Literature Report X

From Conjugated to Enantioenriched Skipped Dienes: Co-Catalyzed Asymmetric Cross-Hydrodimerization of 1,3-Dienes and Alkynes

Reporter: Bao-Qian Zhao
Checker: Yan-Xin Sun
Date: 2025-12-29

Meng, H.; Xia, Y.-L.; Yu, Q.; Li, Y.-L.; Shu, W. *J. Am. Chem. Soc.* **2025**, *147*, 41738

CV of Prof. Shu Wei (舒伟)

Research:

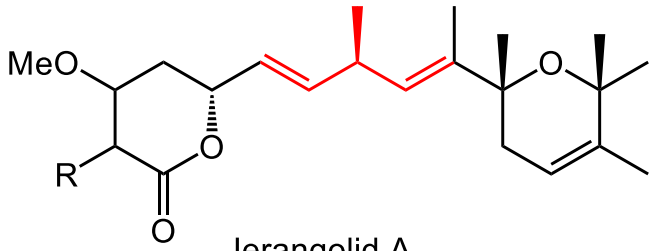
Asymmetric catalysis and synthesis & Merging catalysis of visible light and transition metals

Background:

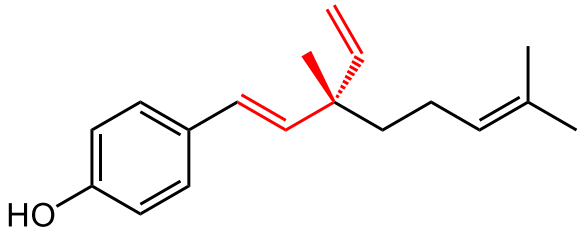
- **2001-2005** B.S., Nankai University
- **2005-2010** Ph.D., Shanghai Institute of Organic Chemistry, CAS
- **2010-2014** Postdoc., University of Zurich
- **2014-2018** Postdoc., Princeton University
- **2018-Now** Professor, Southern University of Science and Technology

Contents

Introduction



Jerangolid A



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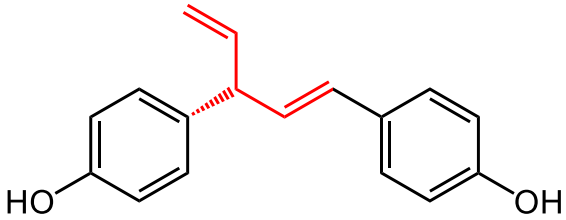
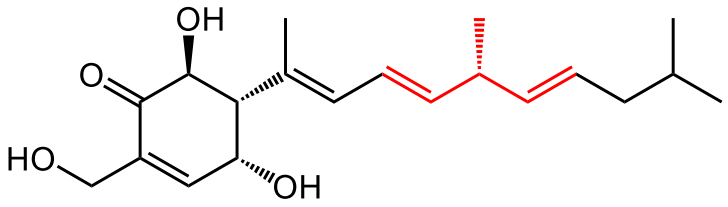


(-)-Hinokiresinol



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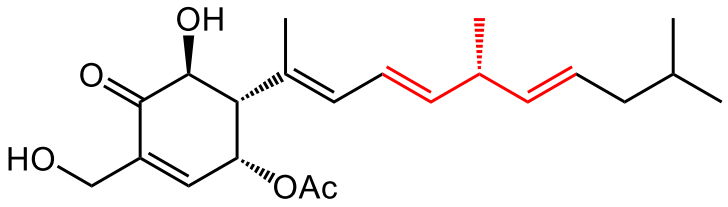
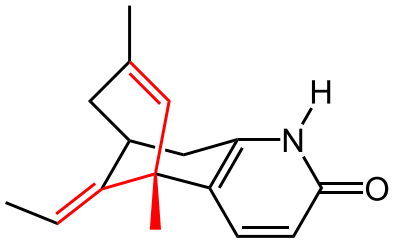
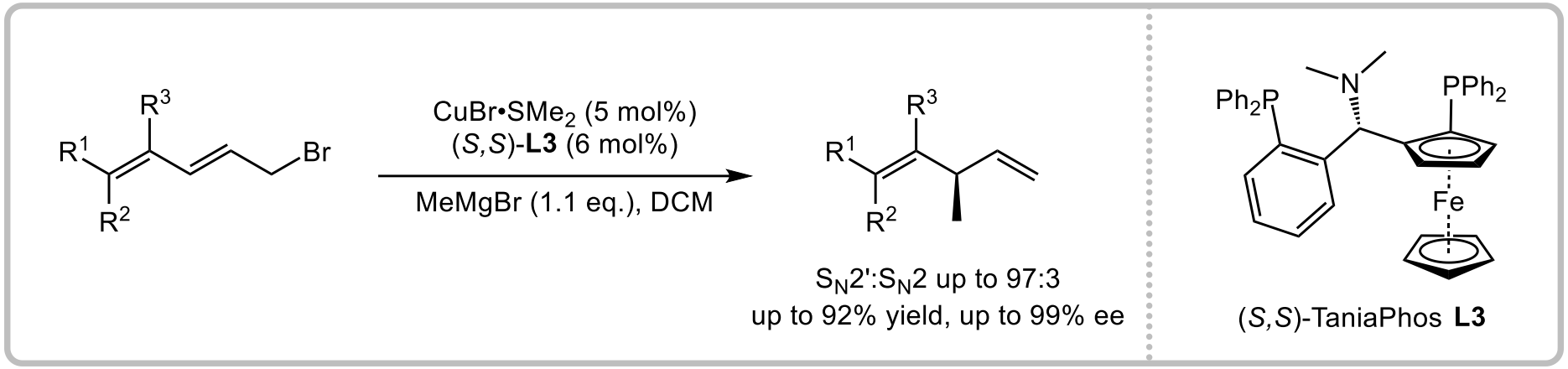


(-)-Phorbasin C



(-)-Huperzine

Introduction



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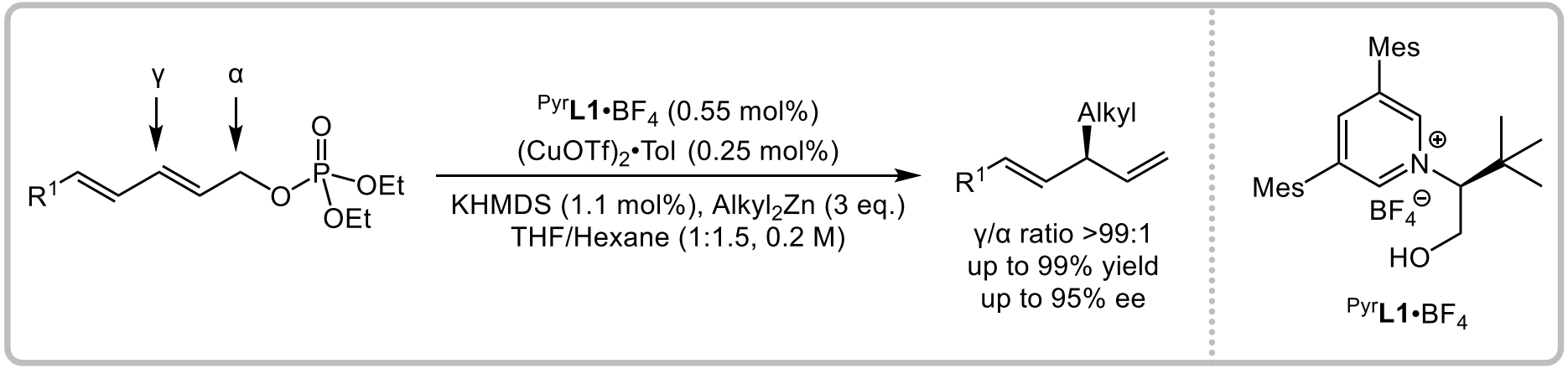

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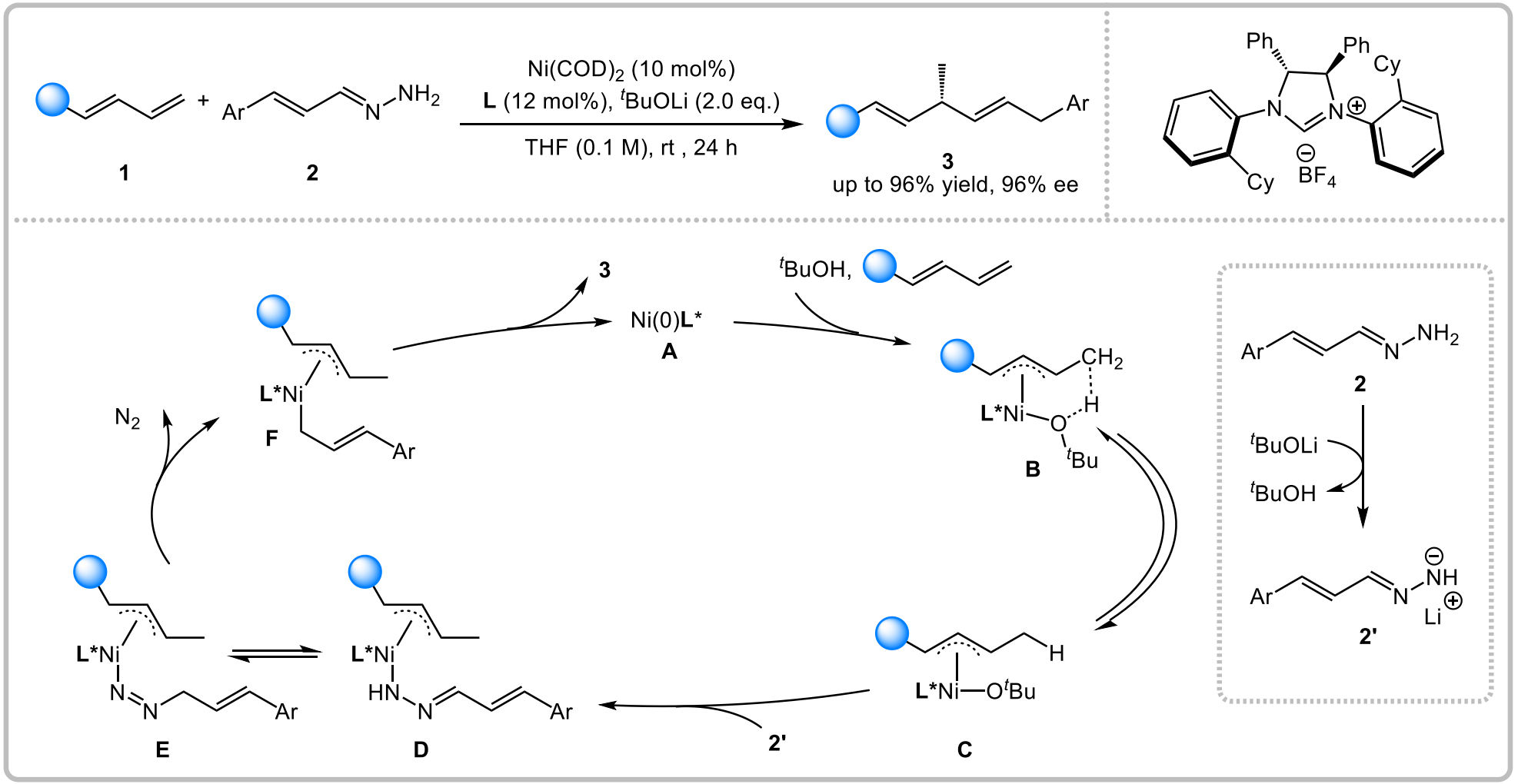
Introduction



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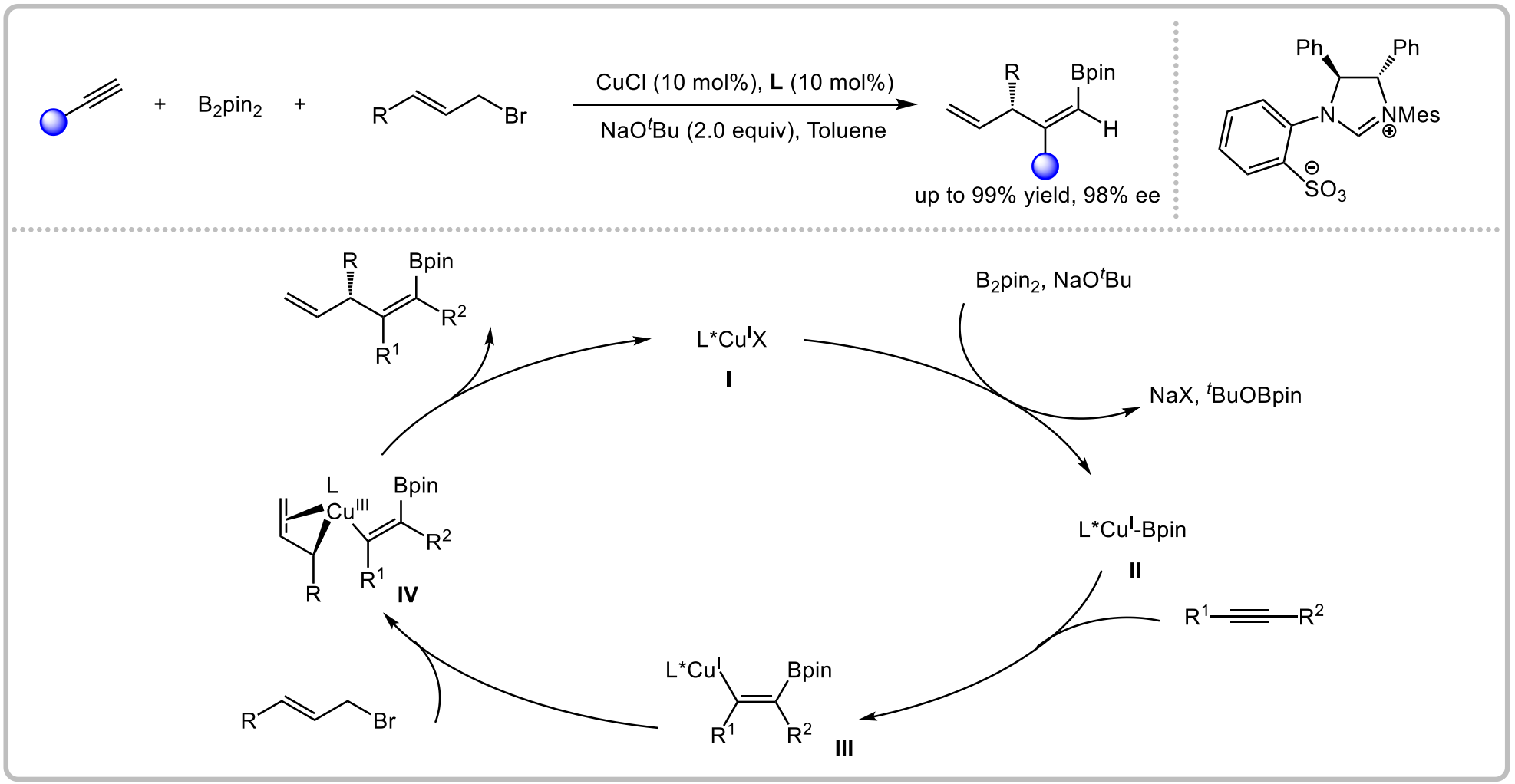

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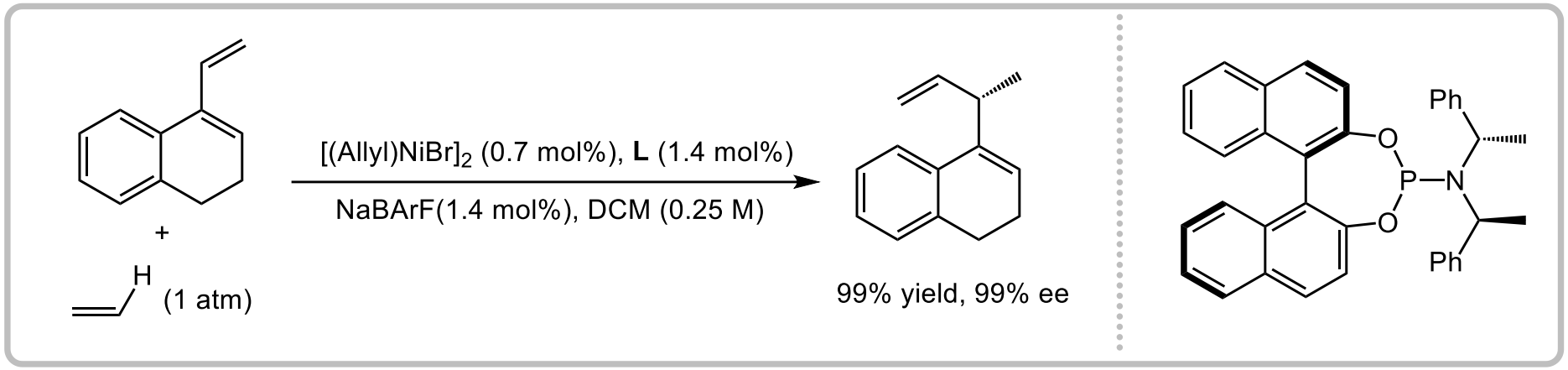
Introduction



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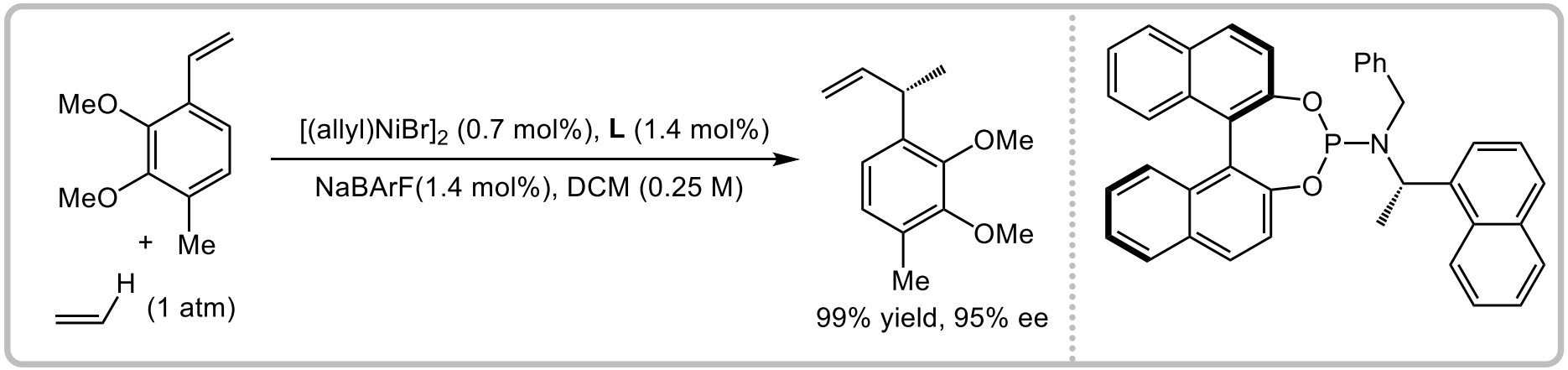

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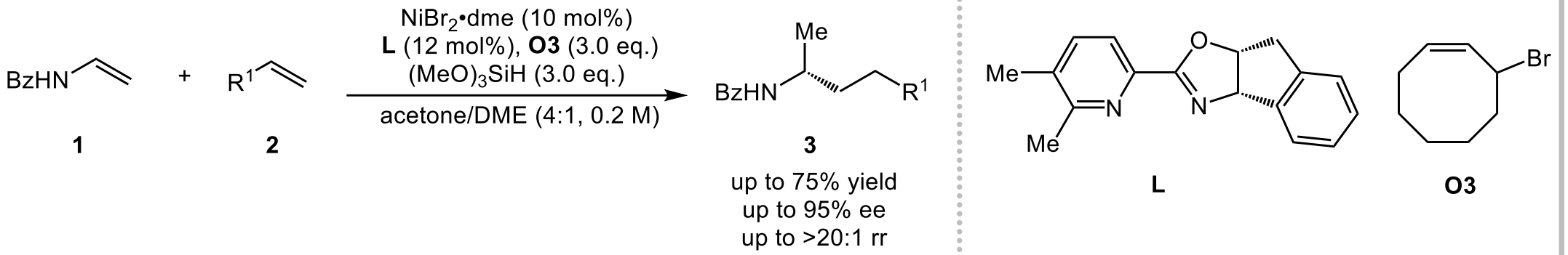
Introduction



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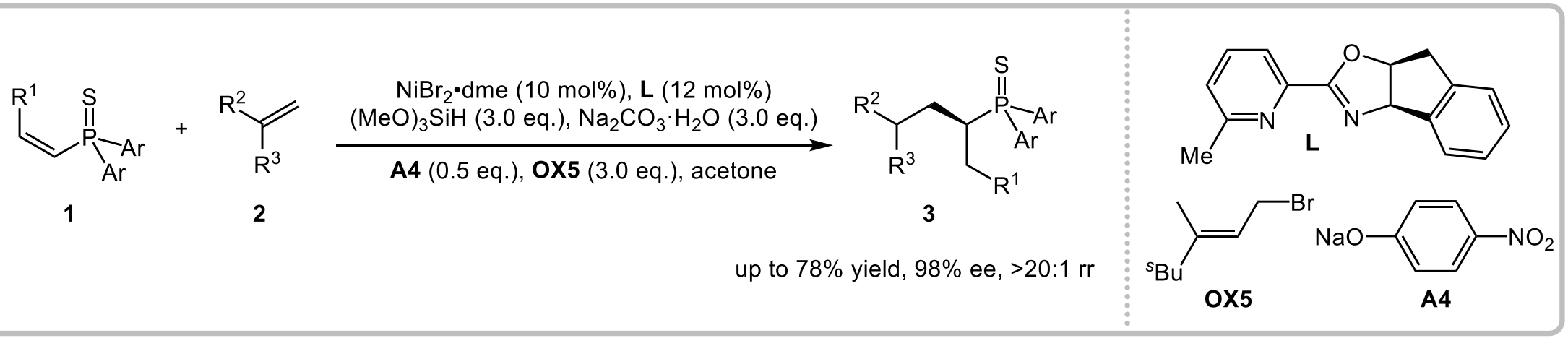
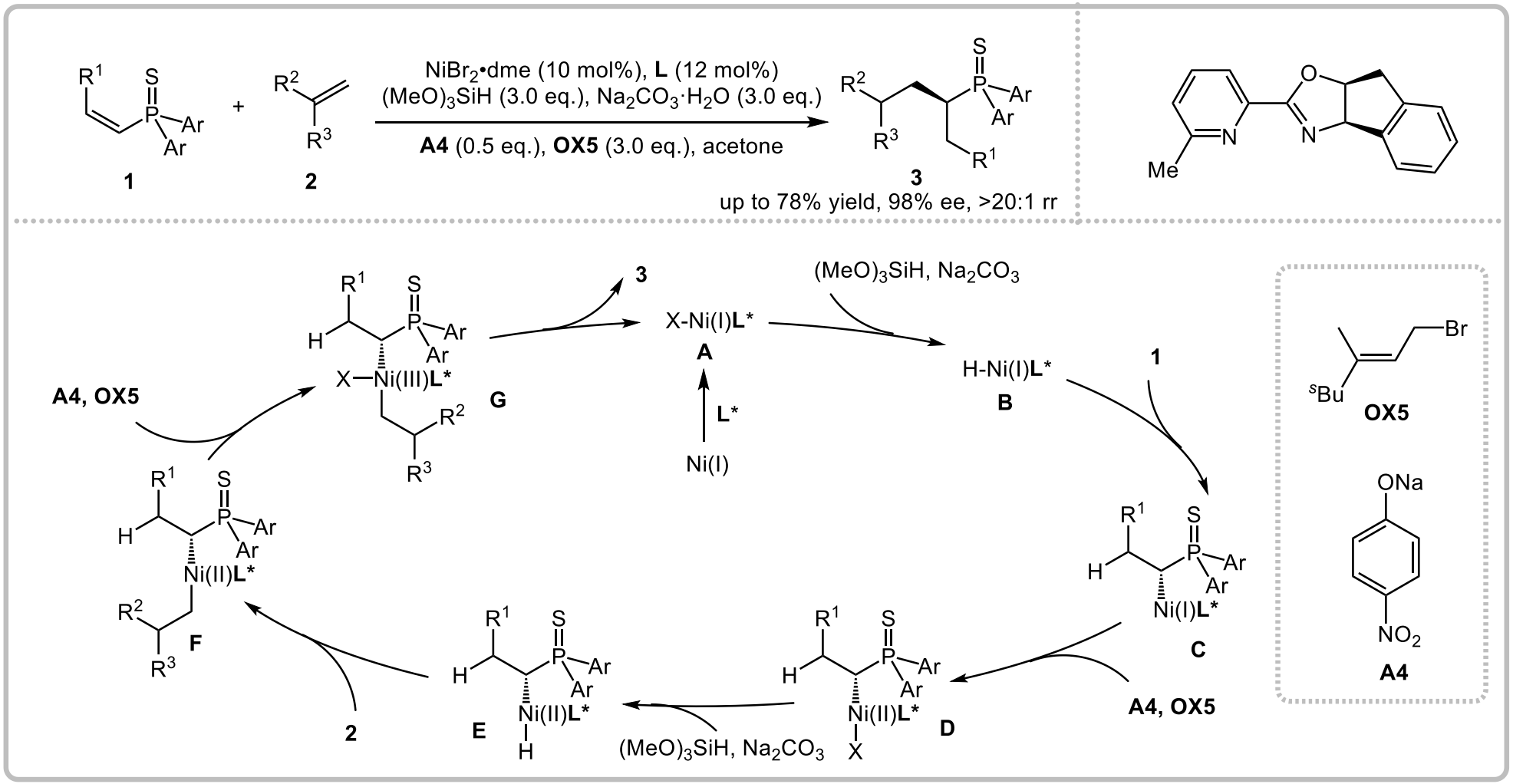


Zou, J.-Y.; Xing, F.-L.; Zi, Q.-X.; Du, H.-W.; Chen, M.; Shu, W. *Sci. Adv.* **2025**, *11*, eadv6571

Introduction



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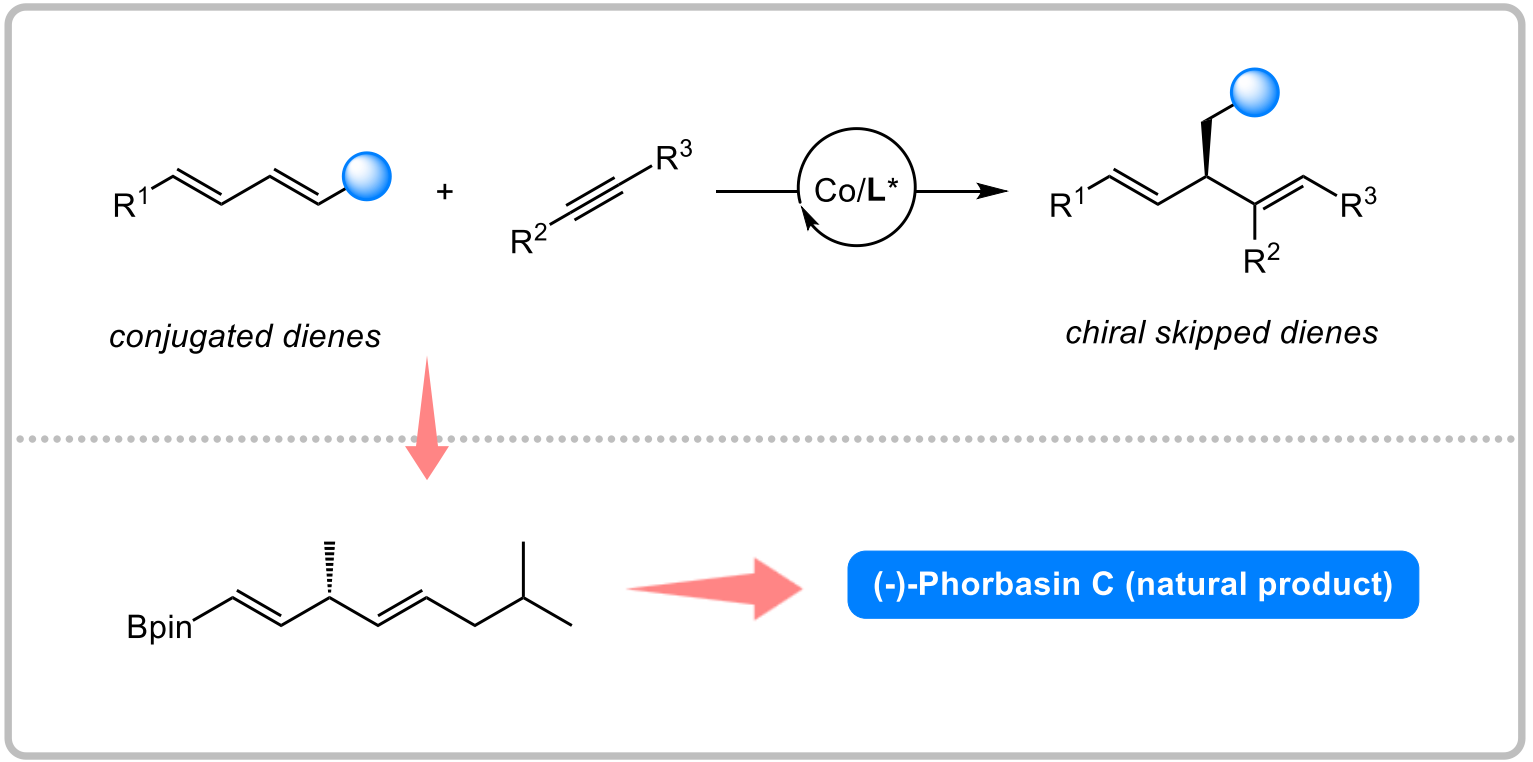
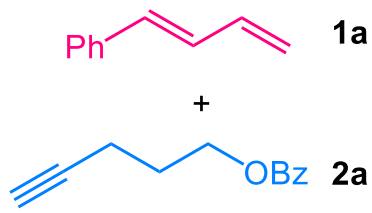
Introduction



✓ **homo-coupling *VS* cross-coupling** ✓ **regio-, and enantioselecivity control**

Optimazation Conditions

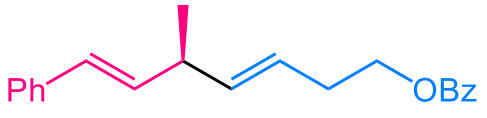


1a

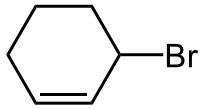
+

2a

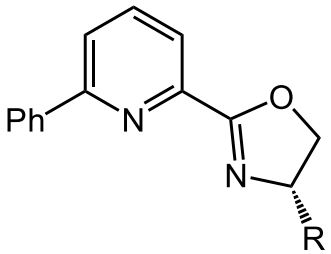
$CoBr_2$•dme (10 mol%), **L** (12 mol%)
$(MeO)_3SiH$ (3.0 equiv), Na_3PO_4 (3.0 equiv)
A1 (3.0 equiv), rt, 14 h, wet THF (0.1 M)



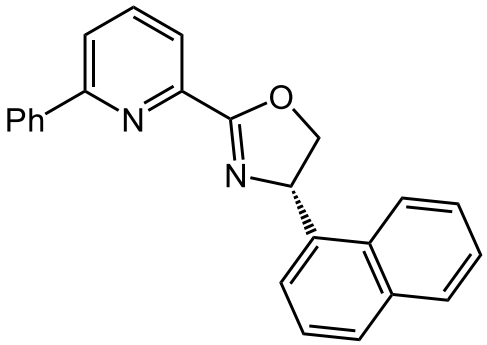
3a



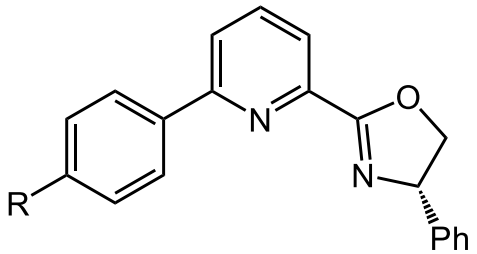
A1



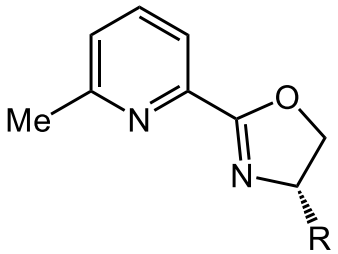
L1: R = Ph, 26%, 95% ee
L2: R = Bn, N.D.
L3: R = ^{t}Bu, N.D.



L4: 24%, 94% ee

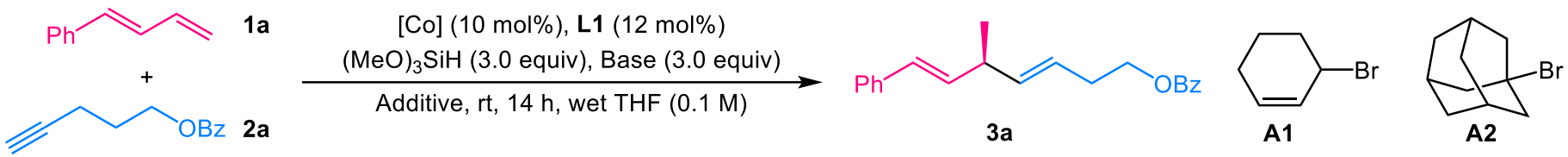


L5: R = OPh, 27%, 94% ee
L6: R = CO_2Me, 22%, 93% ee



L7: R = Ph, trace, 7% ee
L8: R = Bn, 2%, 5% ee

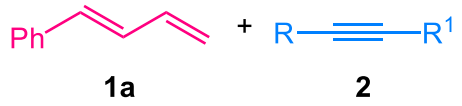
Optimazation Conditions



Entry	[Co]	Base	Additive (eq.)	Yield (%)	Ee (%)
1	$CoBr_2$·dme	Na_3PO_4	**A1 (3.0)**	26	95
2	$CoBr_2$·dme	$KHCO_3$	**A1 (3.0)**	33	94
3	$CoBr_2$·dme	$KHCO_3$	**A2 (3.0)**	41	88
4	$CoBr_2$	$KHCO_3$	**A2 (3.0)**	46	90
5	$CoBr_2$	$KHCO_3$	**A1 (2.0)**, **A2 (3.0)**	52	93
6[b]	$CoBr_2$	$KHCO_3$	**A1 (2.0)**, **A2 (3.0)**	-	-
7[b,c]	$CoBr_2$	$KHCO_3$	**A1 (2.0)**, **A2 (3.0)**	85	94
8[b,c,d]	$CoBr_2$	$KHCO_3$	**A1 (2.0)**, **A2 (3.0)**	90	94
9[b,c,d,e]	$CoBr_2$	$KHCO_3$	**A1 (1.0)**, **A2 (1.5)**	87	92

[a] **1a** (0.10 mmol), **2a** (0.30 mmol). Yield was determined by GC analysis. Ee was determined by HPLC. Isolated yield is shown in parentheses. [b]Dry THF was used. [c]THF/3-methyl-1-butanol (3/7, 0.25 M) was used. [d] using **1a** (1.3 equiv) and **2a** (1.0 equiv). [e] $(MeO)_3SiH$ (2.5 equiv) was used.

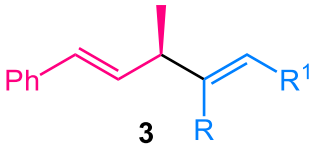
Substrate Scope



1a **2**

$CoBr_2$ (10 mol%), **L1** (12 mol%)
$(MeO)_3SiH$ (2.5 equiv), $KHCO_3$ (3.0 equiv)

A1 (1.0 equiv), **A2** (1.5 equiv), rt, 14 h
THF/3-methyl-1-butanol (3/7, 0.25 M)



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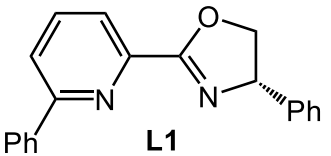
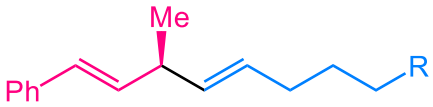
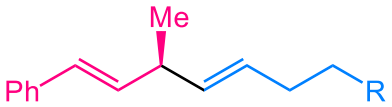


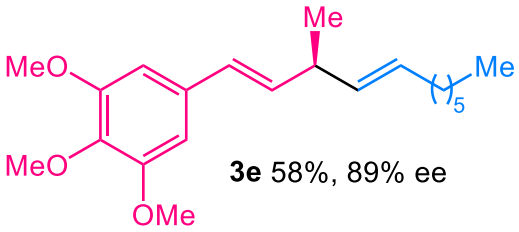
L1



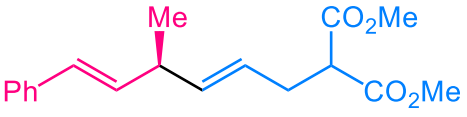
3a R = OBz, 79%, 92% ee
3b R = OH, 67%, 90% ee



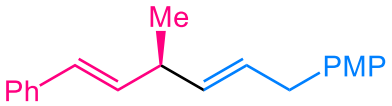
3c R = OTs, 88%, 91% ee
3d R = Ph, 81%, 91% ee



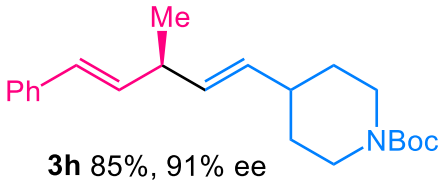
3e 58%, 89% ee



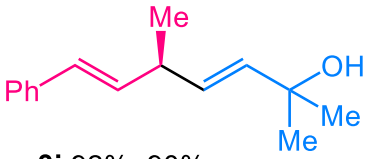
3f 76%, 92% ee



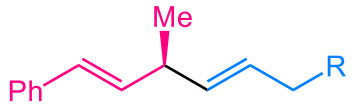
3g 82%, 86% ee



3h 85%, 91% ee

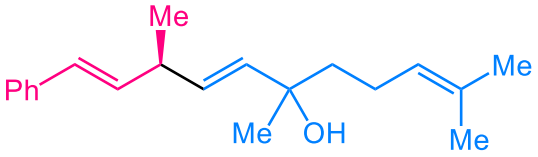


3i 92%, 90% ee

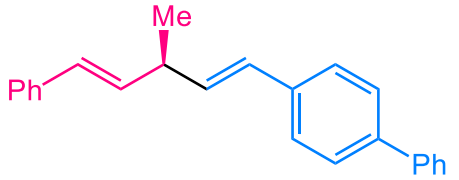


3j R = NHBz, 63%, 90% ee
3k R = OPh, 85%, 91% ee
3l R = OBn, 88%, 91% ee

3m 61%, 90% ee

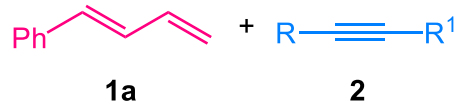


(+/-)-dehydrolinalool
3o 92%, 1.2:1 dr, 88% ee, 90% ee



3p 87%, 95% ee (X-ray)

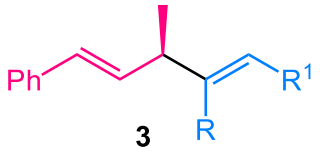
Substrate Scope



1a + **2**

$CoBr_2$ (10 mol%), **L1** (12 mol%)
$(MeO)_3SiH$ (2.5 equiv), $KHCO_3$ (3.0 equiv)

A1 (1.0 equiv), **A2** (1.5 equiv), rt, 14 h
THF/3-methyl-1-butanol (3/7, 0.25 M)



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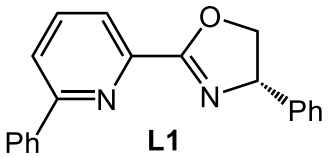
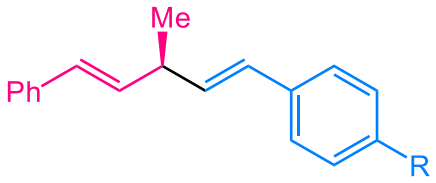
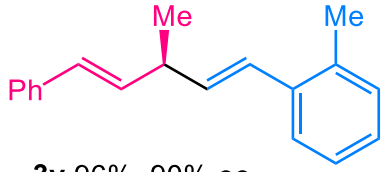


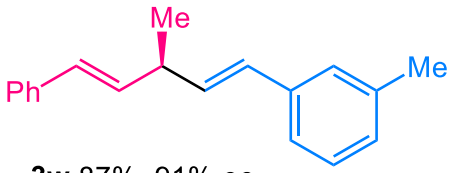
L1



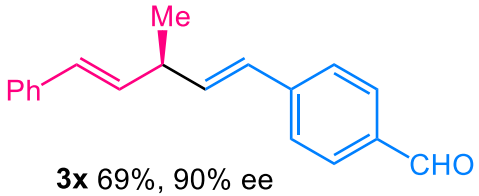
3q R = ^{t}Bu, 98%, 91% ee
3r R = OMe, 87%, 90% ee
3s R = Br, 99%, 90% ee
3t R = Cl, 86%, 91% ee
3u R = CO_2Me, 87%, 89% ee



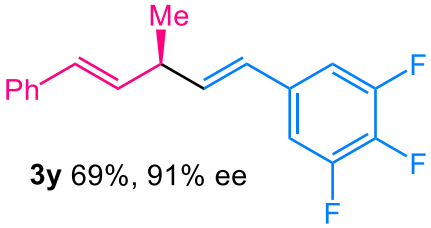
3v 96%, 90% ee



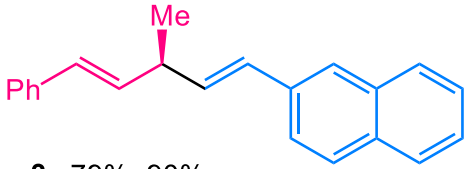
3w 87%, 91% ee



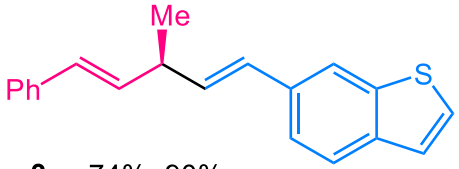
3x 69%, 90% ee



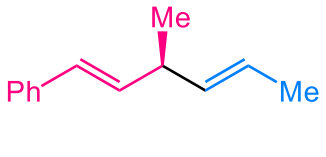
3y 69%, 91% ee



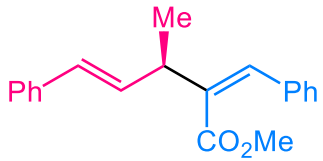
3z 79%, 90% ee



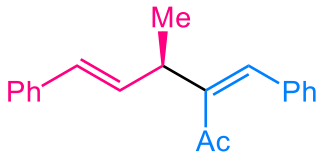
3aa 74%, 90% ee



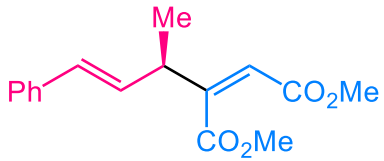
3ab 83%, 90% ee



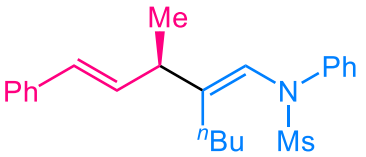
3ac 65%, 92% ee



3ad 66%, 93% ee

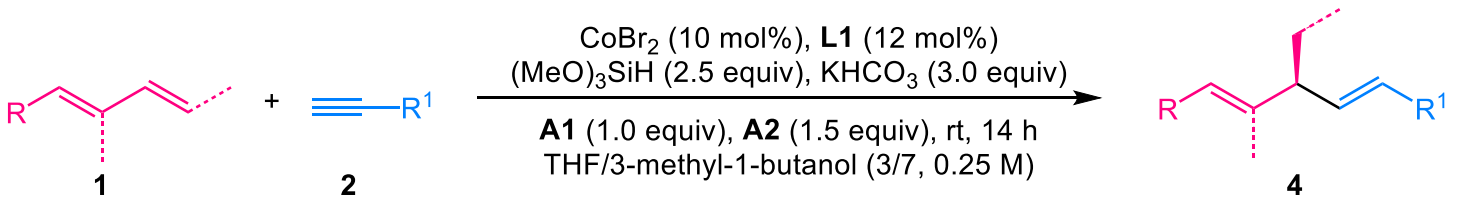


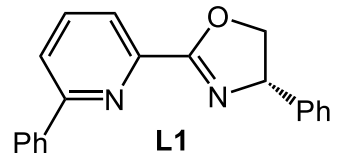
3ae 58%, 91% ee

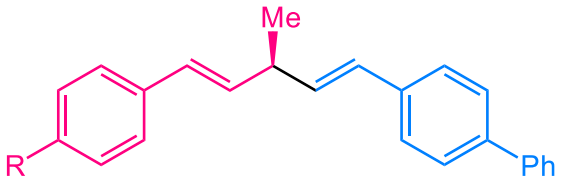


3af 65%, 88% ee

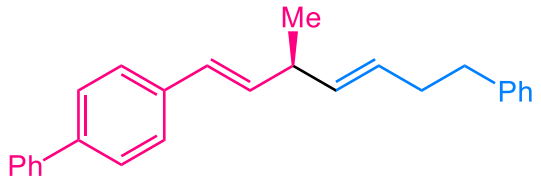
Substrate Scope



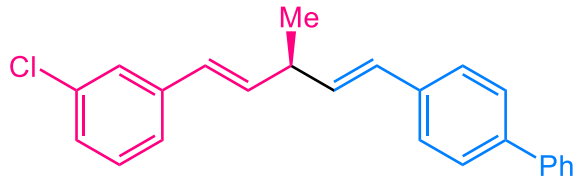




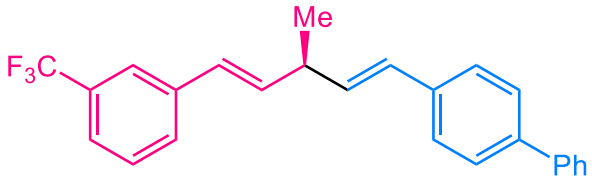
4a R =NMe_2, 71%, 86% ee
4b R = OMe, 68%, 94% ee
4c R = ^{t}Bu, 64%, 90% ee
4d R = Me, 60%, 87% ee
4e R = F, 87%, 93% ee
4f R = Cl, 57%, 91% ee
4g R = Br, 72%, 92% ee



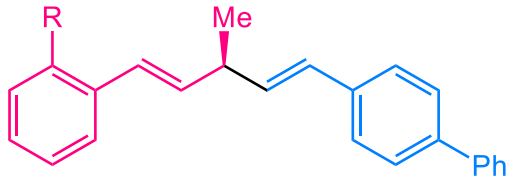
4h 81%, 89% ee



4i 89%, 91% ee

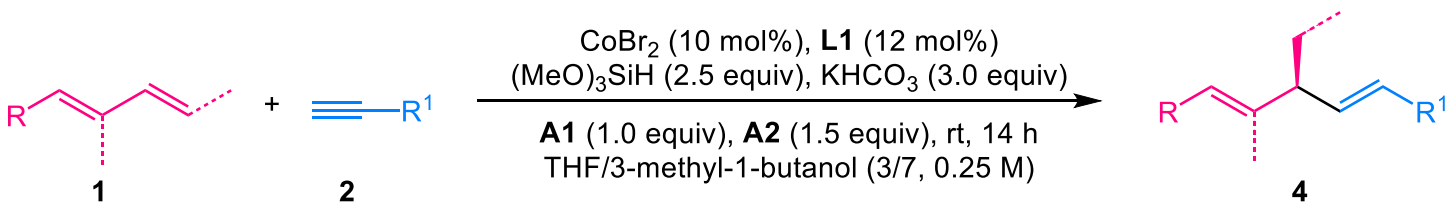


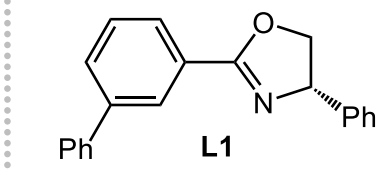
4j 73%, 94% ee

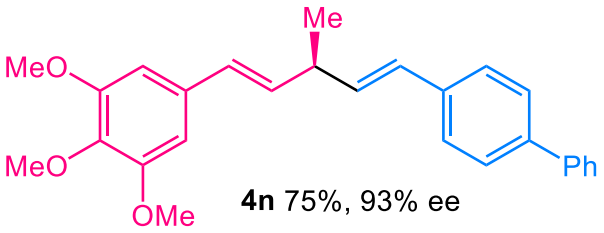


4k R = OMe, 98%, 92% ee
4l R = Me, 82%, 86% ee
4m R = F, 57%, 82% ee

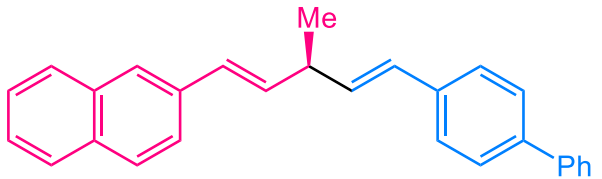
Substrate Scope



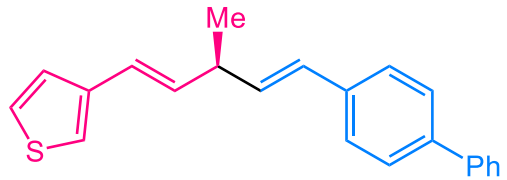




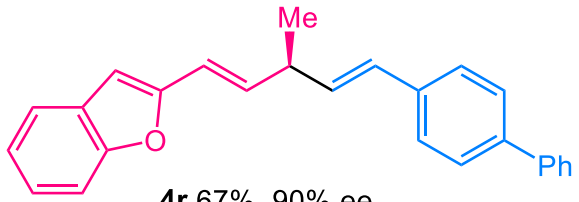
4n 75%, 93% ee



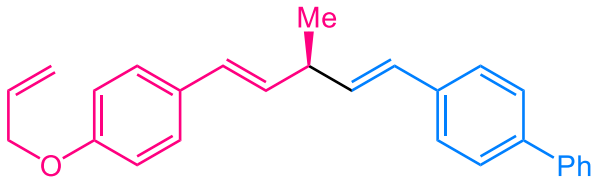
4o 81%, 92% ee



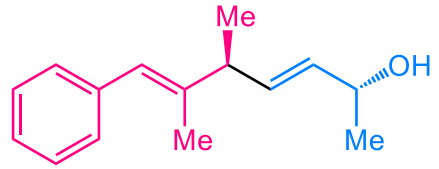
4p 69%, 88% ee



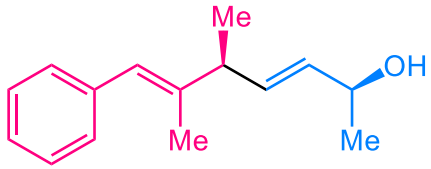
4r 67%, 90% ee



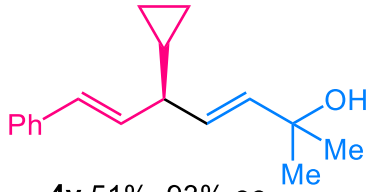
4s 80%, 88% ee



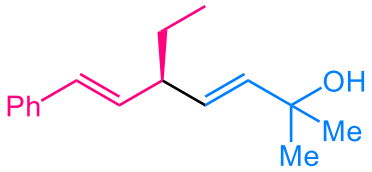
4t 73%, 96% ee, >20:1 dr



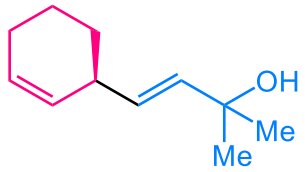
4u 57%, 96% ee, >20:1 dr



4v 51%, 93% ee

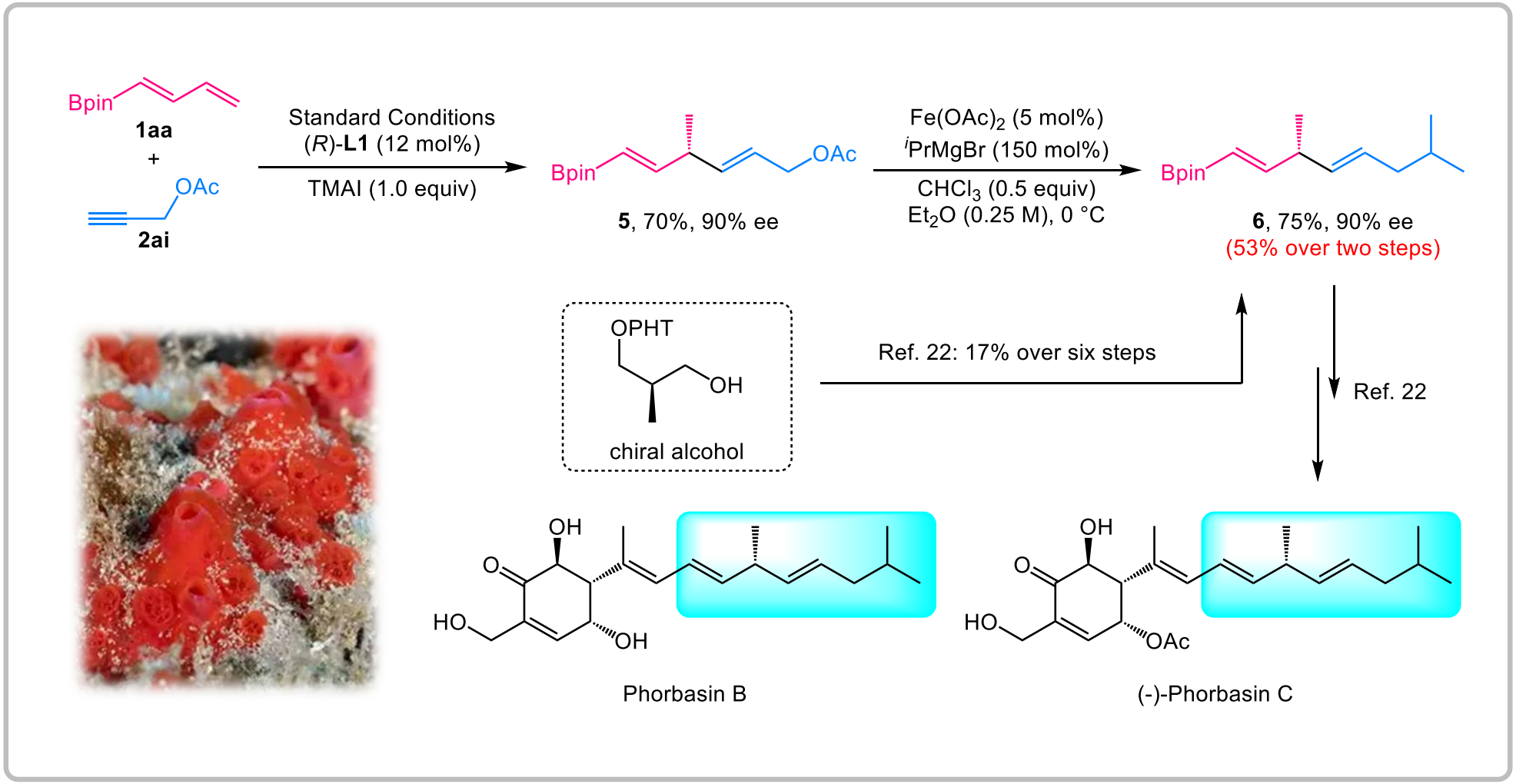


4w 36%, 90% ee



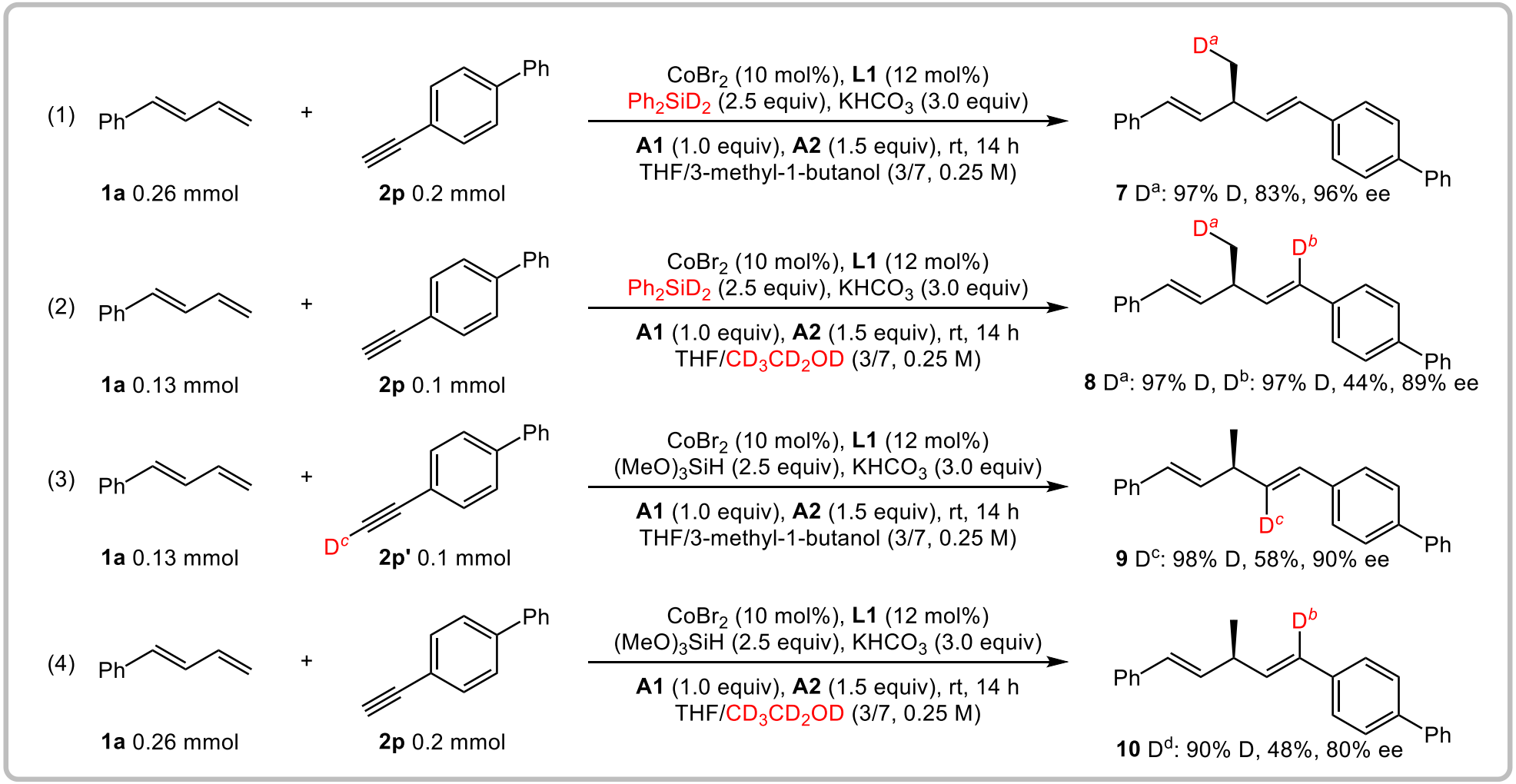
4x 42%, 85% ee

Representative Transformations

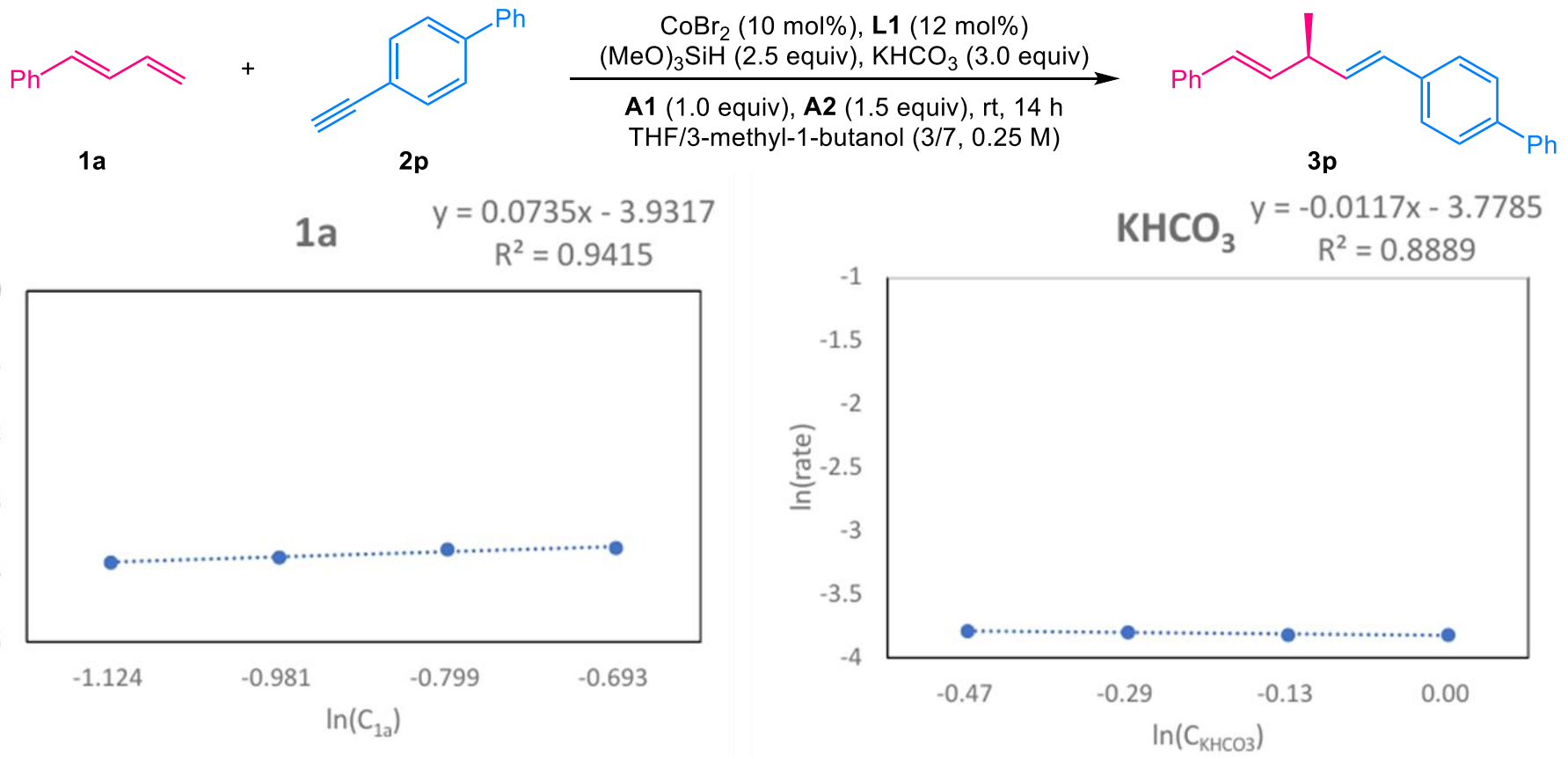


Macklin, T. K.; Micalizio, G. C. *J. Am. Chem. Soc.* **2009**, *131,* 1392

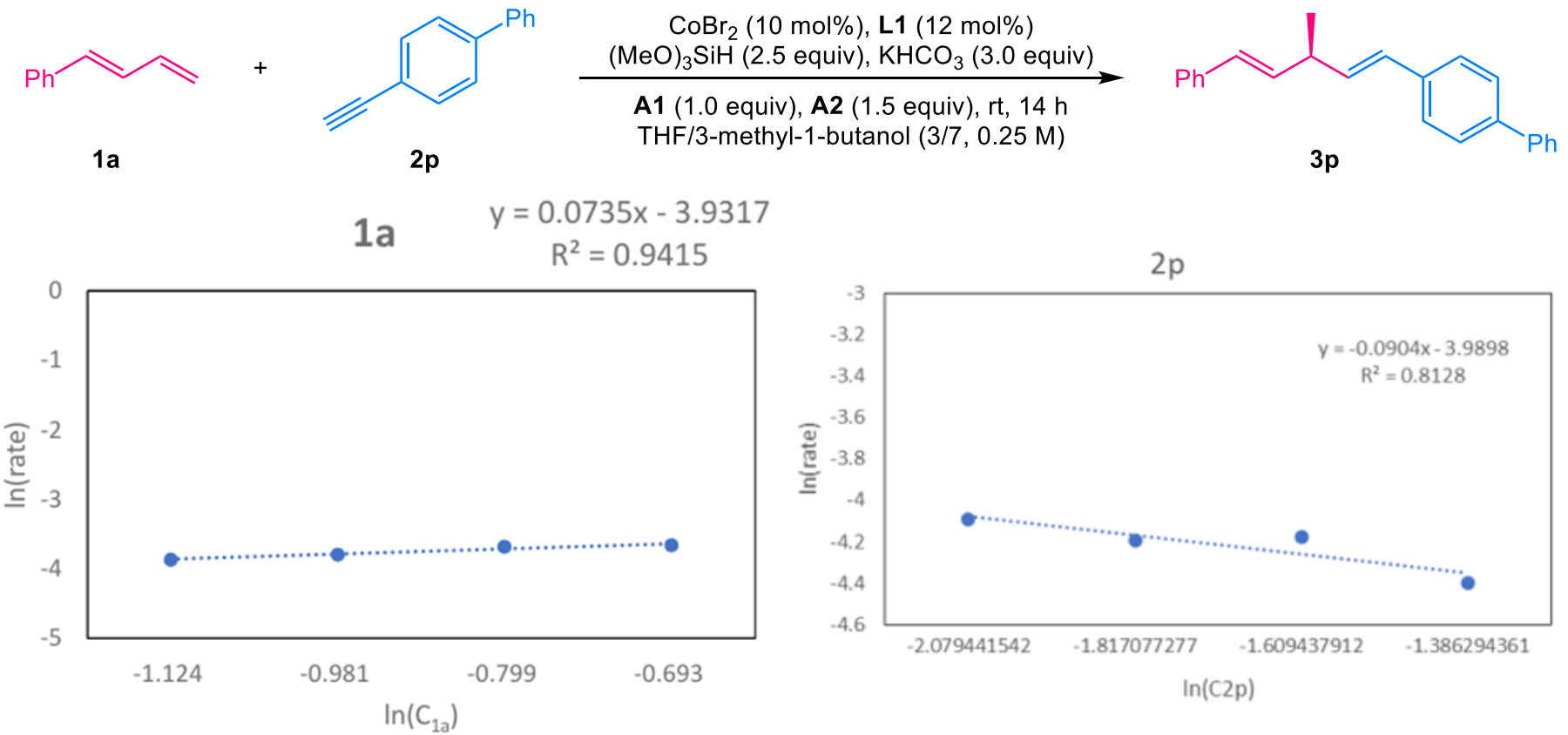
Mechanism Experiment



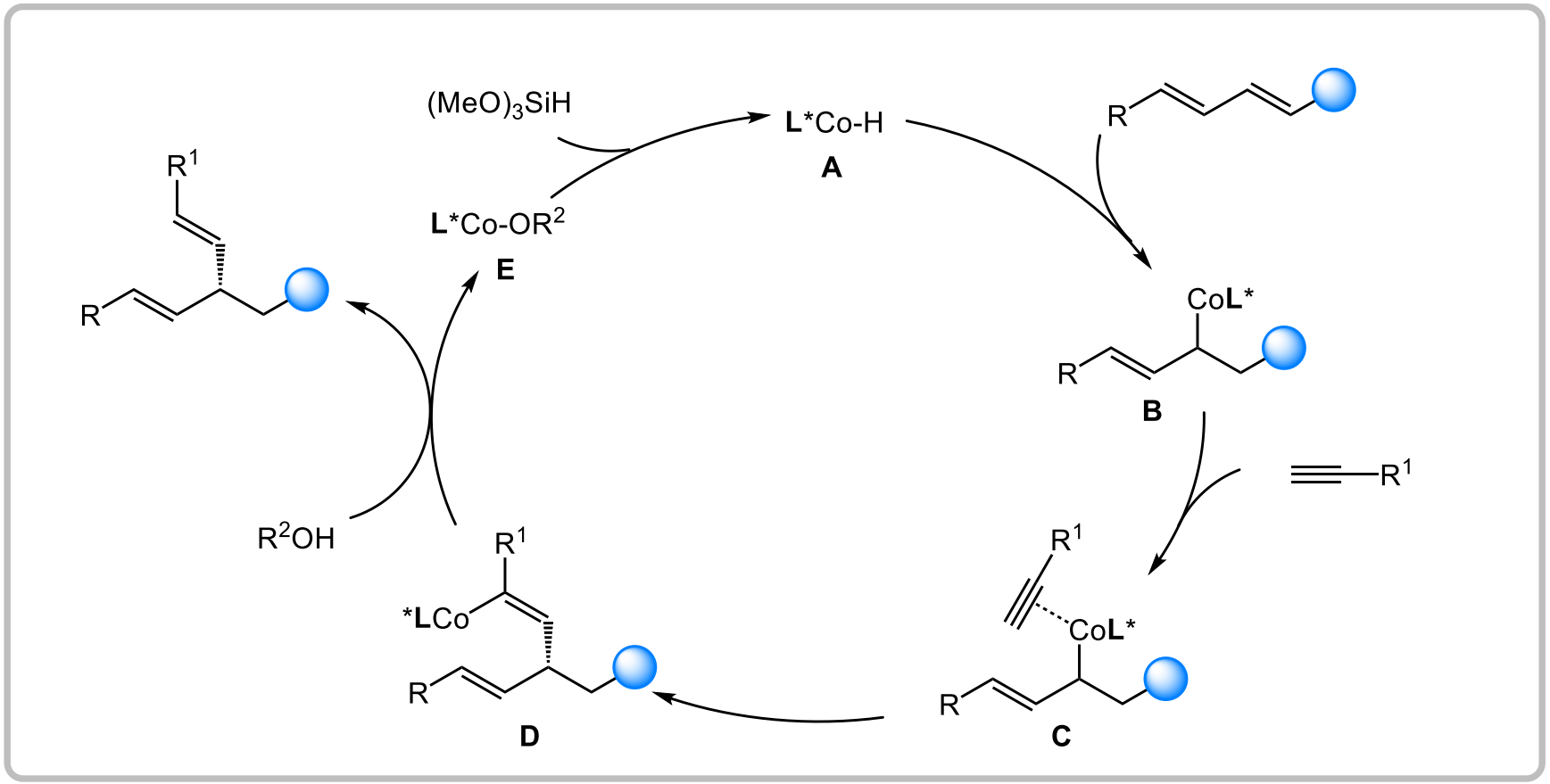
Mechanism Experiment



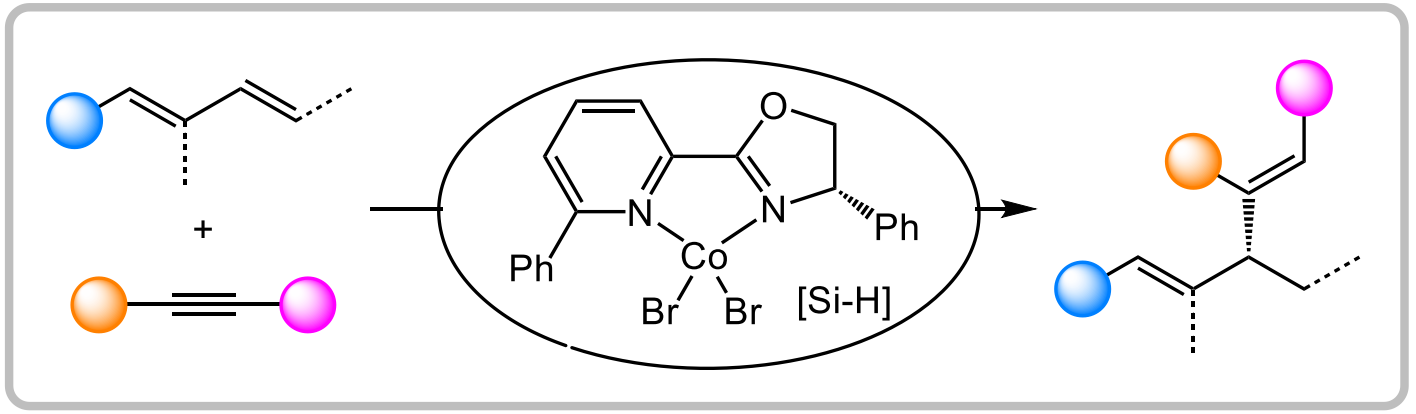
Mechanism Experiment



Plausible Mechanism



Summary



- From Conjugated Dienes to Skipped Dienes
- High Chemo-, Regio-, Enantioselectivity
- Asymmetric Hetero-Hydrodimerization
- Broad Scope and Mild Conditions

Writing Strategies

☐ The First Paragraph

The importance of skipped dienes

✓ Enantioenriched skipped dienes are ubiquitous structural motifs in natural products, terpenoids, alkaloids, and polyketides. Moreover, chiral skipped dienes are important chiral precursors for the synthesis of value-added targets due to their orthogonal reactivity over other polar functional groups.

Few reports about skipped dienes

✓ Over the past decades, Cu- and Ir-catalyzed asymmetric allylic substitution reactions of allylic alcohol derivatives with vinyl metallic reagents (Al, B, ...) have been developed to synthesize enantioenriched skipped dienes. Cu-catalyzed asymmetric alkylation of 1,3-dienyl halides with alkyl metallic reagents has also been established.

Writing Strategies

☐ The Last Paragraph

Summary

of this work

Outlook

of this work

- ✓ In summary, a Cobalt-catalyzed regio- and enantioselective cross-hydrodimerization of 1,3-dienes with alkynes has been developed for the first time, providing straightforward and powerful access to enantioenriched skipped dienes from conjugated dienes in good yields with excellent levels of regio- and enantioselectivity.

- ✓ Mechanistic investigations reveal the reaction undergoes a nontrivial sequential hydrometalation and carbometalation cascade with excellent chemo- and regioselectivity as well as the control of enantioselectivity. The reaction exhibits the tolerance of a wide substrates, including aryl and aliphatic alkynes, terminal and internal alkynes, and 1,3-dienes with diverse substitution patterns.

Representative Examples

- ✓ Herein, an **unprecedented** (**前所未有的，史无前例的**) Co-catalyzed asymmetric cross-hydrodimerization of 1,3-dienes with alkynes has been developed to deliver enantioenriched skipped dienes under mild conditions, representing the first example of a Co-catalyzed asymmetric cross-hydrodimerization of unsaturated hydrocarbons.

- ✓ To further demonstrate the synthetic potential of this Co-catalyzed enantioselective cross-hydrodimerization of 1,3-dienes with alkynes for the synthesis of enantioenriched skipped dienes, the reaction of 1,3-dienyl boronate with propargyl acetate was **conducted** (**引导；指挥**).

- ✓ Moreover, chiral skipped dienes are important chiral precursors for the synthesis of value-added targets due to their **orthogonal** (**正交的**) reactivity over other polar functional groups.

Acknowledgment

Thanks for your attention!