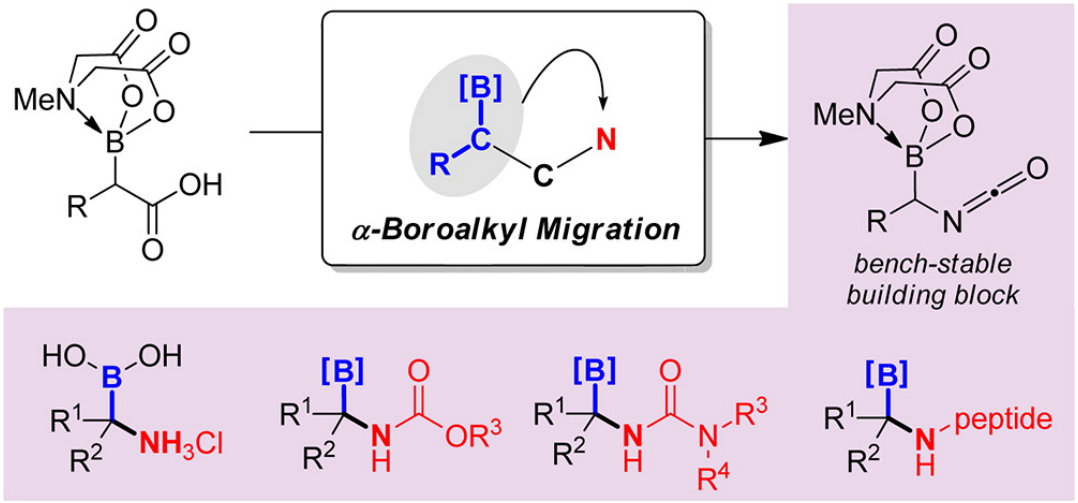
Boroalkyl Group Migration Provides a Versatile Entry into α-Aminoboronic Acid Derivatives

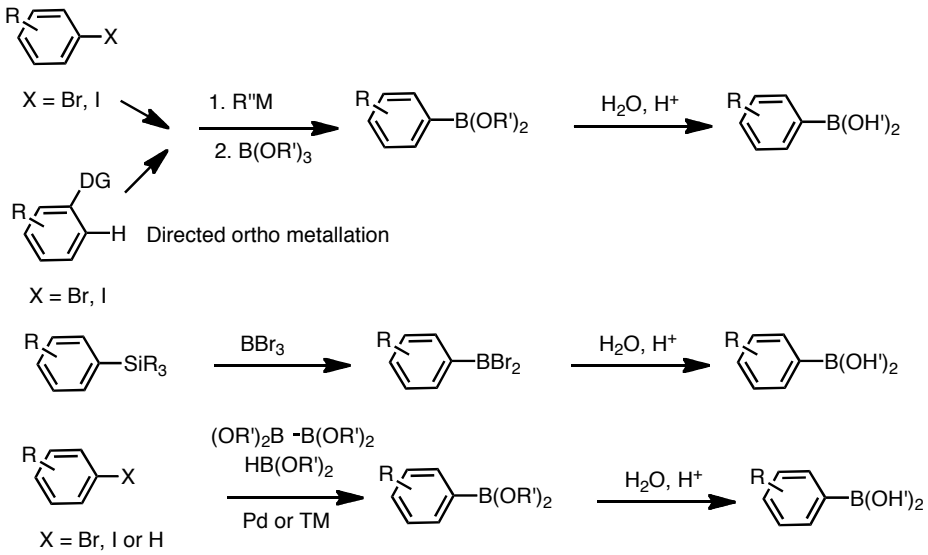
Zhi He, Adam Zadilk, Jeffrey D. St. Denis, Naila Assem and Andrei K. Yudin

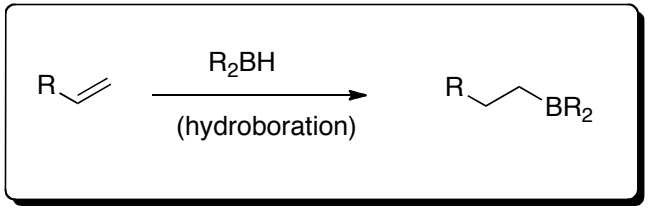
JACS, 2012, 134, 9926

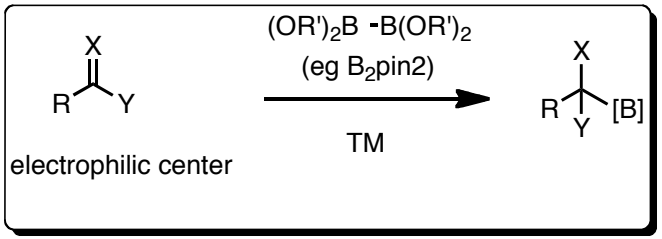


Jaideep Saha
Wipf Group Current Literature
December 1, 2012

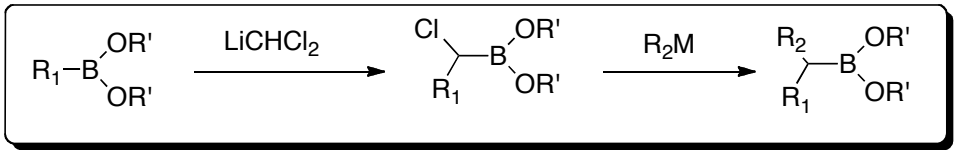
Installation of Boron functionality



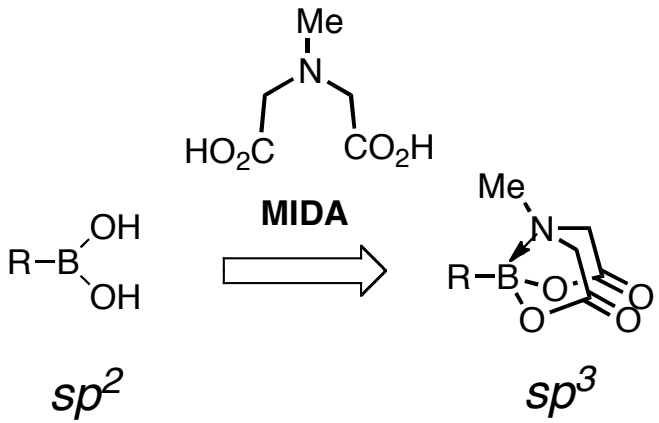




Matteson homologation



MIDA boronates



Burke group, UIUC

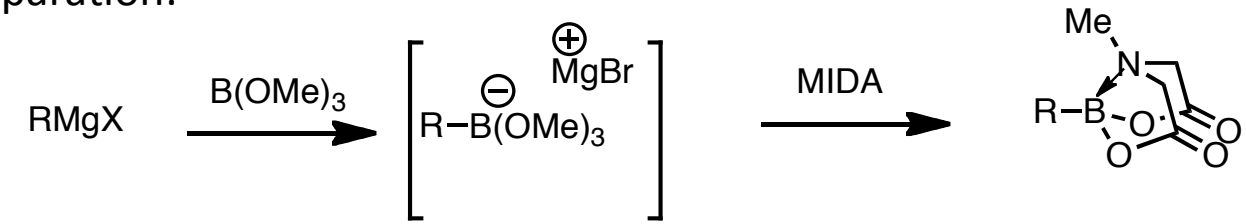
Suzuki-Miyaura cross coupling reaction of boronic acids is a very frequently utilized reaction In organic chemistry.

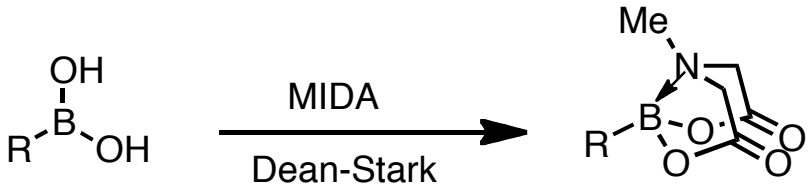
Many boronic acids are unstable and Susceptible for decomposition.

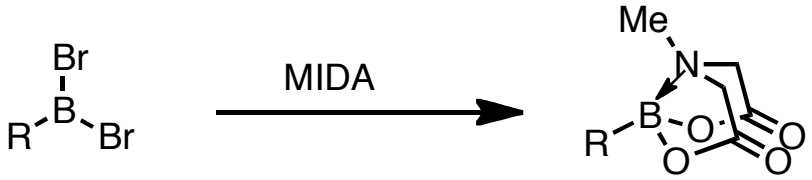
MIDA boronates are chemically compatible To a wide range of reagents, thus allowing Generation of complex boronic acid surrogates

MIDA: *N*-methyliminodiacetic acid

Preparation:

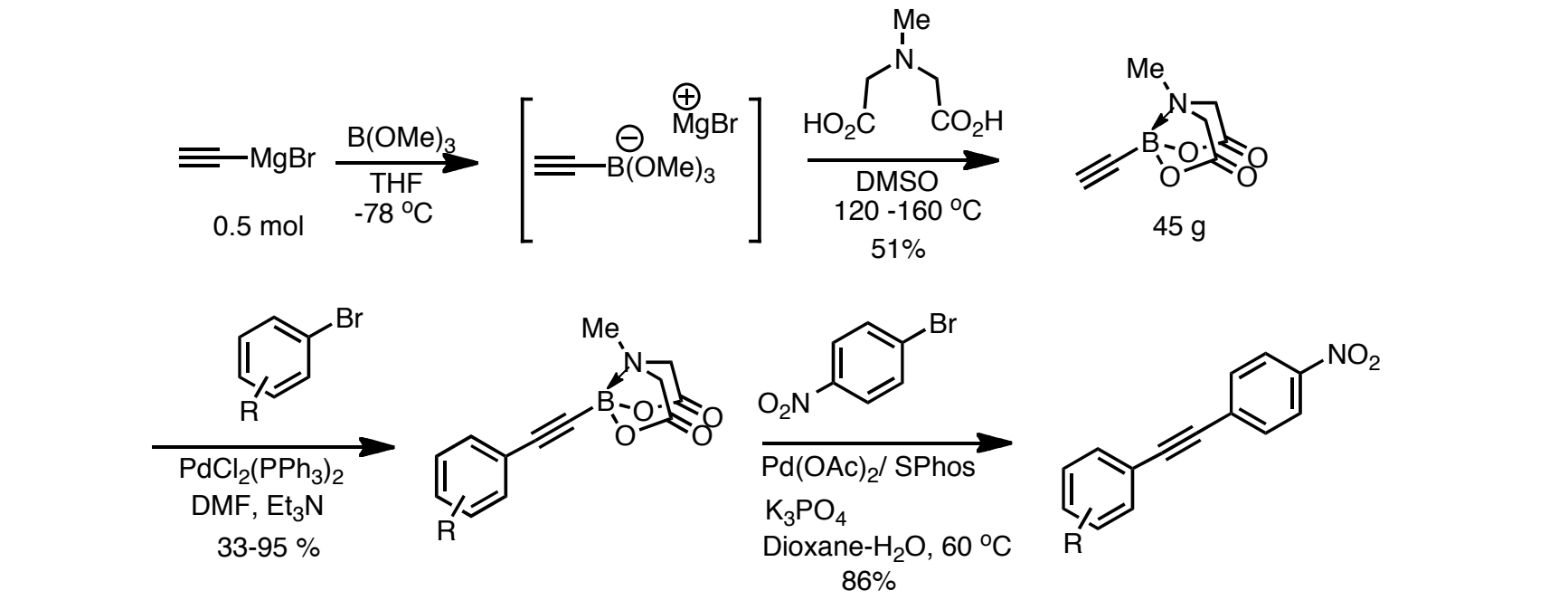


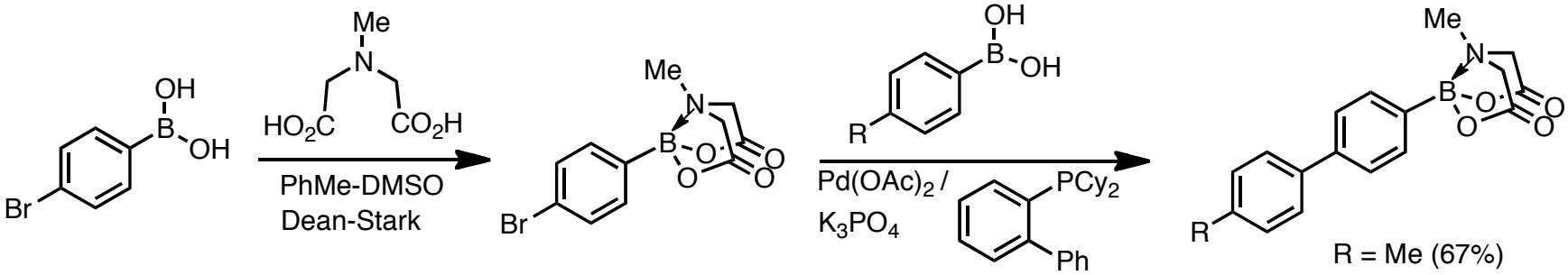




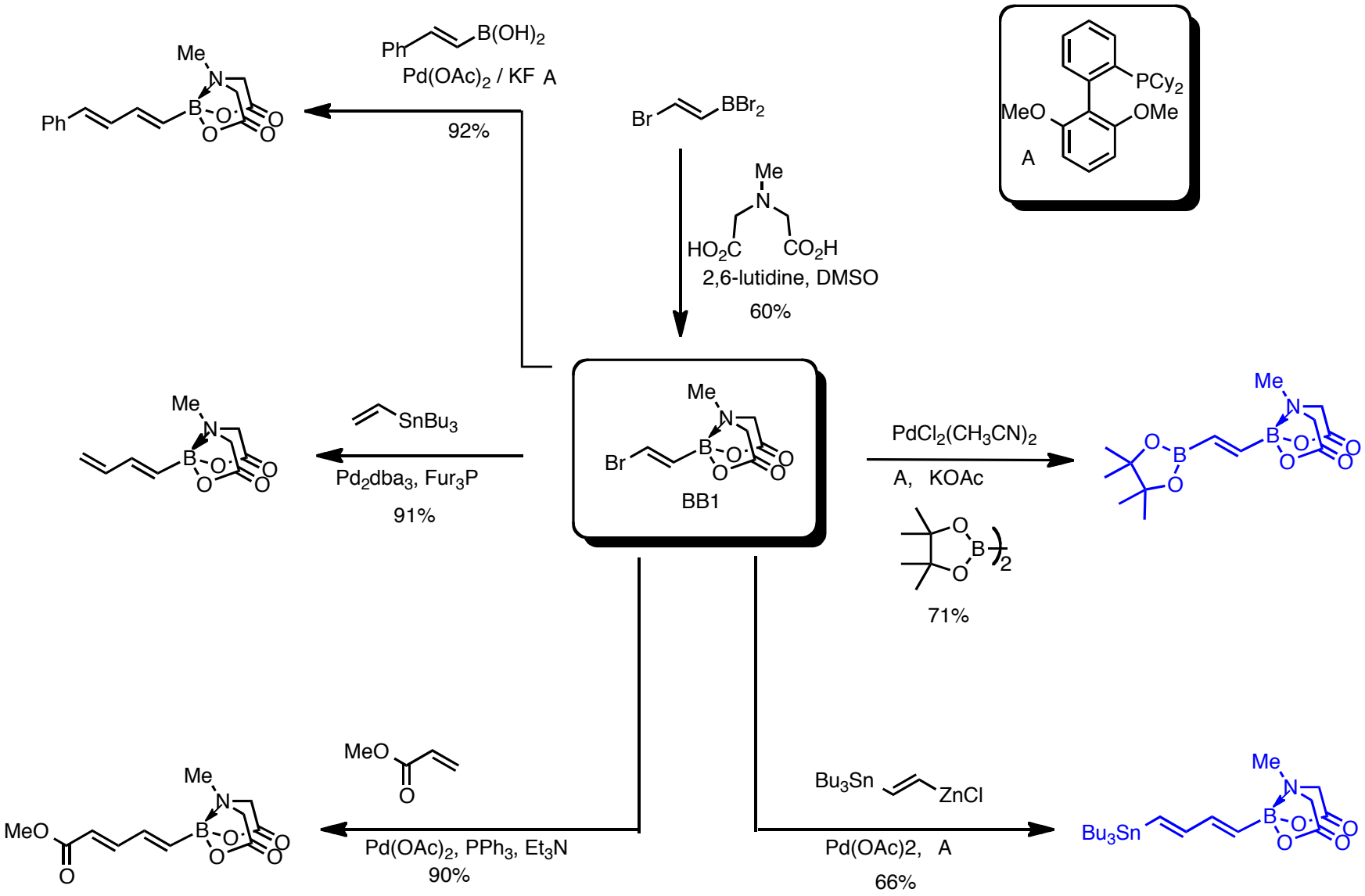
JACS, **2008**, 130, 466

Preparation and reactions

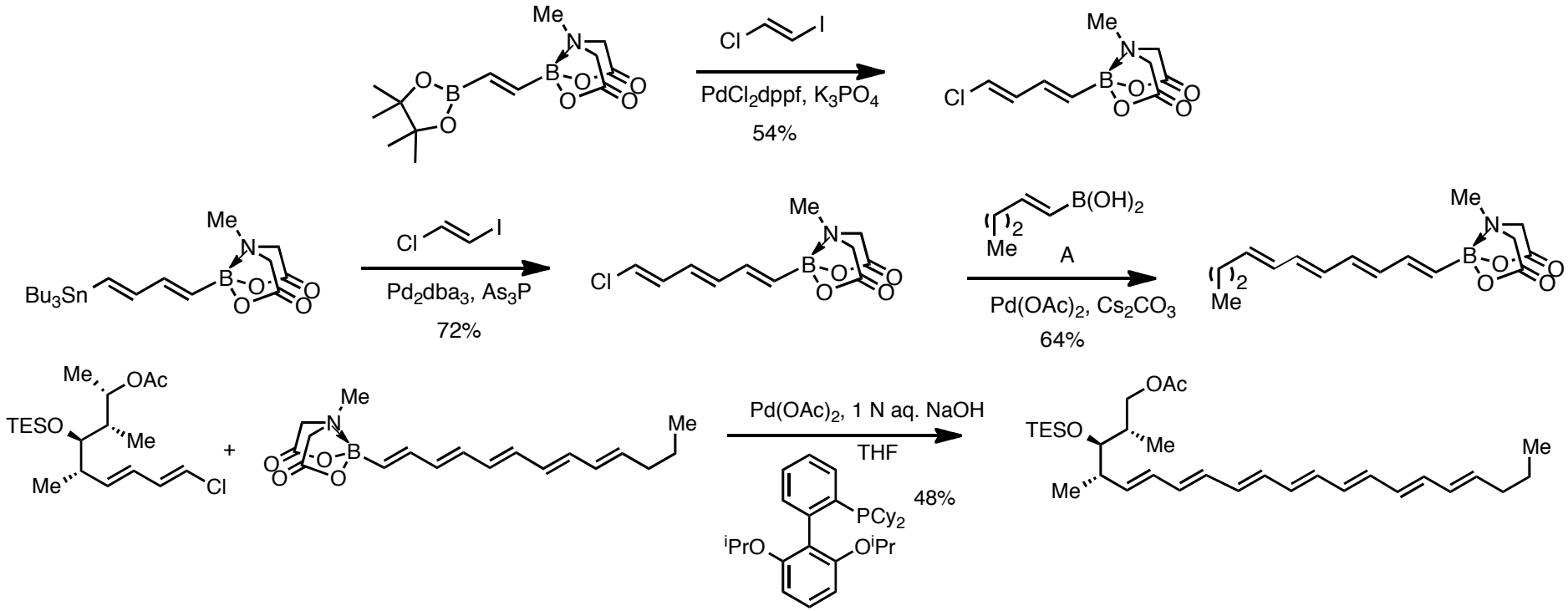


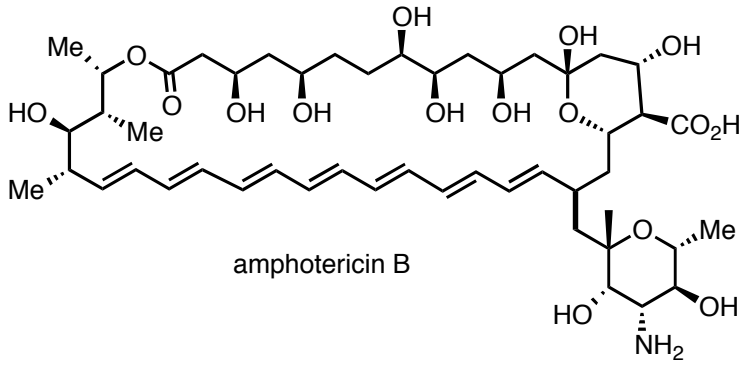


Boronic acid surrogates



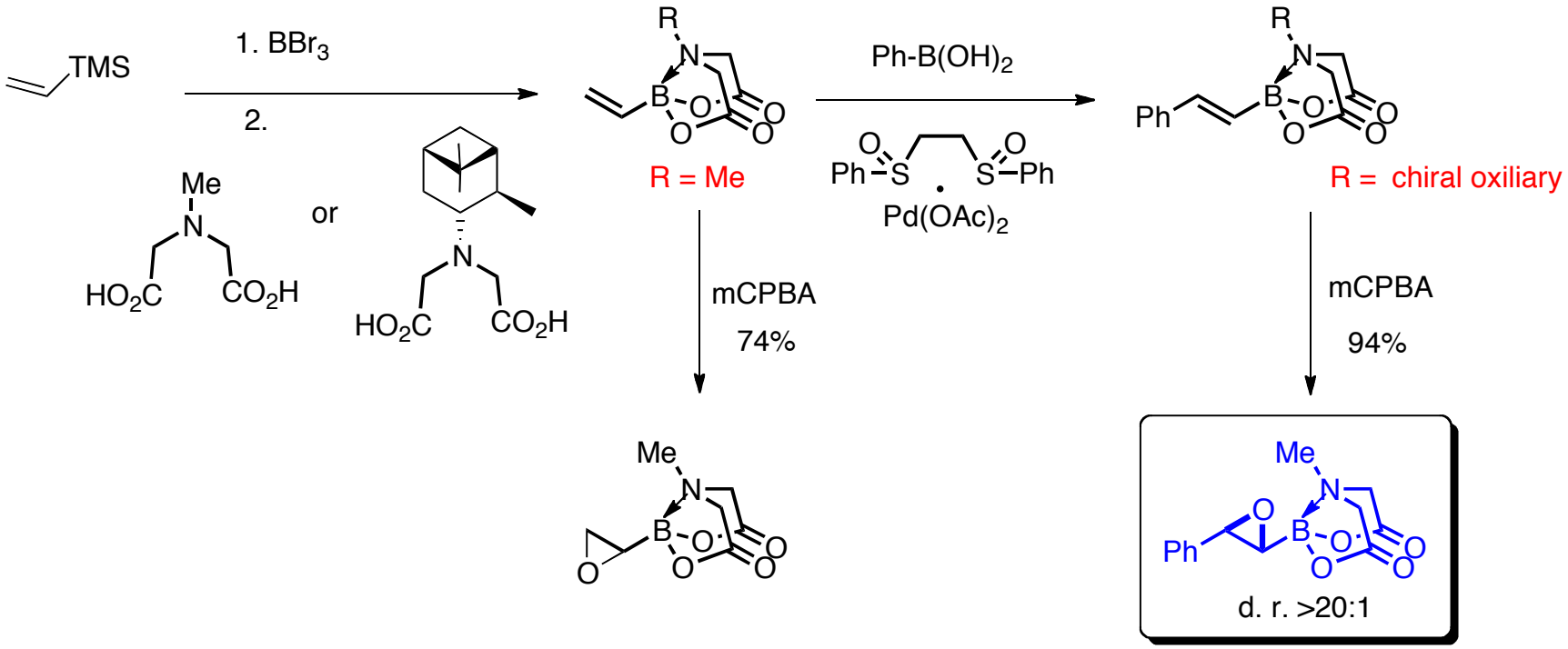
Iterative cross coupling reactions: application in total synthesis





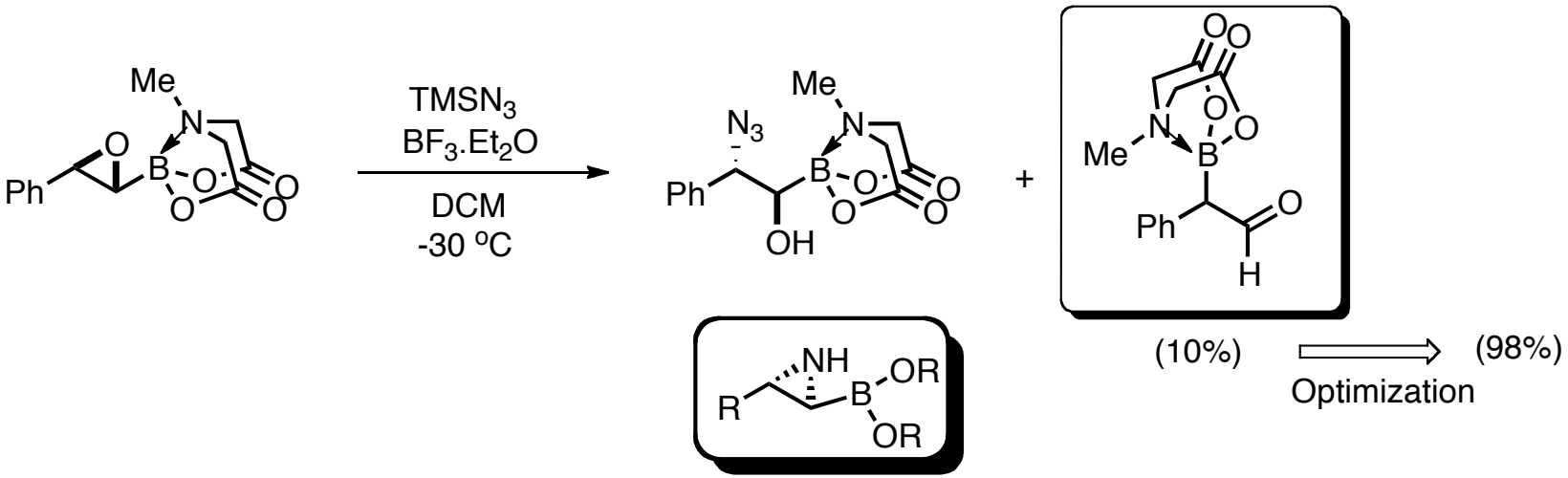
amphotericin B

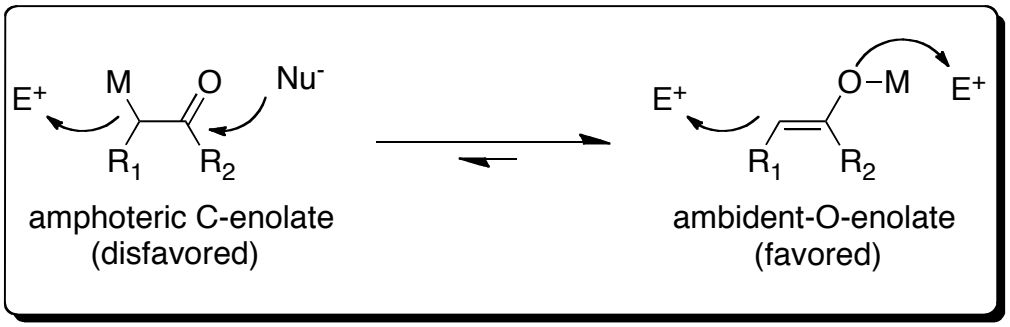
Controlling diastreoselectivity using chiral MIDA boronate



JACS, **2011**, 133, 13774

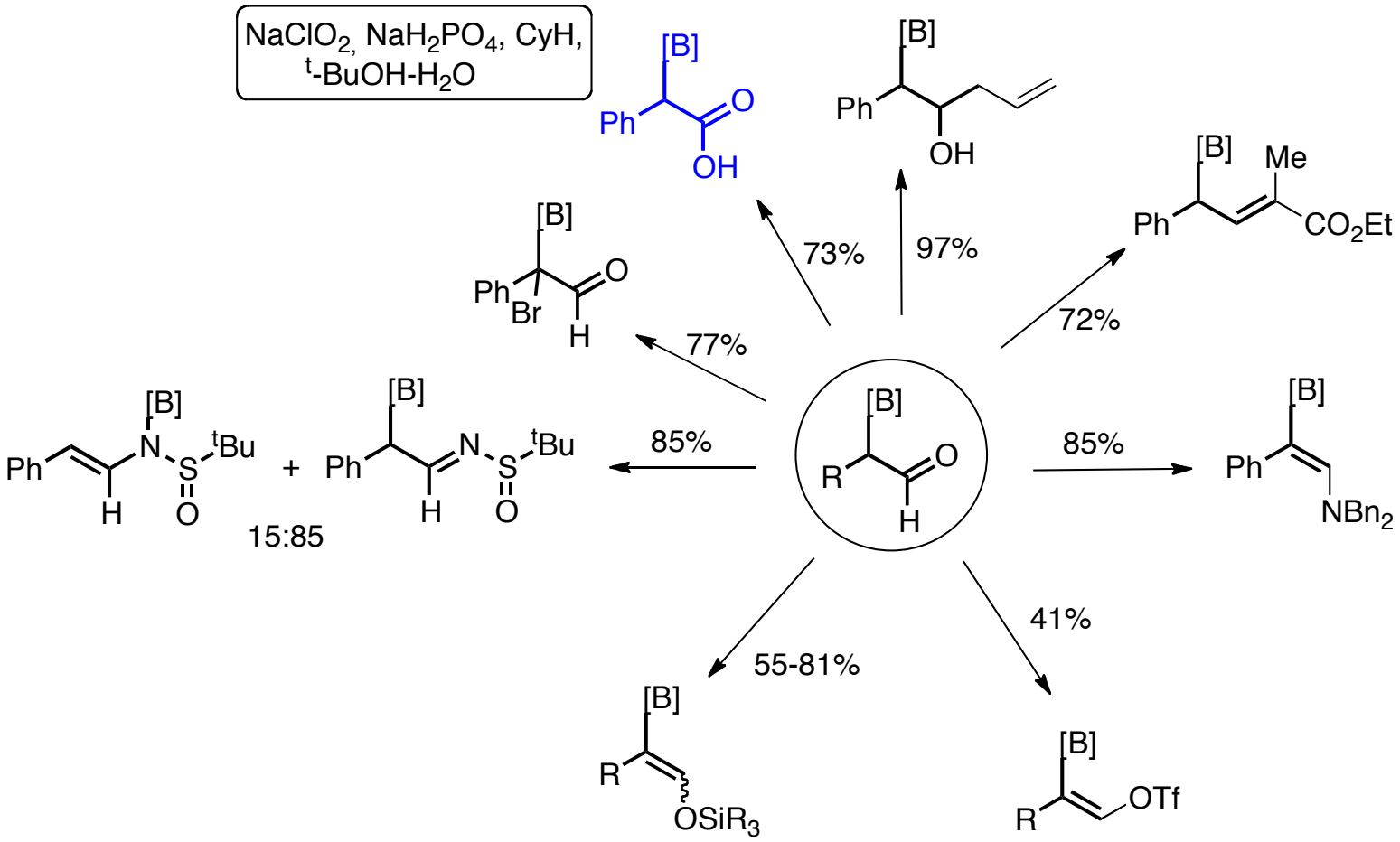
Amphoteric α-boryl aldehyde





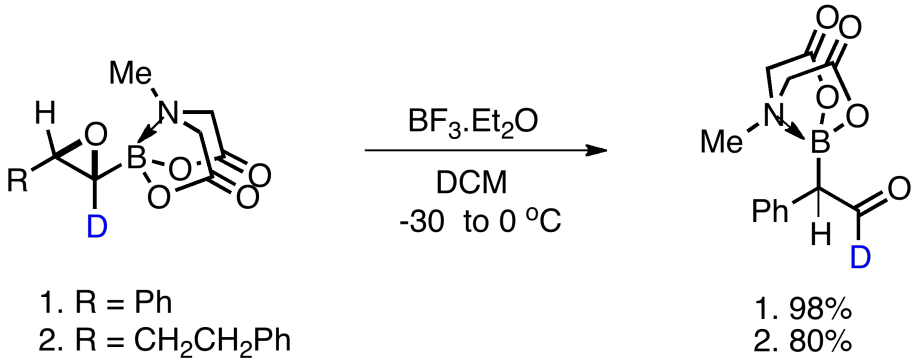
Yudin Group
JACS, **2011**, 133, 13770

Versatility of α-boryl aldehyde intermediate



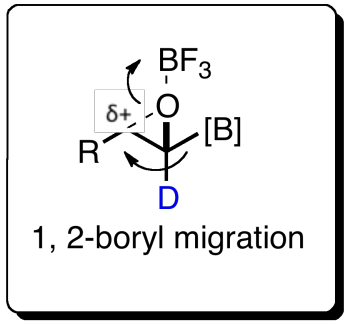
JACS, **2011**, 133, 13770

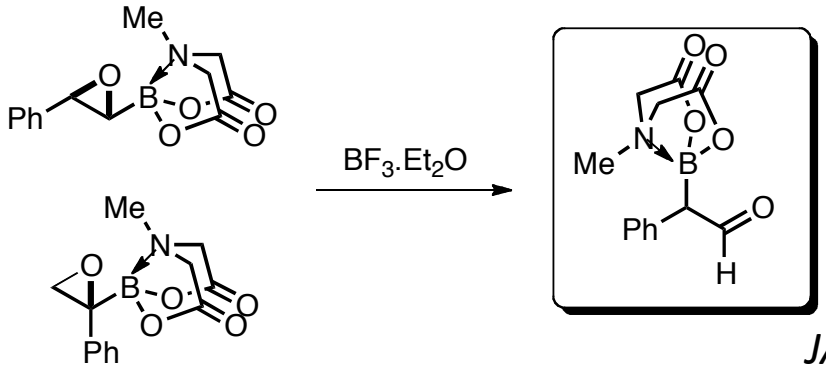
Mechanism: Deuterium labeling experiment



1. R = Ph
2. R = CH_2CH_2Ph

1. 98%
2. 80%



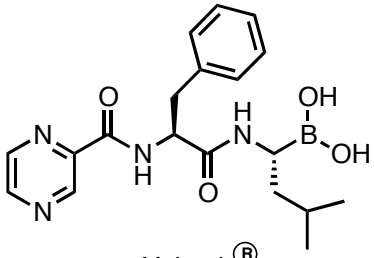


JACS, **2011**, 133, 13770

Title Paper: Boroalkyl group migration-versatile entry into α-aminoboronic acids

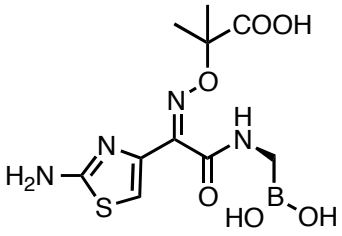
Why α-aminoboronic acids are important ?

Boron-containing therapeutics-

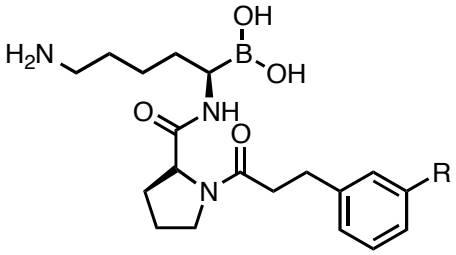


Velcade®

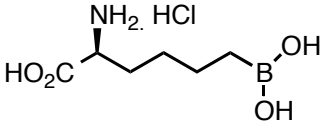
Proteasome Inhibitor



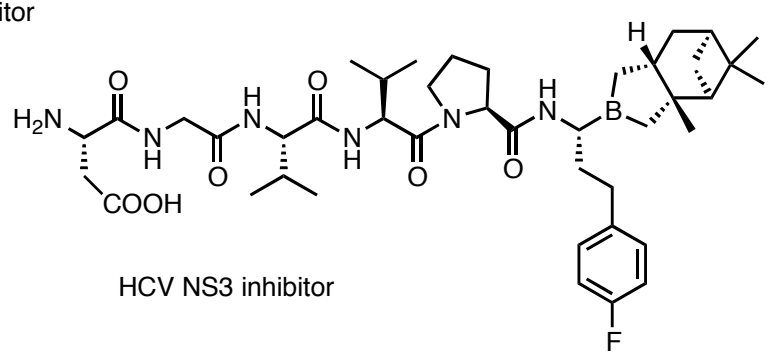
Lactamase Inhibitors



Thrombin inhibitor



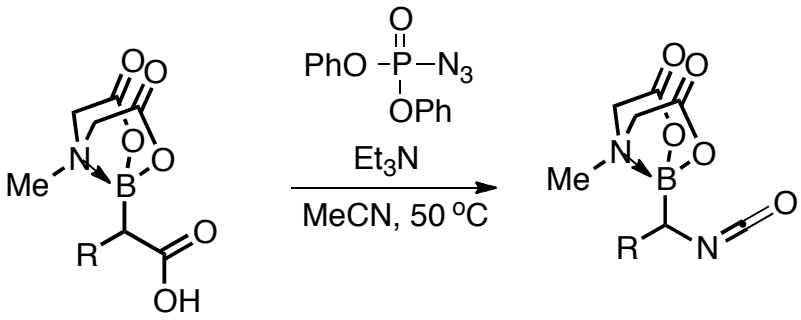
Arginase inhibitor



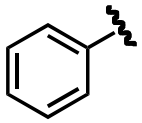
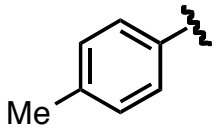
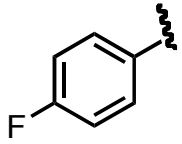
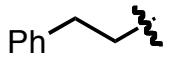
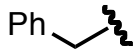
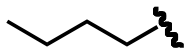
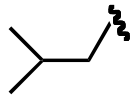
HCV NS3 inhibitor

Chem. Soc. Rev. **2011**, 40, 4279

Title Paper: Boroalkyl group migration-versatile entry into α-aminoboronic acids



Curtius rearrangement

1.		71%
2.		57%
3.		62%
4.		91%
5.		84%
6.		86%
7.		71%
8.		73%

JACS, **2012**, 134, 9926

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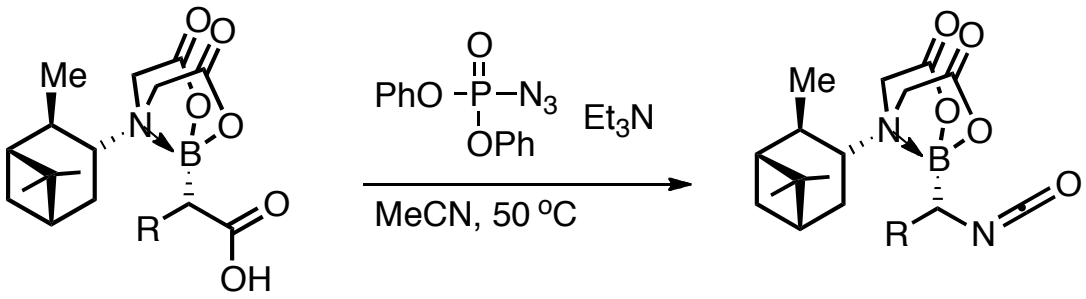
Streochemical Investigation of the migration



R = Ph (d. r. > 95:5)
R = CH_2CH_2Ph (d. r. > 95:5)

R = Ph (d. r. > 85:5)
R = CH_2CH_2Ph (d. r. > 95:5)

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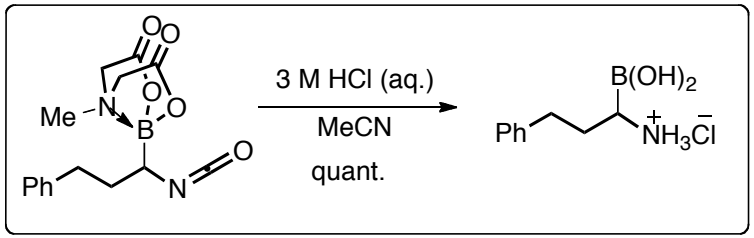
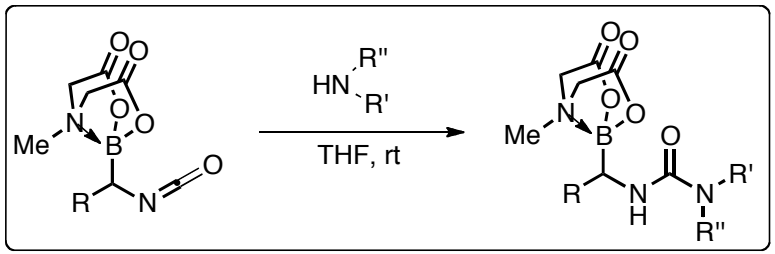
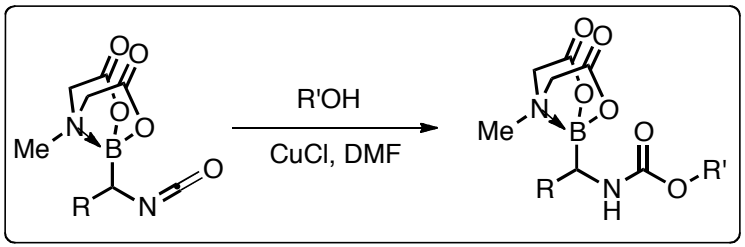
13

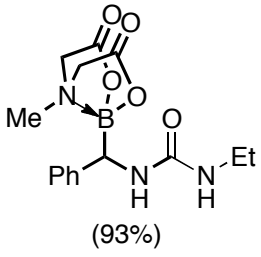
Different transformations of the α-borylisocyanate



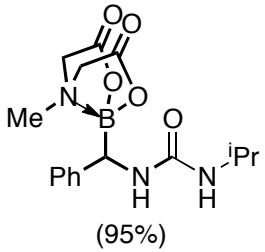
Free amino boronic acid



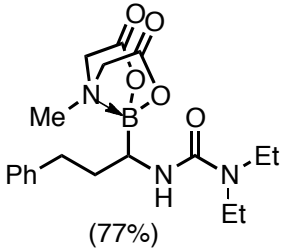




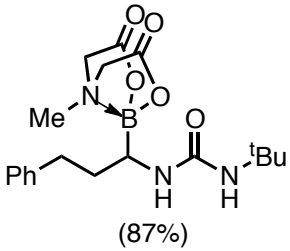
(93%)



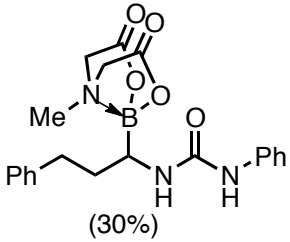
(95%)



(77%)

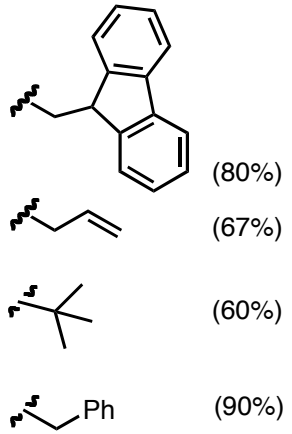


(87%)



(30%)

α-boryl ureas



α-boryl carbamates

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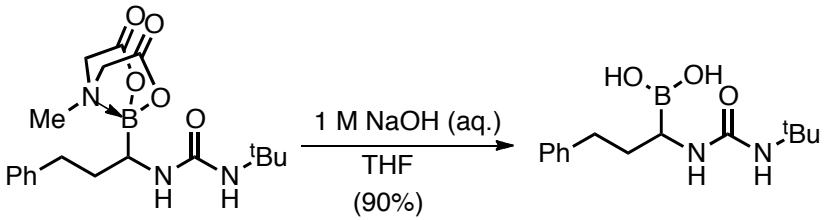
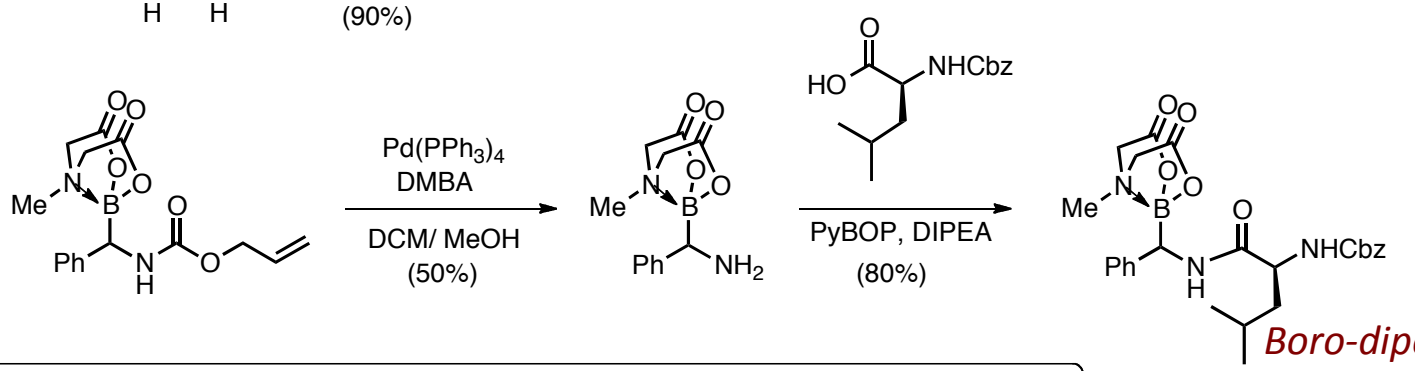
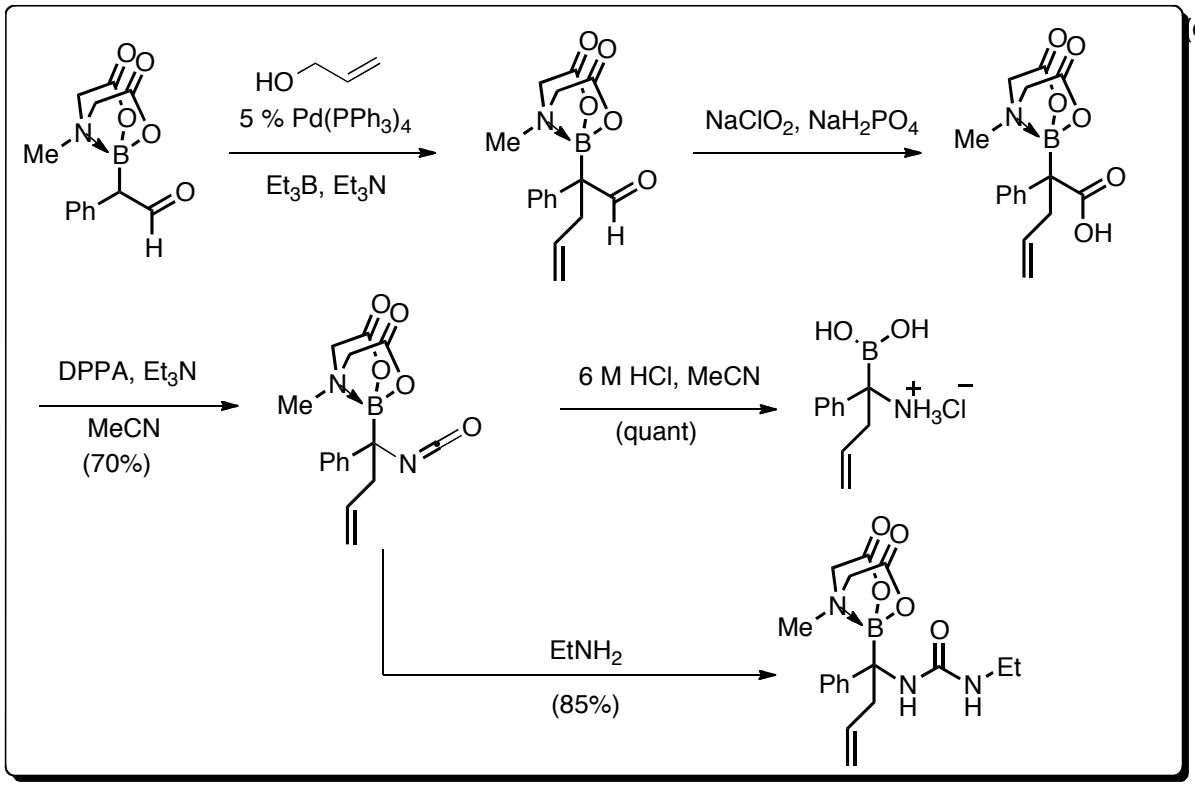


α-ureidoboronic acid



Boro-dipeptide

(d.r. 1:1, separable)



Quaternary boronic acid

Summary and Outlook

- An unprecedented boron-containing alkyl group migration is demonstrated.
- Boryl isocyanate described in the literature is used with nitrogen and oxygen nucleophiles; therefore offers potential for generation of diverse library of boronic acid surrogates.
- This method provides an alternative and versatile method for the generation of α-aminoboronic acids and corresponding peptides which showed promise as drug candidates.

- Screening of other nucleophiles that are compatible to MIDA boronate
- Other reactions involving isocyanate, such as Diels-alder type reactions.