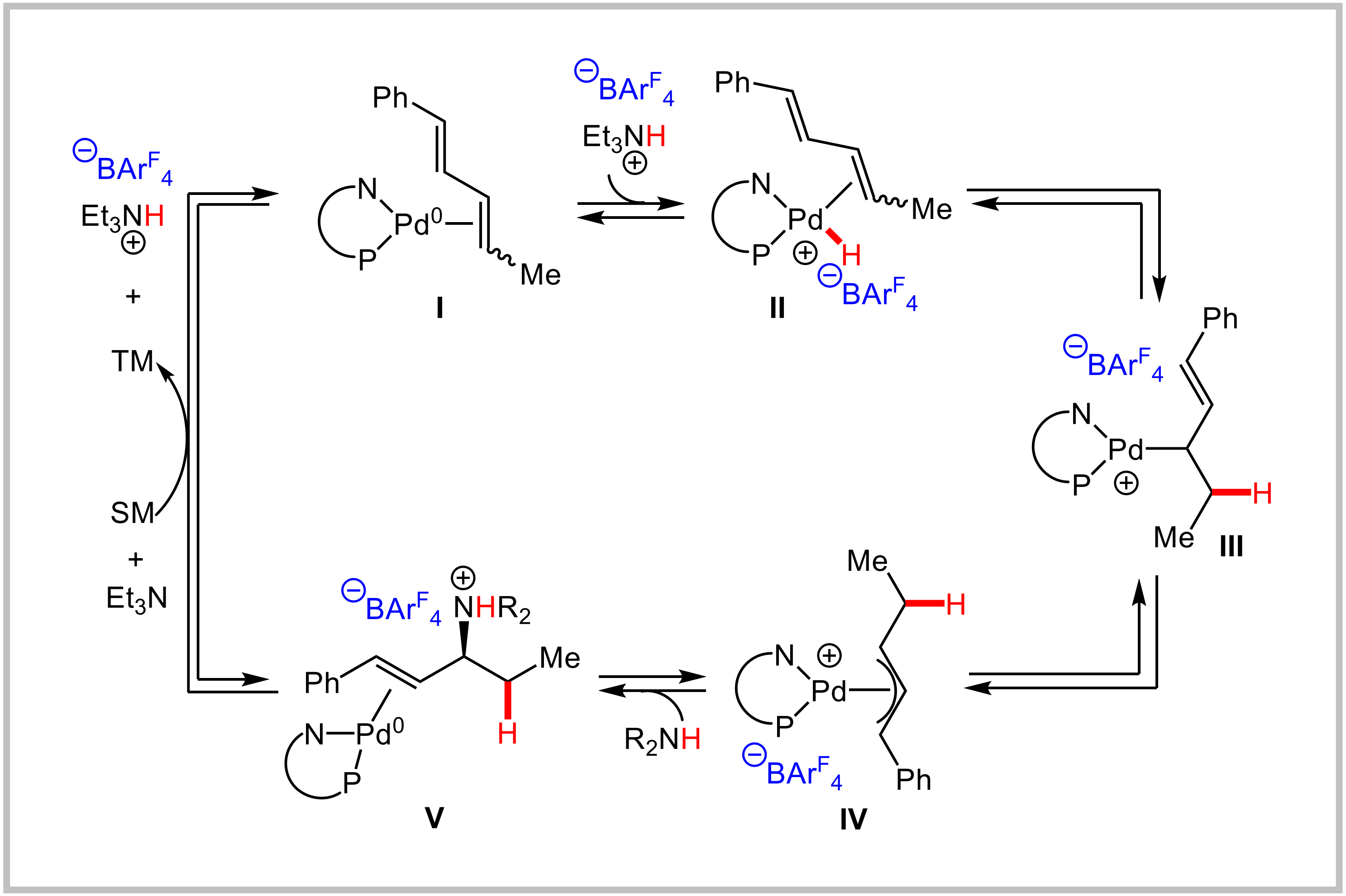
Adamson, N. J.; Hull, E.; Malcolmson, S. J. *J. Am. Chem. Soc.* **2017**, *139*, 7180



Park, S.; Malcolmson, S. J. *ACS Catal.* **2018**, *8*, 8468

Introduction

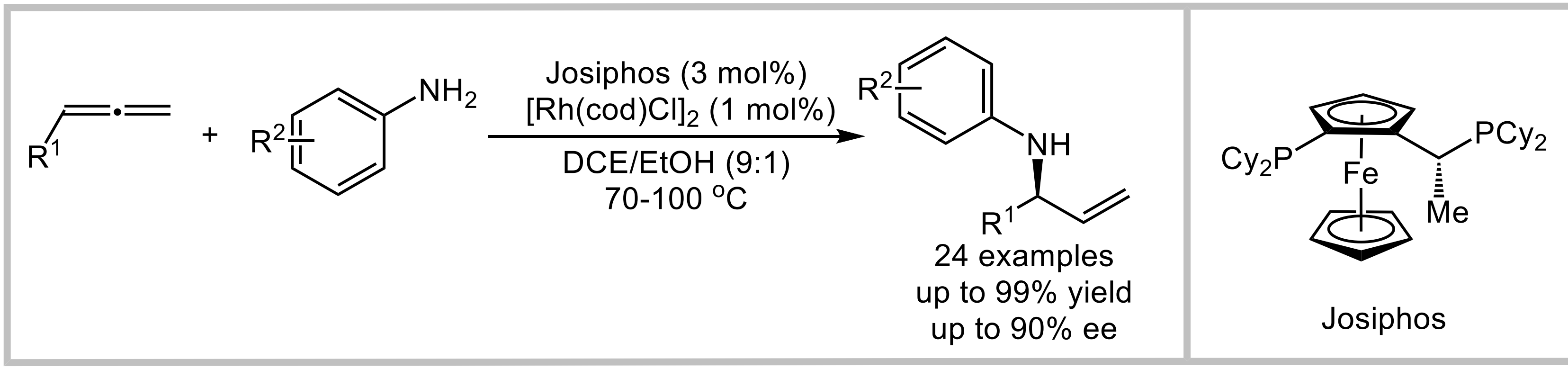
Palladium-Catalyzed Hydroamination



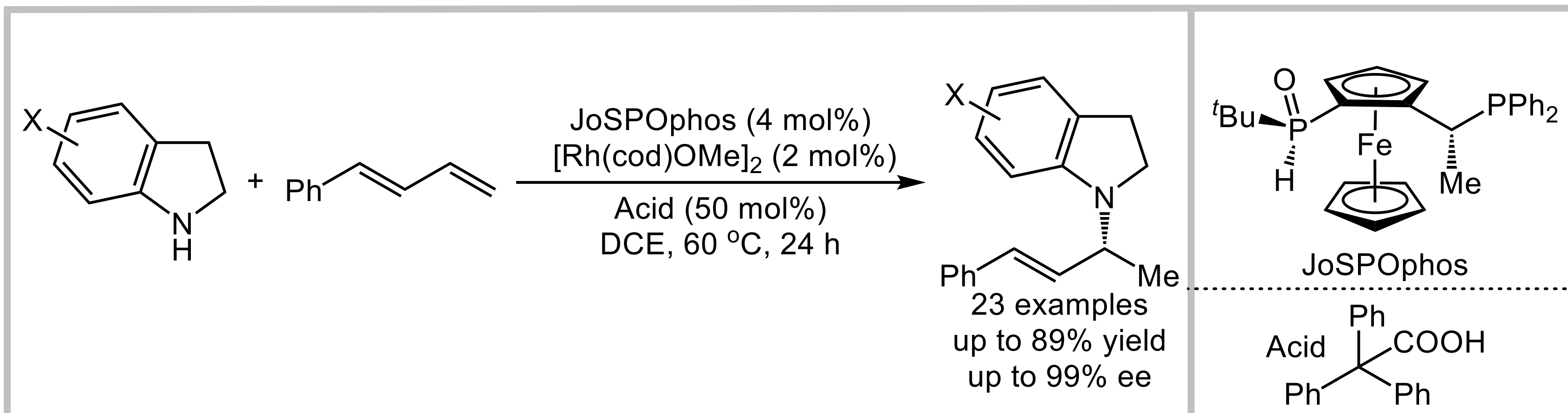
Park, S.; Malcolmson, S. J. *ACS Catal.* **2018**, *8*, 8468

Introduction

Rhodium-Catalyzed Hydroamination



Cooke, M. L.; Xu, K.; Breit, B. *Angew. Chem. Int. Ed.* **2012**, *51*,10876



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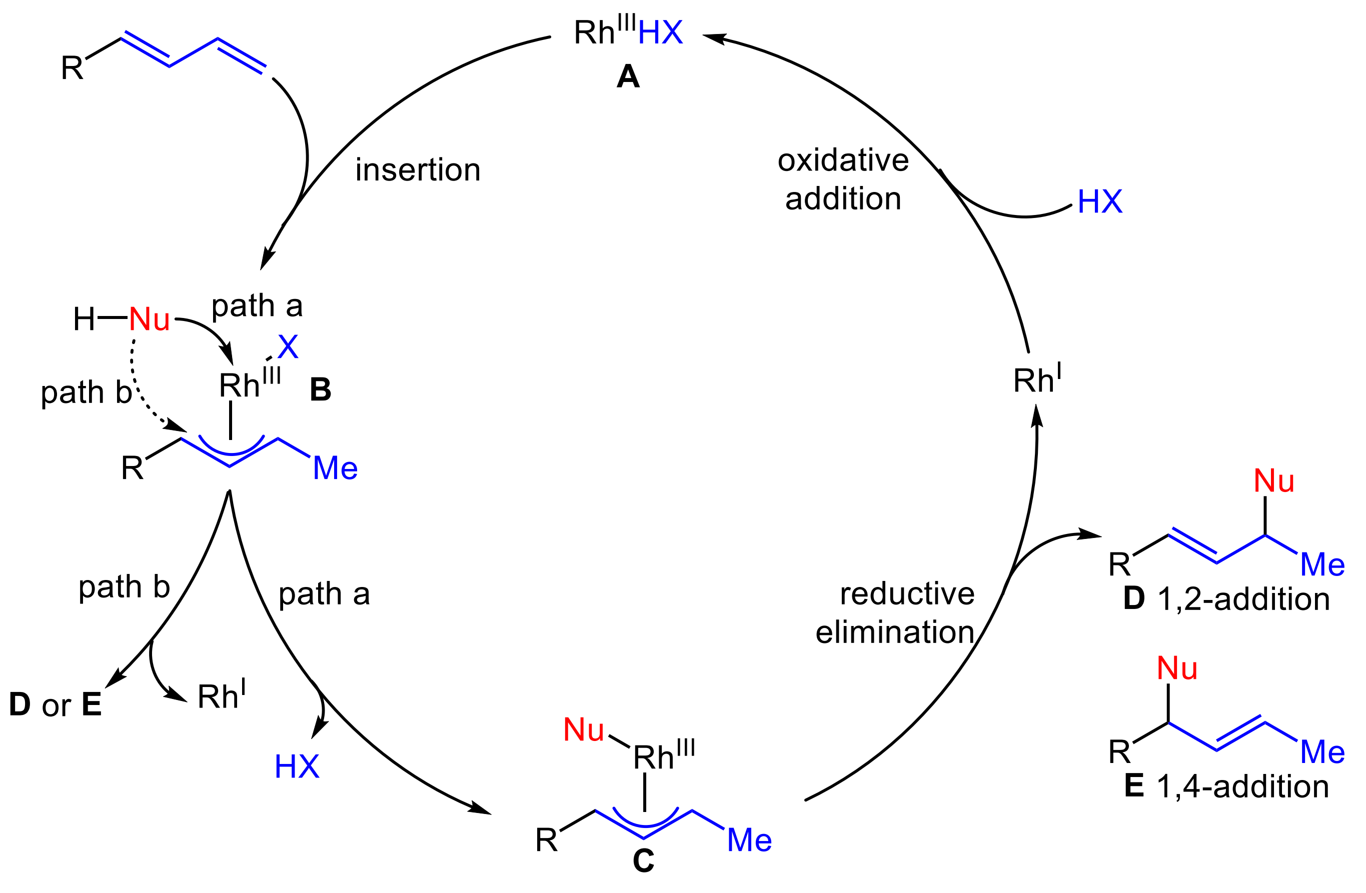
Introduction

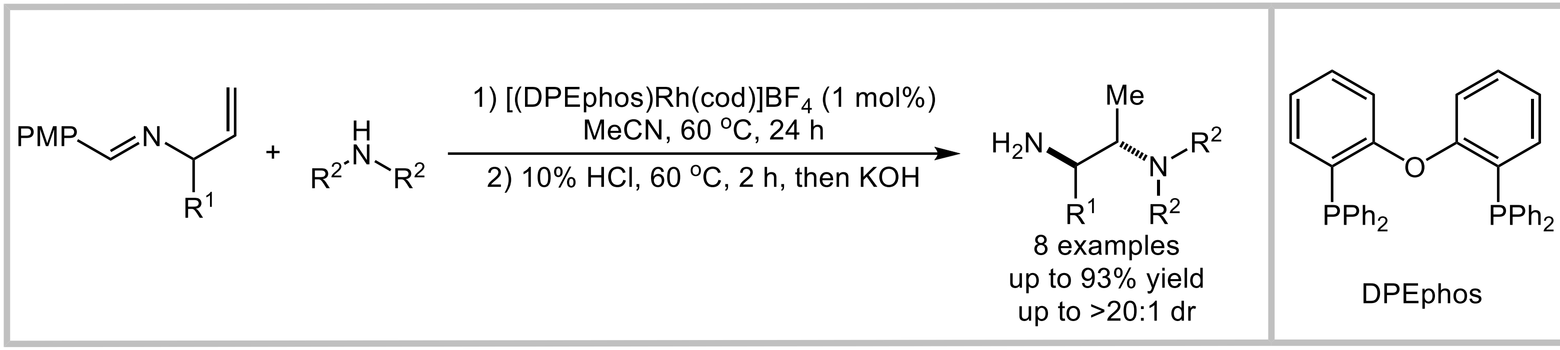
Rhodium-Catalyzed Hydroamination



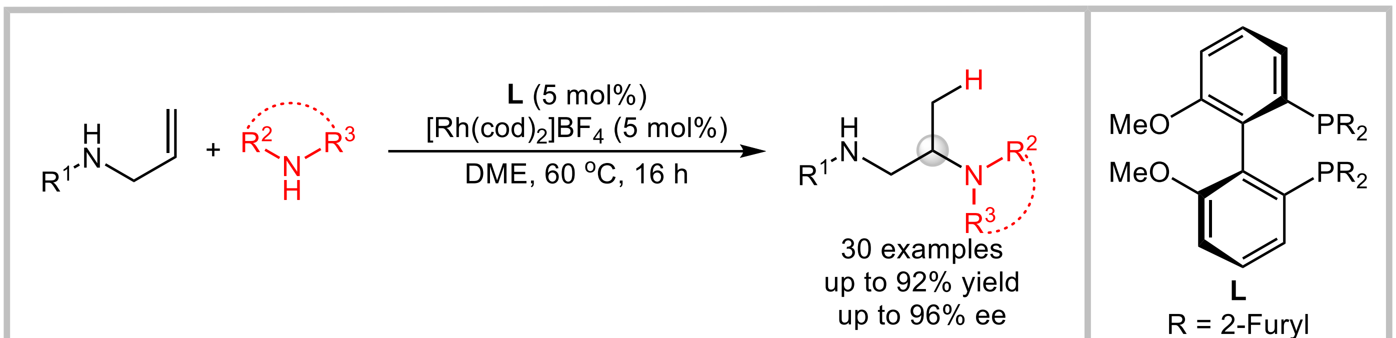
Yang, X.-H.; Dong, V. M. *J. Am. Chem. Soc.* **2017**, *139*, 1774

Introduction

Rhodium-Catalyzed Hydroamination



Ickes, A. R.; Ensign, S. C.; Hull, K. L. *et al*. *J. Am. Chem. Soc.* **2014**, *136*, 11256



Vanable, E. P.; Kennemur, J. L.; Hull, K. L. *et al*. *J. Am. Chem. Soc.* **2019**, *141*, 739

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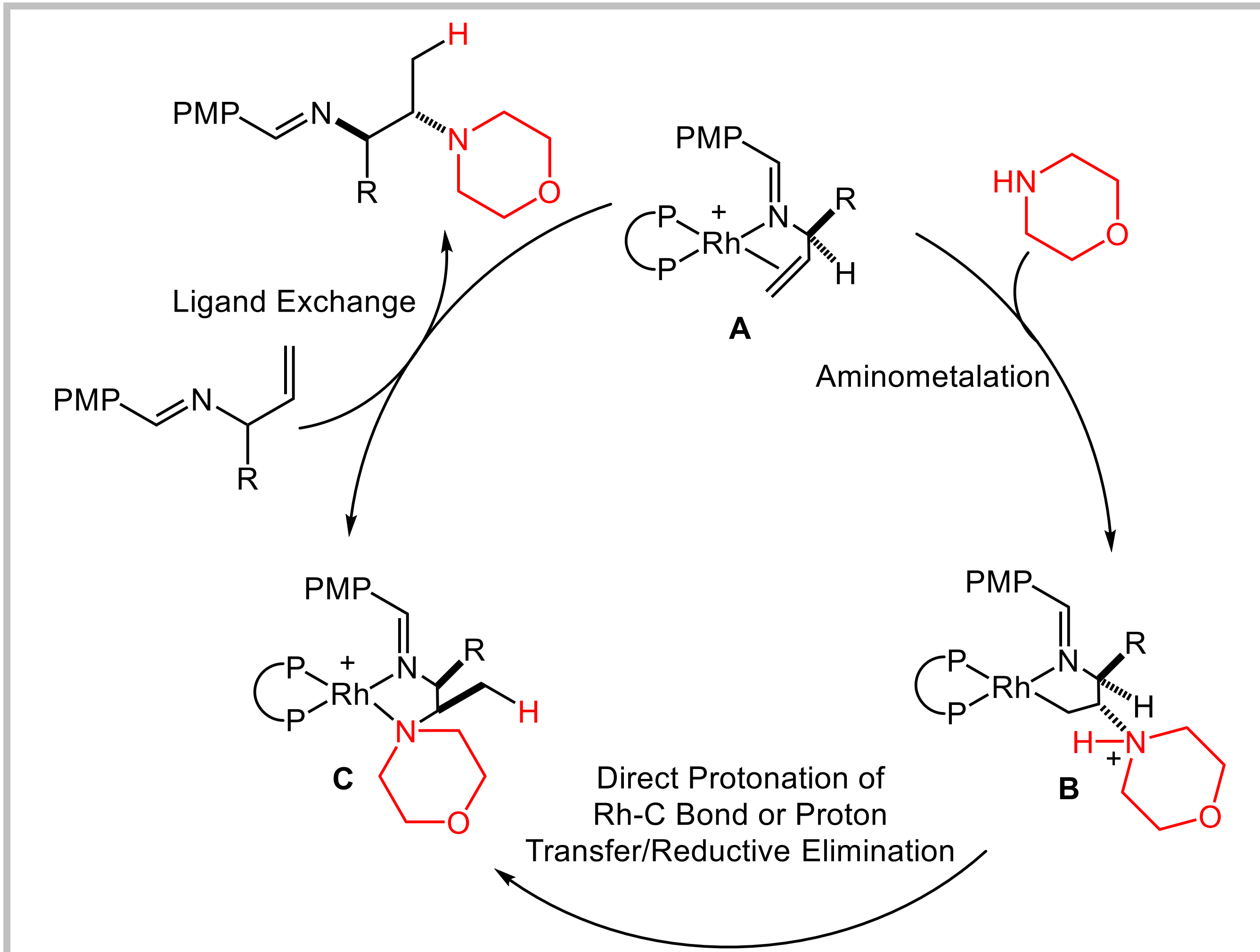
Rhodium-Catalyzed Hydroamination



Ickes, A. R.; Ensign, S. C.; Hull, K. L. *et al*. *J. Am. Chem. Soc.* **2014**, *136*, 11256

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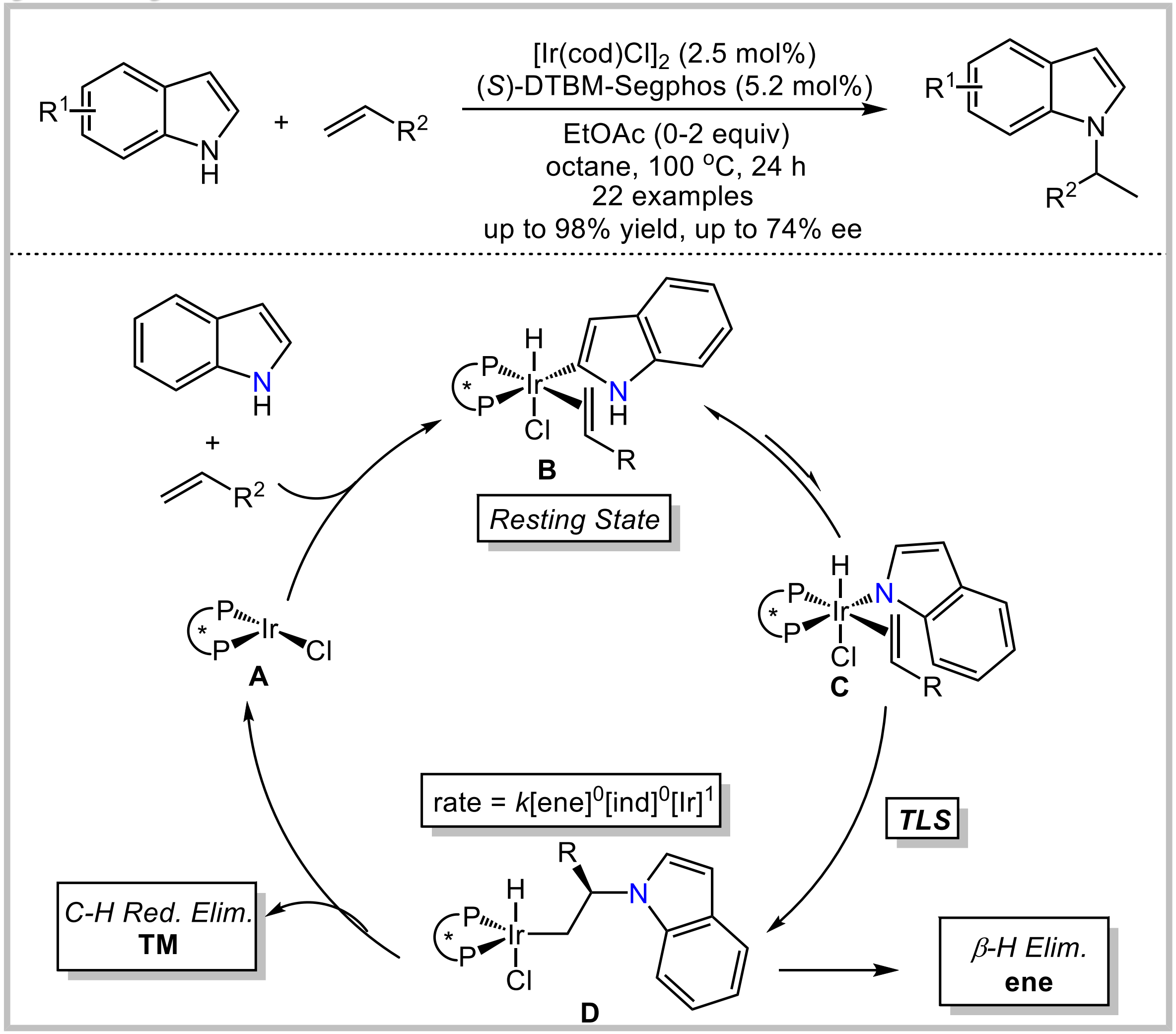
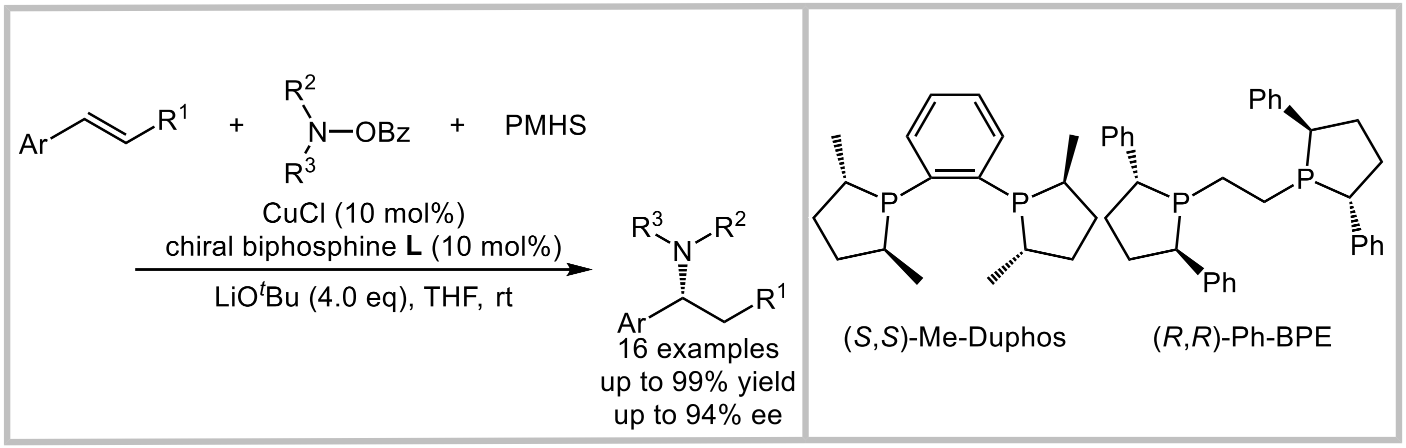
Iridium-Catalyzed Hydroamination



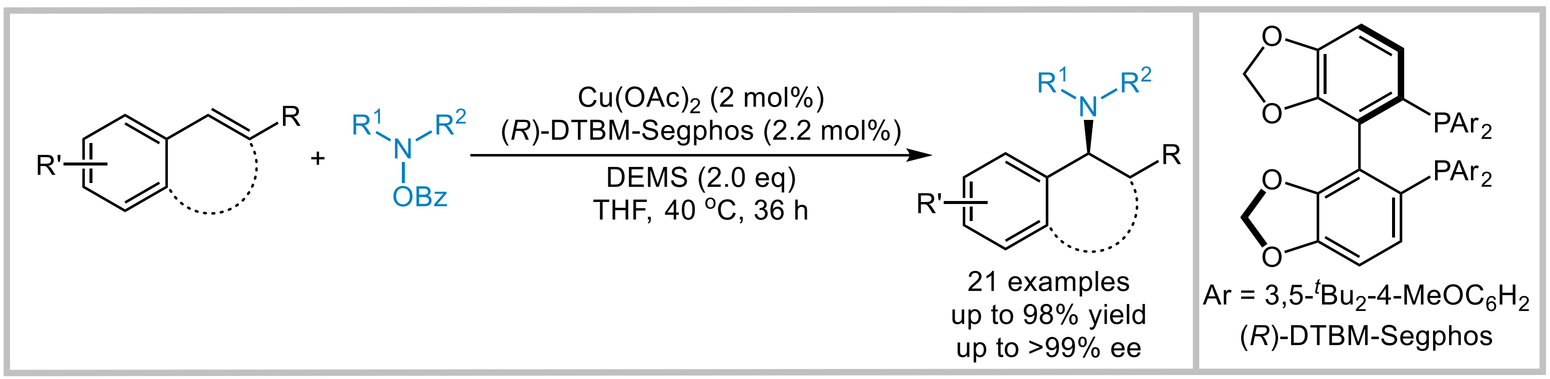
Sevov, C. S.; Zhou, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 3200

Introduction

Copper-Catalyzed Hydroamination



Miki, Y.; Hirano, K.; Miura, M. *et al*. *Angew. Chem. Int. Ed.* **2013**, *52*, 10830



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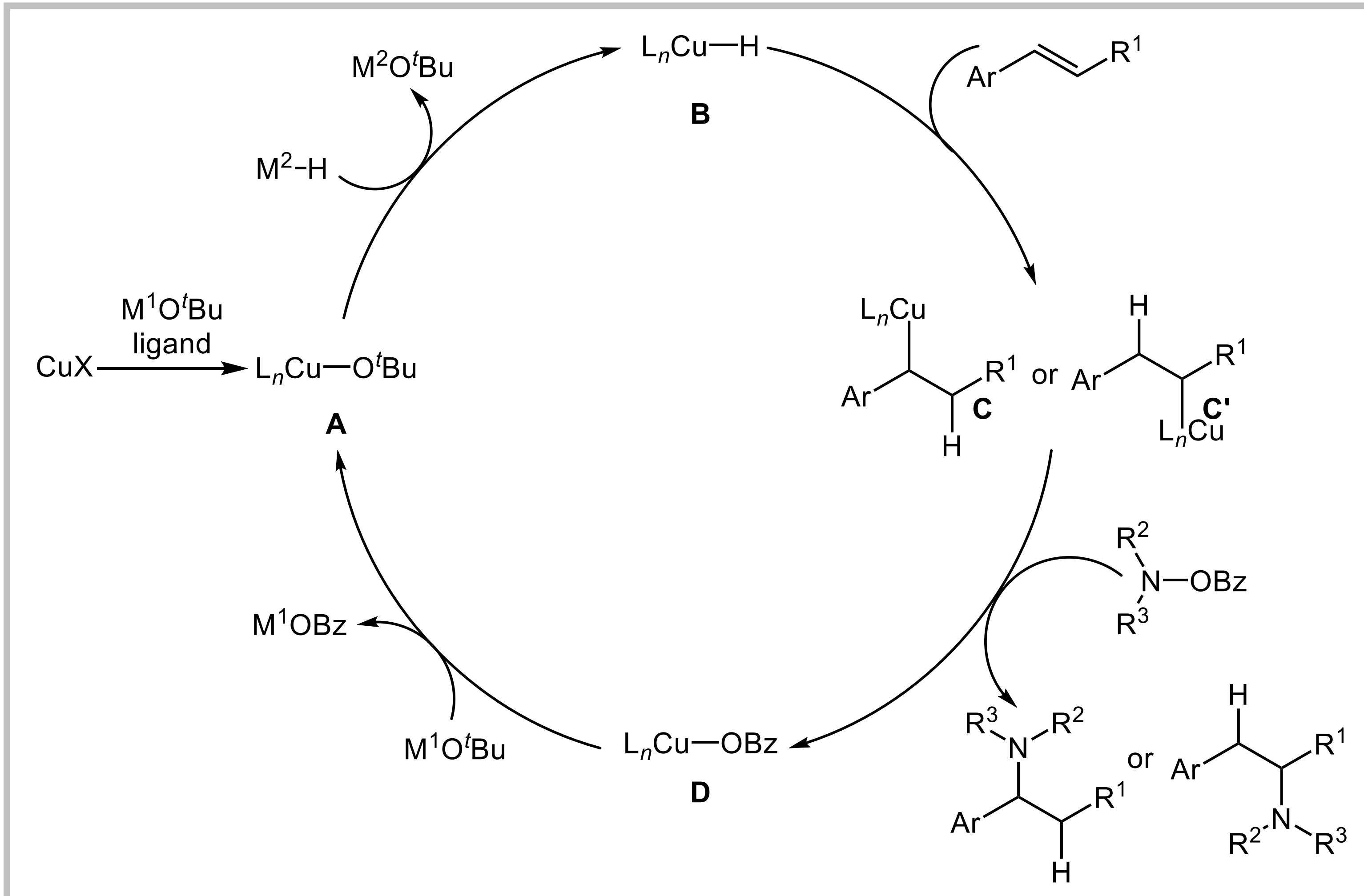
Copper-Catalyzed Hydroamination



Miki, Y.; Hirano, K.; Miura, M. *et al*. *Angew. Chem. Int. Ed.* **2013**, *52*, 10830

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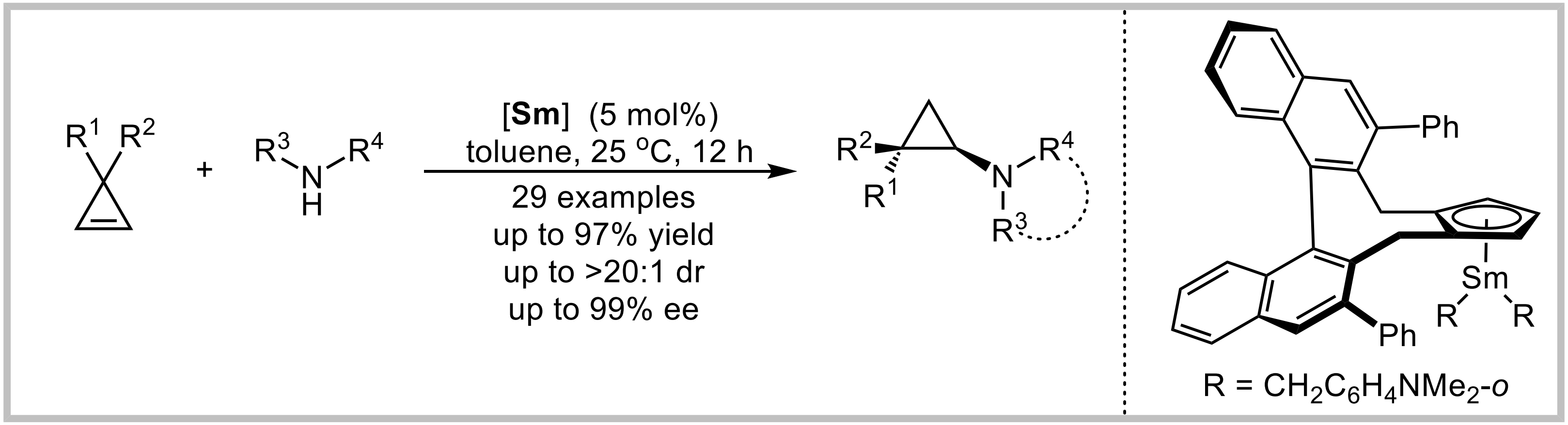
Rare-Earth-Metal-Catalyzed Hydroamination



Teng, H.-L.; Luo, Y.; Hou, Z. M. *et al*. *Angew. Chem. Int. Ed.* **2016**, *55*, 15406

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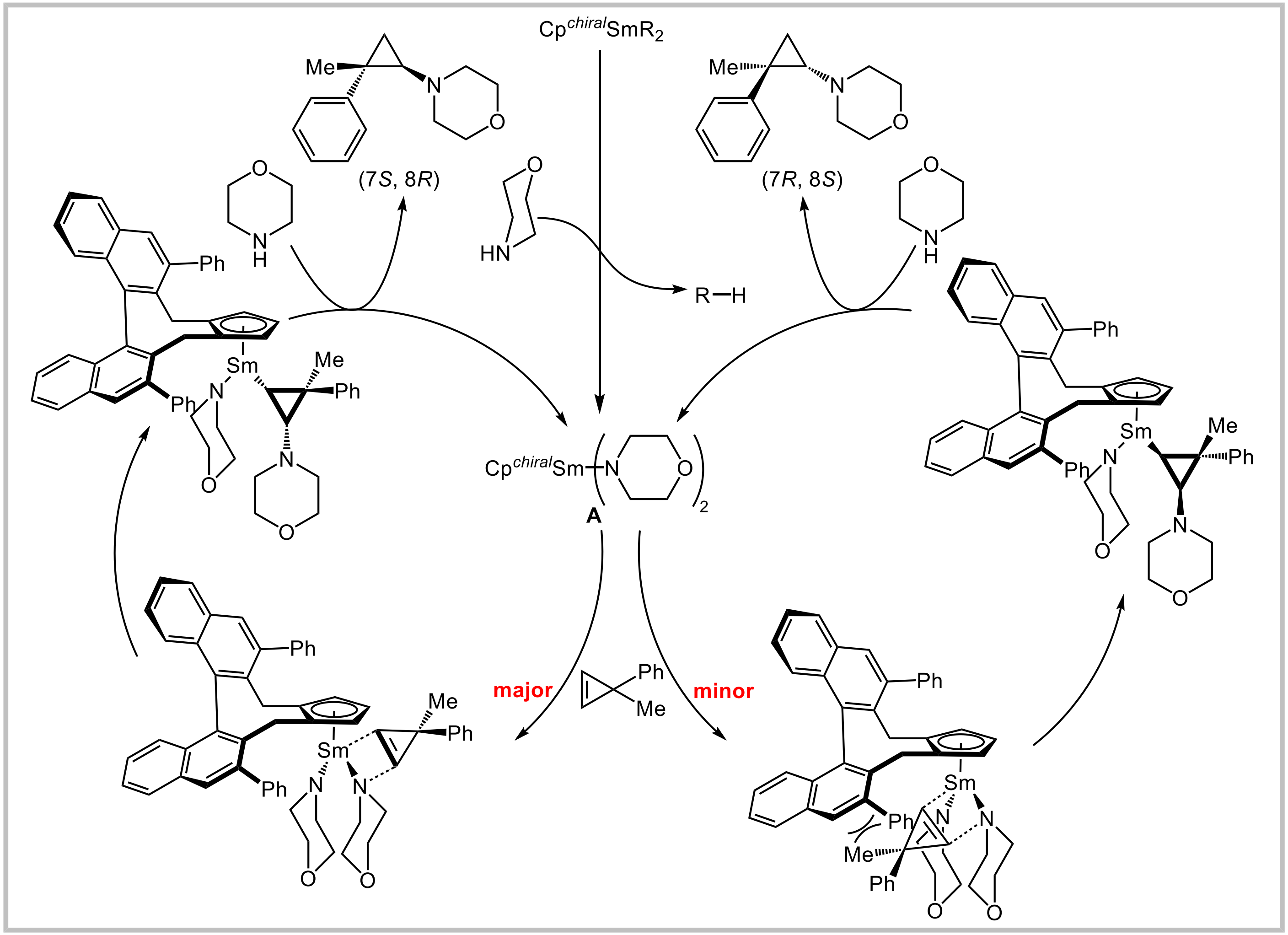
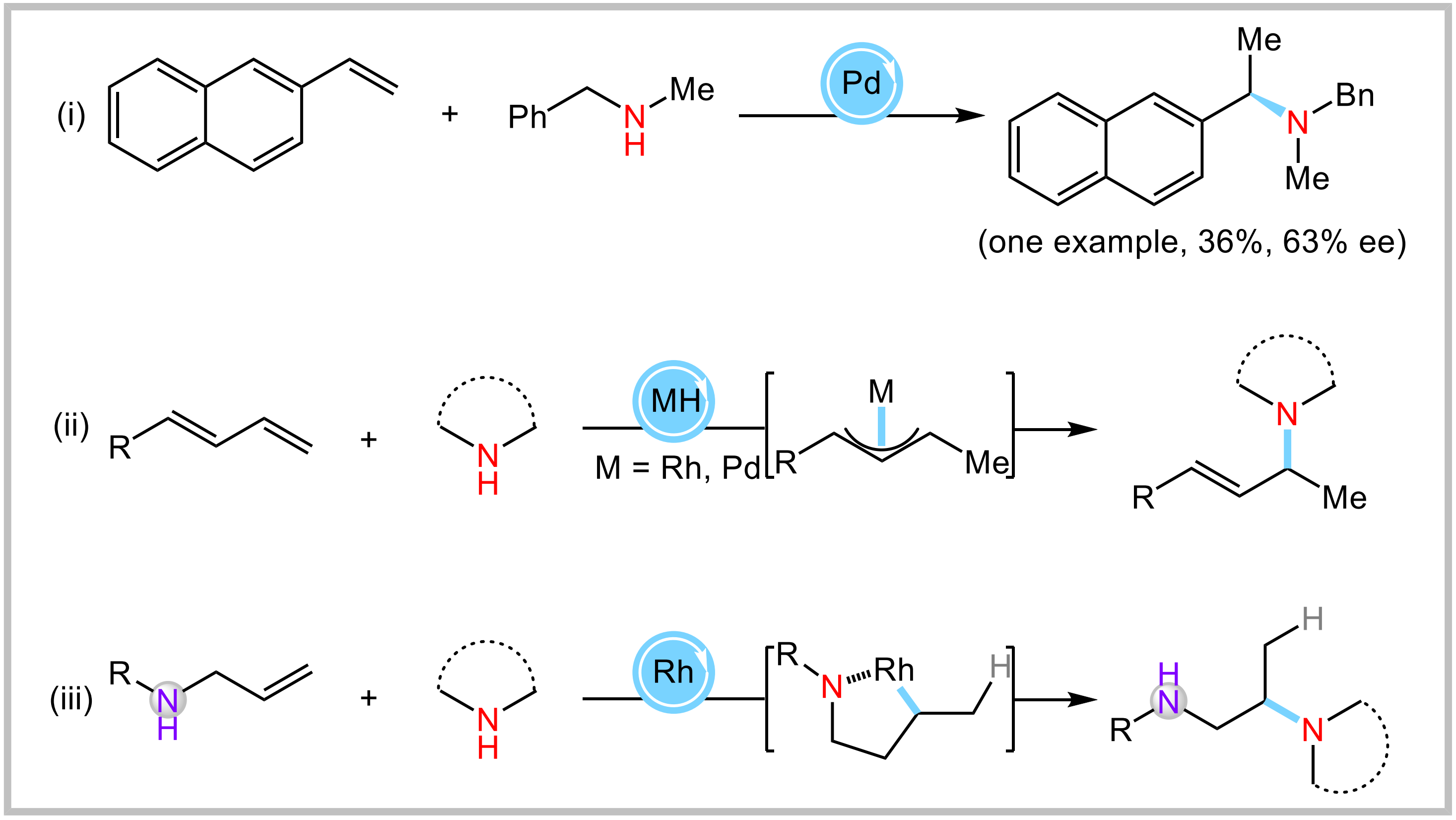
Rare-Earth-Metal-Catalyzed Hydroamination



Teng, H.-L.; Luo, Y.; Hou, Z. M. *et al*. *Angew. Chem. Int. Ed.* **2016**, *55*, 15406

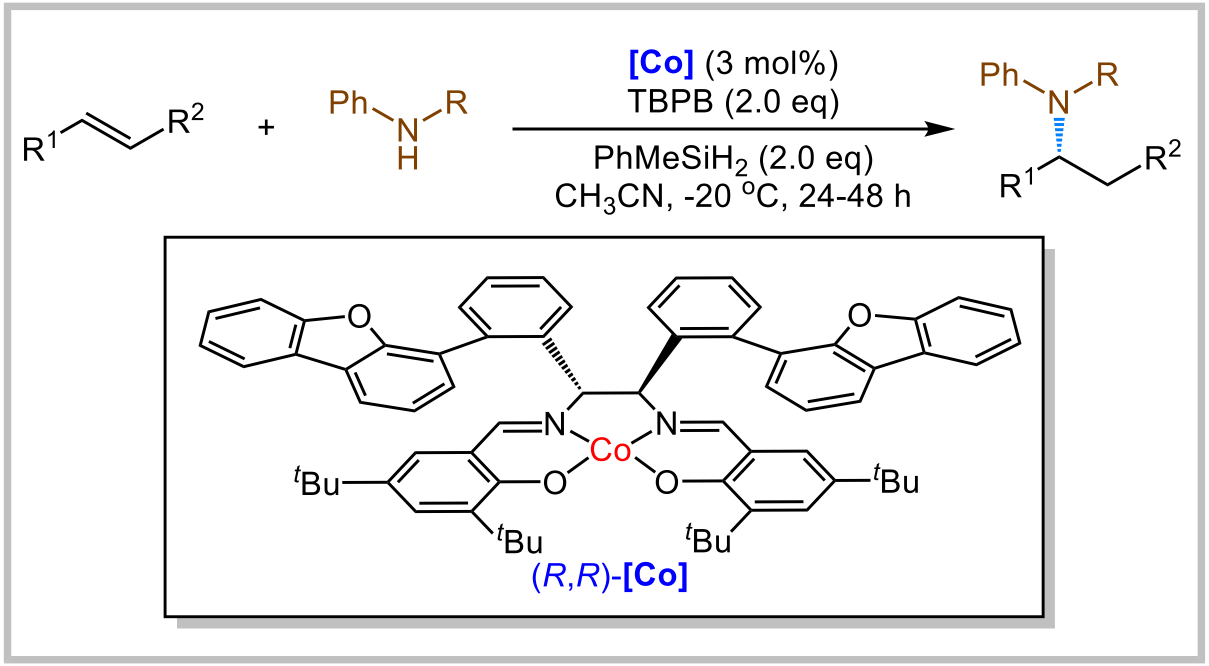
Introduction

Cobalt-Catalyzed Enantioselective Hydroamination



Introduction

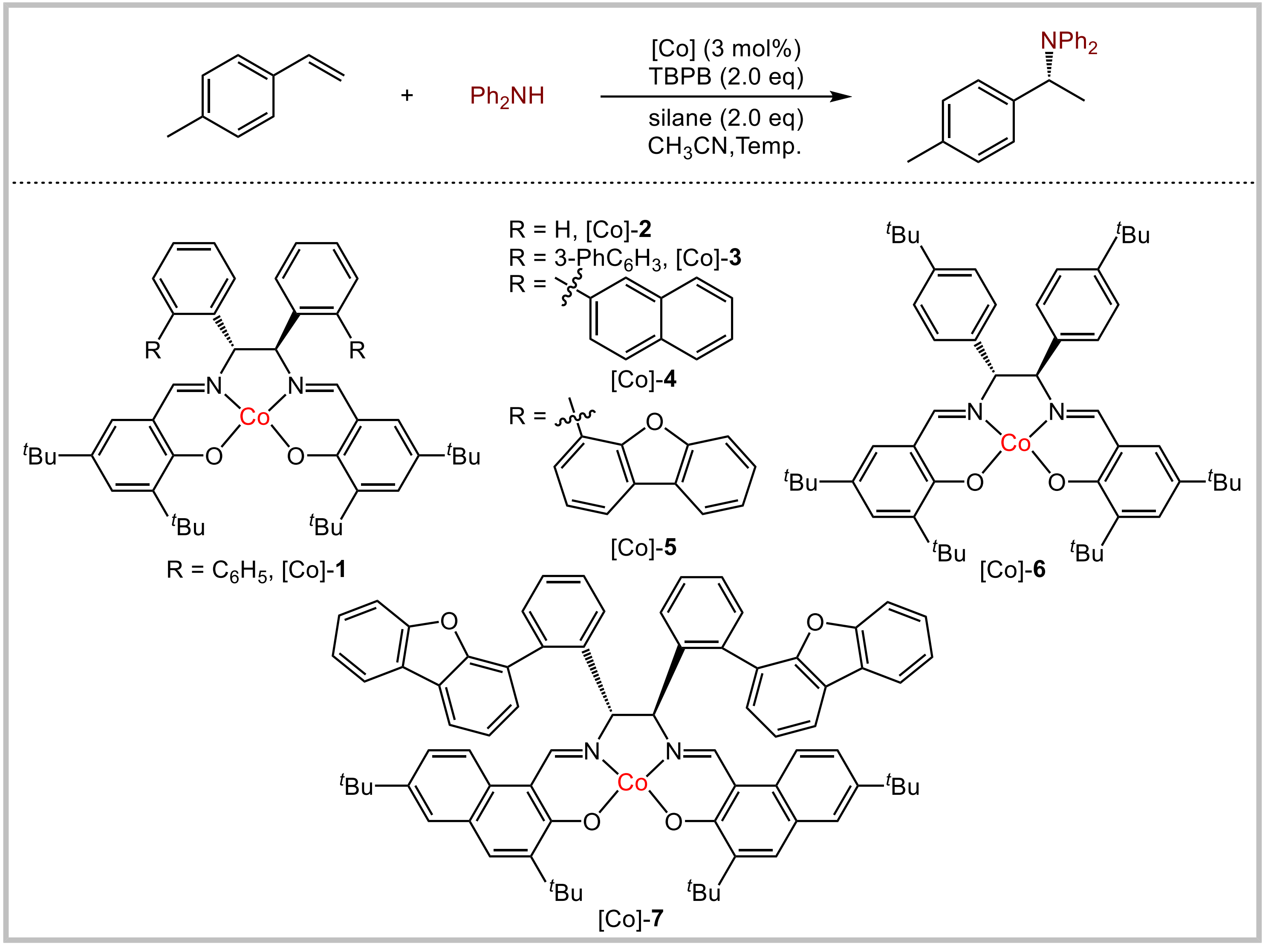
Cobalt-Catalyzed Enantioselective Hydroamination



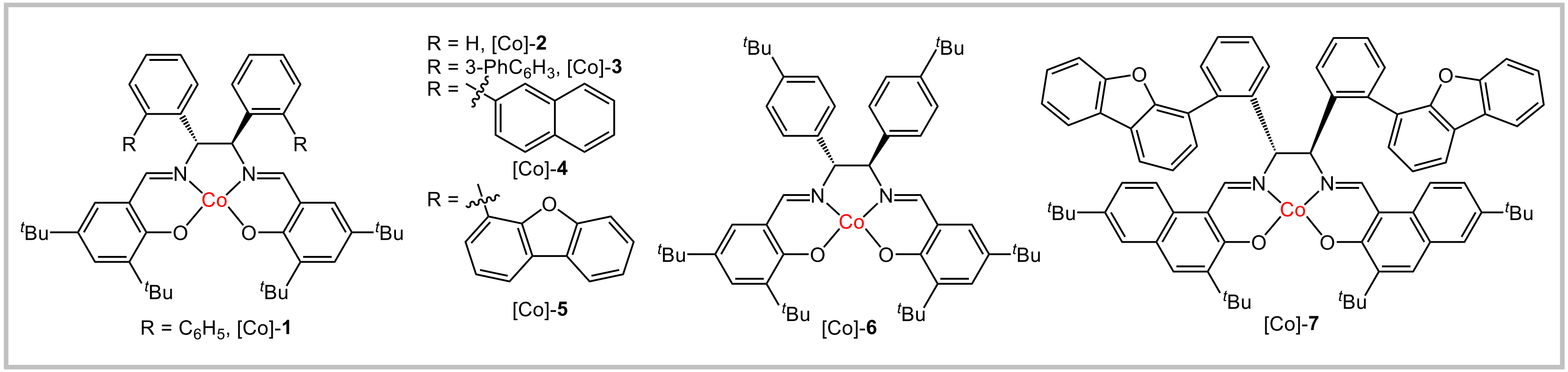
Challenges:

- Reversible homolysis of the C-Co bond in alkylcobalt(III) species;
- Bond cleavage of the C-Co bond in alkylcobalt(IV) species;
- Chain reaction.

Optimization of the Reaction Conditions



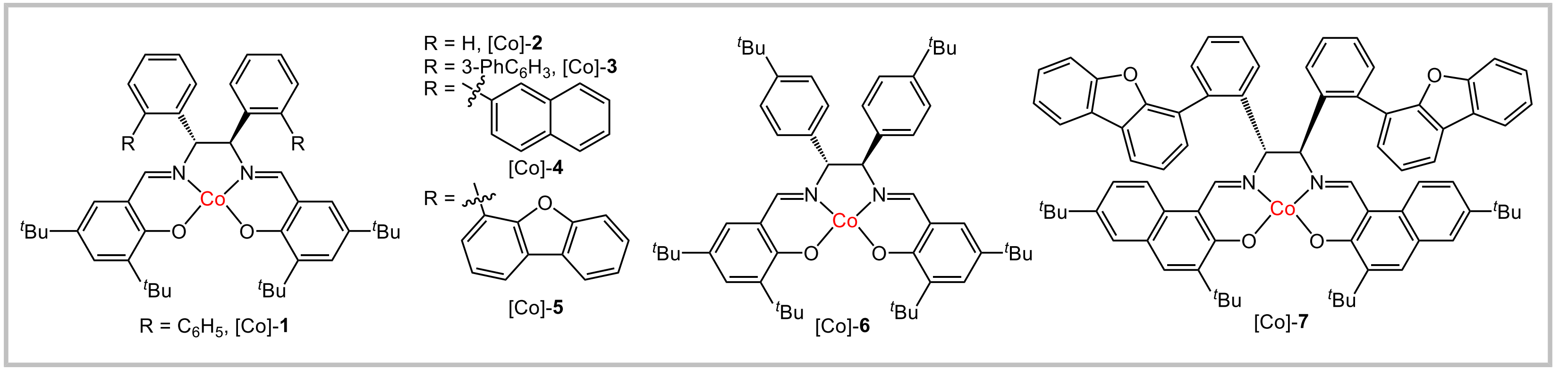
Optimization of the Reaction Conditions



Entry[a]	Catalyst	Silane	Yield	ee
1	[Co]-**1**	TMDS	76%	51%
2	[Co]-**2**	TMDS	60%	3%
3	[Co]-**3**	TMDS	76%	55%
4	[Co]-**4**	TMDS	56%	55%
5	[Co]-**5**	TMDS	94%	81%
6	[Co]-**6**	TMDS	58%	-17%
7	[Co]-**7**	TMDS	48%	35%

[a] Reaction conditions: styrene **1a** (0.2 mmol), amine **2a** (2.0 eq), TBPB (2.0 eq), silane (2.0 eq) and [Co] catalyst (3 mol%) in CH_3CN at 0 °C for 24 h. TBPB = *tert-butyl* peroxybenzoate

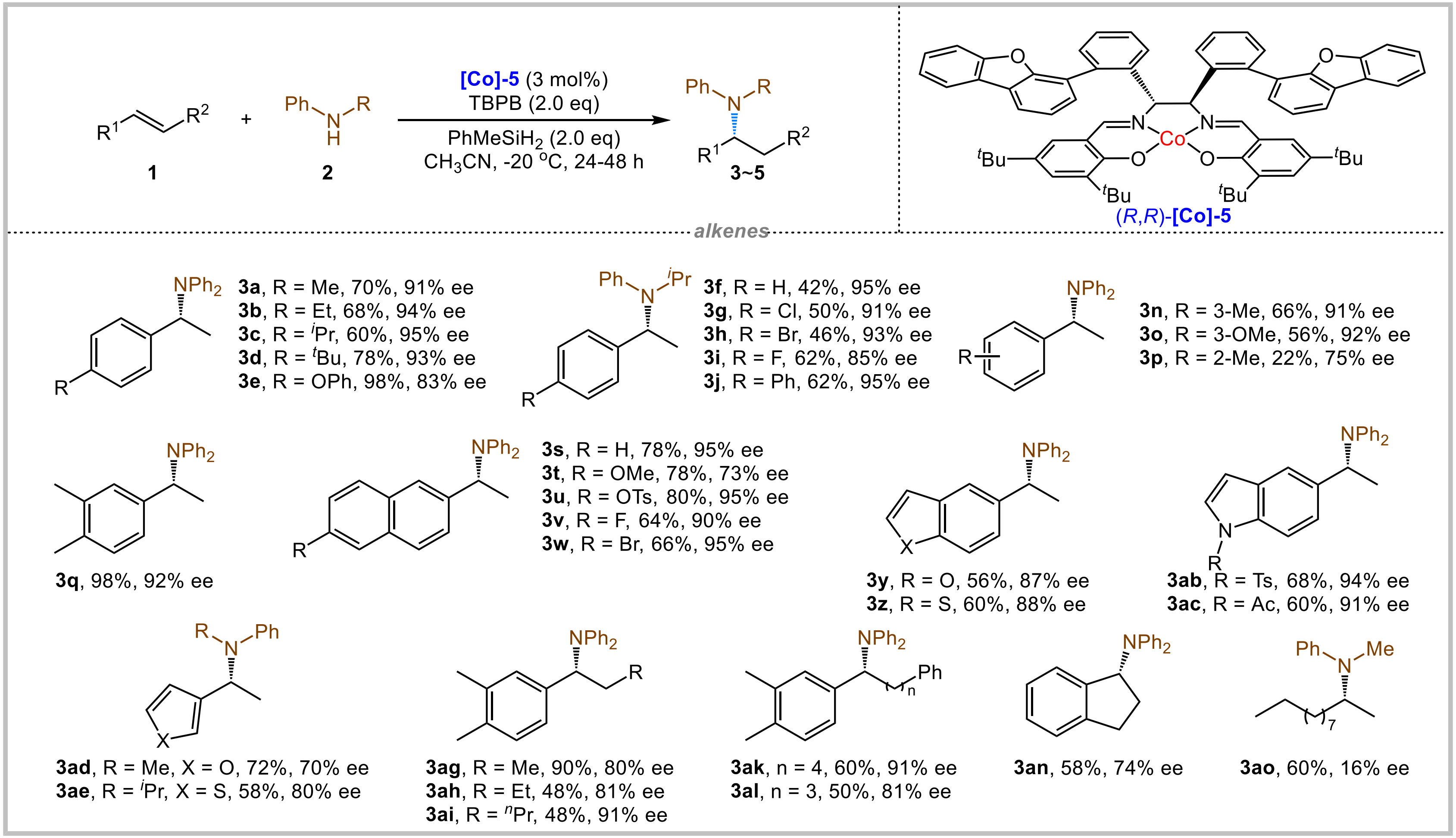
Optimization of the Reaction Conditions



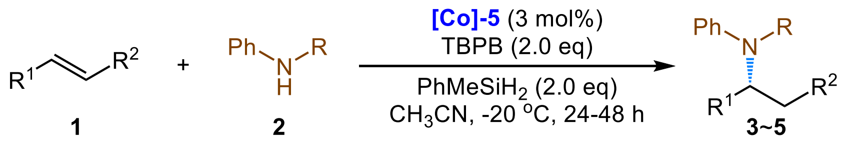
Entry[a]	Catalyst	Silane	Yield	ee
5	[Co]-**5**	TMDS	94%	81%
8[b]	[Co]-**5**	TMDS	72%	83%
9[b]	[Co]-**5**	$PhSiH_3$	60%	89%
10[b]	[Co]-**5**	Et_2SiH_2	76%	89%
11[b]	[Co]-**5**	$PhMe_2SiH$	60%	89%
12[b]	[Co]-**5**	$PhMeSiH_2$	72%	90%
13[b,c]	[Co]-**5**	$PhMeSiH_2$	70%	91%

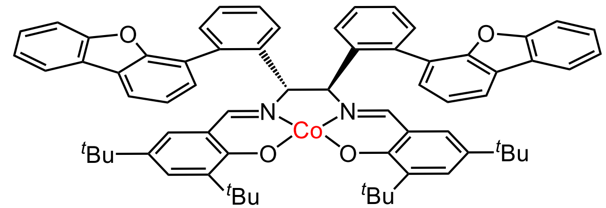
[a] Reaction conditions: styrene **1a** (0.2 mmol), amine **2a** (2.0 eq), TBPB (2.0 eq), silane (2.0 eq) and [Co] catalyst (3 mol%) in CH_3CN at 0 ^oC for 24 h. [b] -20 ^oC for 48 h. [c] Using 1.5 eq of **2a**. TBPB = *tert-butyl* peroxybenzoate

Substrate Scope



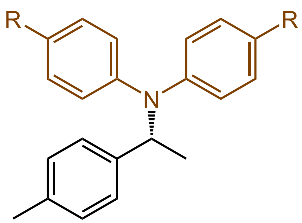
Substrate Scope

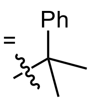


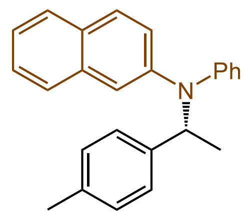


(*R*,*R*)-**[Co]-5**

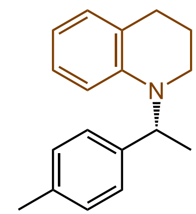
secondary amines



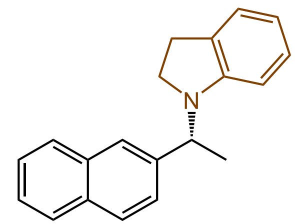
4a, R = Me, 70%, 92% ee
4b, R = *t*Bu, 55%, 92% ee
4c, R = OMe, 98%, 71% ee
4d, R = Br, 50%, 53% ee
4e, R =  , 54%, 90% ee



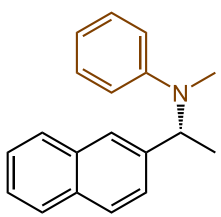
4f, 50%, 87% ee



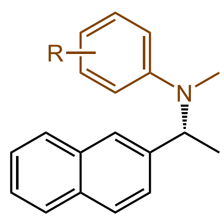
4h, 46%, 76% ee



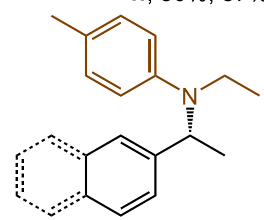
4i, 44%, 81% ee



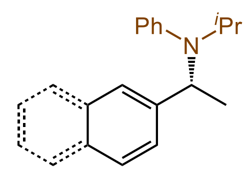
4j, 74%, 77% ee



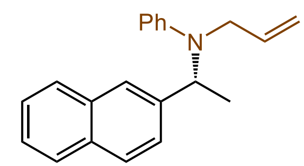
4k, R = 4-Me, 40%, 87% ee
4l, R = 4-Cl, 62%, 81% ee
4m, R = 4-OMe, 44%, 79% ee



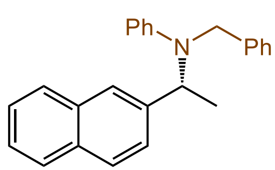
4n, from **1s**, 90%, 71% ee
4o, from **1a**, 55%, 71% ee



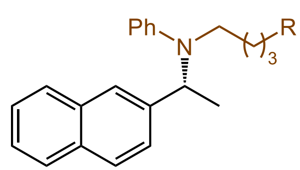
4p, from **1s**, 42%, 97% ee
4q, from **1a**, 60%, 91% ee



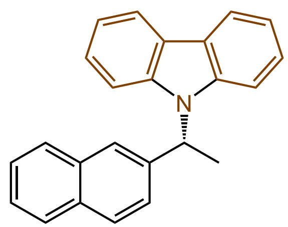
4s, 72%, 77% ee



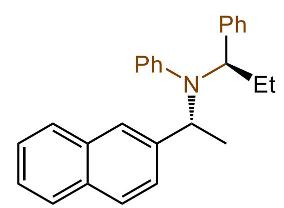
4t, 84%, 83% ee



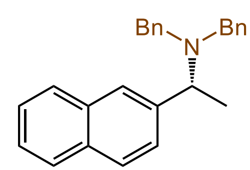
4u, R = Ph, 72%, 91% ee
4v, R = CN, 40%, 91% ee



4x, 44%, 80% ee

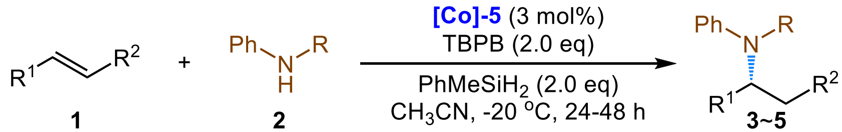


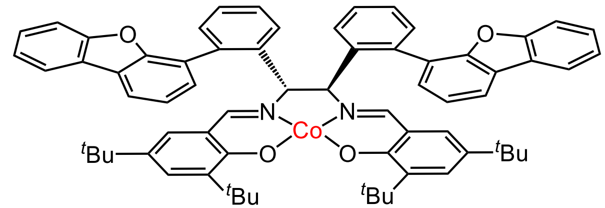
4y, using **(*R*,*R*)-L***, 58%, 99% de
4z, using **(*S*,*S*)-L***, 50%, -99% de



4aa, 22%, 92% ee

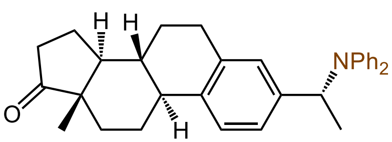
Substrate Scope



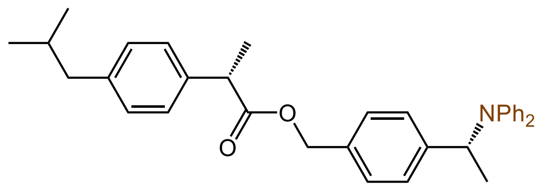


(*R*,*R*)-[Co]-5

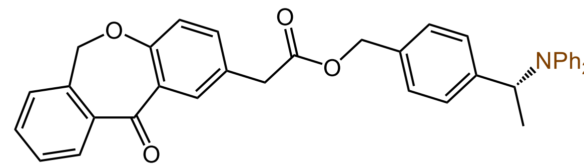
late-stage functionalization of complicated molecules



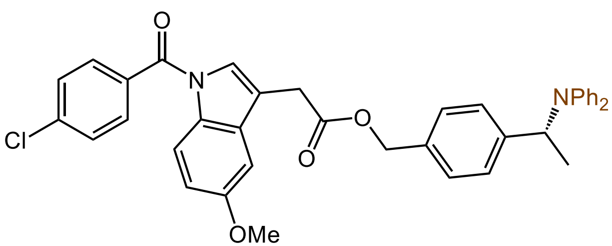
5a, 88%, 96% de



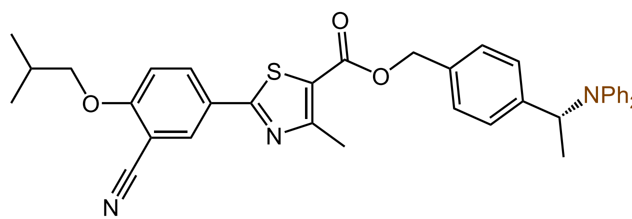
5b, 42%, 92% de



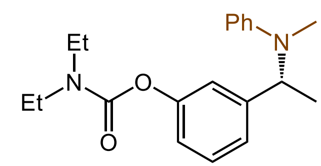
5c, 61%, 93% ee



5d, 76%, 85% ee

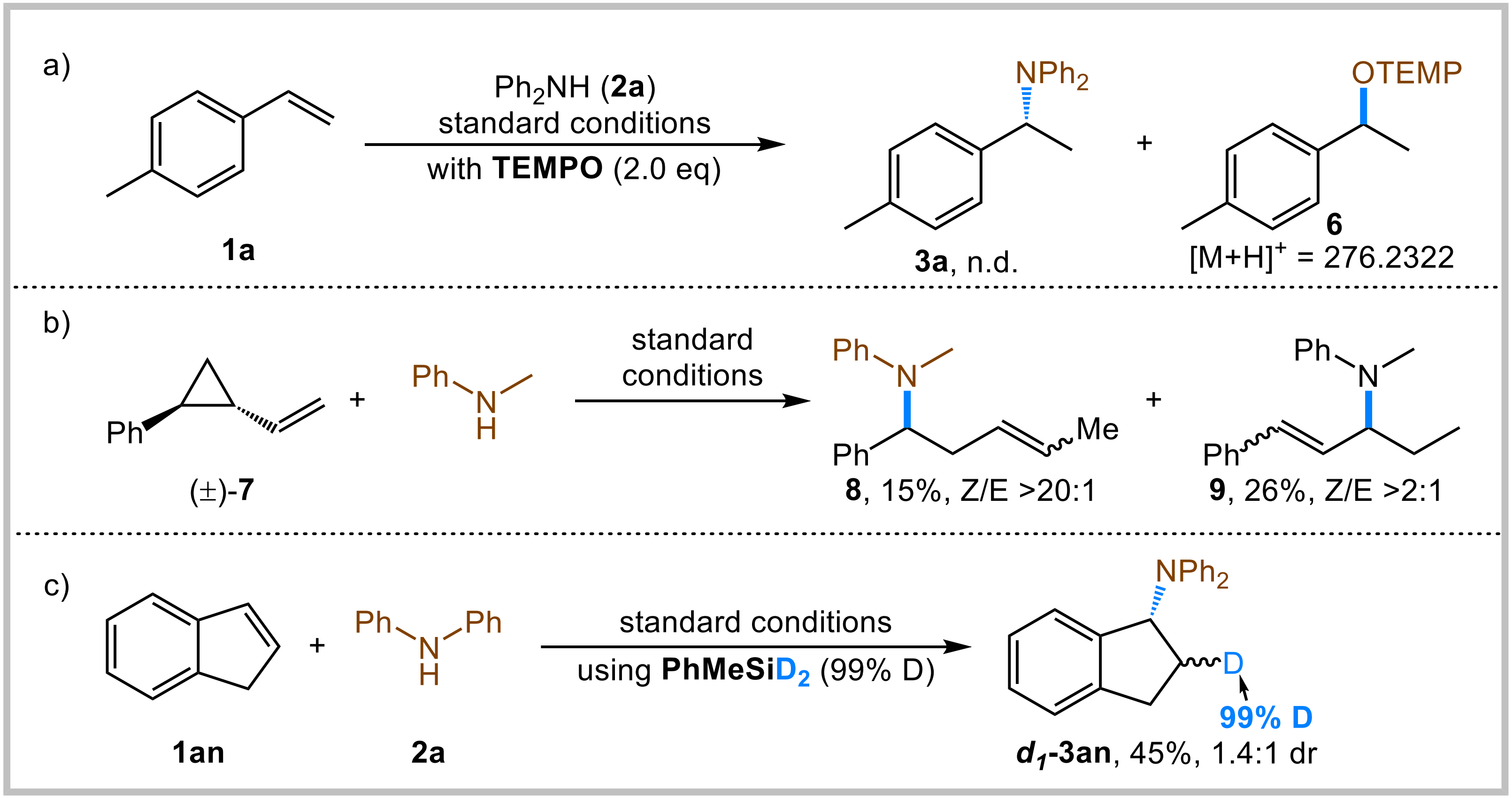


5e, 64%, 91% ee

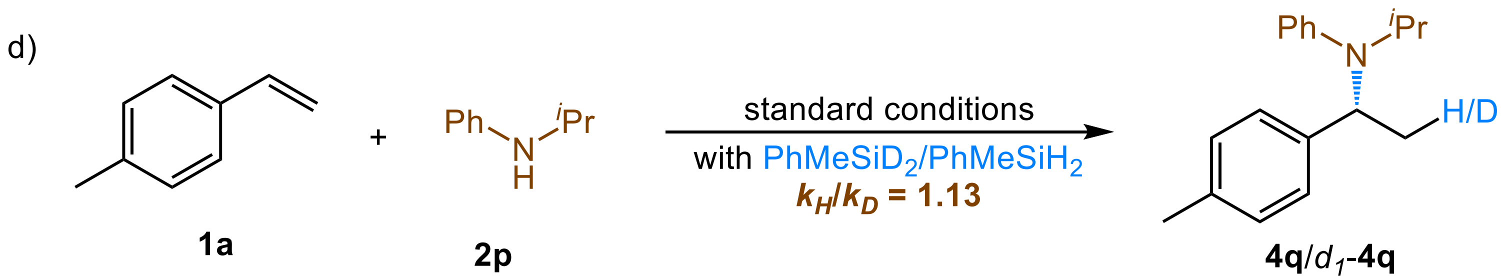


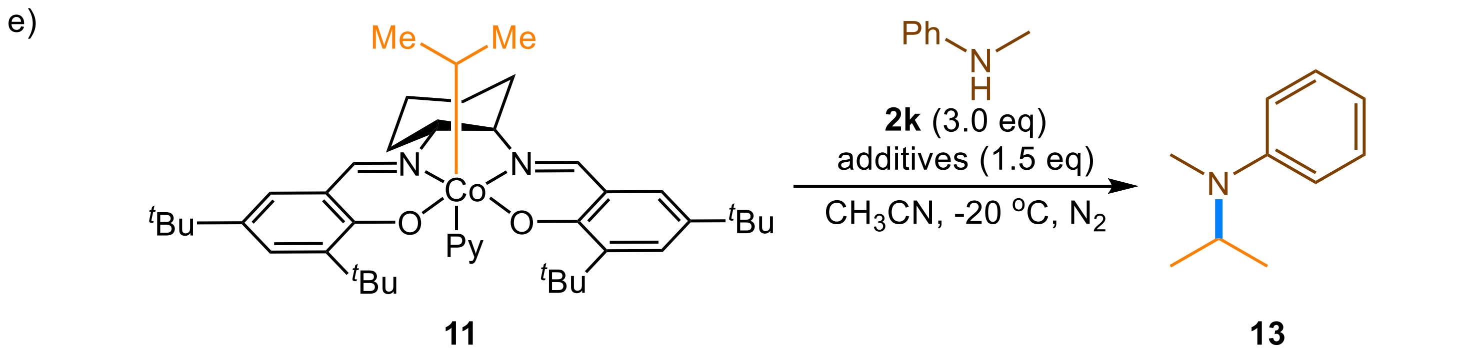
5f, 46%, 85% ee

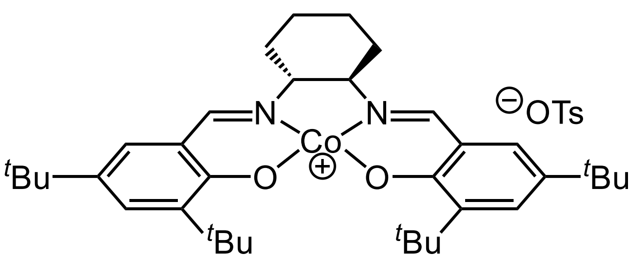
Control Experiments



Control Experiments



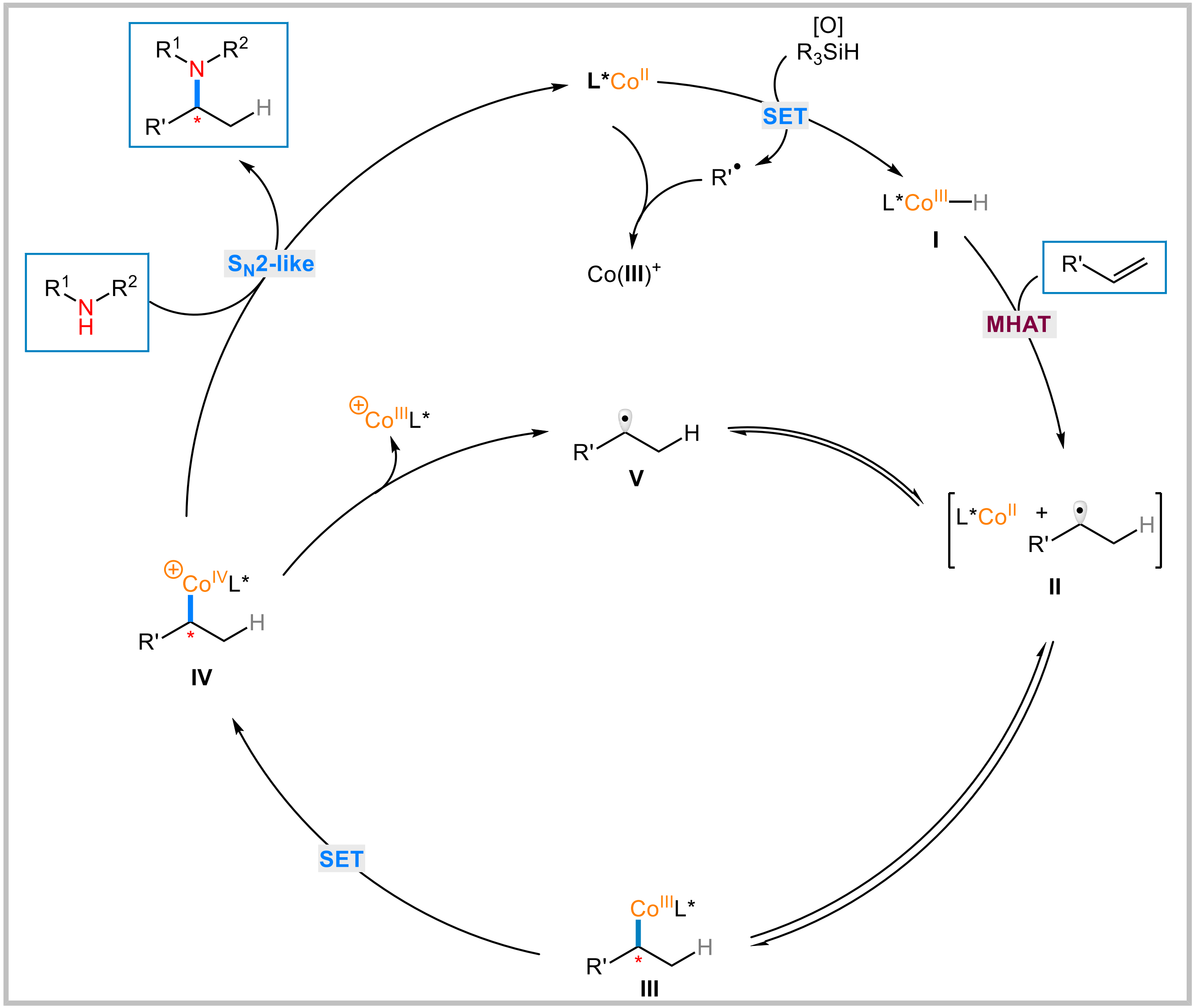




Co(III)·OTs (**12**)

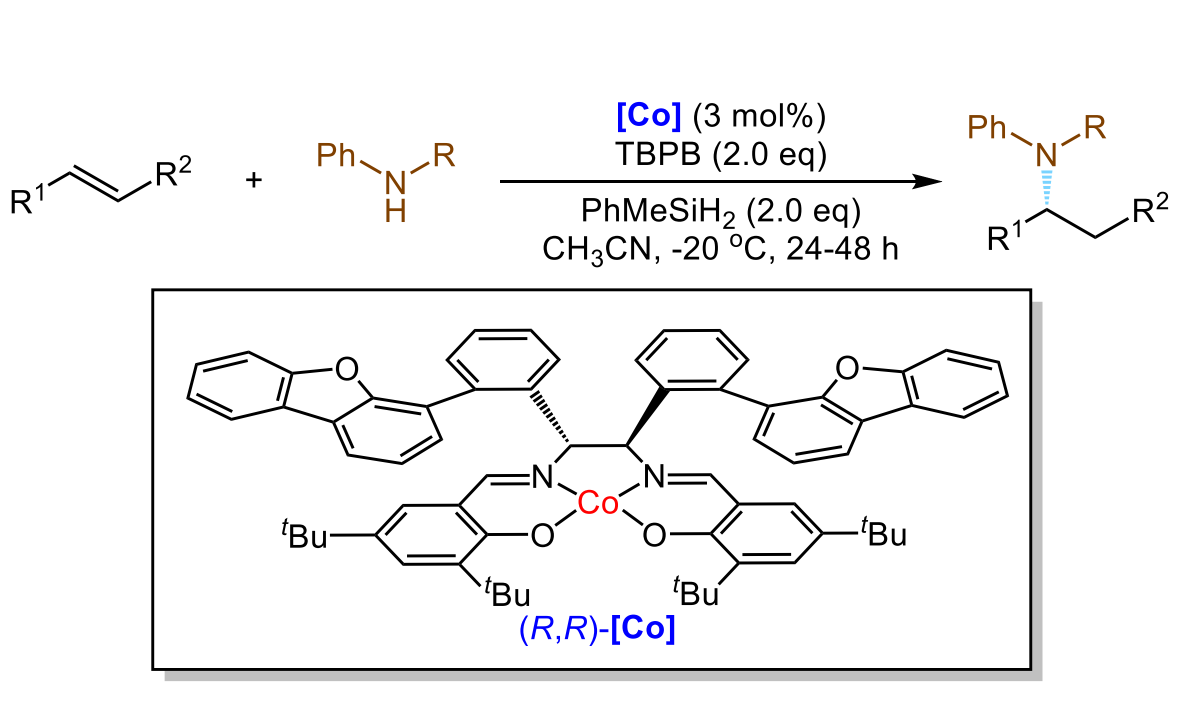
additives	yield of **13**
---	0
Co(III)·OTs (**12**)	38%
TBPB	15%

Proposed Mechanism



Summary

Cobalt-Catalyzed Enantioselective Hydroamination



- Mild conditions;
- Good functional group tolerance;
- Broad substrate scope;
- Application in bioactive compounds.

The First Paragraph

介绍手性叔胺及其重要性

↓

总结不对称氢胺化反应的进展及挑战

↓

指出廉价金属催化体系仍待开发

The First Paragraph

The enantioselective synthesis of α-chiral tertiary amine derivatives is an important undertaking due to the prevalence of this motif in a large number of biologically active natural products and pharmaceuticals as well as agrochemicals. The asymmetric hydroamination of alkenes undoubtedly offers a direct, effective, and atom-economical approach to these important motifs from readily available starting materials. However, the intermolecular enantioselective hydroamination of alkenes directly using Lewis basic amines as nucleophiles has long been a challenging task in synthetic chemistry.

The First Paragraph

This is mainly due to the intrinsic strong coordination of Lewis basic amines with transition metal and the electrostatic repulsion between the olefin π-system and the nitrogen lone pair, thus most reported asymmetric alkene hydroamination are limited to reactions of amines preinstallated with an electro-withdrawing group. Significant progress recently has been made in ···. Despite with these advances, the development of efficient methods for enantioselective alkene hydroamination of secondary amines, especially using the cheap first-row transition metal catalysts, is still an ideal strategy for synthetically important *α*-chiral tertiary amines and particularly appealing.

The Last Paragraph

总结本文工作

↓

强调方法优势

↓

展望未来发展

The Last Paragraph

In conclusion, by exploiting Co(II)H catalysis, we have accomplished an enantioselective radical hydroamination of arylalkenes with Lewis basic secondary amine, thereby enabling an efficient and alternative strategy for the asymmetric synthesis of α-branched tertiary amines in which the key chiral C−N bond formation via TM-HAT integrated with radical-polar crossover process. This mode reaction operates under mild conditions, displays good functional group tolerance, broad substrate scope, and can be used in the last-stage functionalization of complex bioactive compounds. Further investigations on the development of new cobalt catalytic systems and their application in oxidative MHAT with various free nucleophiles are underway in our laboratory.

Representative Examples

- Due to **the prevalence of this motif in**··· （该结构在··· 中广泛存在）

- This approach **furnishes an expedient and straightforward route to** the synthesis of chiral α-tertiary amines ··· （提供方便和直接的路线）

- To **gain more insight into** the mechanism, ··· （深入了解）

Thanks

for your attention !