Nickel-Catalyzed Hydroarylation of Styrenes

Reporter: Bo Wu
Checker: Yang Zhao
Date: 2019/07/01

Xiao, L.-J.; Zhou, Q.-L. *et al*. *Angew. Chem. Int. Ed.* **2018**, *57*, 461
Chen, Y.-G.; Mei, T.-S. *et al*. *J. Am. Chem. Soc.* **2019***, 141,* 3395

Contents

CV of Prof. Tian-Sheng Mei

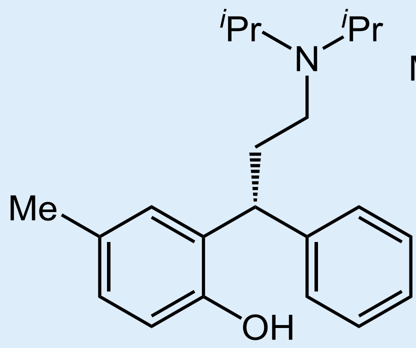
Background:

- **1997-2001** B.S., Lanzhou University
- **2005-2007** M.S., Brandeis University
- **2007-2012** Ph.D., The Scripps Research Institute
- **2012-2014** Postdoc, University of Utah
- **2014-Now** Professor, SIOC

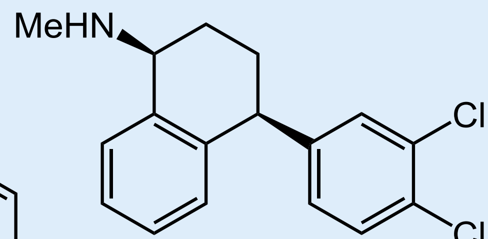
Research Interests:

- ✓ Exploring transition-metal-catalyzed highly stereoselective reactions
- ✓ Applying electrochemistry to organometallic chemistry

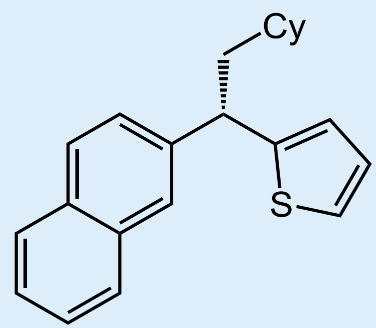
Introduction



tolterodine

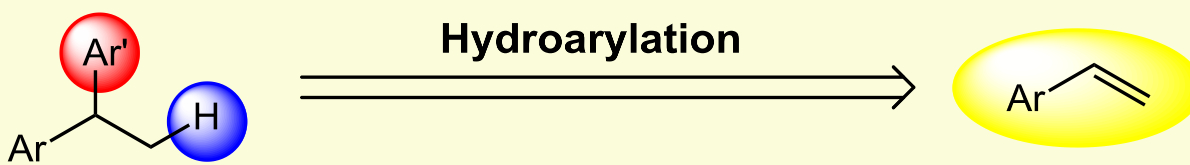


sertraline



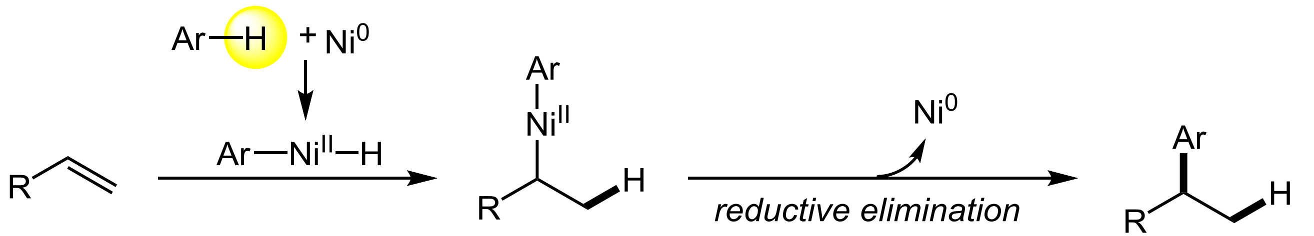
anti breast cancer agent

A facile method for the synthesis of 1,1-diarylalkanes

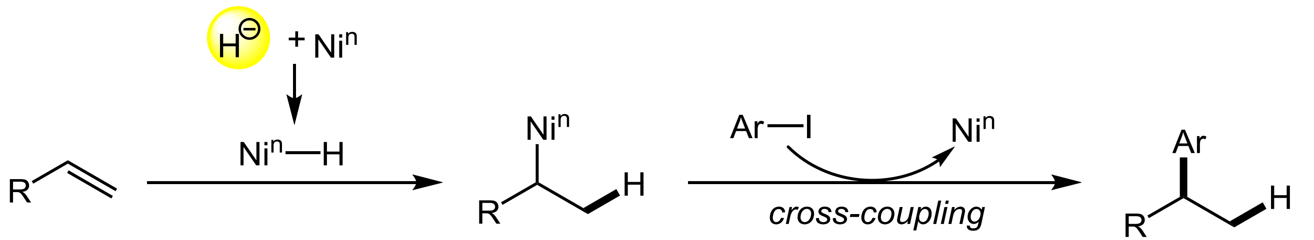


Nickel-Catalyzed Hydroarylation of Alkenes

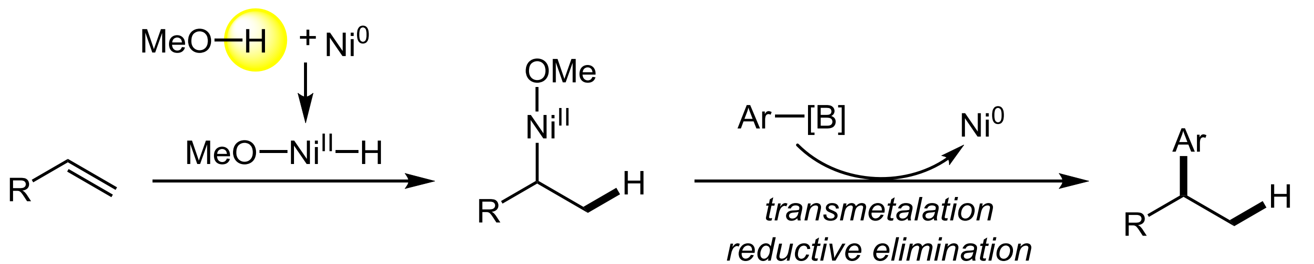
a) sp^2 C-H as H-atom source to form Ni-H



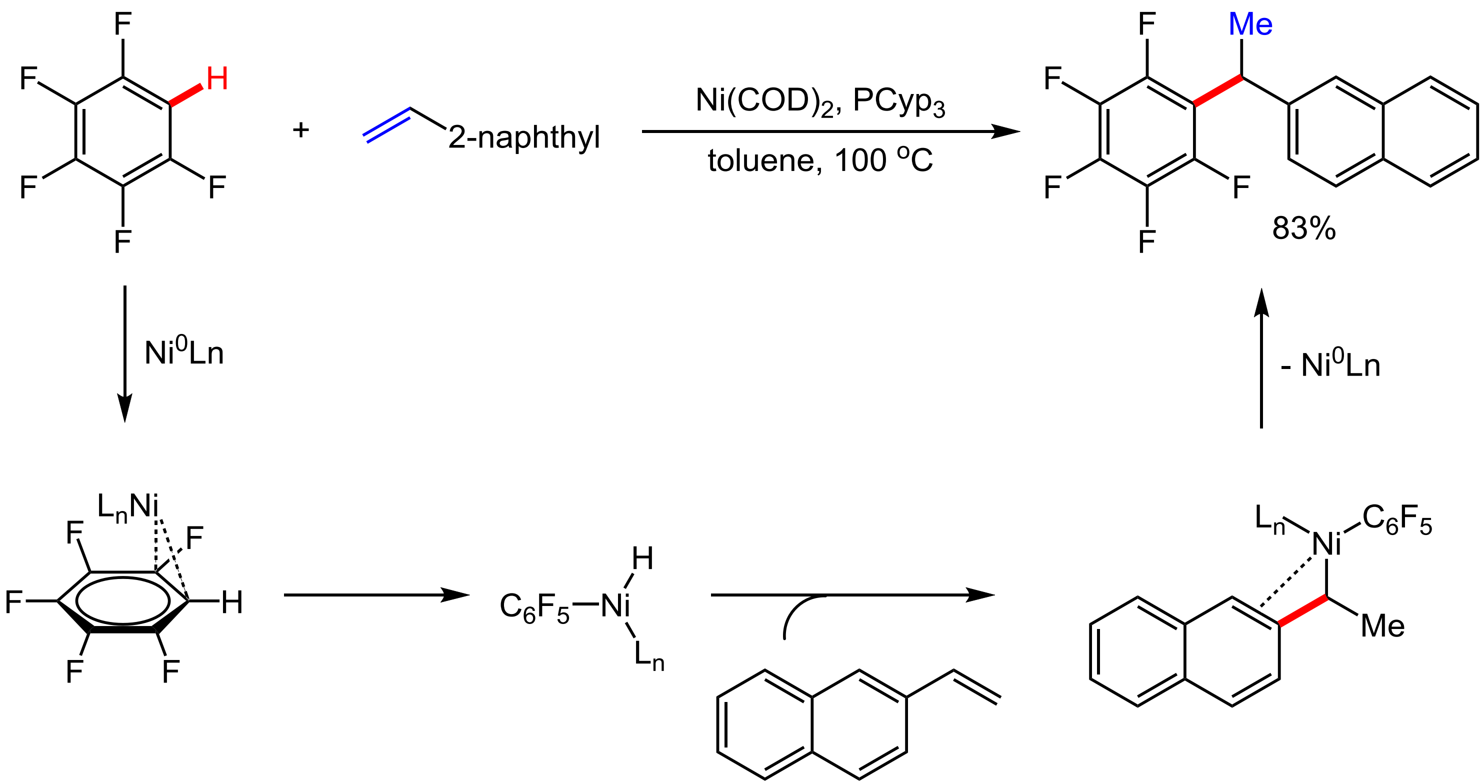
b) Hydride reagent as H-atom source to form Ni-H



c) Proton of alcohol as H-atom source to form Ni-H

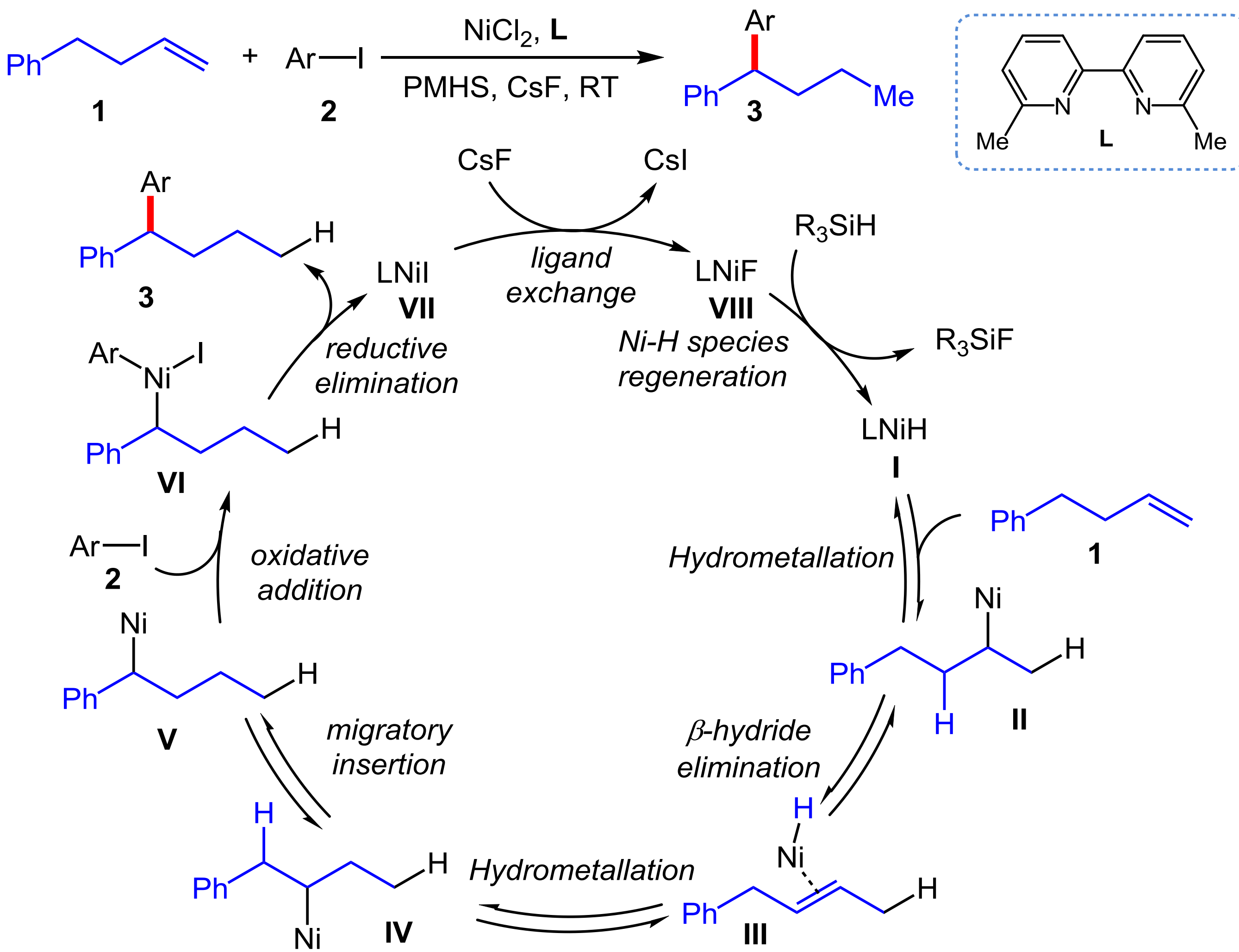


sp^2 C-H as H-Atom Source



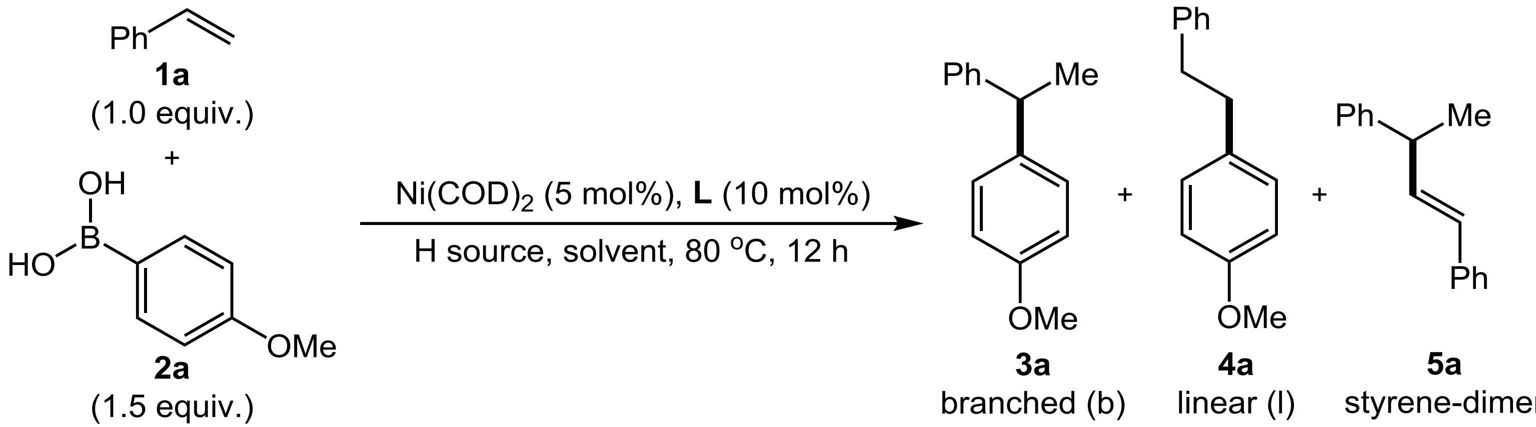
Hiyama, T. *et al. J. Am. Chem. Soc.* **2008**, *130*, 16170

Hydride Reagent as H-Atom Source



Zhu, S. *et al. J. Am. Chem. Soc.* **2017**, *139*, 1061

Proton of Alcohol as H-Atom Source



Entry[a]	L	Solvent	H source	Yield of **3a** (%)[b]	b/l[b]	Yield of **5a** (%)[b]
1	PCy_3	THF	none	14	93/7	84
2	PCy_3	toluene	none	21	95/5	76
3[c]	PCy_3	toluene	AcOH	trace	--	6
4[c]	PCy_3	toluene	PhOH	13	99/1	32
5[c]	PCy_3	toluene	H_2O	64	96/4	22
6[c]	PCy_3	toluene	MeOH	36	99/1	42

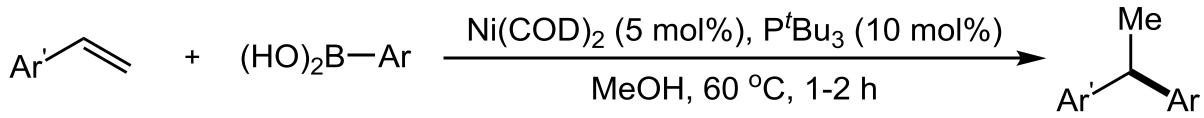
Zhou, Q.-L. *et al. Angew. Chem. Int. Ed.* **2018**, *57*, 461

Proton of Alcohol as H-Atom Source

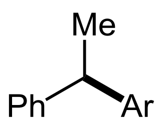
Entry[a]	L	Solvent	H source	Yield of **3a** (%)[b]	b/l[b]	Yield of **5a** (%)[b]
7	PCy_3	MeOH	MeOH	70	> 99/1	20
8	PCy_3	EtOH	EtOH	45	> 99/1	21
9	PCy_3	^{i}PrOH	^{i}PrOH	31	> 99/1	27
10	PCy_3	^{t}BuOH	^{t}BuOH	32	> 99/1	20
11	$P^{n}Bu_3$	MeOH	MeOH	4	> 99/1	27
12	$PCyp_3$	MeOH	MeOH	45	> 99/1	37
13	PPh_3	MeOH	MeOH	11	> 99/1	0
14[d]	$P^{t}Bu_3$	MeOH	MeOH	90 (88)	> 99/1	trace

[a] Reaction conditions: styrene **1a** (0.5 mmol), (4-methoxyphenyl)boronic acid **2a** (0.75 mmol), $Ni(COD)_2$ (0.025 mmol), ligand (0.050 mmol), solvent (1.0 mL). [b] Yields and b/l ratio were determined by GC with an internal standard; yield of isolated product is given in parenthesis. [c] H source (2.0 equiv.). [d] At 60 ^{o}C for 1 h.

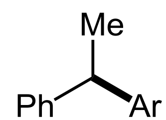
Substrate Scope



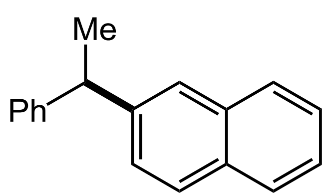
1 **2** (1.5 equiv.) **3**



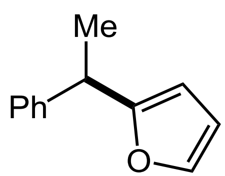
3a: Ar = 4-MeOC_6H_4, 88%
3b: Ar = C_6H_5, 73%
3c: Ar = 4-MeC_6H_4, 92%



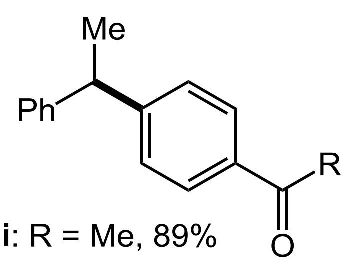
3d: Ar = 4-$F_3CC_6H_4$, 50%
3e: Ar = 2-MeC_6H_4, 61%
3f: Ar = 3,5-$Ph_2C_6H_3$, 86%



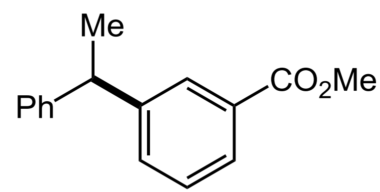
3g: 91%



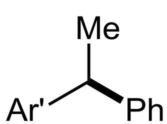
3h: 40%



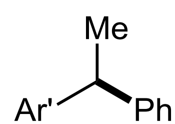
3i: R = Me, 89%
3j: R = NMe_2, 74%



3k: 85%

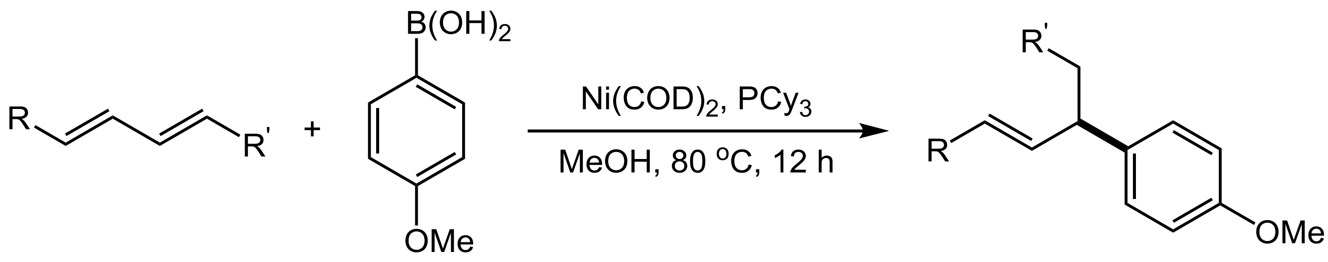


3l: Ar' = 4-MeOC_6H_4, 82%
3m: Ar' = 4-MeC_6H_4, 94%
3n: Ar' = 4-FC_6H_4, 83%

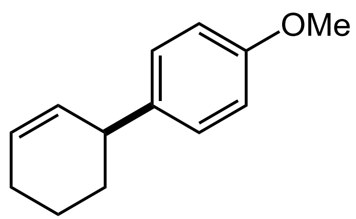


3o: Ar' = 4-$F_3CC_6H_4$, 63%
3p: Ar' = 3-MeC_6H_4, 89%
3q: Ar' = 2-MeC_6H_4, 60%

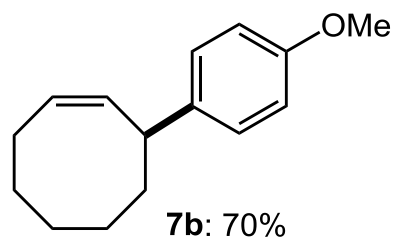
Hydroarylation of 1,3-Dienes



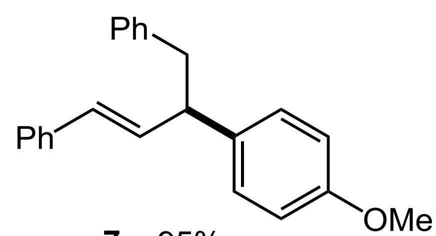
6 **2a** (1.5 equiv.) **7**



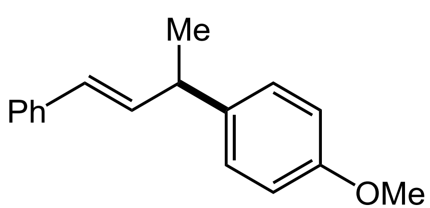
7a: 72%

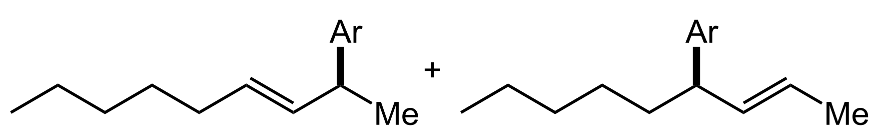


7b: 70%



7c: 95%



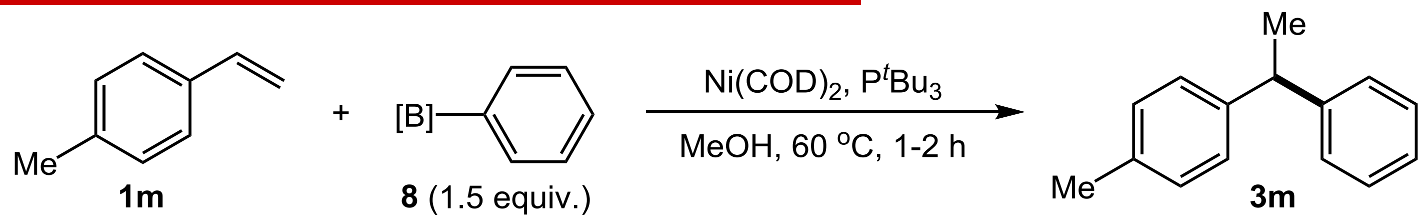


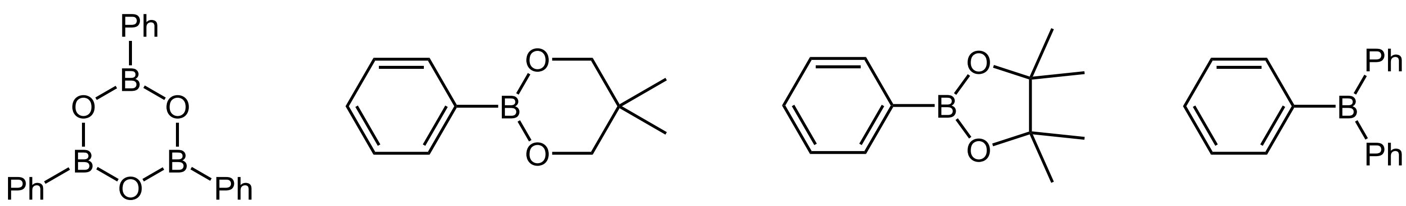
7e **7e'**

7d: 91% (PPh_3 was used)

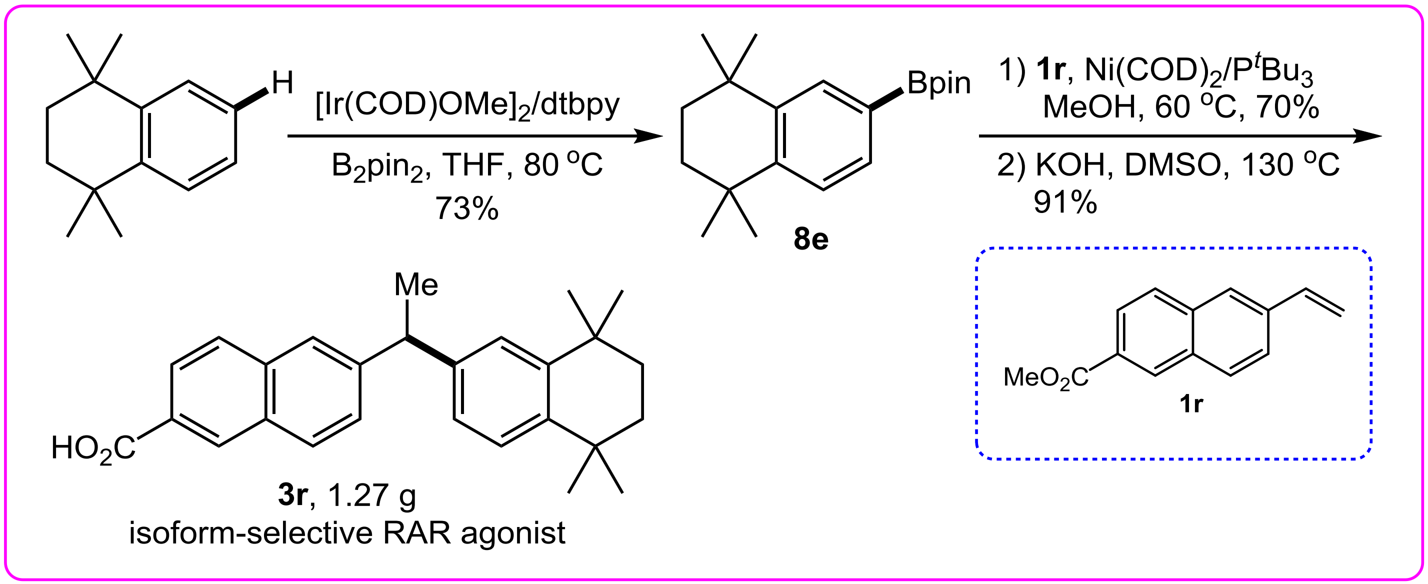
7e + **7e'** = 88%, **7e**/**7e'** = 1:1, Ar = 4-$MeOC_6H_4$, (PPh_3 was used)

Arylboron Reagent Scope and Application

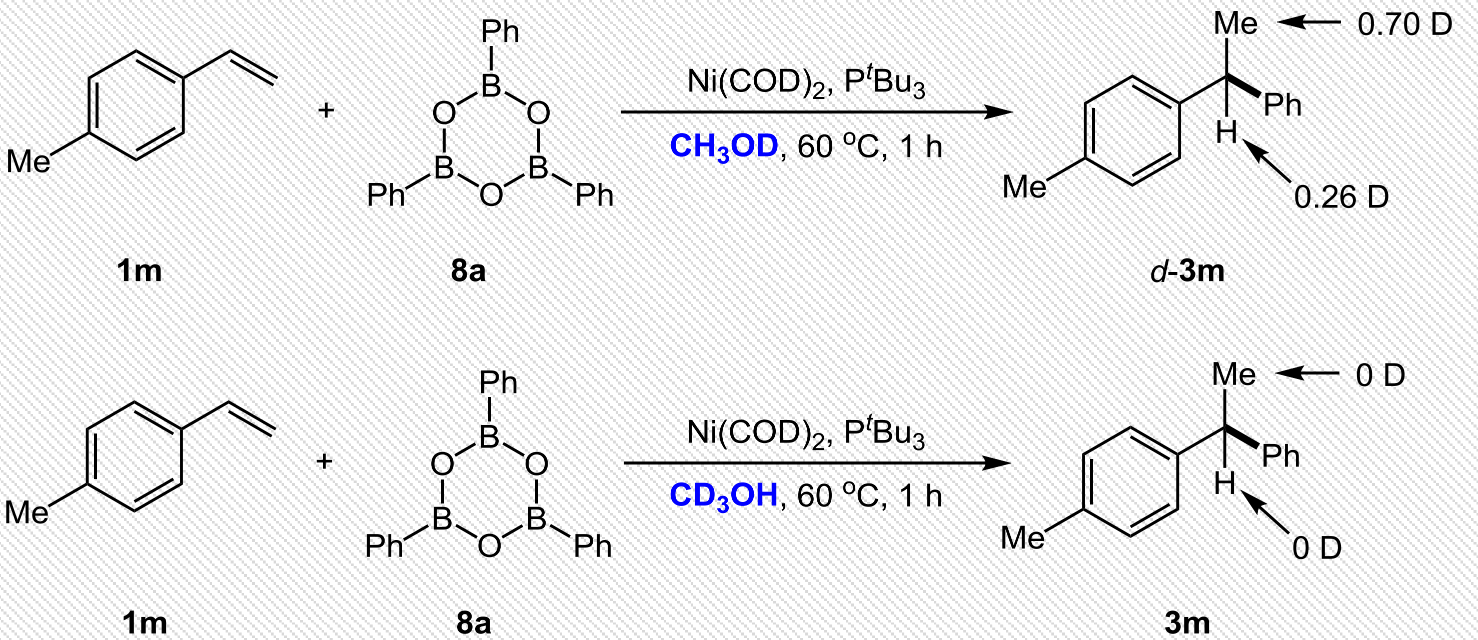




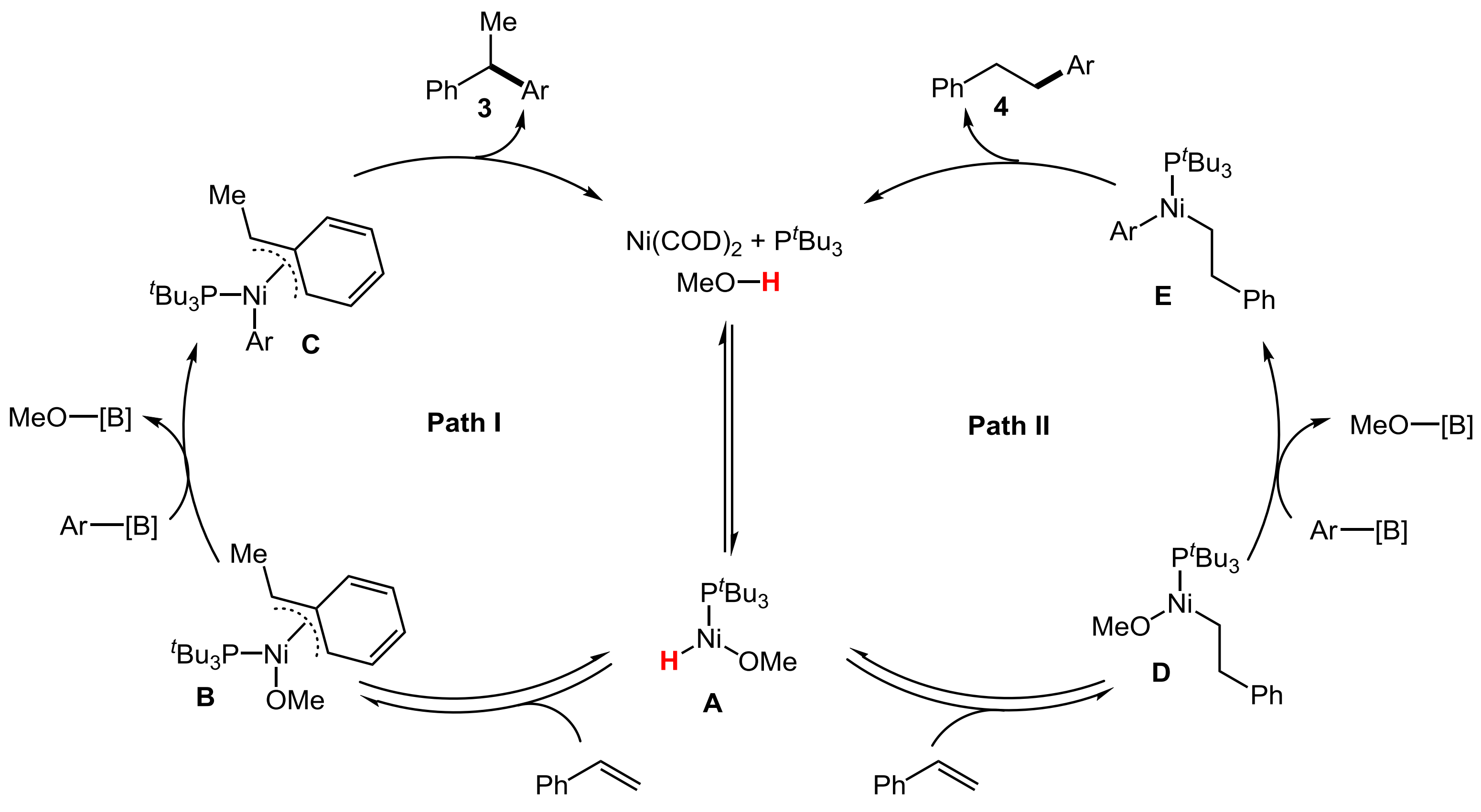
8a, 95% **8b**, 84% **8c**, 94% **8d**, 71%



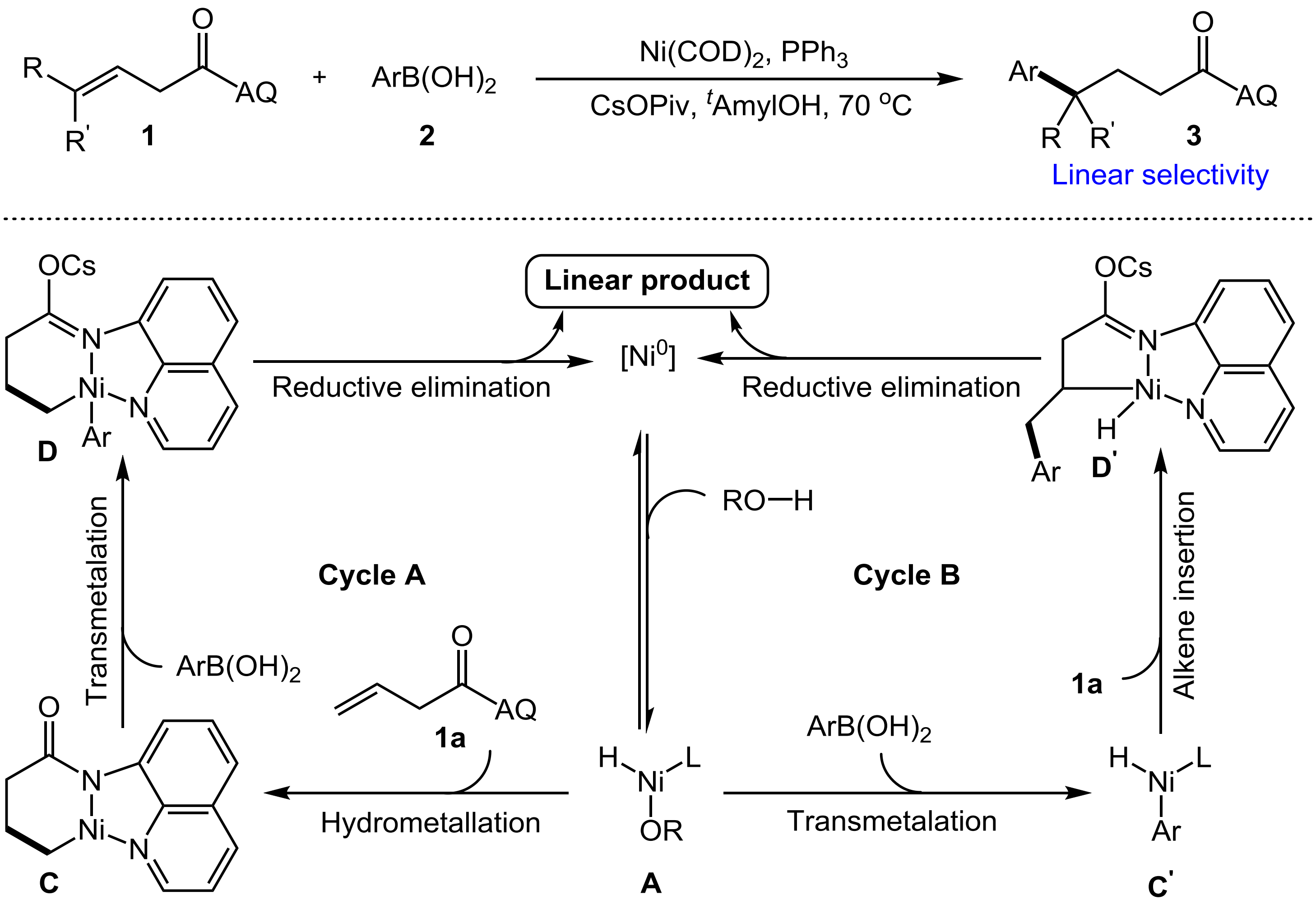
Deuterium-labeling Experiments



Proposed Mechanism

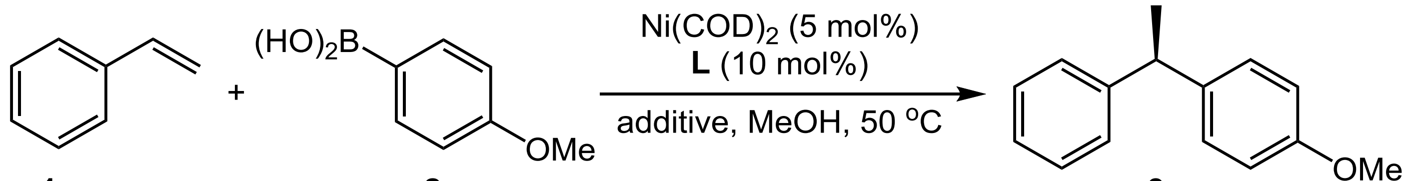


Linear-selective Hydroarylation



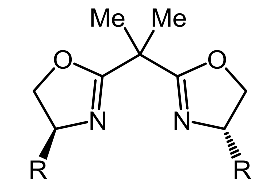
Zhao, D. *et al. Chem. Sci.* **2018**, *9*, 6839

Ni-Catalyzed Enantioselective Hydroarylation

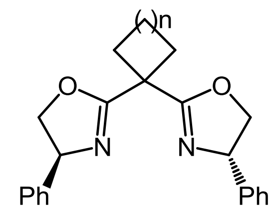


1a 2a 3a

Entry	L	Additive	Yield (%)	Ee (%)
1	**L1**	EtOLi	< 5	--
2	**L2**	EtOLi	76	40
3	**L3**	EtOLi	49	85
4	**L4**	EtOLi	88	84
5	**L5**	EtOLi	96	76
6	**L6**	EtOLi	96 (92)	92
7	**L7**	EtOLi	62	90
8	**L6**	--	64	63
9	**L6**	MeOLi	82	90
10	**L6**	^{t}BuOLi	95	89



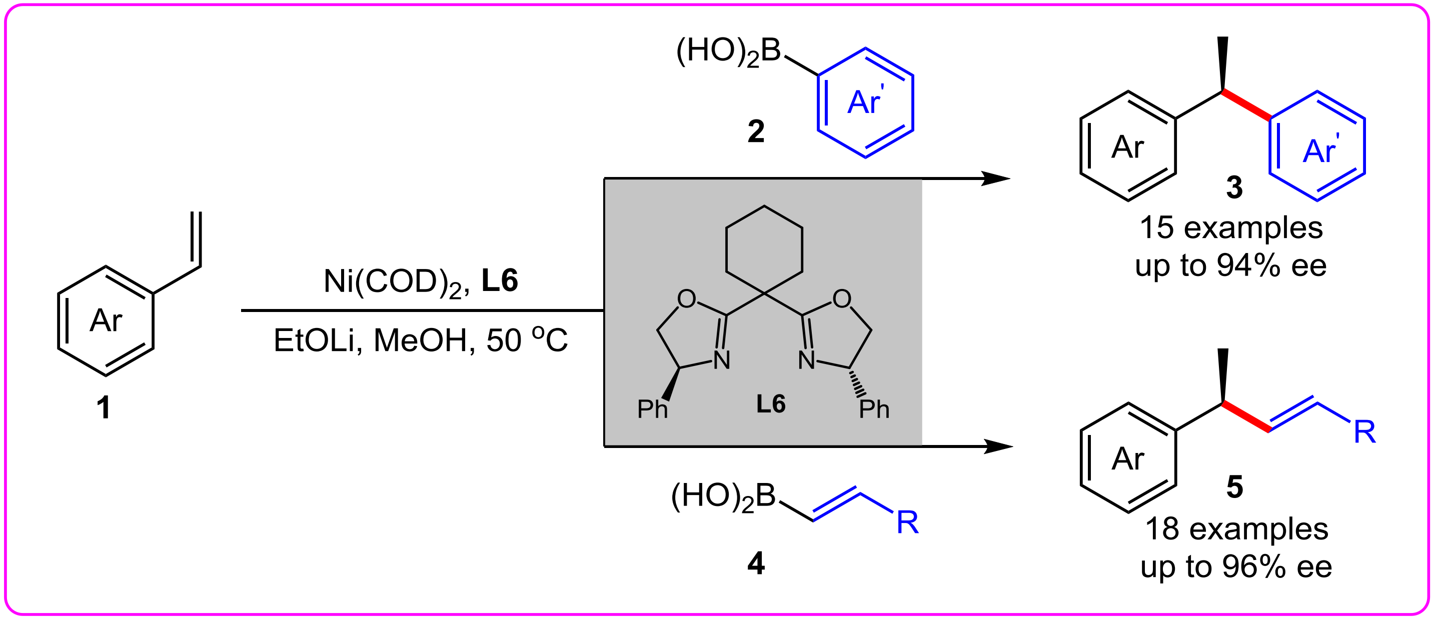
L1, R = ^{i}Pr
L2, R = Bn
L3, R = Ph

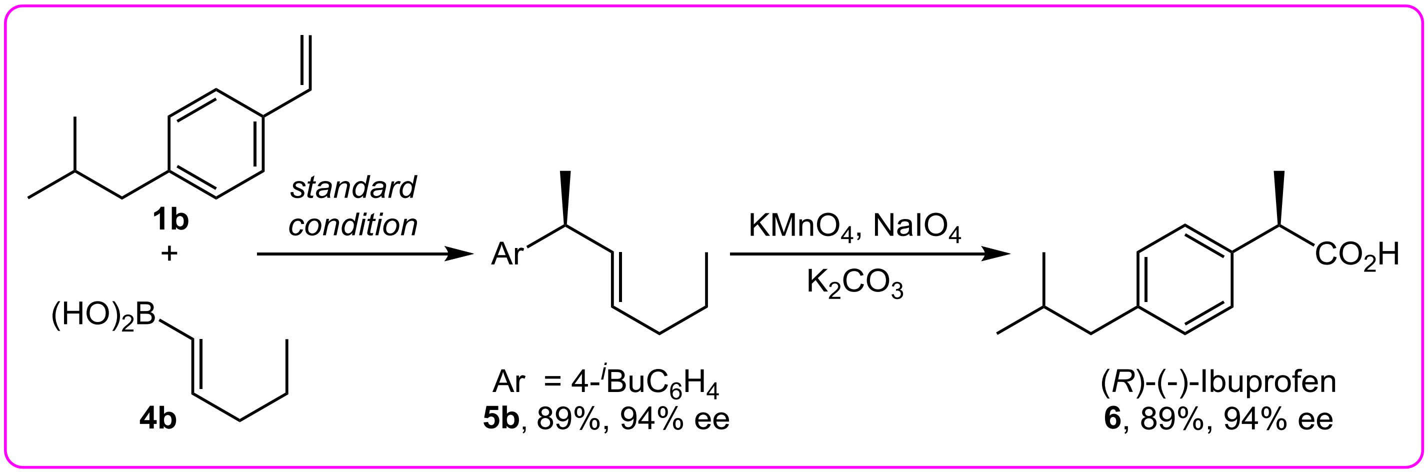


L4, n = 1
L5, n = 2
L6, n = 3
L7, n = 4

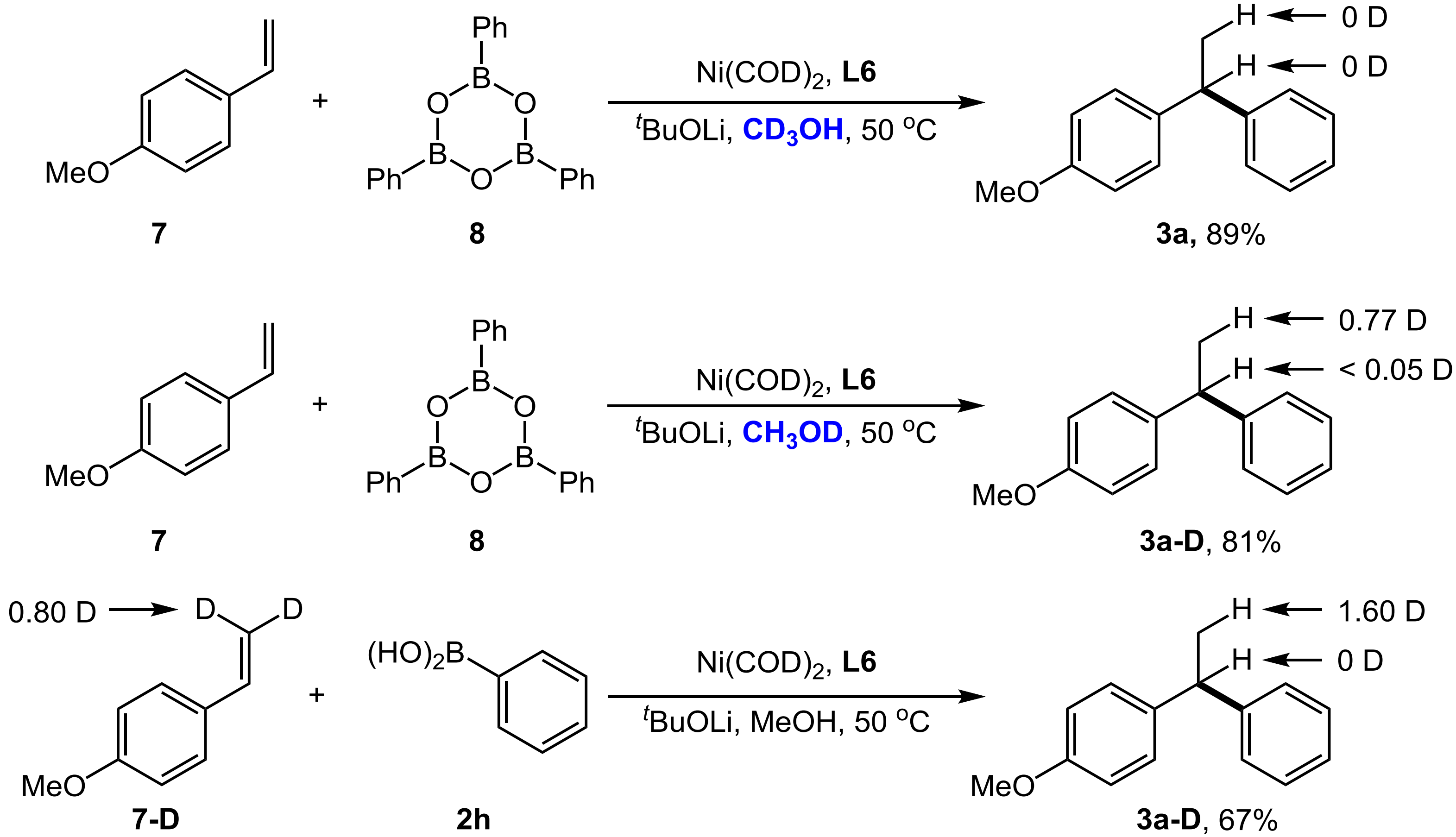
Mei, T.-S. *et al. J. Am. Chem. Soc.* **2019**, *141*, 3395

Substrate Scope and Application

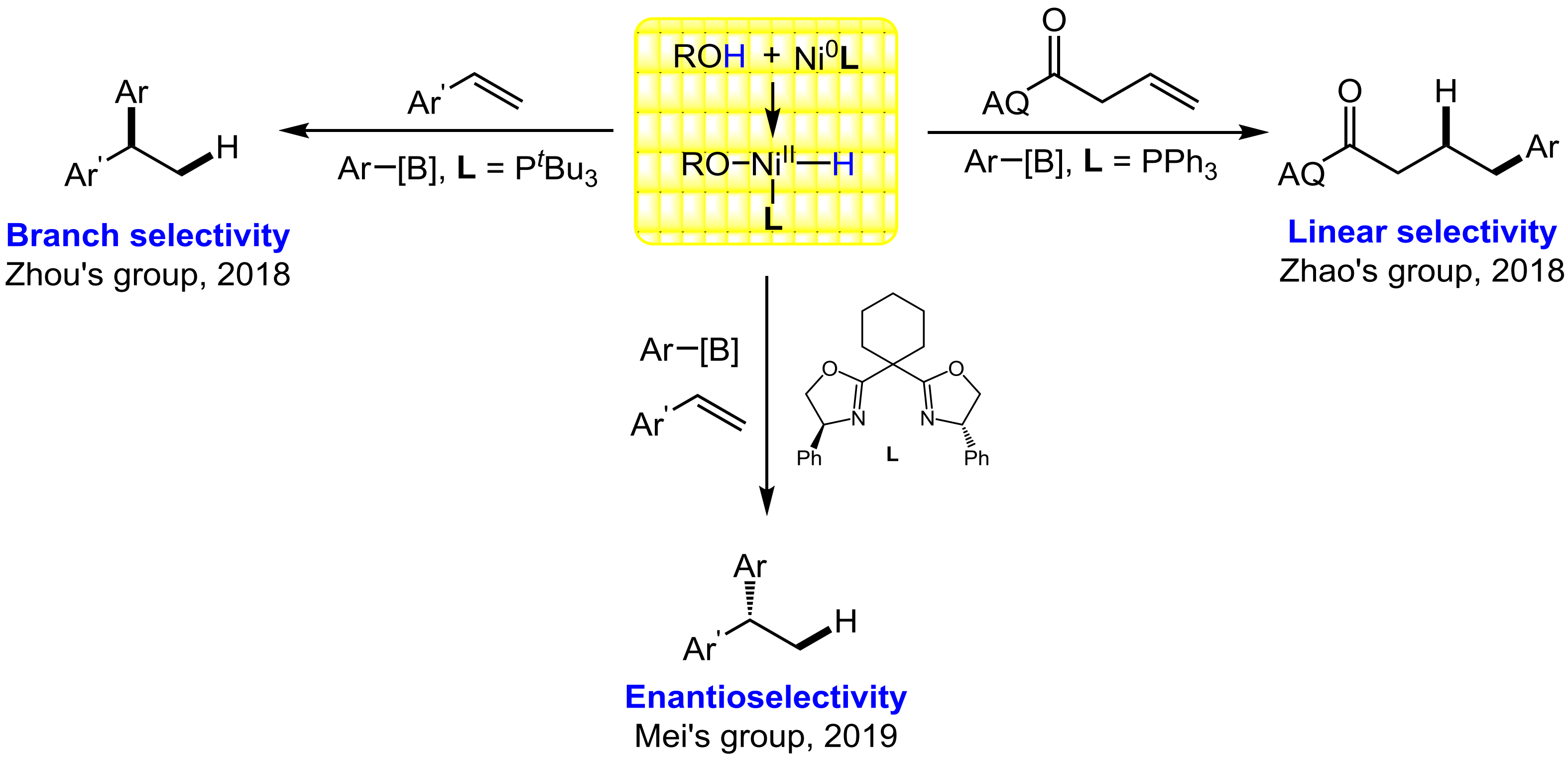




Deuterium-labeling Experiments



Summary


ROH + Ni^{0}L
RO–Ni^{II}–H
L
Ar'
Ar–[B], L = P^{t}Bu$_3$
Ar
Ar'
H
Branch selectivity
Zhou's group, 2018
O
AQ
Ar–[B], L = PPh$_3$
O
H
AQ
Ar
Linear selectivity
Zhao's group, 2018
Ar–[B]
Ar'
O
N
N
O
Ph
L
Ph
Ar
Ar'
H
Enantioselectivity
Mei's group, 2019

The First Paragraph

Transition-metal-catalyzed functionalization of alkenes is a highly efficient C-C bond forming reaction that makes use of abundant feedstocks to produce value-added products and it has received increasing attention. Hydroarylation, the addition of hydrogen and an aryl group to alkenes offers a straightforward method for the synthesis of alkylarenes. Among hydroarylations, reaction with styrenes can produce 1,1-diarylalkanes, which often show biological activity. To date, two strategies have been developed for achieving the hydroarylation of alkenes, and they are characterized by using different way to generate active catalyst species M-H. One uses C-H bond activation of arenes to form M-H, and the other uses hydride reagents to form M-H.

The First Paragraph

The former strategy usually requires arenes with a directing group or heteroarenes. The latter strategy works only under reductive conditions. As a part of our efforts toward the development of catalysis based on earth-abundant nickel, we herein report the hydroarylation of alkenes under redox-neutral conditions. In our hydroarylation reaction, the proton of methanol was used to react with Ni^0 to generate the active catalyst species Ni-H, which represents a unique example in which the catalytic process is initiated by the protonation of a low-valence metal.

The Last Paragraph

In summary, we have developed a highly selective Ni-catalyzed hydroarylation of styrenes and 1,3-dienes with arylboron compounds under redox-neutral conditions. This reaction offers a new approach to the selective preparation of diarylalkanes and allylarenes. In this hydroarylation reaction, a new strategy that uses the proton of methanol to generate active catalyst species Ni-H was developed. These results shed light on the origins of the reactivity and regioselectivity of the reaction and may be useful for the development of new functionalization reactions of alkenes catalyzed by nickel or other transition metals.

Acknowledgement

Thanks

for your attention