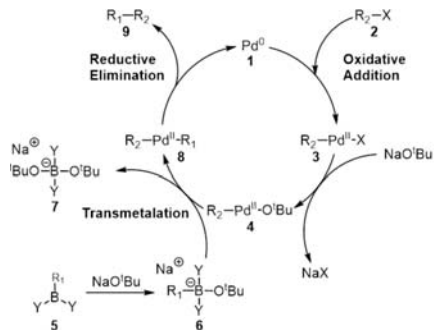


J. P. Morken: (*Chem. Comm.* **2007**, 4717)

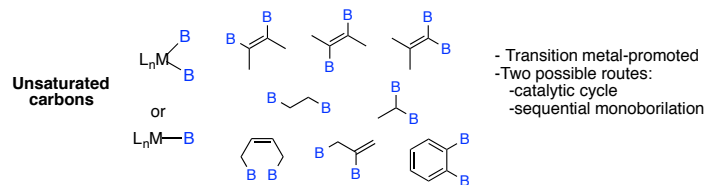
- Organoboranes are versatile reagents for organic synthesis due, in part, to a combination of accessibility, stability, and reactivity.
- While organoboronic esters are stable to air and moisture, under appropriate reaction conditions, they participate in oxidation, amination, sulfination, phosphination, halogenation and a variety of catalyzed and non-catalyzed C–C bond forming reactions.
- **Multiborylated compounds** are currently emerging as useful conjunctive reagents for asymmetric synthesis.
- They can be crafted or manipulated in an enantioselective catalytic fashion and they provide opportunities for multiple sequential bond-forming transformations.

Cross-coupling reactions



Preparation of diboronates

From unsaturated carbons



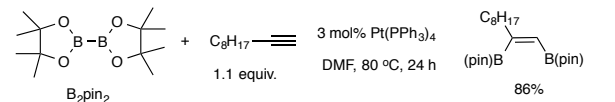
- Transition metal-promoted
- Two possible routes:
- catalytic cycle
- sequential monoboration

This work is exclusively centered in diboration of unsaturated substrates because diboration of saturated systems are *nowhere to be found*. Also, although transition metal-catalysis is the most common form of catalysis for these systems, a metal-free example (not discussed here) was developed by Hoveyda and his lab (*JACS* **2012**, *134*, 8277)

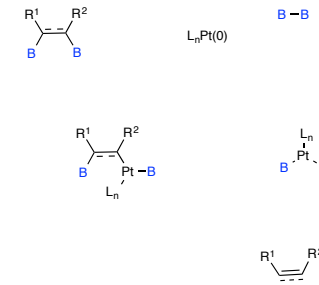
Alkynes

Pt-catalyzed

First discovered by Suzuki, Miyaura, and co-workers in 1993 (*JACS* **1993**, *115*, 11018)



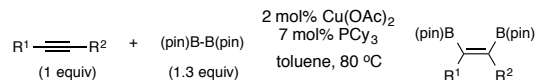
inactive toward diboration.¹⁰ Since the pinacol ester derivative **1** is thermally stable and can be easily handled in air, the reaction should allow the synthesis of a wide range of stereodefined bis(boryl)alkenes and their additional synthetic applications.



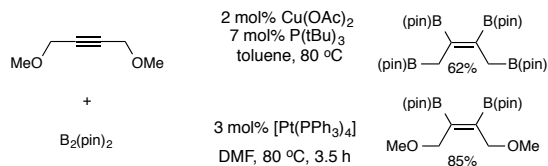
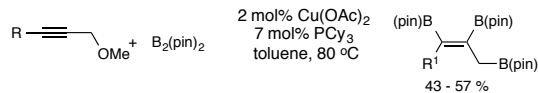
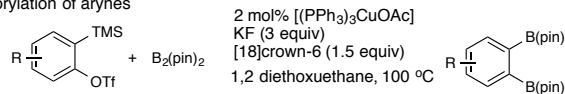
Catalytic cycle for the Pt-catalyzed diboration of unsaturated hydrocarbons

Cu-catalyzed

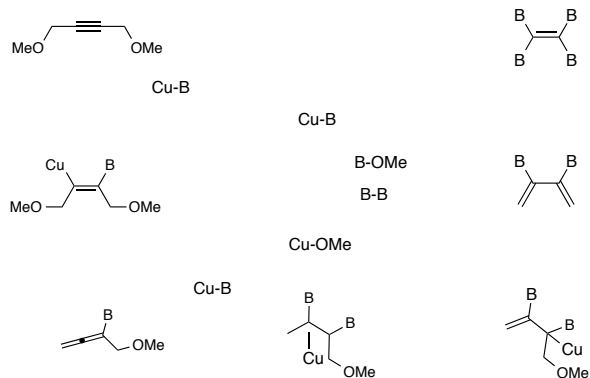
ACIE **2011**, *51*, 235.



Diborylation of arynes

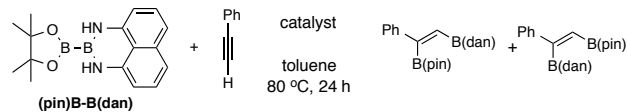


Proposed catalytic cycle for the tetraborylation



Differentially-protected diborons from alkynes

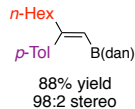
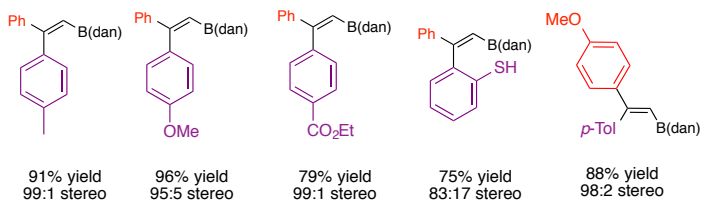
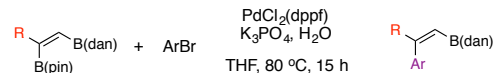
JACS. **2010**, *132*, 2548.



Catalyst screening

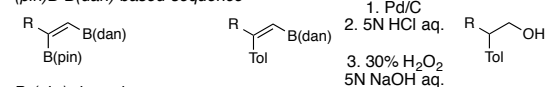
5	Pt(dba) ₂ (2)	(4-CF ₃ C ₆ H ₄) ₂ P (2.2)	83	84:16
6	Pt(dba) ₂ (2)	[3,5-(CF ₃) ₂ C ₆ H ₃] ₂ P (2.2)	74 ^d	96:4
13	[IrCl(cod)] ₂ (1)	—	51	98:2

Suzuki-Miyaura Scope

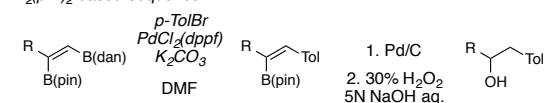


Reaction is regiocomplementary to the 'common' symmetrical diborons
stepwise reactions!

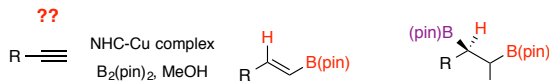
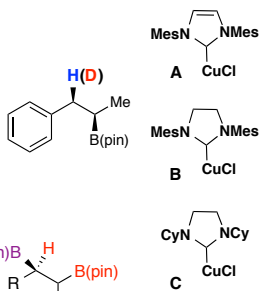
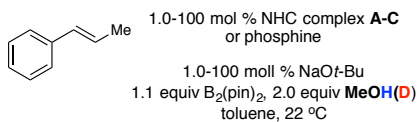
(pin)B-B(dan)-based sequence



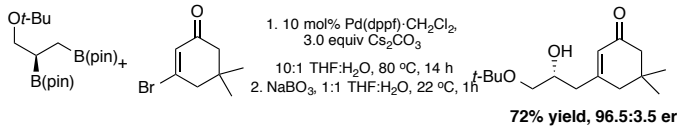
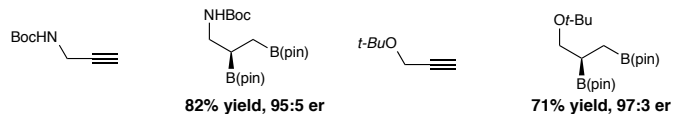
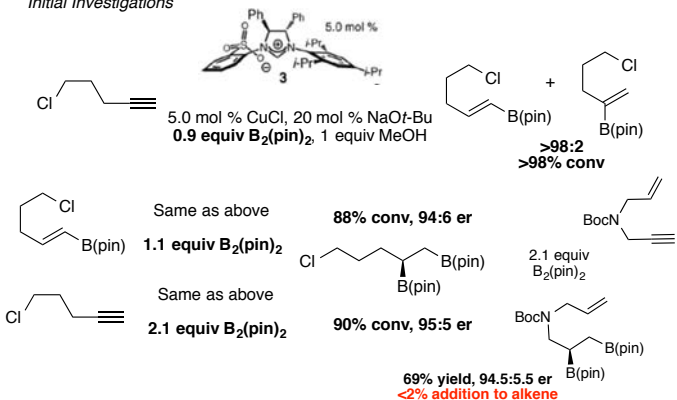
B₂(pin)₂-based sequence



Terminal Alkynes to saturated diboronates
JACS, **2009**, *131*, 18234.



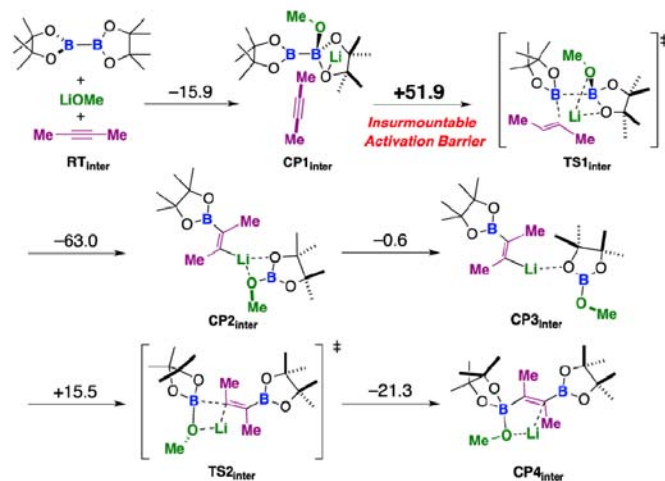
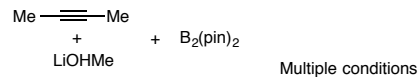
Initial Investigations



First Trans Diborylation

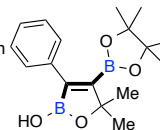
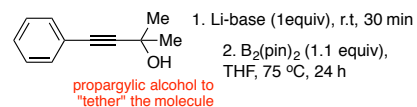
JACS, **2014**, *136*, 8532.

- Key transition state: Anionic mechanism (*trans*) vs. interactions between orbitals of the transition metal and the alkyne (*cis*)

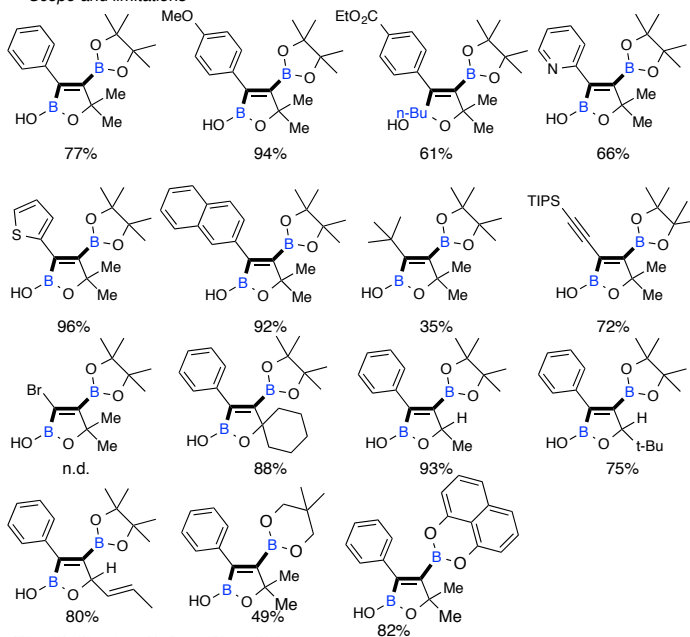


Solution?

Pseudo-Intramolecular Approach



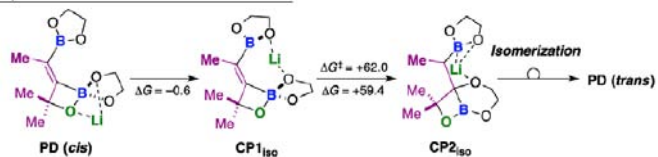
Scope and limitations



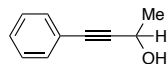
Pseudo-intramolecular trans-Diborylation:



Equilibrium between *cis*- and *trans*-Products:

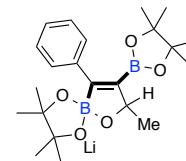


Applications?

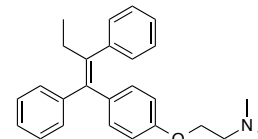
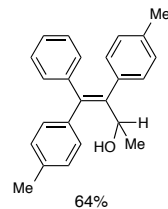


1. *n*-BuLi (1 equiv)
dioxane, r.t., 30 min

2. B₂(pin)₂ (1.1 equiv)
75 °C, 24 h



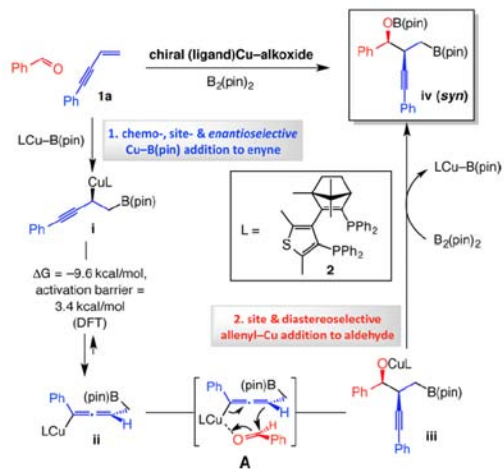
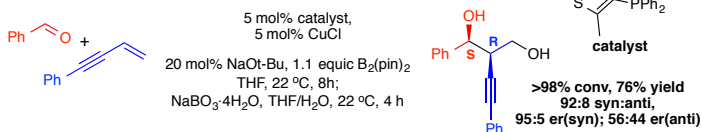
3. (2.2 equiv)
PdCl₂(dppf) (5 %)
dioxane/aq, KOH
120 °C, 24 h



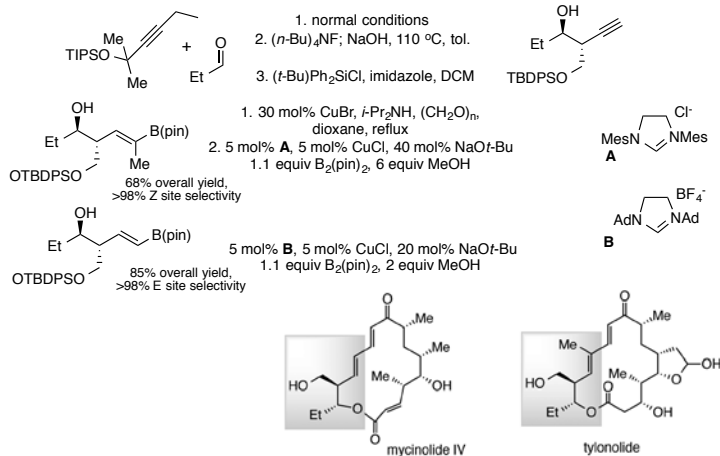
tamoxifen

Others

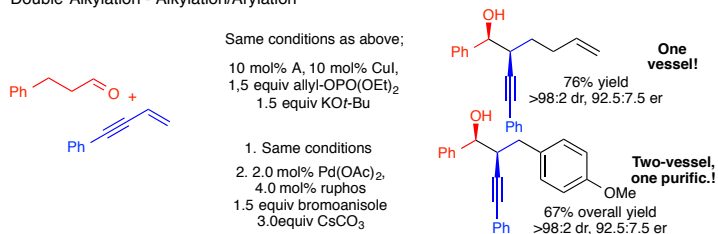
1,3-enynes
JACS 2014, 136, 11304.



Application to fragments of Tylonolide and Mycinolide IV

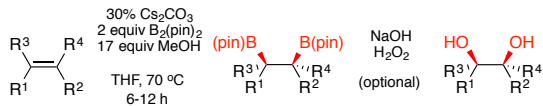


Double Alkylation - Alkylation/Arylation



Alkenes

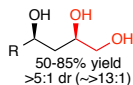
Hydroxyl-directed
Morken. *JACS*, **2014**, *136*, 9264.



-Cyclic and acyclic homoallylic and bis-homoallylic alcohols
-Alternative to OsO₄-promoted dihydroxylations

Scope

Terminal alkenes

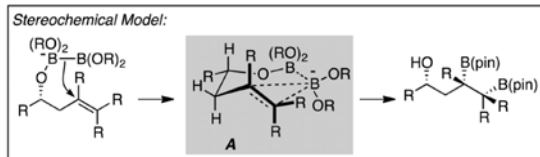
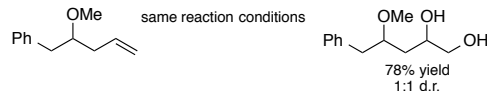


1,1-disubstituted alcohols

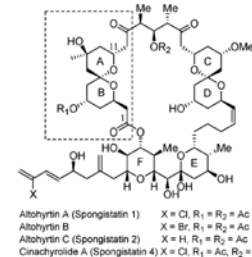
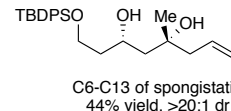
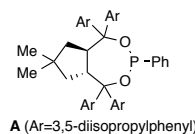
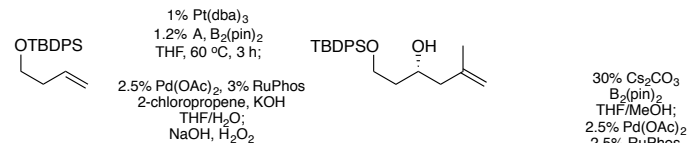


-Cyclic alkenes (syn diols)
-Allylic alcohols suffer from diminished dr

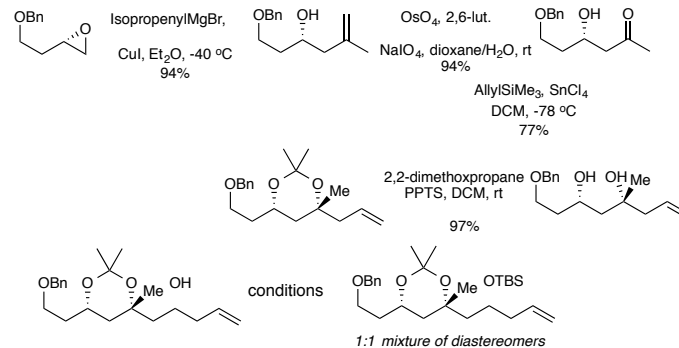
DR is lowered when methoxy-derivative is used instead



Application to the synthesis of C6-C13 spongistatin

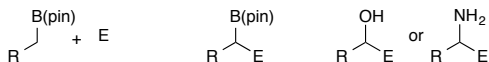


In comparison, look at this old-fashioned synthesis....



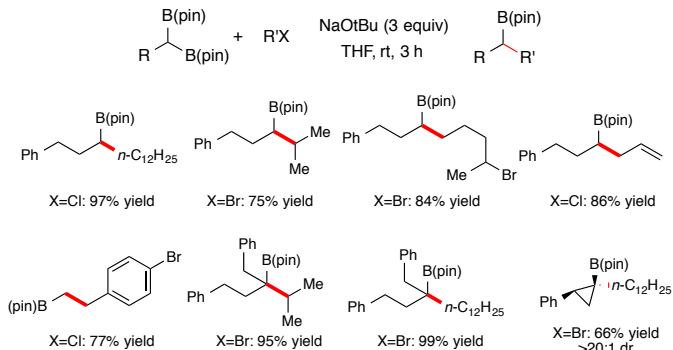
Geminal diborons

JACS, 2014, 136, 10581.



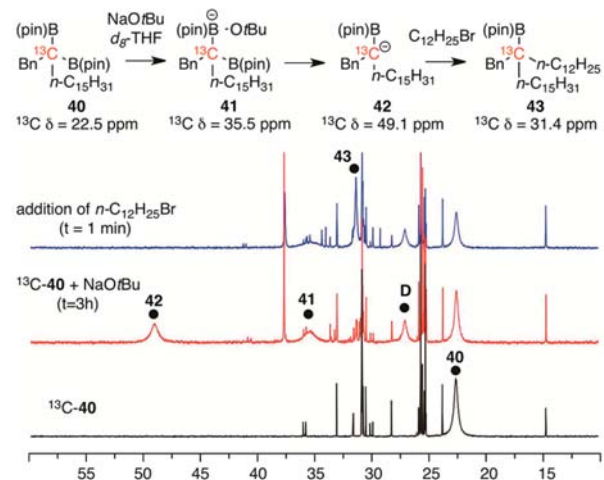
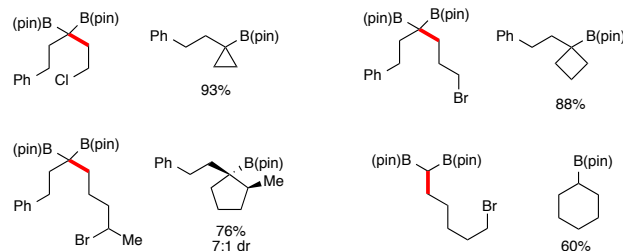
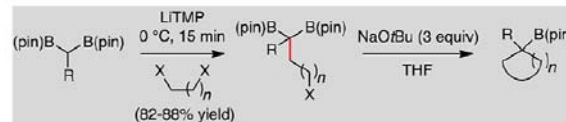
- The valence deficiency of three-coordinate boron can be used to stabilize anions at adjacent carbon centers
- They report an alkoxide-promoted deborylative alkylation of geminal boronates that applies to aliphatic primary, secondary, and tertiary derivatives
- can enable highly hindered C-C couplings between geminal boronates and alkyl halide electrophiles
- They also provide the first experimental evidence that these reactions proceed through the intermediacy of alpha-boryl carbanions
- Given that geminal bis(boronates) are easily accessed on a large scale, this reactivity pattern constitutes a practical strategy for the construction of common alkyl pinacol boronic esters.

Scope



- mono- and di-substituted geminal boronates
- primary and secondary halides
- Cl or Br (I gives lower yields)
- Allylic electrophiles
- Diborylmethane: efficient strategy for single-carbon homologation

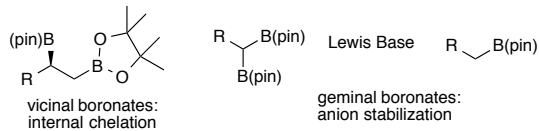
The coolest thing!



Enantioselective boronation of vinyl boronates

JACS. 2014, 136, 16140.

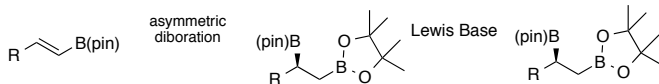
There is inherently distinctive reactivity in bis(boronate) esters



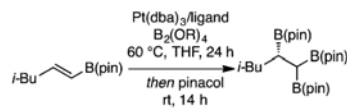
The possibilities of mixing them together....

JACS. 2014. ASAP DOI: 10.1021/ja510081r

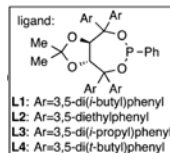
Chiral tris(boronates)



Enantioselective vinylboronate diboration



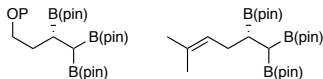
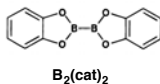
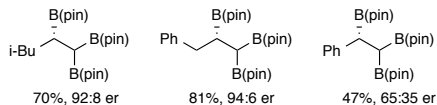
7 ⁺	L3	B ₂ (cat) ₂	3/6	>98	70	92:8
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-Since Pt/phosphonite complexes are effective in the enantioselective diboration of terminal alkenes, dienes, and imines, they considered them as prospective catalysts for vinyl boronate diboration

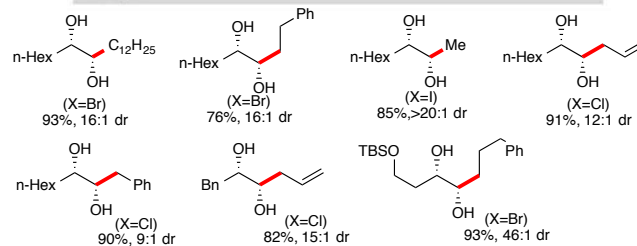
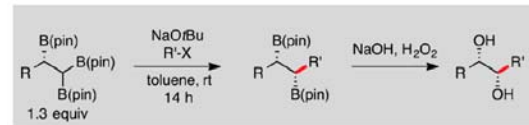
Note the use of a "more reactive" reagent.

Scope

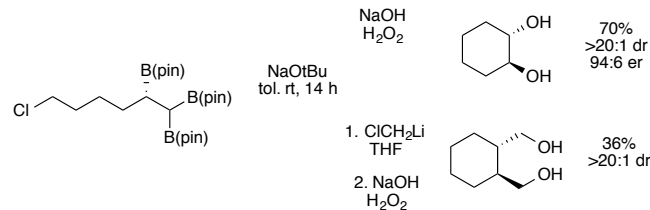
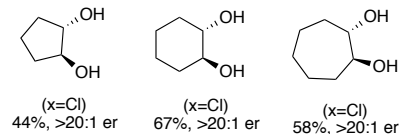
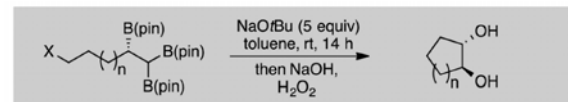


P=TBS 78%, 81:19 er
P=TBDPS 81%, 83:17 er

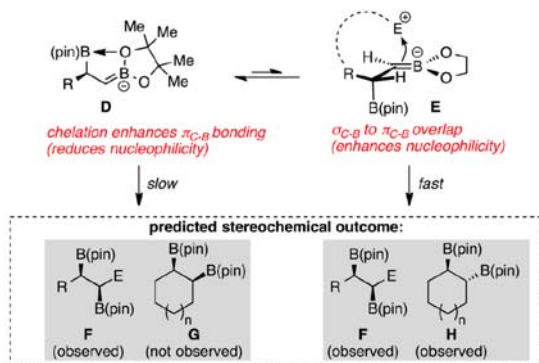
Deborlyative Alkylation



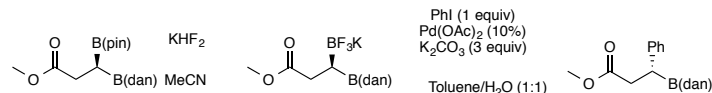
Stereoselective Intramolecular Deborylative Alkylation



Stereochemical Analysis

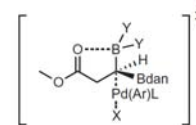


Nature Chem. 2011, 3, 894.

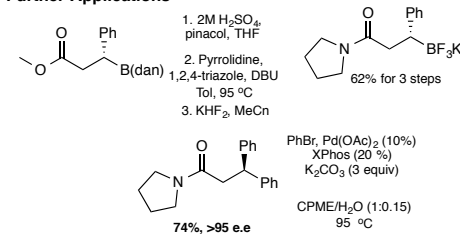


-Differentiated geminal diborons

Proposed TS

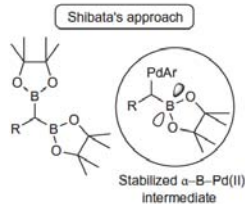
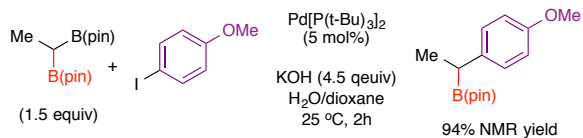


Further Applications

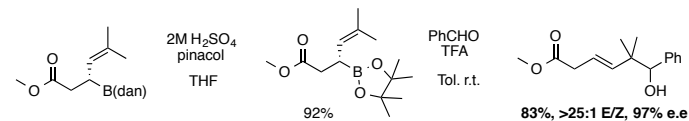


Honorary Mention

Shibata and coworkers were the first to demonstrate that achiral 1,1-diboronate esters undergo cross coupling in a chemoselective fashion affording only the mono-coupled product. (*JACS*. 2010, 132, 11033)

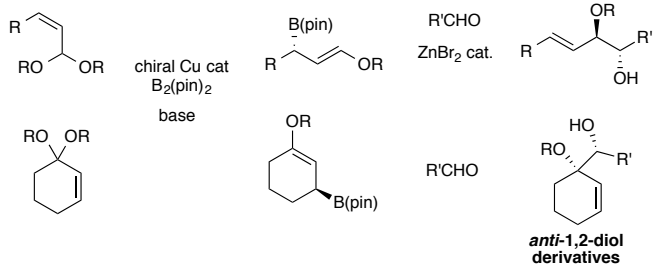


Or even further applications...

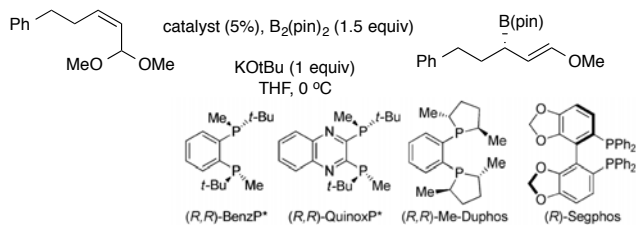


Access to linear and carbocyclic α -chiral (δ -alkoxyallyl) boronates

JACS. ASAP. DOI:10.1021/ja506284w



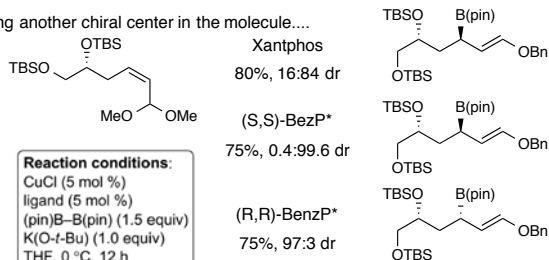
What do they do? Screening....



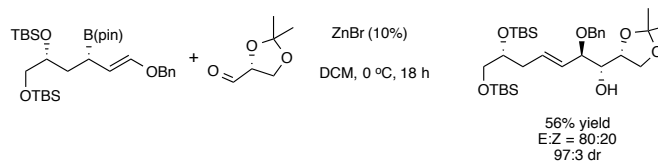
entry	catalyst	time (h)	yield ^b (%)	ee ^c (%)
1	CuCl/(<i>R,R</i>)-BenzP*	3	95 (83)	97

Pretty normal scope

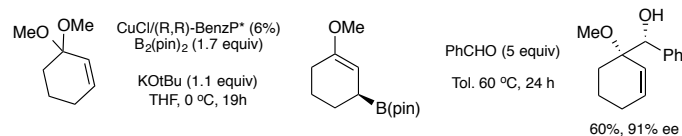
Having another chiral center in the molecule....



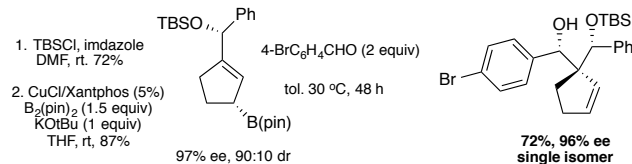
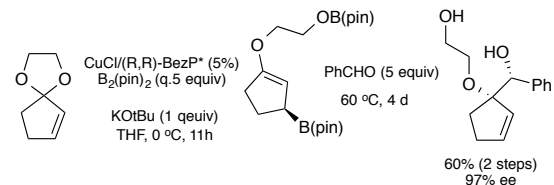
Convergent coupling for polyol derivatives



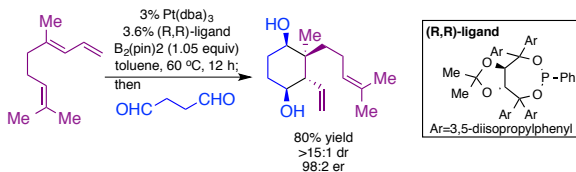
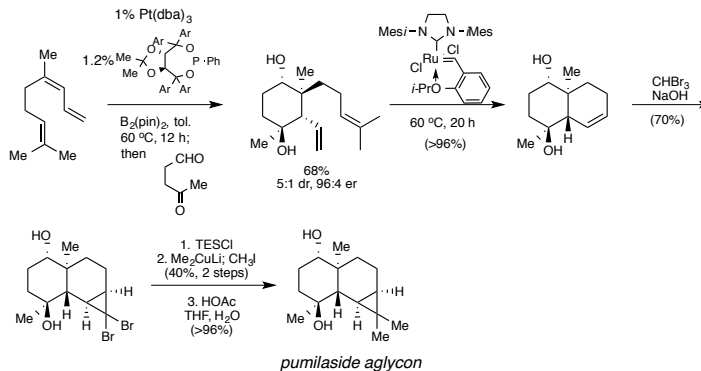
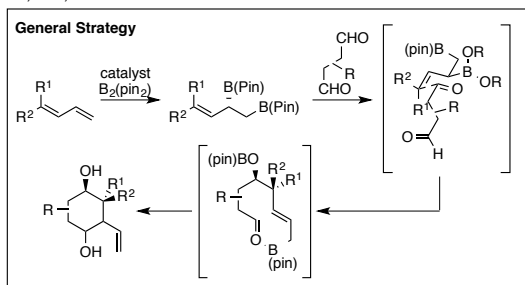
Enantioselective boryl substitution in cyclic substrates



Stereoselective modular construction of complex 3,3-disubstituted cyclopentenes



Strategy for rapid terpene construction:
Application to the synthesis of Pumiliside Aglycon
JACS. 2013, 135, 2501.



Scope

