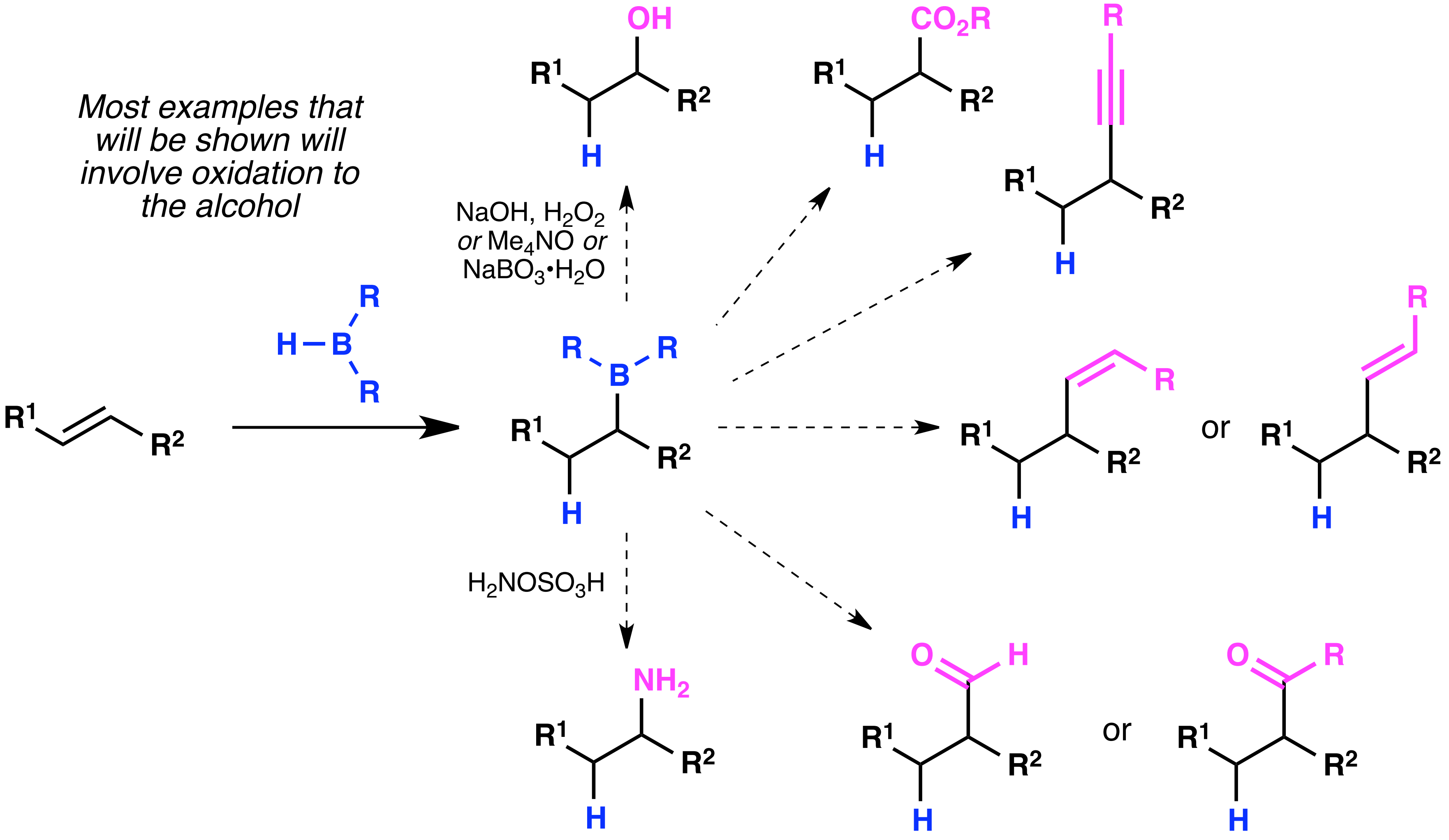
Hydroboration

Carreira: Chapter 7

Hydroboration of alkenes/alkynes is one of the most versatile reactions available. Most commonly, the resulting alkyl borane intermediates are not isolated, but are used in subsequent reactions for forming a wide range of functional groups.

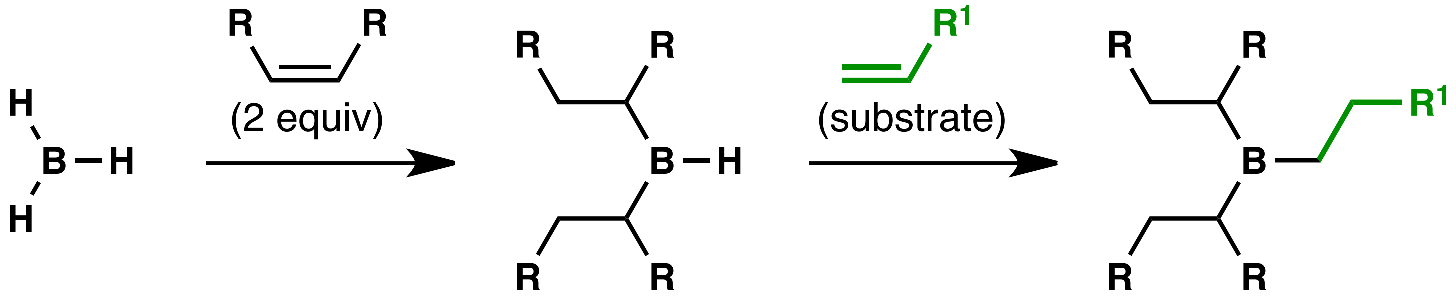
Most examples that will be shown will involve oxidation to the alcohol



Monograph: Brown, H. C. *Organic Synthesis Via Boranes*; Wiley: New York, 1975; Brown, H. C. *Organic Synthesis Via Boranes Volume 2*; Aldrich Chemical Company: Milwaukee, WI, 2001.

Many Different Reagents

There are several reagent options available depending on selectivity/reactivity concerns. Generally, boranes (B–H compounds) can be prepared easily from inexpensive reagents. Many are air and moisture sensitive. Most are prepared by initial hydroboration of a different olefin with borane (BH_3).

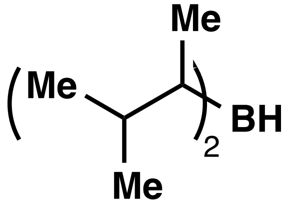


the addition of the first two alkyl groups is usually rapid

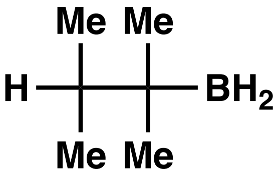
the addition of the third alkyl group is slower and quite dependent on the substitution pattern of the olefin

Some Commonly used hydroborating agents

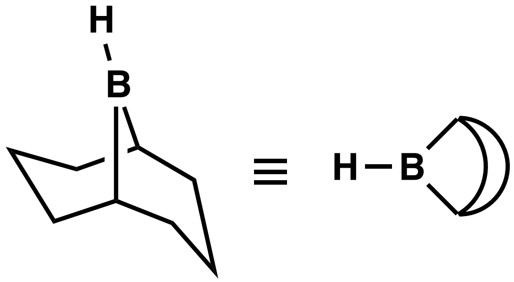
BH_3•SMe_2
(BMS, air stable, neat liquid, ~10 M)



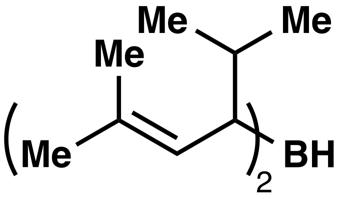
diisoamylborane
(Sia_2BH)



thexylborane
(Thx_2BH)

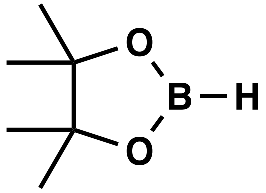


9-borabicyclo-[3.3.1]nonane (9-BBN)

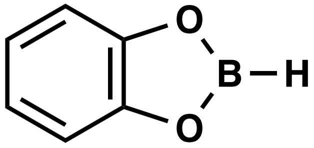


di(isopropylprenyl)borane
(*i*PP_2BH)

useful for catalytic HB



pinacolborane
(PinBH)

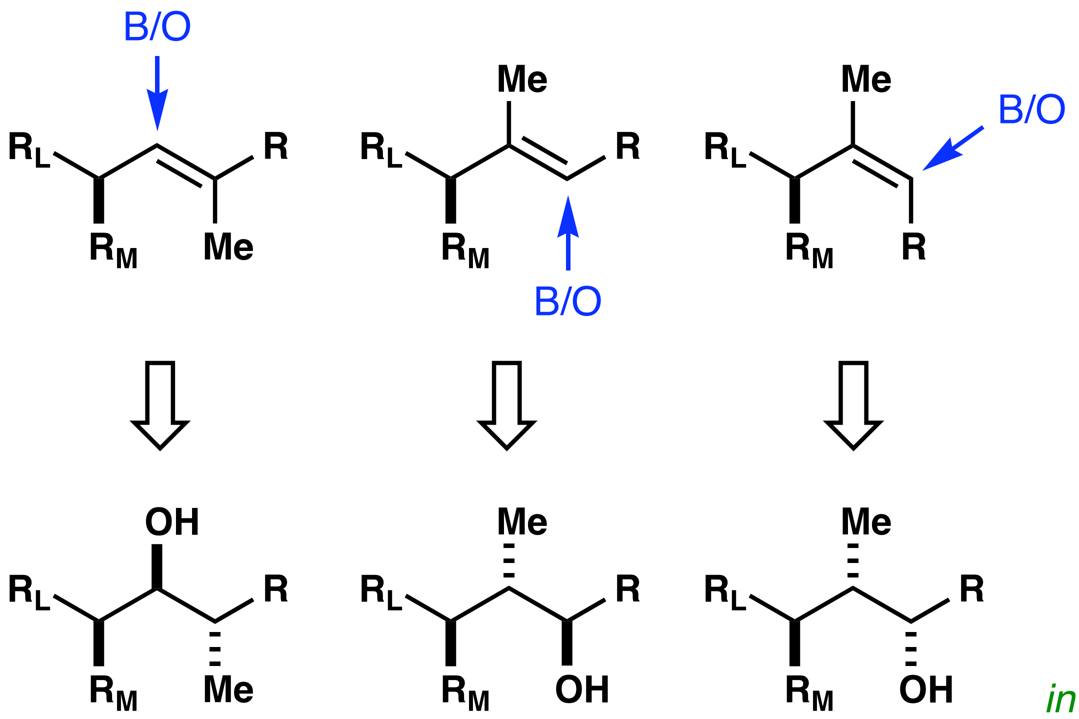


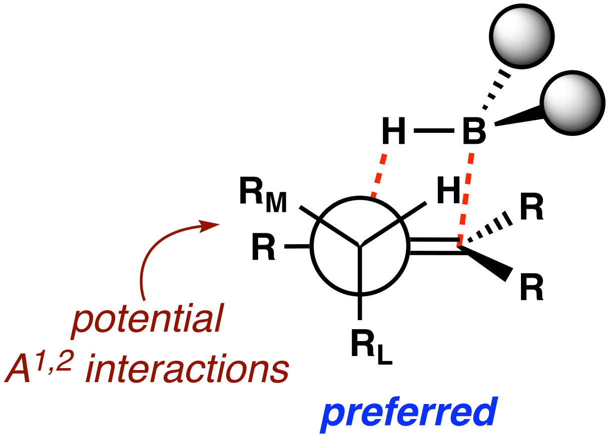
catecholborane
(CatBH)

Stereoselectivity With Acyclic Olefins

Hydroboration involves a four-membered transition state with *syn*-addition across the alkene/alkyne. Conversion of C–BR$_2$ into C–OH is stereospecific with *retention* of configuration. The boron usually ends up on the less substituted end of the olefin.

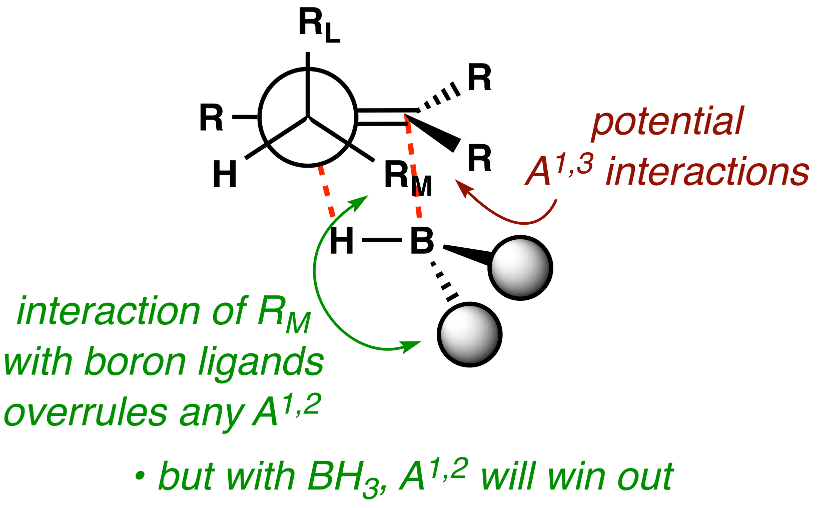
trisubsubstituted olefins – similar arguement can be made for disubstituted, but regioselectivity now becomes important.





potential
$A^{1,2}$ interactions

preferred



potential
$A^{1,3}$ interactions

interaction of R$_M$
with boron ligands
overrules any $A^{1,2}$

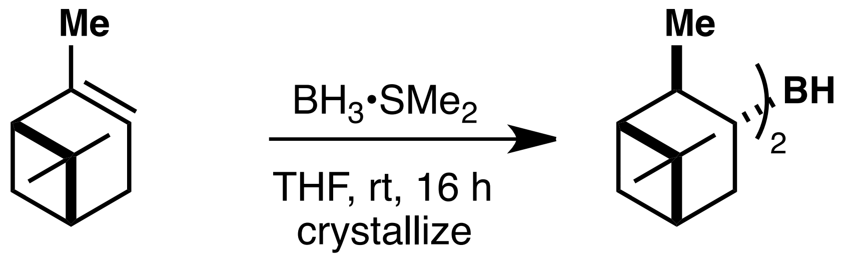
- but with BH_3, $A^{1,2}$ will win out

Asymmetric Hydroboration

Asymmetric hydroborations were among the first examples of non-enzymatic transformations to proceed with high enantiomeric excess (*J. Am. Chem. Soc.* **1961**, *83*, 486).

Several reagents have been developed, but those derived from α-pinene (Brown) are still the most widely used.

diisopinocamphenylborane – sterically demanding reagent, reacts with unhindered alkenes



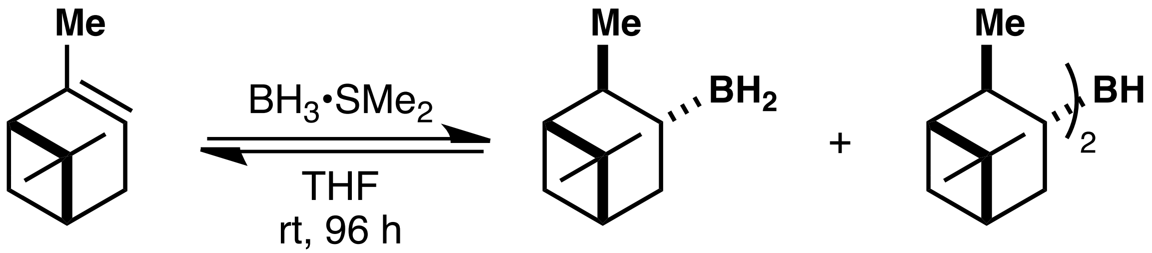
(+)-α-pinene
(excess)
91% ee

(–)-Ipc_2BH
> 99% ee
(note change in rotation)

solid, can be stored at 0 ºC under N_2

J. Org. Chem. **1982**, *47*, 5065

monoisopinocamphenylborane – unhindered reagent, reacts will all classes of alkenes

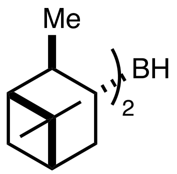


(+)-α-pinene
(1 equiv)
4.5%

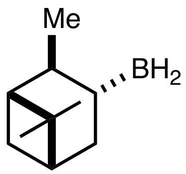
(+)-$IpcBH_2$
91%

(–)-Ipc_2BH
4.5%

Asymmetric Hydroboration



(–)-Ipc_2BH

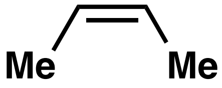


(+)-$IpcBH_2$

(–)-Ipc_2BH – 1,2-*cis*-olefins give high selectivity, others react slowly

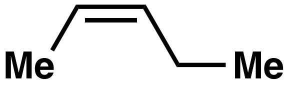
(+)-$IpcBH_2$ – 1,2-*trans*- and trisubstituted olefins give high to moderate selectivity

1,1-disubstituted olefins are still troublesome, with no general reagent available

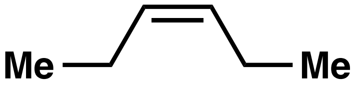


98% ee

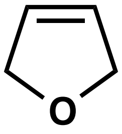
24% ee



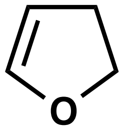
92% ee



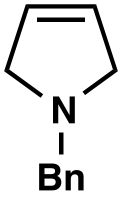
93% ee



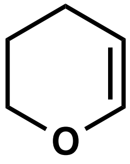
99% ee



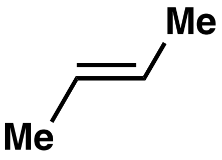
99% ee



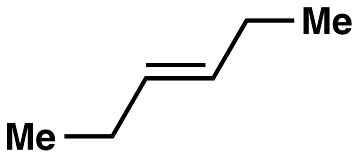
99% ee



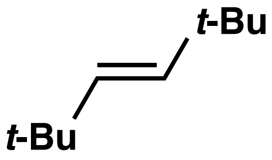
83% ee



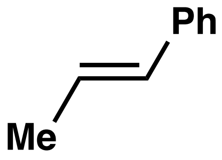
73% ee



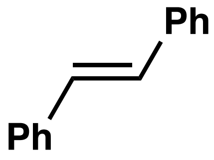
75% ee



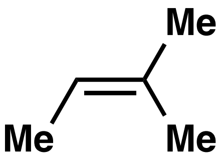
92% ee



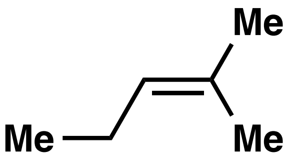
76% ee



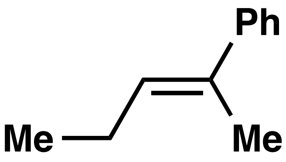
65% ee



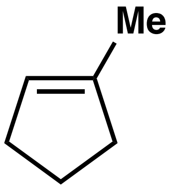
53% ee



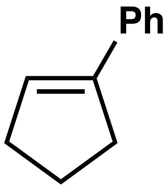
58% ee



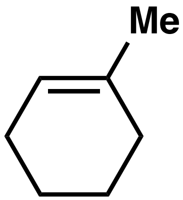
86% ee



66% ee



> 99% ee



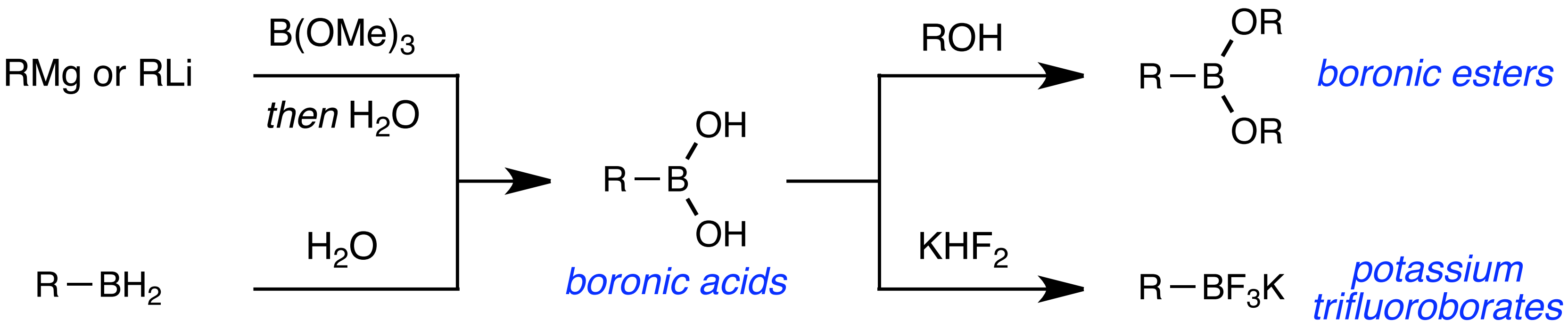
72% ee

(–)-Ipc_2BH: *J. Org. Chem.* **1982**, *47*, 5065; *J. Am. Chem. Soc.* **1986**, *108*, 2049; *J. Org. Chem.* **1986**, *51*, 4296

(+)-$IpcBH_2$: *J. Org. Chem.* **1982**, *47*, 5074; *J. Org. Chem.* **1987**, *52*, 310; *J. Org. Chem.* **1980**, *45*, 3543; *Bull. Chem. Soc. Jpn* **1988**, *61*, 93

Conversion to Other Organoboron Compounds

Boronic acids, boronic esters, and organotrifluoroborates are useful intermediates for cross-coupling and other reactions. Their preparation from alkenes is complicated by needing to perform a monohydroboration with BH_3. Snieckus and co-workers reported a nice solution to this problem.



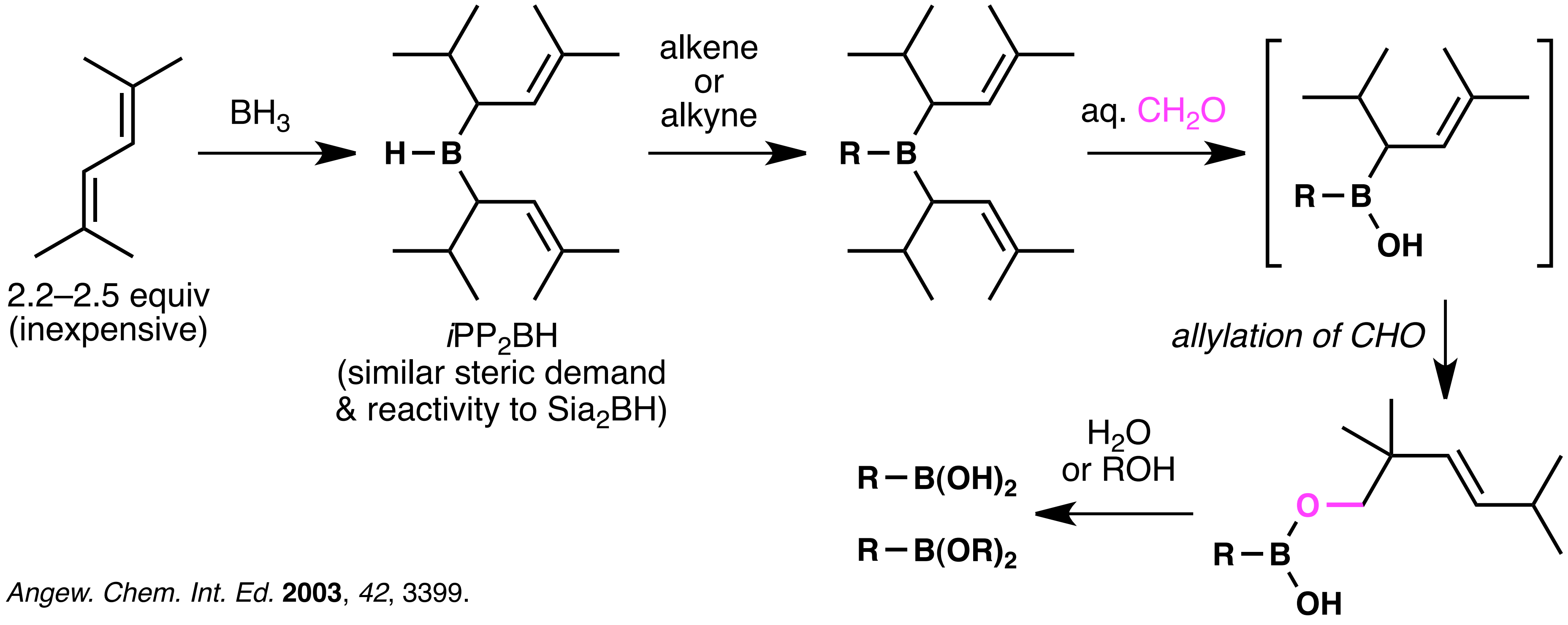
RMg or RLi $\xrightarrow{B(OMe)_3 \text{ then } H_2O}$

R–BH₂ $\xrightarrow{H_2O}$

R–B(OH)₂ *boronic acids*

$\xrightarrow{ROH}$ R–B(OR)₂ *boronic esters*

$\xrightarrow{KHF_2}$ $R{-}BF_3K$ *potassium trifluoroborates*



2.2–2.5 equiv
(inexpensive)

BH_3

iPP$_2$BH
(similar steric demand & reactivity to Sia$_2$BH)

alkene or alkyne

aq. CH_2O

allylation of CHO

H_2O or ROH

R–B(OH)₂

R–B(OR)₂

Angew. Chem. Int. Ed. **2003**, *42*, 3399.