Literature Report 7

Stereodivergent Coupling of 1,3-Dienes with Aldimine Esters Enabled by Synergistic Pd and Cu Catalysis

Reporter: Zhou-Hao Zhu
Checker: Yi-Xuan Ding
Date: 2019-10-14

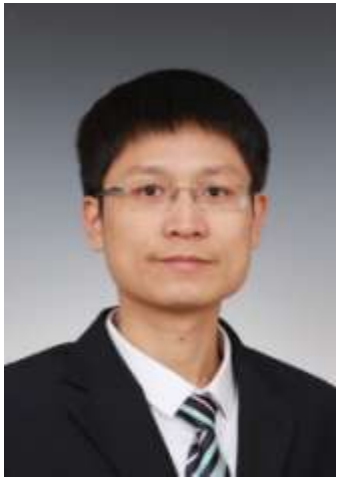
Cruz, F. A.; Dong, V. M.*
J. Am. Chem. Soc. **2017**, *139*, 1029

Zhang, Q.; Yu, H.; Shen, L.; Tang, T.; Dong, D.; Chai, W.; Zi, W.*
J. Am. Chem. Soc. **2019**, *141*, 14554

Contents

CV of Prof. Weiwei Zi

Background:



Weiwei Zi

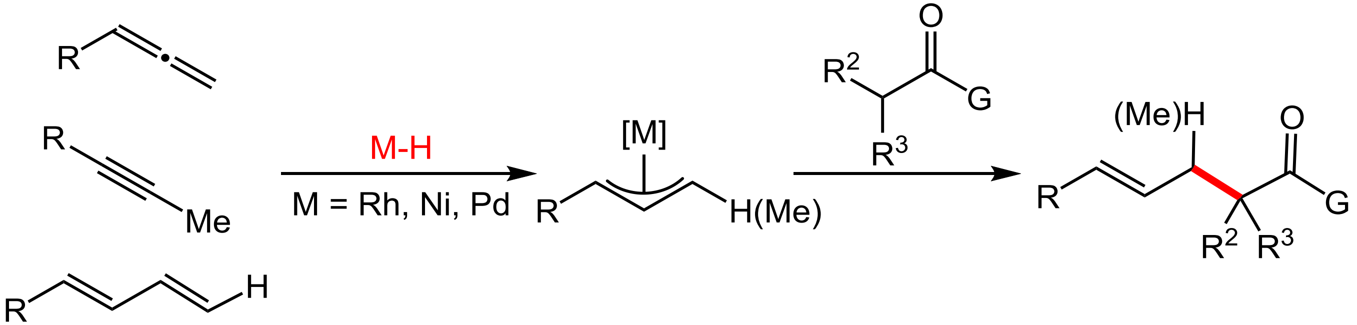
- ☐ **2002-2006** B.S., Lanzhou University (with Prof. Haoli Zhang)
- ☐ **2006-2011** Ph.D., Shanghai Institute of Organic Chemistry (with Prof. Dawei Ma)
- ☐ **2011-2012** Assistant Researcher, Shanghai Institute of Organic Chemistry
- ☐ **2012-2016** Postdoctoral Associate, Department of Chemistry, University of California at Berkeley (with Prof. F. Dean Toste)
- ☐ **2016-now** Professor, Institute of Elemento-Organic Chemistry, Nankai University

Research Interests:

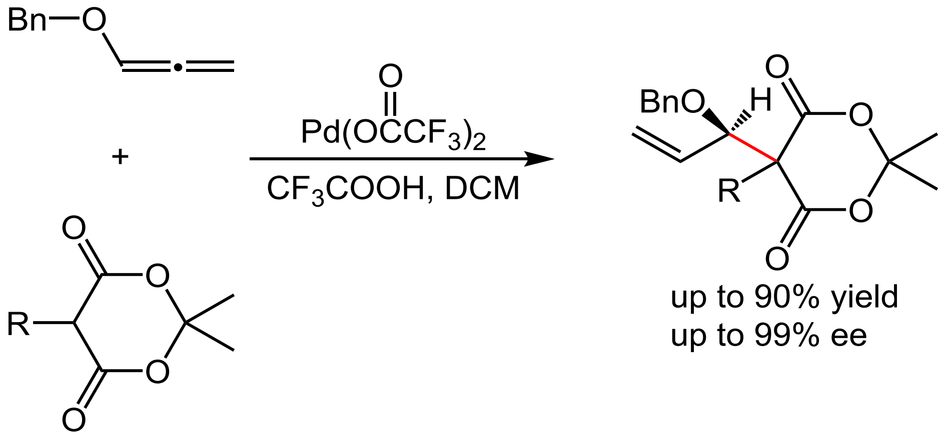
- ➢ Natural Products Synthesis
- ➢ Transition-Metal Catalysis

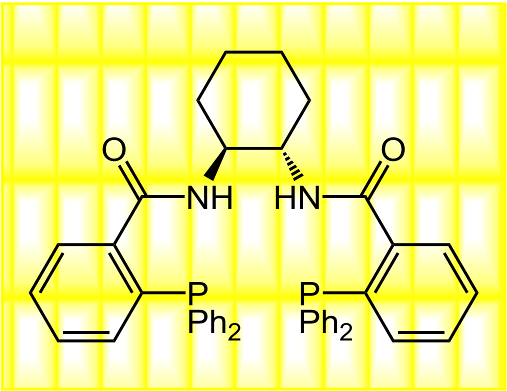
Introduction

M-H catalyzed coupling unsaturated hydrocarbons with carbon nucleophiles



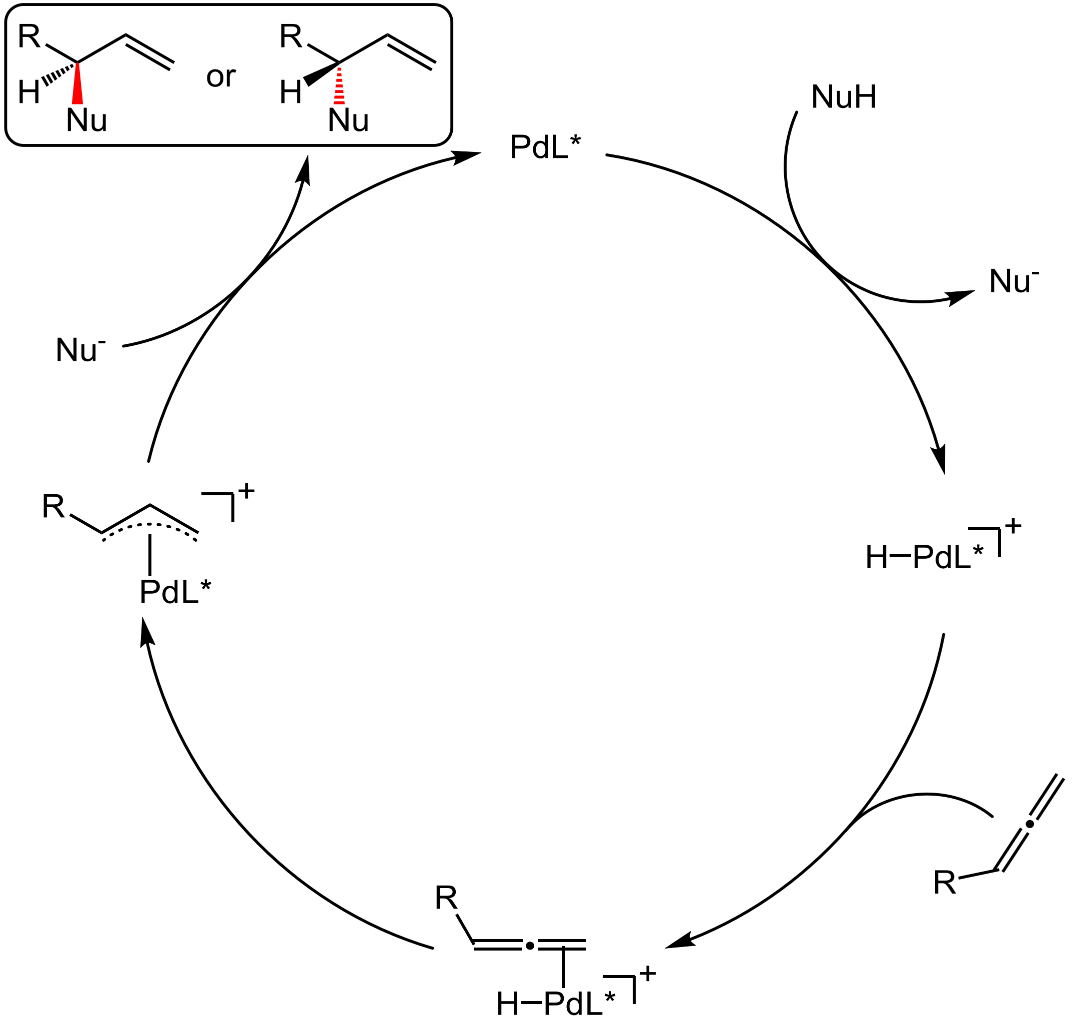
Introduction (Pd-H)



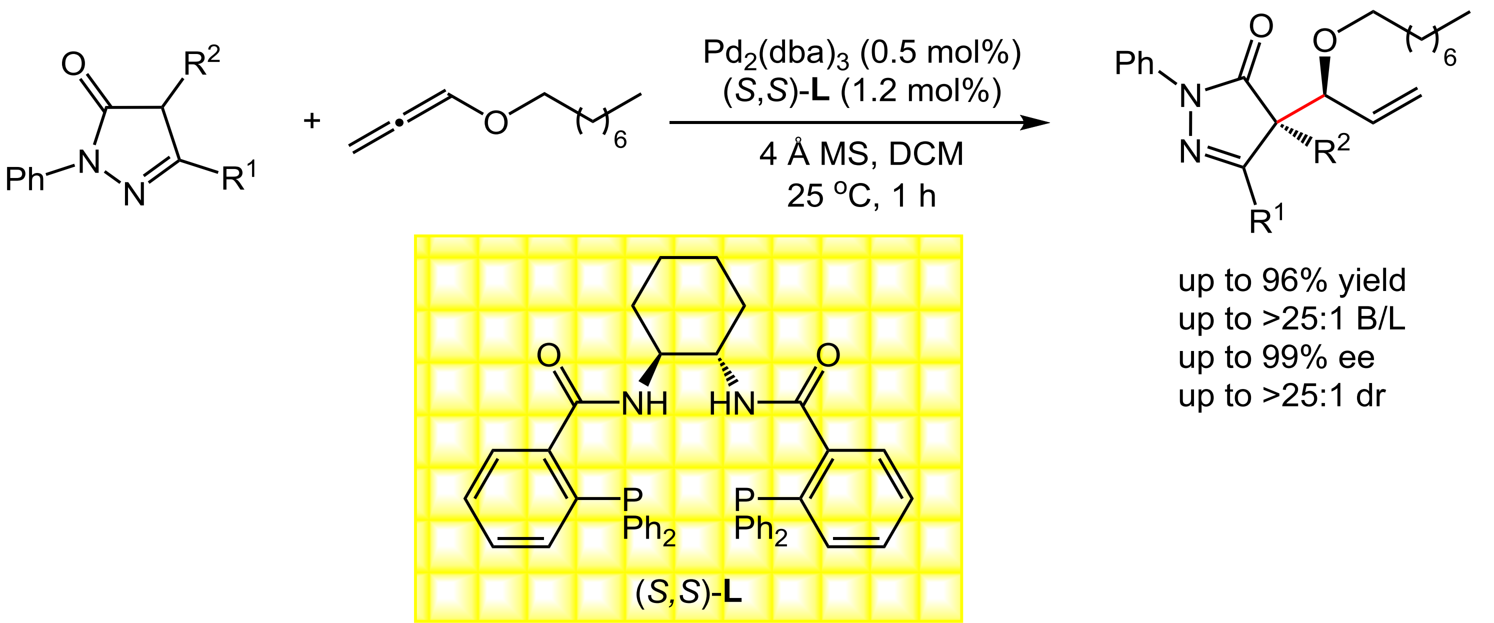


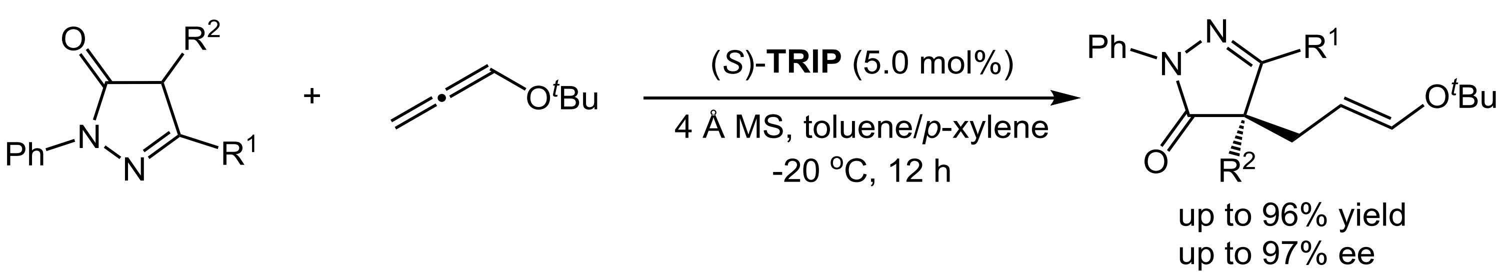
Trost, B. M.* *et al. J. Am. Chem. Soc.* **2003**, *125*, 4438

Introduction (Pd-H)



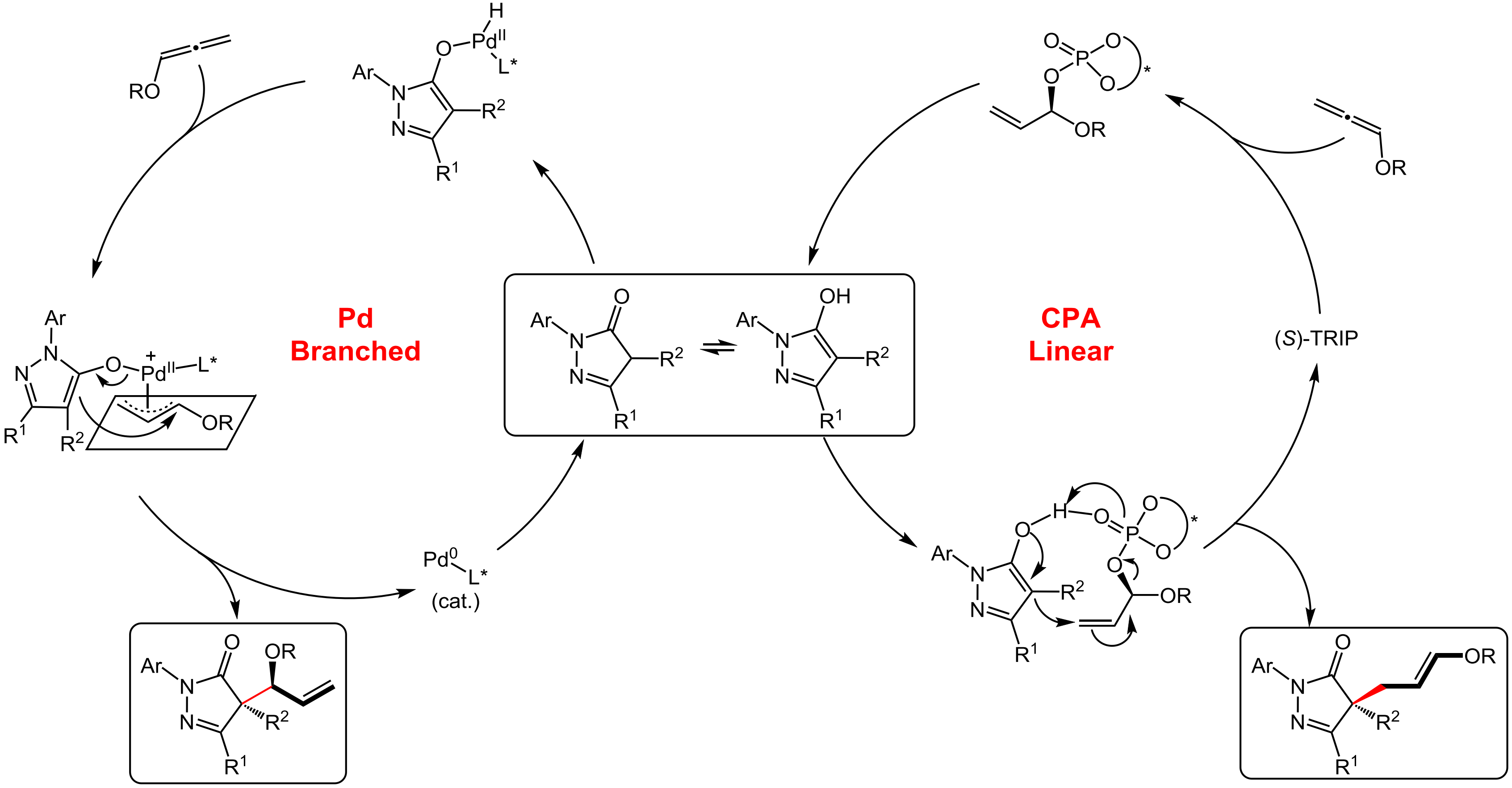
Introduction (Pd-H)



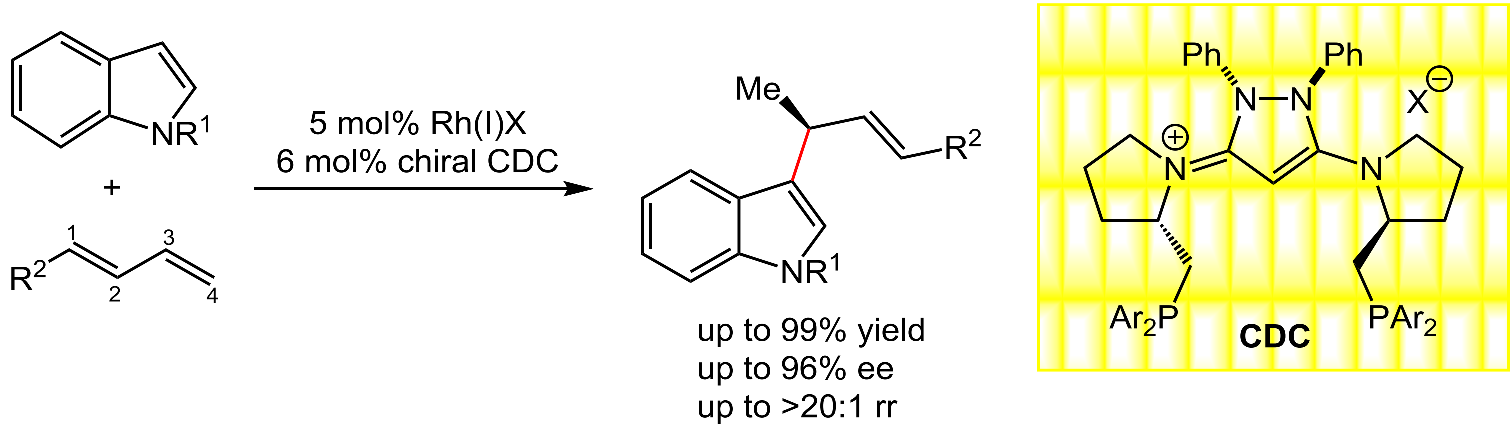


Jiang, G.* *et al.* Angew. *Chem. Int. Ed.* **2017**, *56*, 1077

Introduction (Pd-H)

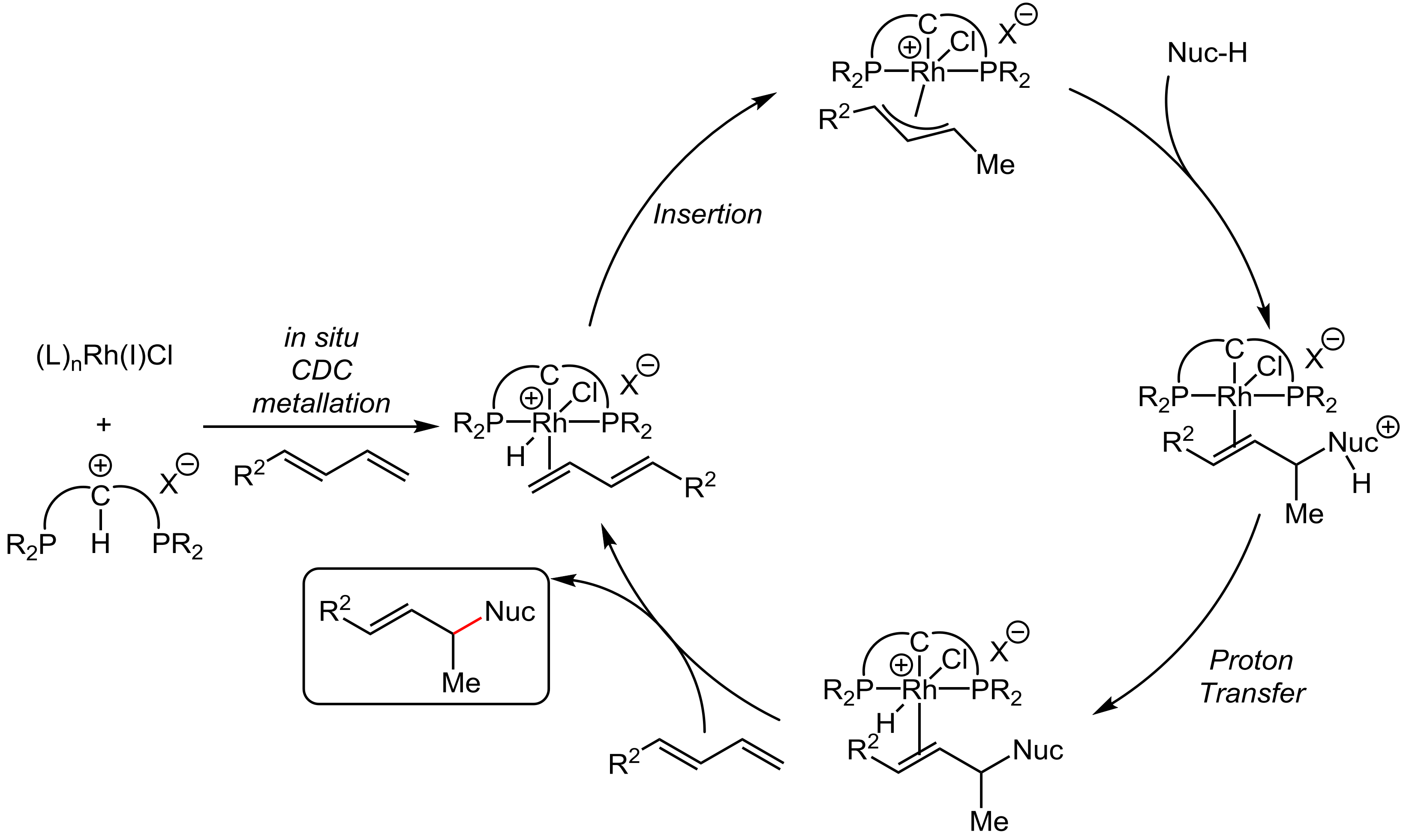


Introduction (Rh-H)

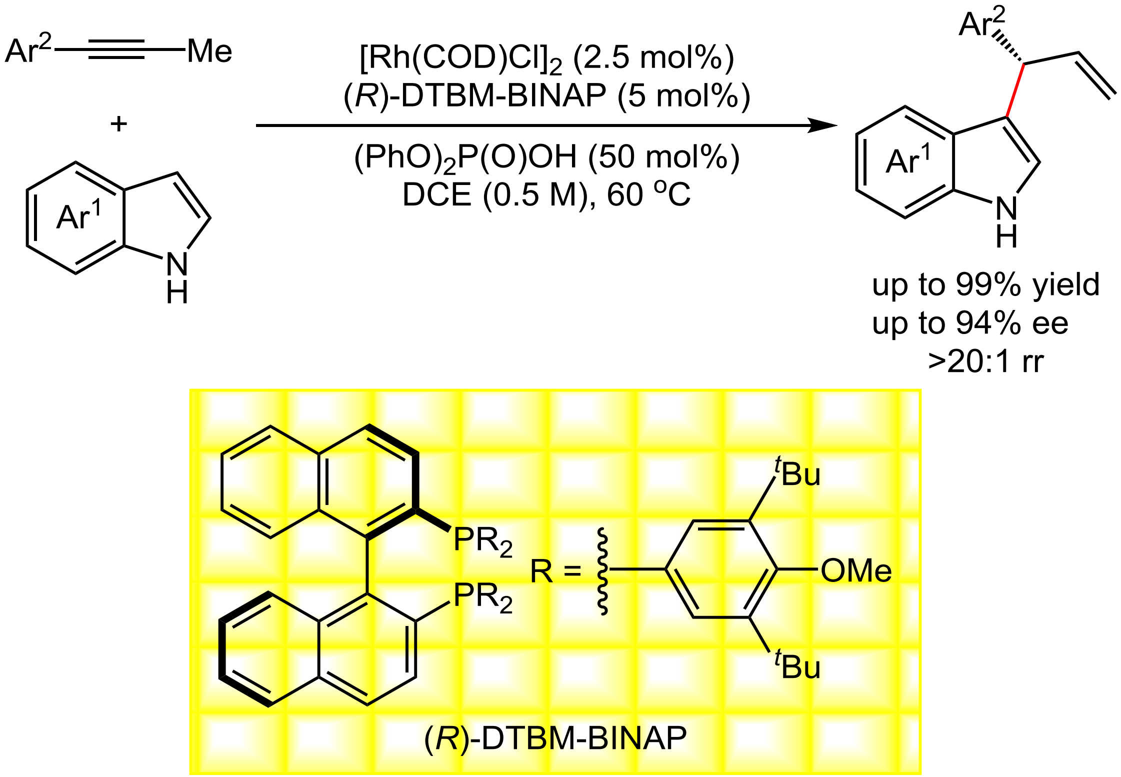


Meek, S. J.* *et al. J. Am. Chem. Soc.* **2017**, *139*, 15580

Introduction (Rh-H)

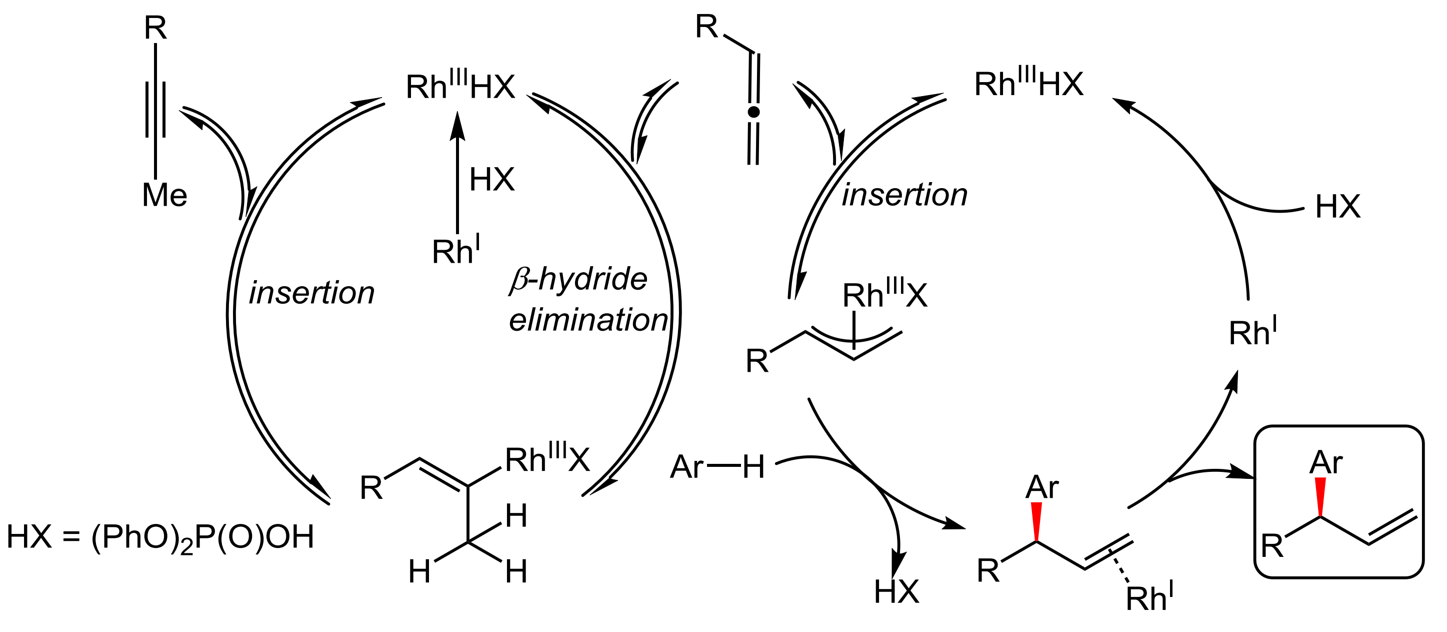


Introduction (Rh-H)



Dong, V. M.* *et al. J. Am. Chem. Soc.* **2017**, *139*, 10641

Introduction (Rh-H)



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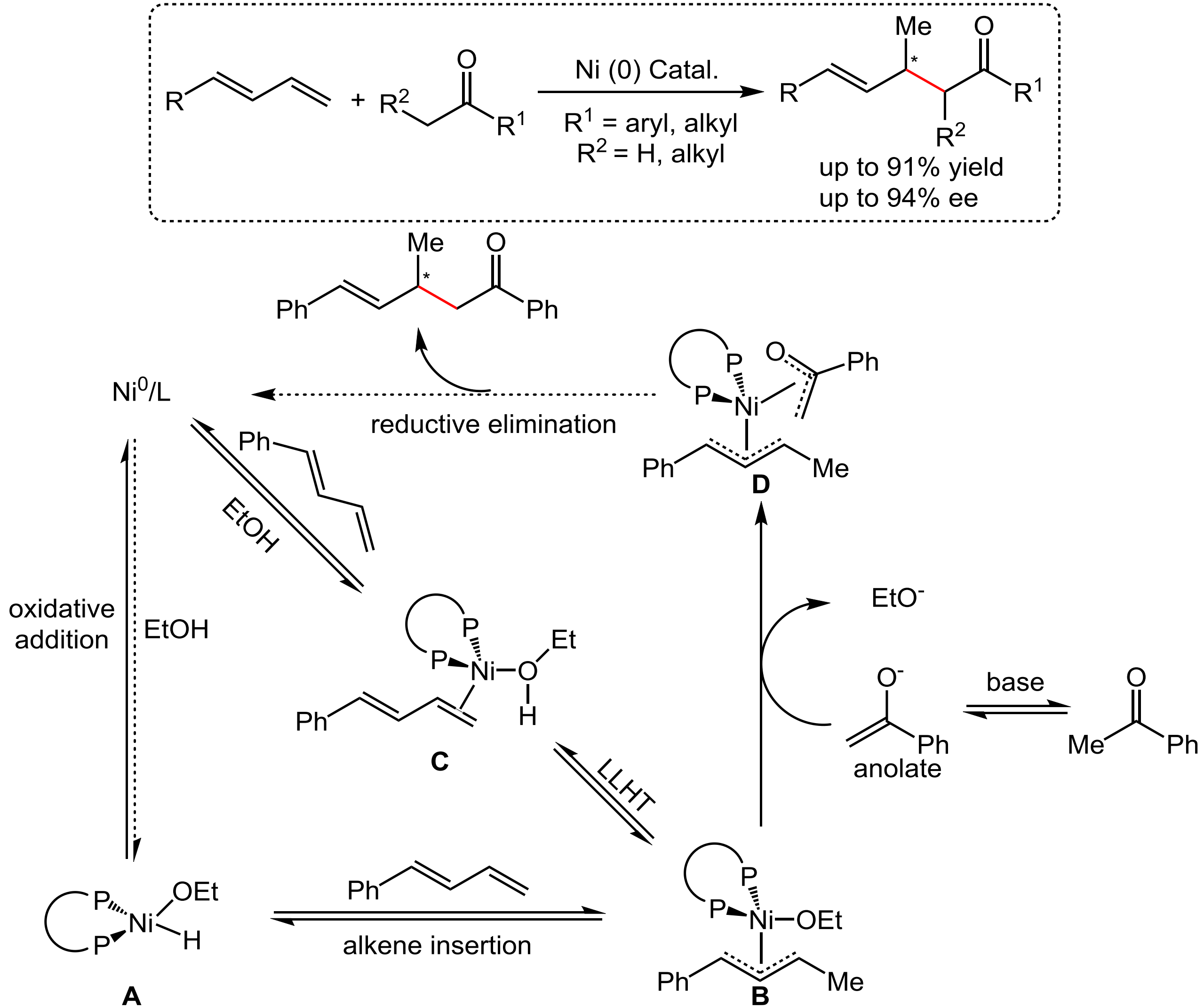
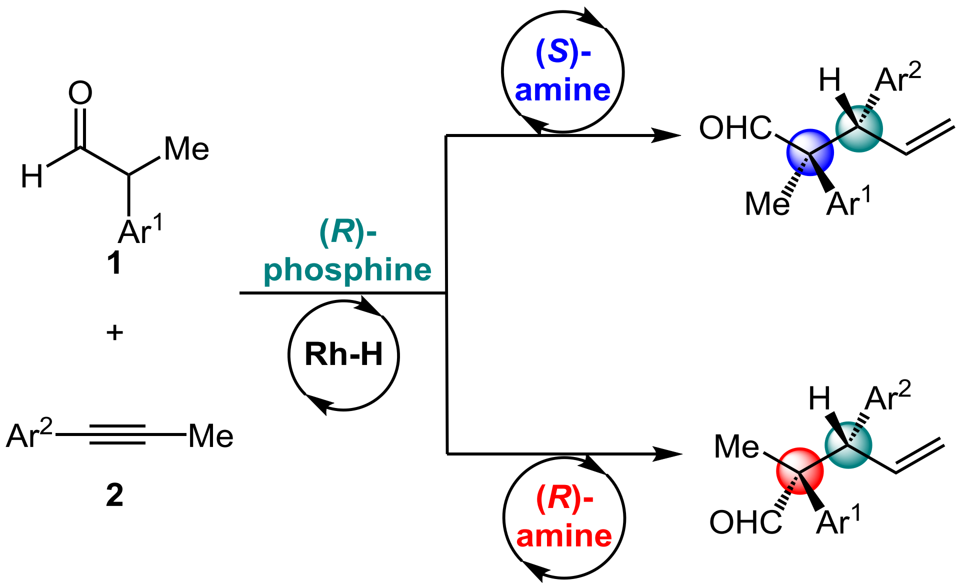


Zhou, Q.-L.* *et al. J. Am. Chem. Soc.* **2018**, *140*, 11627

Stereodivergent Coupling of Aldehydes and Alkynes

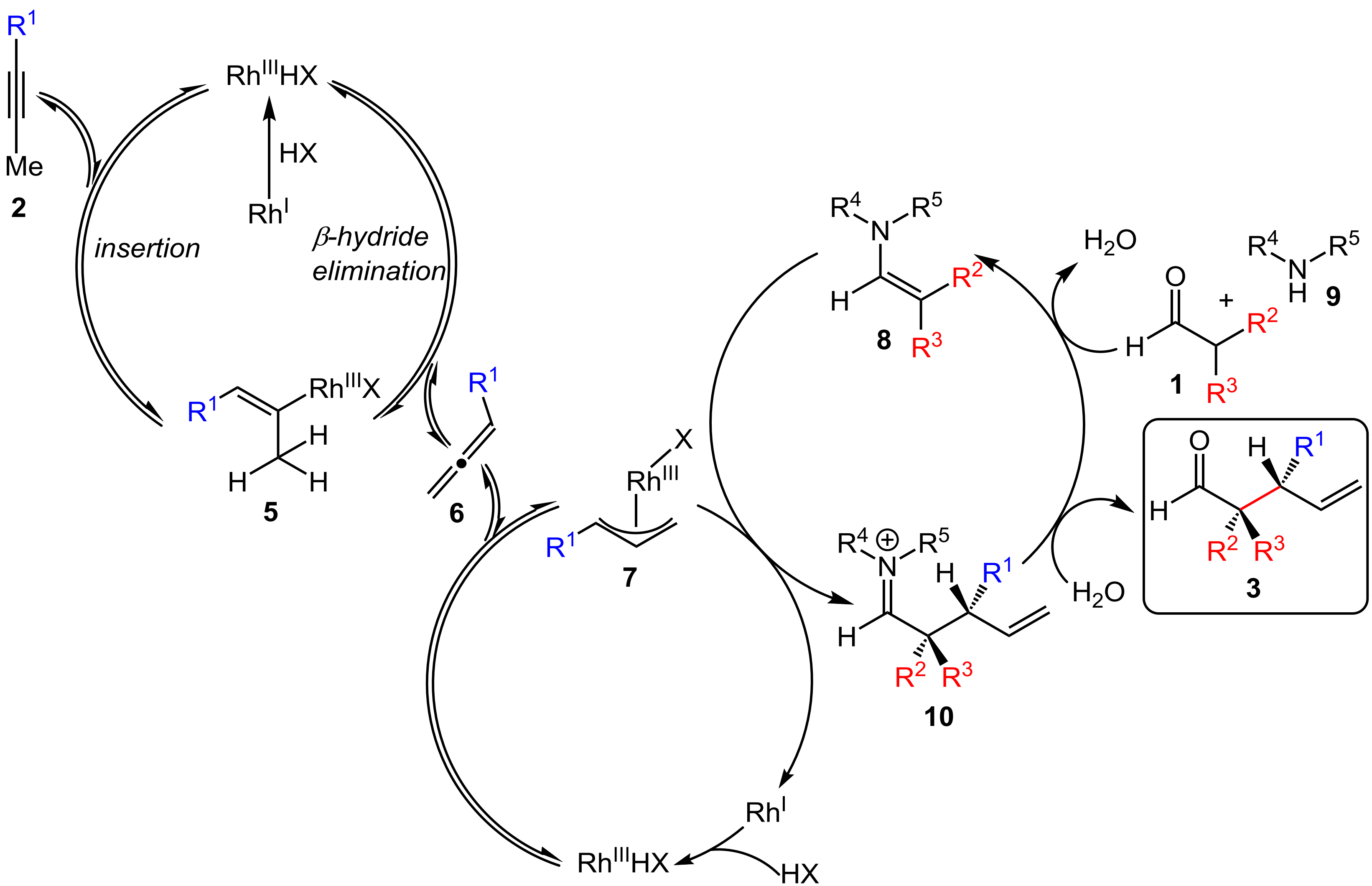


(*S*,*S*)-**3**
anti
up to 96% yield
>20:1 dr
>99% ee
>20:1 rr

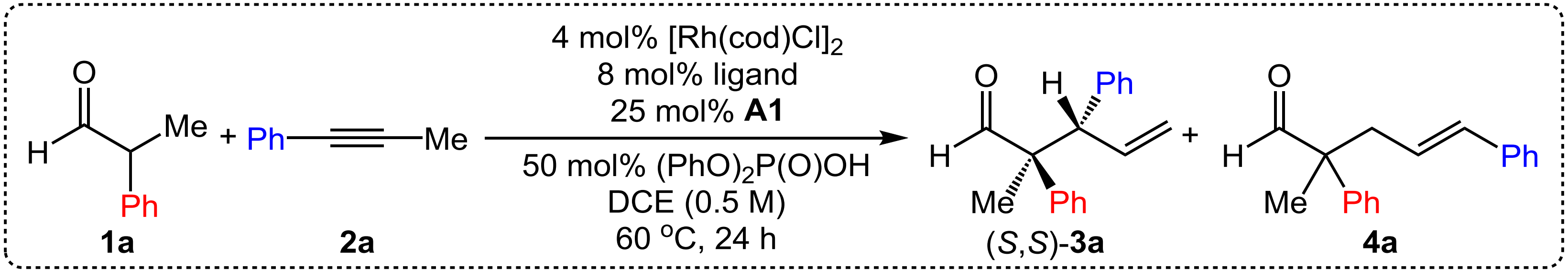
(*R*,*S*)-**3**
syn
up to 93% yield
12:1 dr
>99% ee
>20:1 rr

Cruz, F. A.; Dong, V. M.* *J. Am. Chem. Soc.* **2017**, *139*, 1029

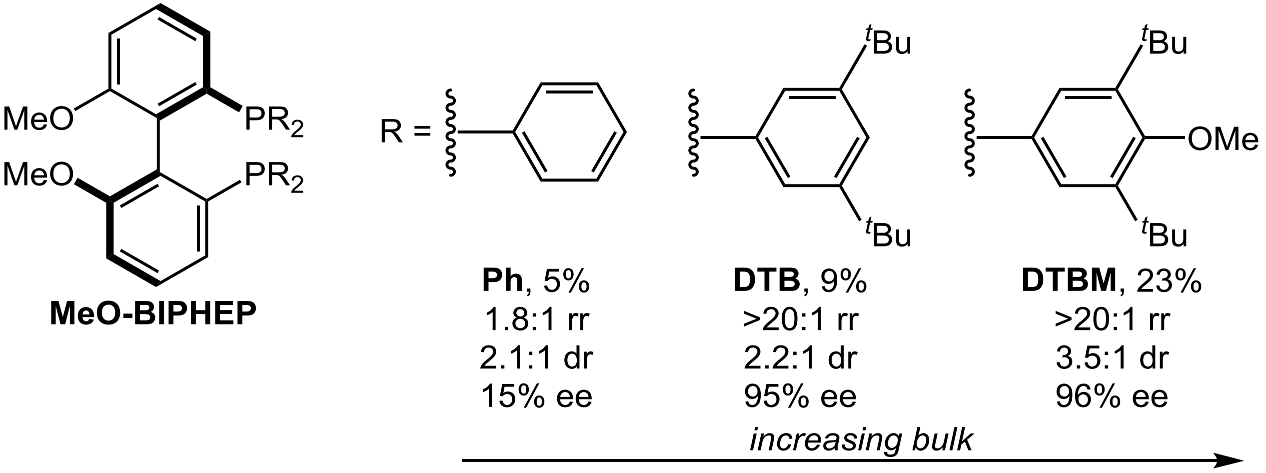
Proposed Mechanism



Optimization of the Reaction Parameters[a]

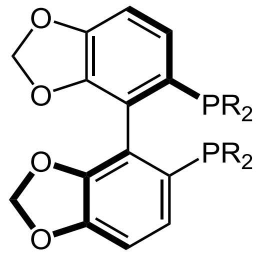


a) Phosphine Substituent

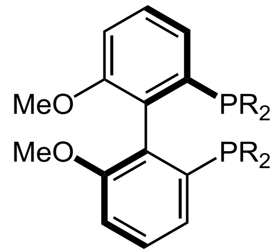


Optimization of the Reaction Parameters[a]

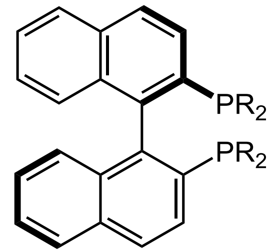
b) Ligand Scaffold, *R = DTBM*



SEGPHOS, 11%
4.1:1 dr, 92% ee



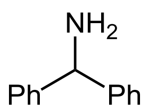
MeO-BIPHEP, 23%
3.5:1 dr, 96% ee



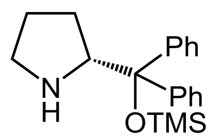
BINAP, 37%
3.7:1 dr, 92% ee

increasing dihedral angle

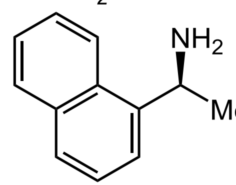
c) Amine Catalyst, *w/ (R)-DTBM-BINAP and $MeNO_2$*



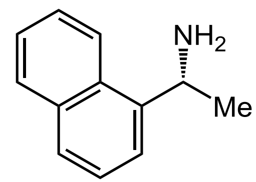
A1, 66%
5.1:1 dr, 98% ee



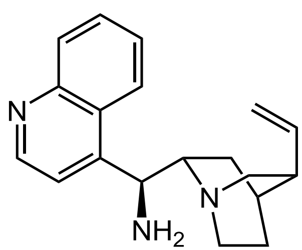
A2
N.R.



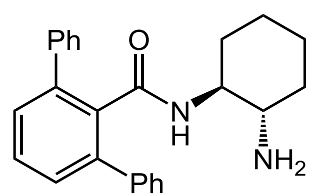
(*S*)-**A3**, 68%
5:1 dr, 98% ee



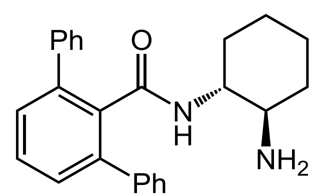
(*R*)-**A3**, 63%
5:1 dr, 96% ee



A4, 18%
8.8:1 dr, 77% ee



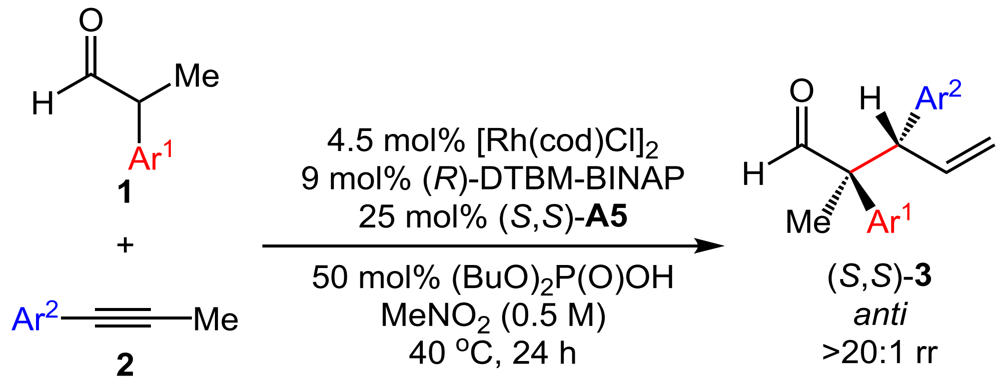
(*S*,*S*)-**A5**, 75%[b]
>20:1 dr, >99% ee

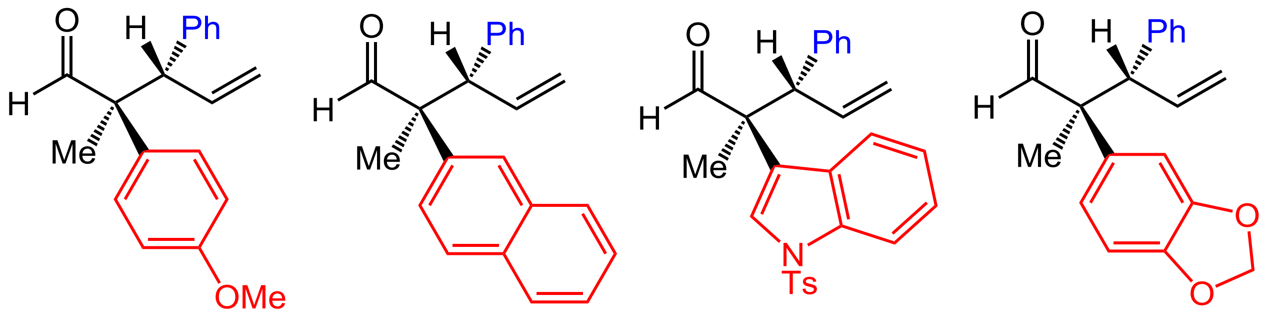


(*R*,*R*)-**A5**, 75%[b]
1:8 dr, >99% ee

[a]Yields determined by ^{1}H NMR using an internal standard. Rr's and dr's determined by ^{1}H NMR analysis of the crude reaction mixture. Ee's determined by SFC analysis. [b]4.5 mol% $[Rh(cod)Cl]_2$, 50 mol% $(BuO)_2P(O)OH$ instead, run at 40 ^oC.

Substrate Scope





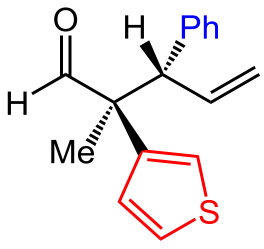
3b, 86%
11:1 dr
>99% ee

3c, 83%
16:1 dr
>99% ee

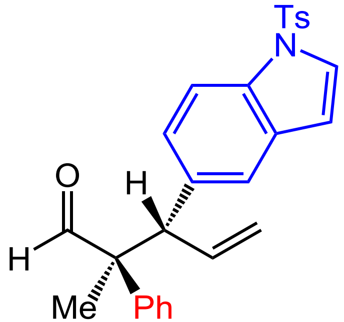
3d, 86%
>20:1 dr
>99% ee

3e, 91%
12:1 dr
>99% ee

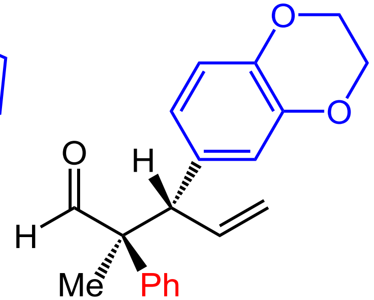
Substrate Scope



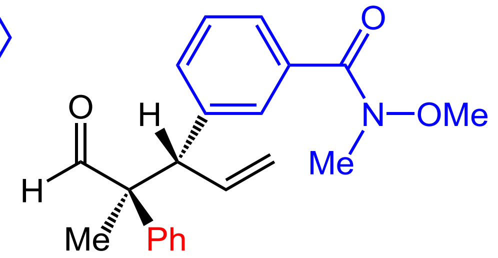
3f, 81%
10:1 dr
>99% ee



3g, 71%
20:1 dr
93% ee



3h, 96%
16:1 dr
>99% ee

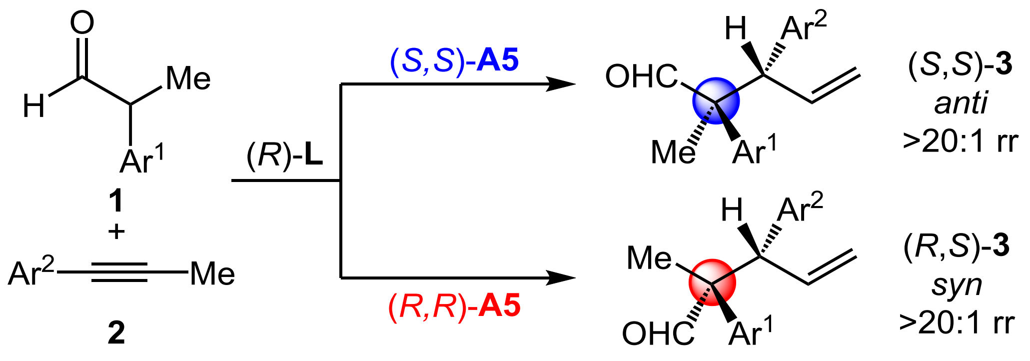


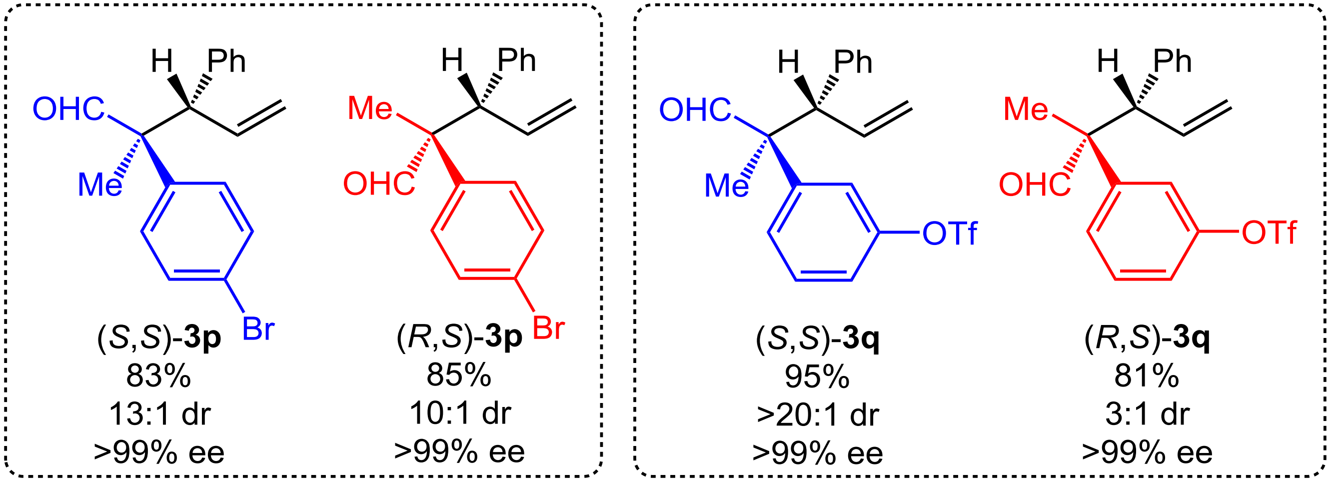
3i, 77%
17:1 dr
4% ee

Ar[1] = Ph, Ar[2] =

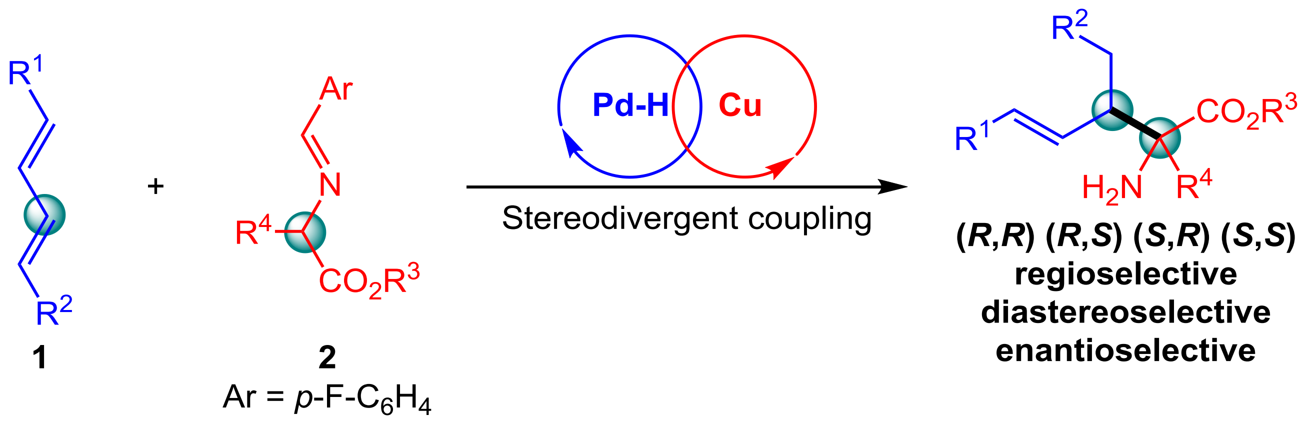
4-OMeC_6H_4	4-$CF_3C_6H_4$	4-BrC_6H_4	4-TMSC_6H_4	4-$CO_2MeC_6H_4$	3-$NO_2C_6H_4$
3j, 64%	**3k**, 81%	**3l**, 69%	**3m**, 83%	**3n**, 80%	**3o**, 75%
17:1 dr	15:1 dr	16:1 dr	20:1 dr	>20:1 dr	>20:1 dr
>99% ee	>99% ee	>99% ee	>99% ee	>99% ee	72% ee

Stereodivergent Aldehyde-Alkyne Coupling



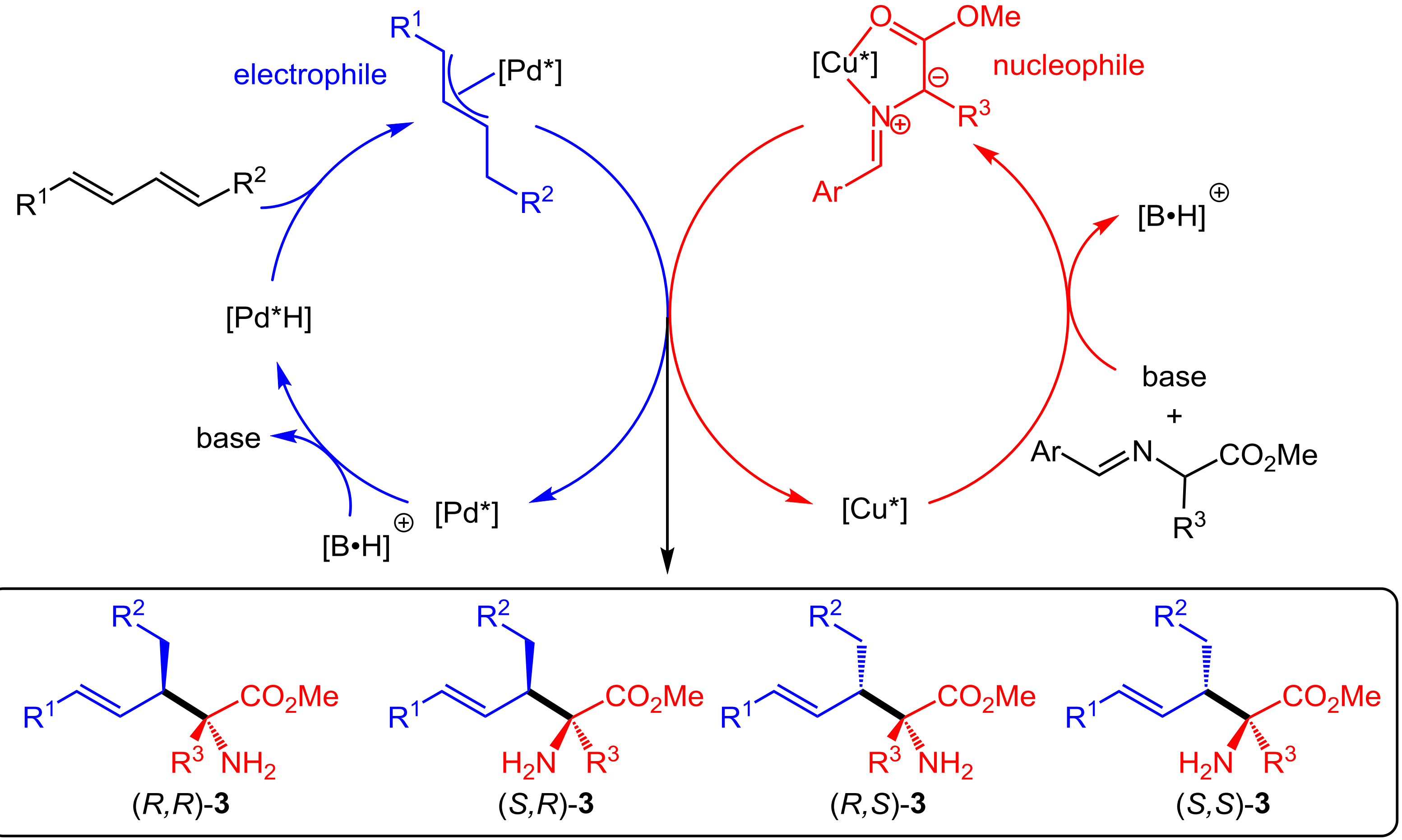


Stereodivergent Coupling of Dienes with Aldimine Esters



Zhang, Q.; Yu, H.; Shen, L.; Tang, T.; Zi, W.* *J. Am. Chem. Soc.* **2019**, *141*, 14554

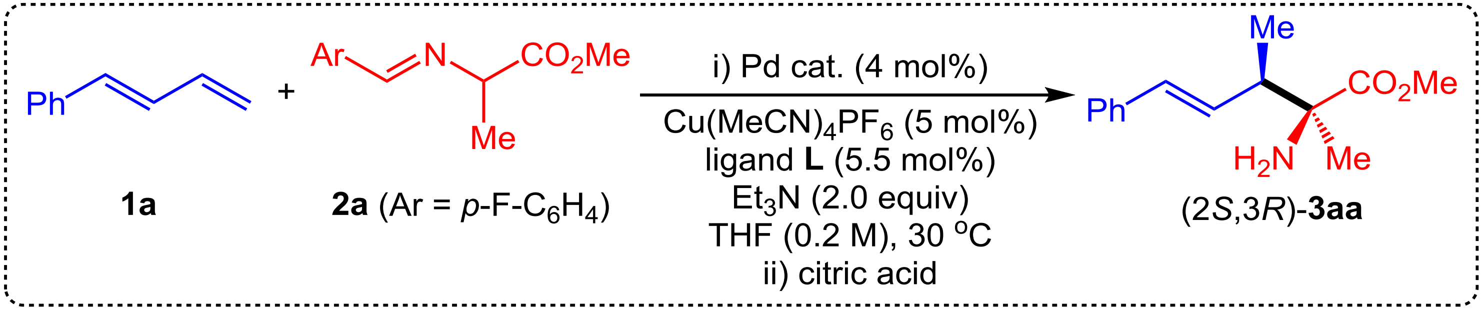
Proposed Mechanism

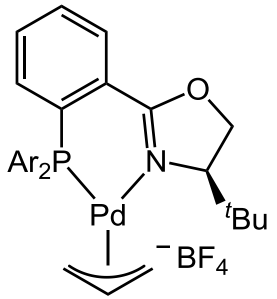


all stereoisomers accessible

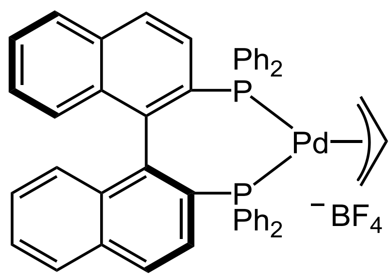
♦regioselective ♦enantioselective ♦diastereoselective ♦stereodivergent

Optimization of the Reaction Parameters

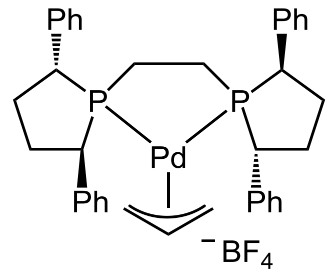




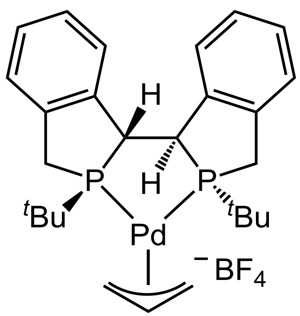
Pd-1
Ar = 4-CF$_3$C$_6$H$_4$



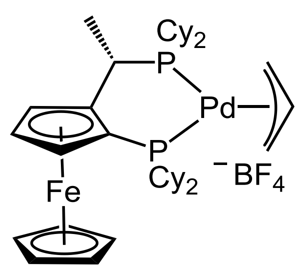
Pd-2



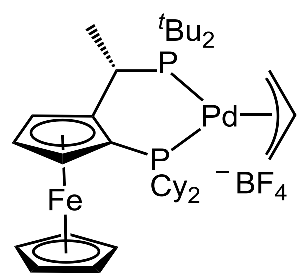
Pd-3



Pd-4



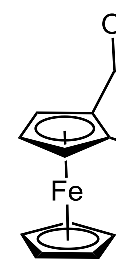
Pd-5



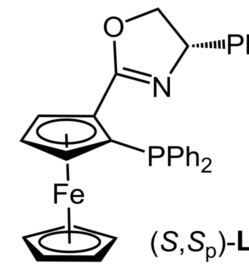
Pd-6

Optimization of the Reaction Parameters

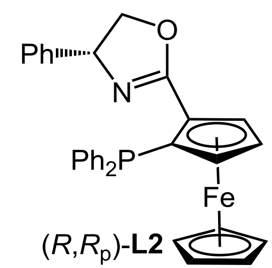
entry[a]	Pd cat.	Cu ligand	yield (%)[b]	dr[b]	ee (%)[c]
1	**Pd-1**	(S,S_p)-**L1**	53	1.6:1	95/67
2[d]	**Pd-1**	(S,S_p)-**L1**	<5	--	--
3	**Pd-1**	(S,S_p)-**L2**	75	2:1	95/83
4	**Pd-2**	(S,S_p)-**L2**	81	4.5:1	97/95
5	**Pd-3**	(S,S_p)-**L2**	62	3.5:1	94/94
6	**Pd-4**	(S,S_p)-**L2**	85	4.4:1	99/94
7	**Pd-5**	(S,S_p)-**L2**	79	7:1	98/90
8	**Pd-6**	(S,S_p)-**L2**	99	>20:1	>99/--
9	**Pd-6**	(R,R_p)-**L2**	90	1:14	--/>99
10	**--**	(S,S_p)-**L2**	NR	--	--
11	**Pd-6**	--	NR	--	--



(S,S_p)-**L1**



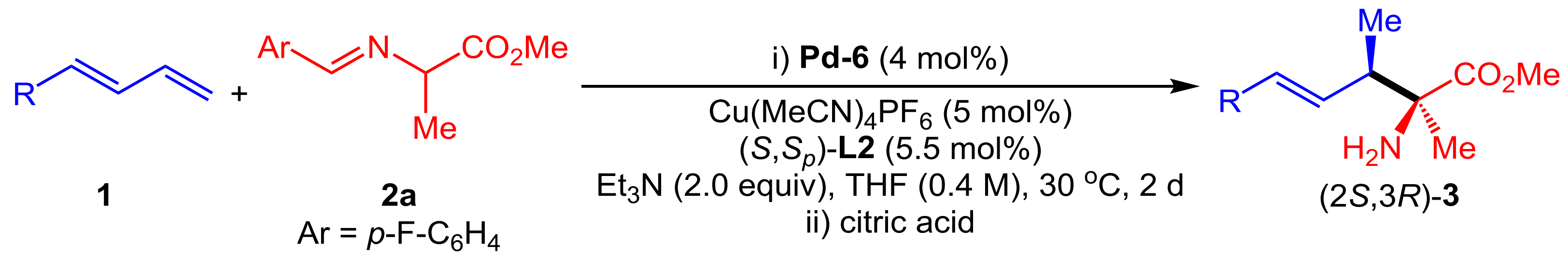
(S,S_p)-**L2**



(R,R_p)-**L2**

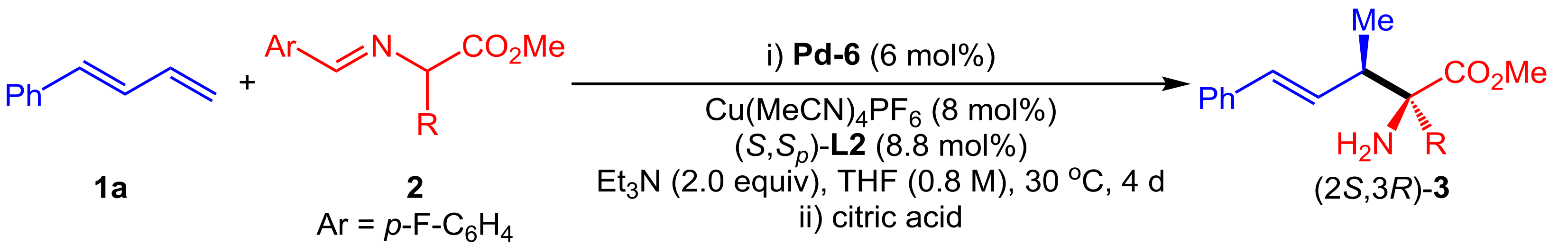
[a]Reaction conditions: (i) **1a** (0.2 mmol), **2a** (0.1 mmol), Pd cat. (4 mol%), $Cu(MeCN)_4PF_6$ (5 mol%), (S,S_p)-**L** or (R,R_p)-**L** (5.5 mol%), Et_3N (200 mol%), THF (0.5 mL), 30 °C, 36 h; (ii) citric acid (10%, 4 mL). In all cases, the regioselectivity was >20:1. [b]Determined by ^{1}H NMR analysis of the crude product. NR, no reaction. Isolated yields are provided in parentheses. [c]Determined by HPLC. [d]Cs_2CO_3, DBU, $^i Pr_2NEt$, or DABCO was used instead of Et_3N.

Substrate Scope



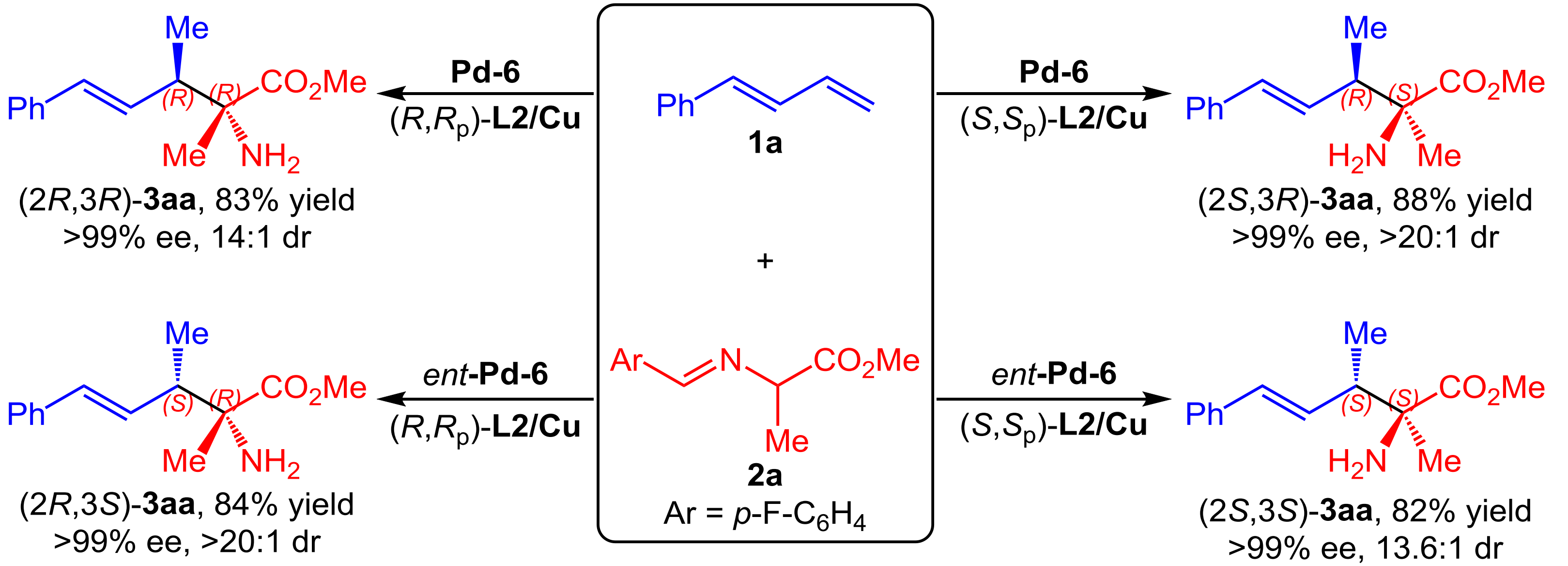
entry	(2S,3R)-3	R	yield (%)	dr	ee (%)
1	3ba	*p*-Me-C_6H_4	68	>20:1	>99
2	3ca	*m*-Me-C_6H_4	83	>20:1	>99
3	3da	*o*-F-C_6H_4	83	>20:1	>99
4	3ea	*m*-F-C_6H_4	82	>20:1	>99
5	3fa	*p*-F-C_6H_4	70	>20:1	>99
6	3ga	*p*-Cl-C_6H_4	72	>20:1	>99
7	3ha	*p*-CF_3-C_6H_4	70	>20:1	>99
8	3ia	*p*-MeO-C_6H_4	78	>20:1	>99
9	3ja	2-naphthyl	73	>20:1	>99
10	3ka	2-furyl	69	>20:1	>99
11	3la	2-thiophenyl	67	>20:1	>99
12	3ma	$(CH_2)_2OAc$	46	>20:1	93

Substrate Scope

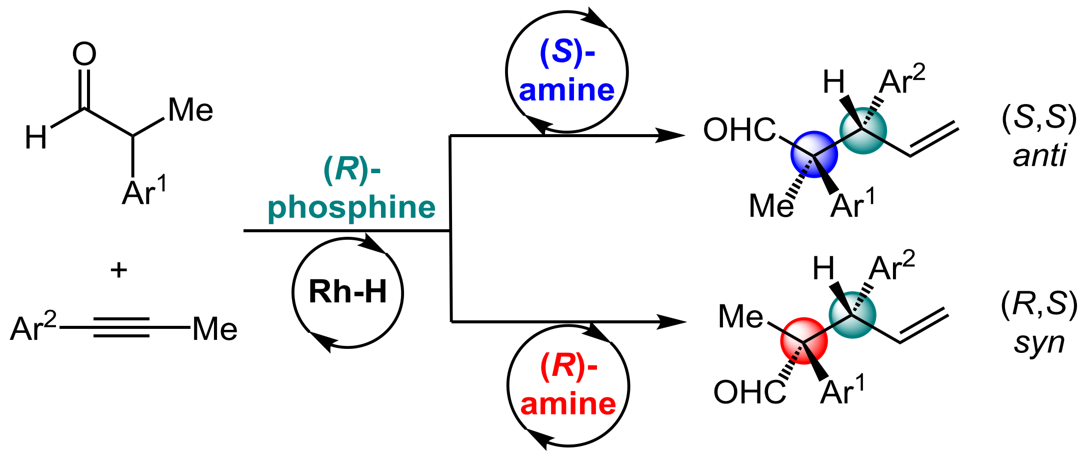


entry	(2*S*,3*R*)-3	R	yield (%)	dr	ee (%)
1	**3ab**	Et	85	>20:1	>99
2	**3ac**	^{n}Pr	86	>20:1	>99
3	**3ad**	^{n}Bu	88	>20:1	>99
4	**3ae**	CH_2CH_2Ph	95	>20:1	>99
5	**3af**	Bn	46	>20:1	98
6	**3ag**	CH_2CO_2Me	92	>20:1	>99
7	**3ah**	$(CH_2)_2NHCbz$	89	>20:1	>99
8	**3ai**	$(CH_2)_2SMe$	95	>20:1	>99
9	**3aj**	allyl	59	>20:1	>99

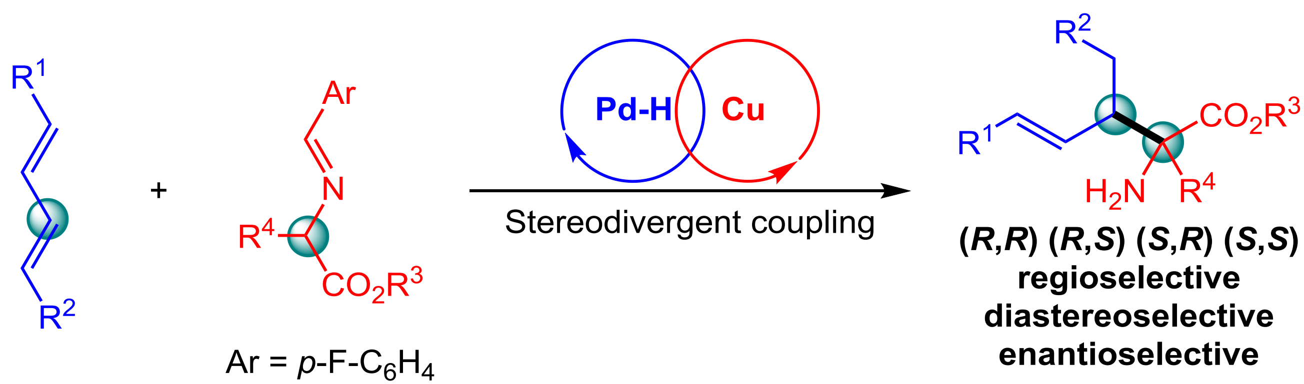
Stereodivergent Access to All Four Stereoisomers



Summary



Cruz, F. A.; Dong, V. M.* *J. Am. Chem. Soc.* **2017**, *139*, 1029



Zhang, Q.; Yu, H.; Shen, L.; Tang, T.; Zi, W.* *J. Am. Chem. Soc.* **2019**, *141*, 14554

The First Paragraph

As an atom-economical strategy for C-C bond formation, coupling reactions between enols/enolates and unsaturated hydrocarbons with catalysis by transition-metal hydrides (M-H) have been attracting increasing attention. These reactions are initiated by addition of M-H to the unsaturated hydrocarbon to form an electrophilic π-allyl metal intermediate, which reacts with the enolizable carbonyl compound to form a C-C bond. Substantial progress on asymmetric versions of these reactions has been made. However, controlling the stereochemistry when two contiguous stereocenters are generated by these methods remains a formidable challenge; Dong and co-workers reported the only successful example to date. These investigators developed a cooperative system involving Rh-H and Jacobsen's amine for stereodivergent coupling of aldehydes with alkynes.

The First Paragraph

Inspired by this work, as well as recent advances in Ir-catalyzed stereodivergent allylic alkylation reactions, we herein report a protocol for asymmetric coupling reactions between 1,3-dienes and aldimine esters with synergistic catalysis by Pd and Cu; all four possible stereoisomers of the coupling products could be obtained regio-, enantio-, and diastereoselectively by using various combinations of different enantiomers of the two catalysts.

The Last Paragraph

In summary, we have developed a protocol for stereodivergent coupling reactions between 1,3-dienes and aldimine esters with synergistic catalysis by Pd and Cu. This protocol has a wide substrate scope and could be used to prepare all four possible stereoisomers of synthetically useful amino acid esters with two vicinal stereogenic centers (at the α- and β-positions) with high diastereo- and enantioselectivities, simply by varying the configurations of the two chiral metal catalysts. Our work represents the first example of a stereodivergent coupling reaction catalyzed by Pd−H, and insights from this study can be expected to shed light on other Pd−H related synergistic catalyses.

Thanks
for your attention