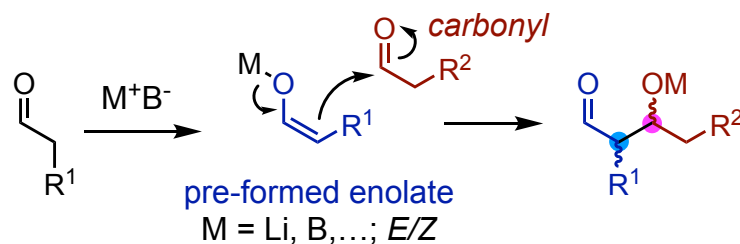


Stereoselectivity in the Aldol reaction



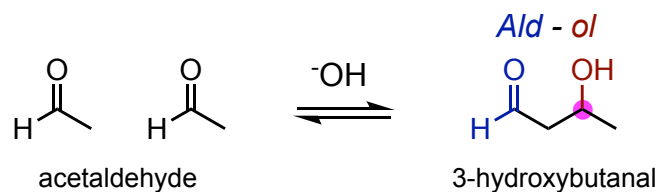
Oliver Thorn-Seshold
LMU Munich

doi.org/ABCD (key papers)

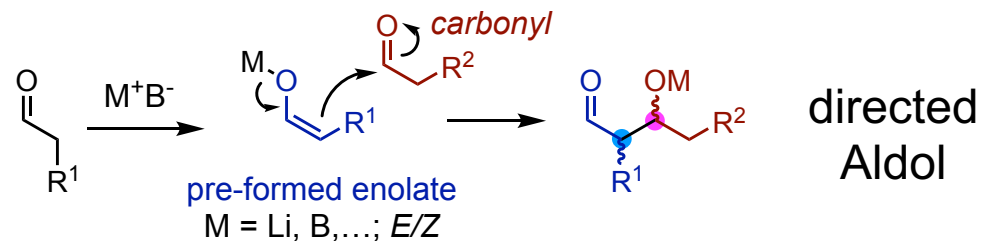
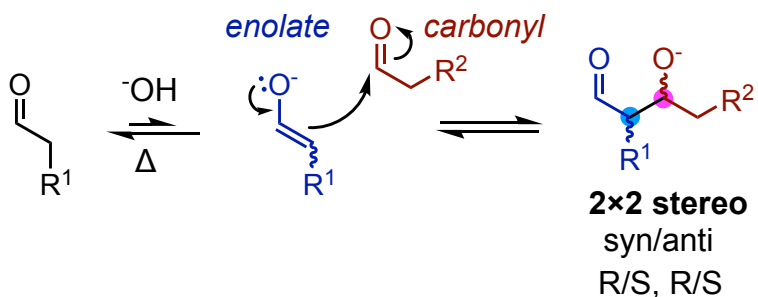
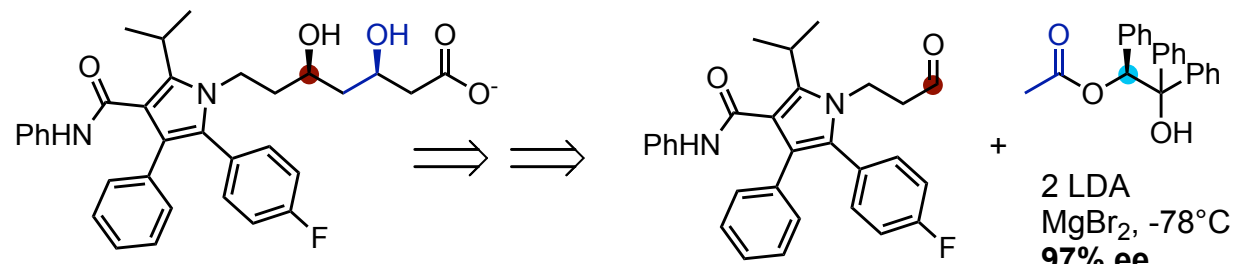
tinyurl.com/aldol-flashback

Carey & Sundberg Part B Ch 2

The Aldol Reaction - Stereoselectivity



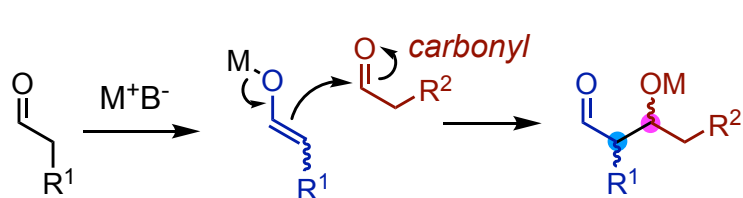
Borodin **1869** [tinyurl.com/borodin1869]
 & Wurtz **1872** [tinyurl.com/wurtz1872]



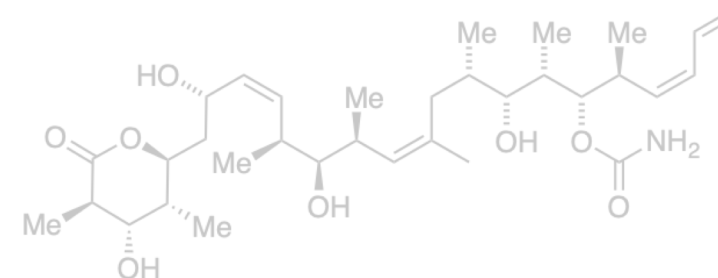
Expected Stereocontrol?

99% de (relative; *syn/anti*)
 97% ee (absolute; e.g. *R,S*)

The Aldol Reaction - Stereoselectivity

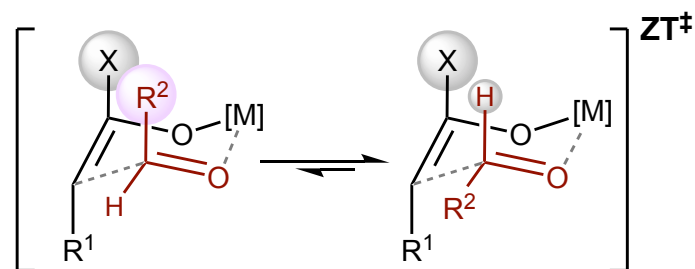


Stereocontrol?



discodermolide (antimitotic NP)

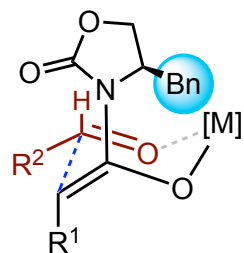
without
chirality



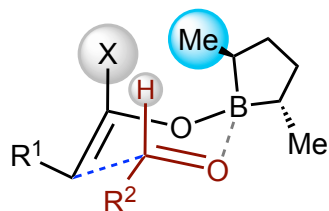
relative stereochemistry

2 new stereocentres in *syn*- or *anti*

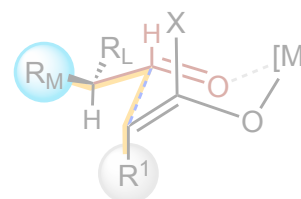
+ chirality



auxiliary
(Evans)



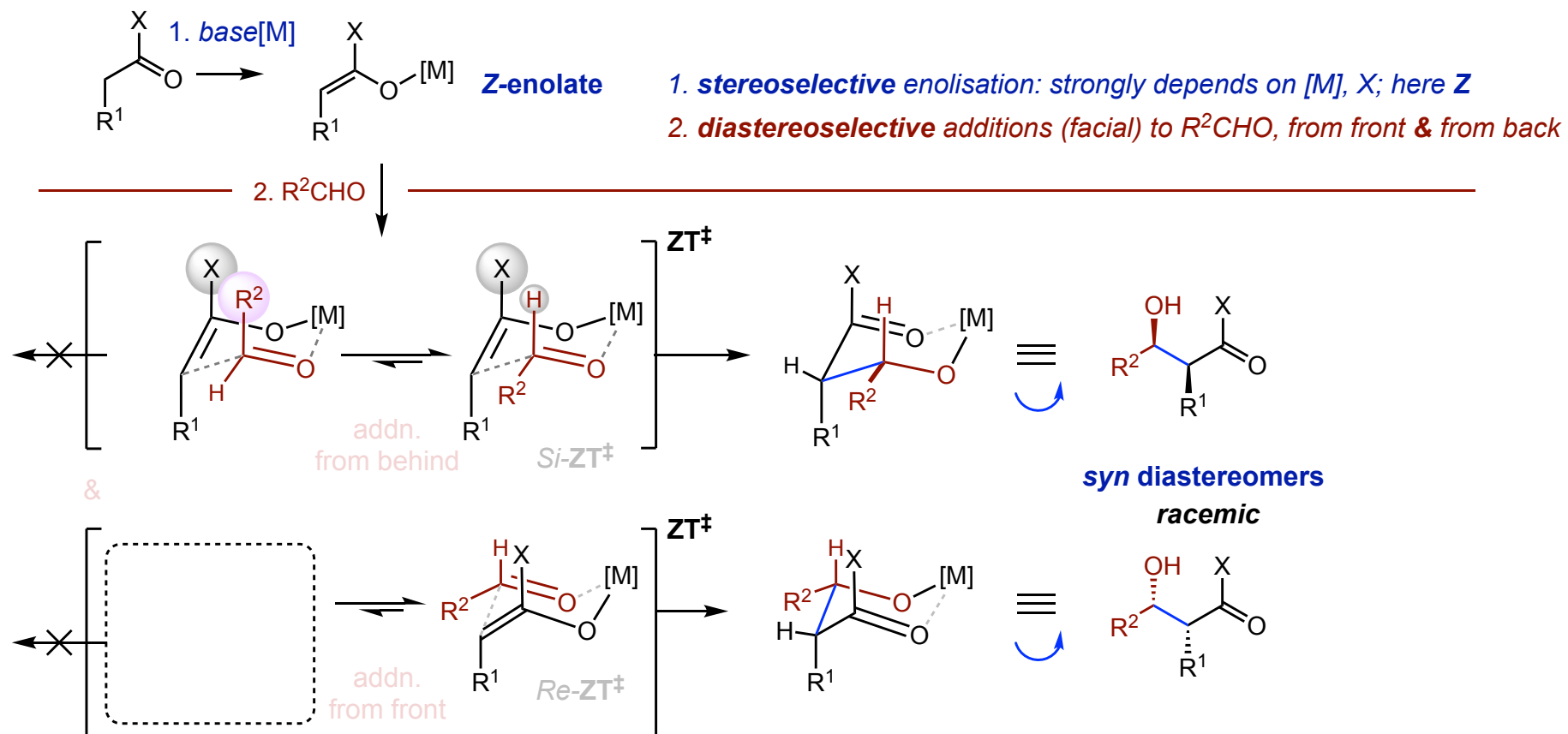
ligand
(Masamune)



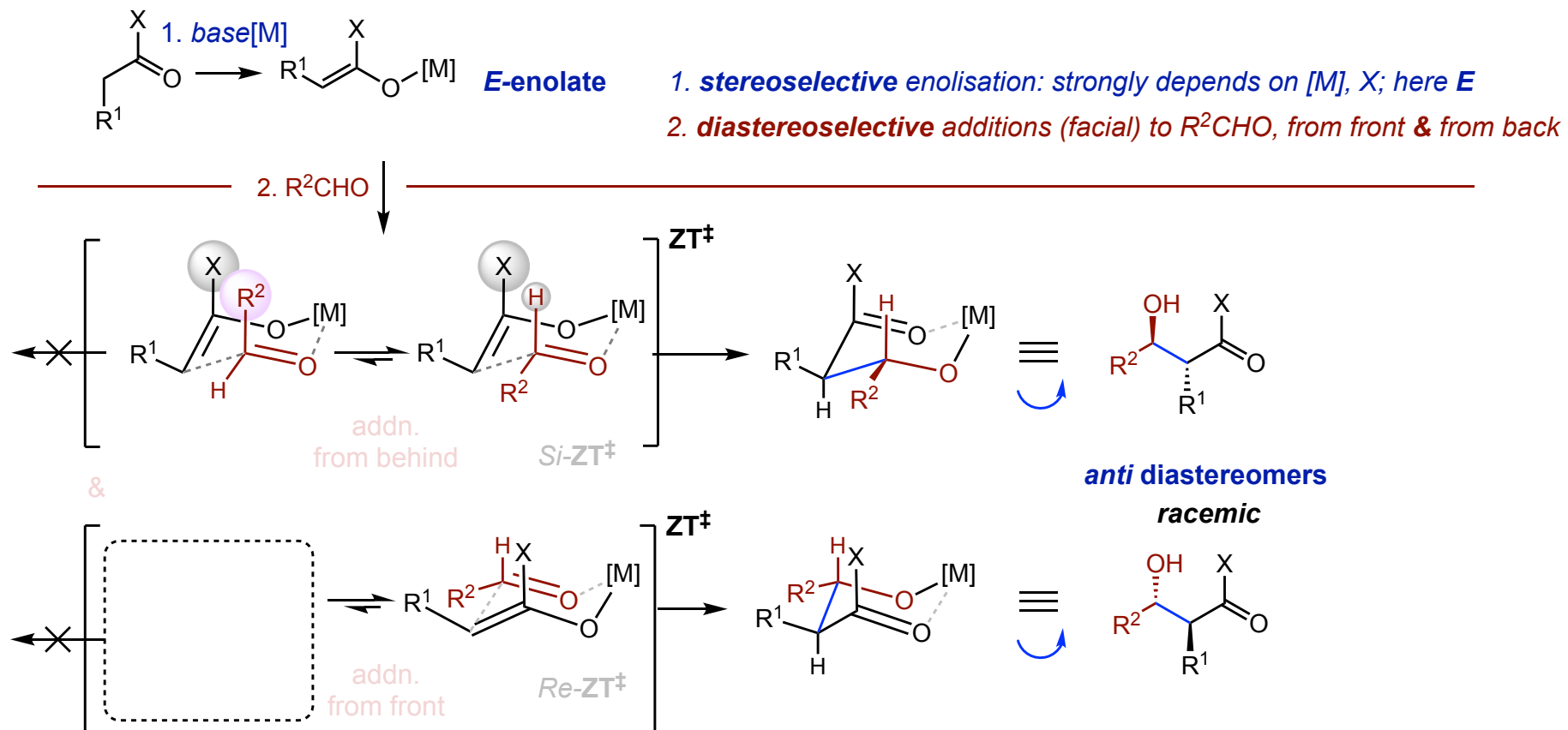
carbonyl
(Felkin-Anh)

**absolute
stereochemistry**

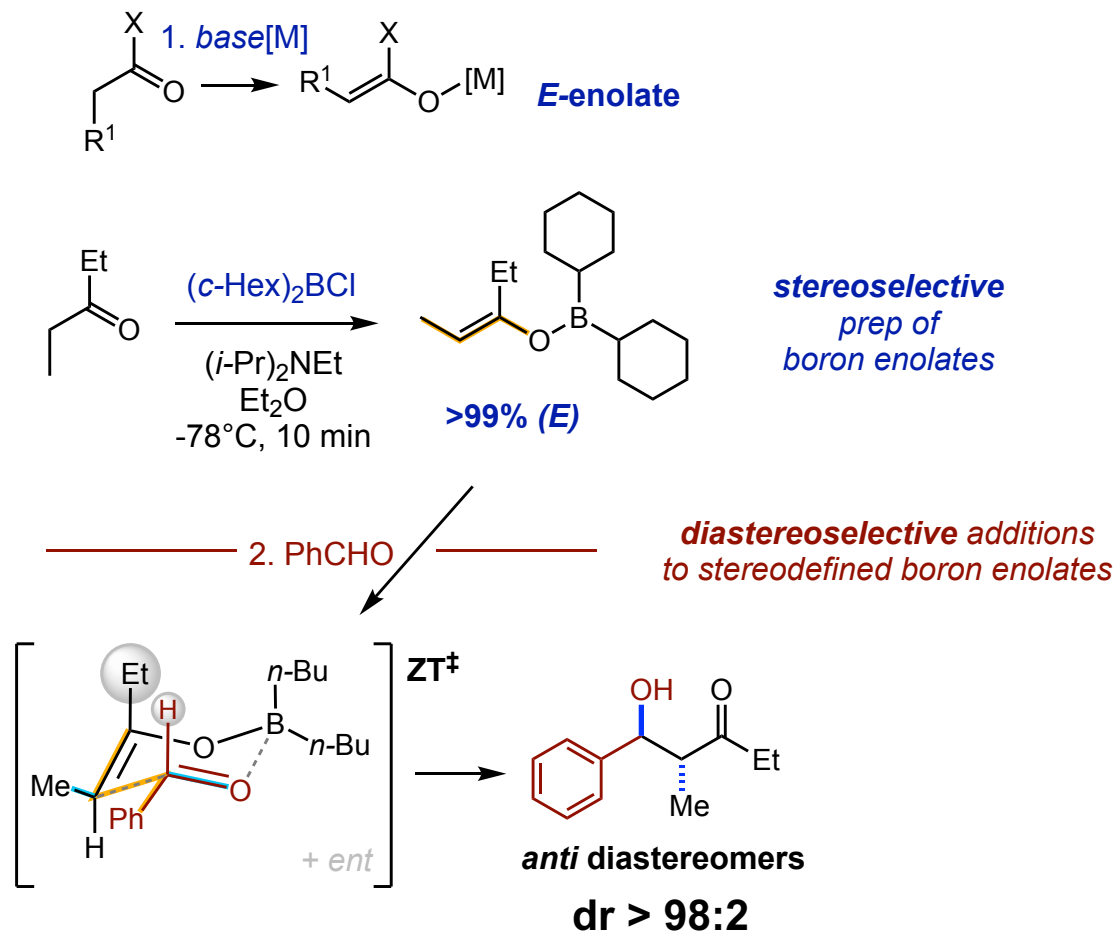
1. Achiral Substrates + Chelation → Diastereoselective



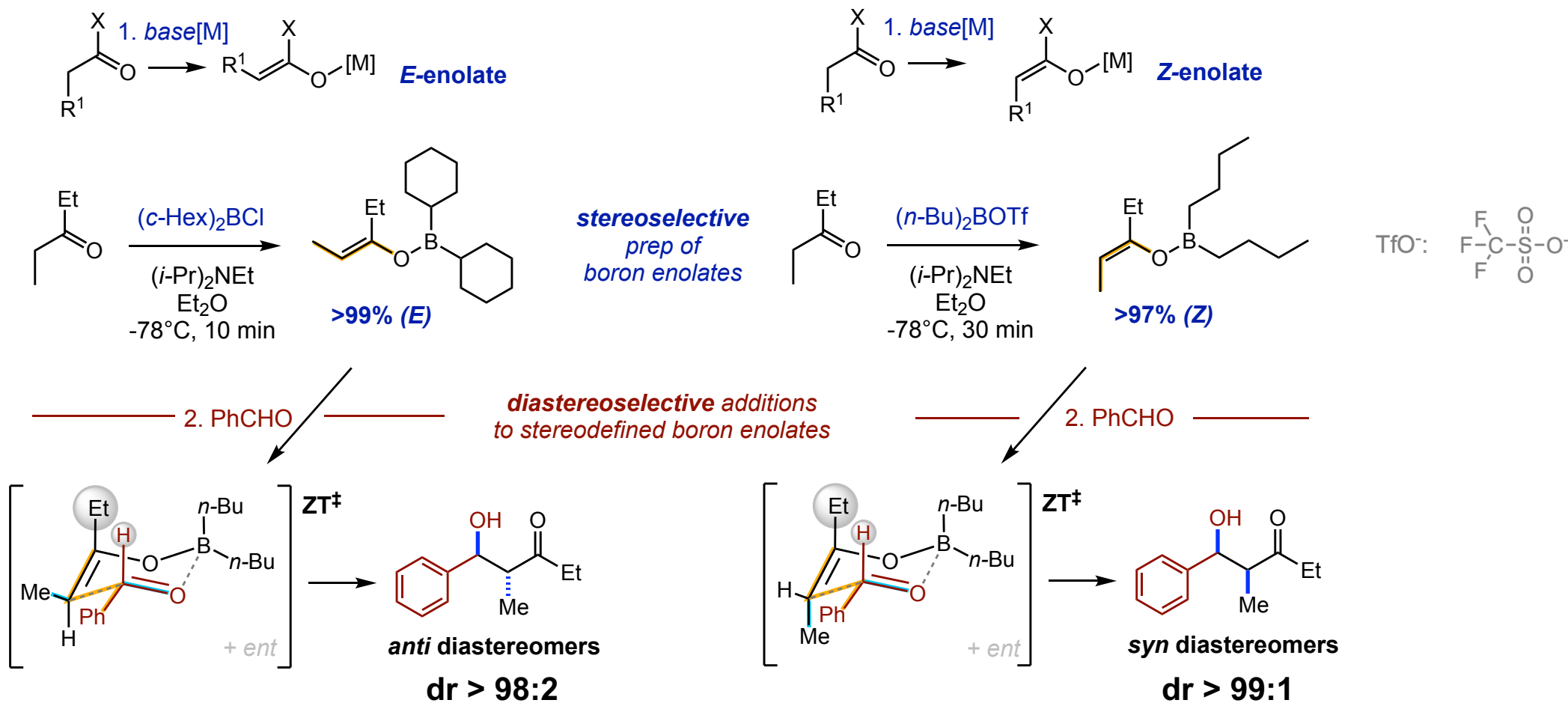
1. Achiral Substrates + Chelation → Diastereoselective



Example: stereoselective prep of (*E*)-/(*Z*)-boron enolates

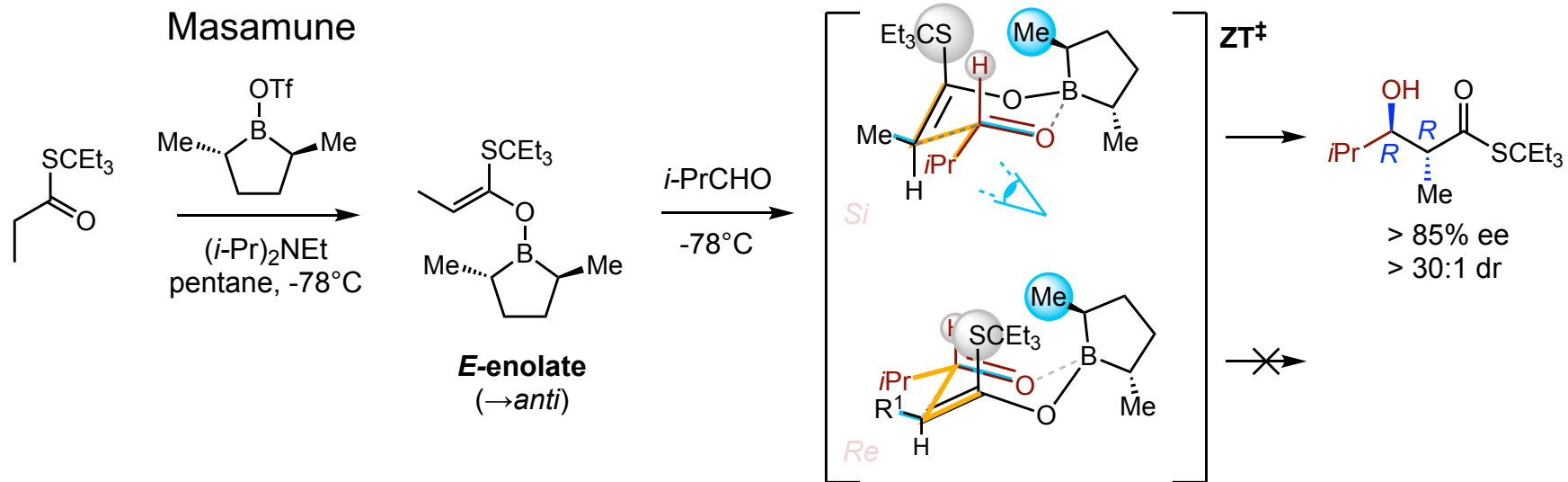


Example: stereoselective prep of (*E*)-/(*Z*)-boron enolates



Zimmerman-Traxler chelate: *E* → anti, *Z* → syn

2. Chiral [B]*

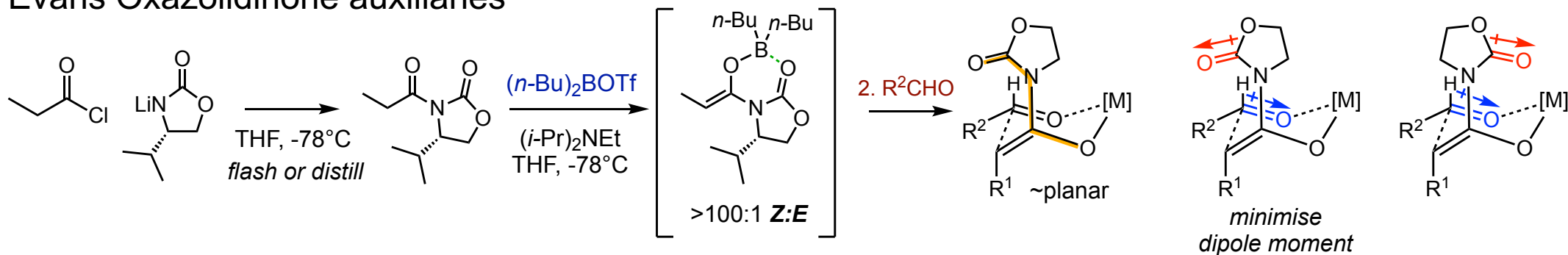


enantioselectivity from **[B]*** (here: $2R,3R$ vs $2S,3S$)
related: Corey diazaborolidines; Peterson chiral B-ligands; ...

+ Zimmerman-Traxler: $E \rightarrow$ anti, $Z \rightarrow$ syn

3. Chiral Auxiliaries - Evans

Evans Oxazolidinone auxiliaries

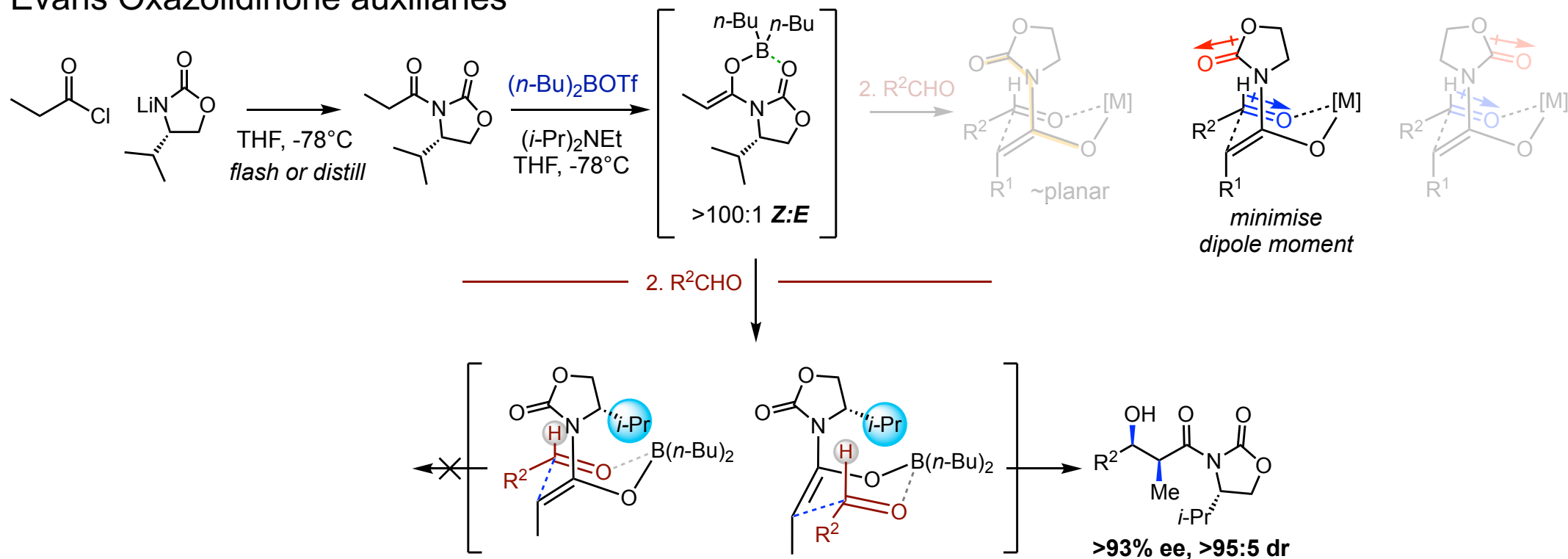


Evans 1981 JACS [doi.org/bshp6p]

“One of the most reliable and predictable reactions in organic synthesis, *and* industrially useful”

3. Chiral Auxiliaries - Evans

Evans Oxazolidinone auxiliaries

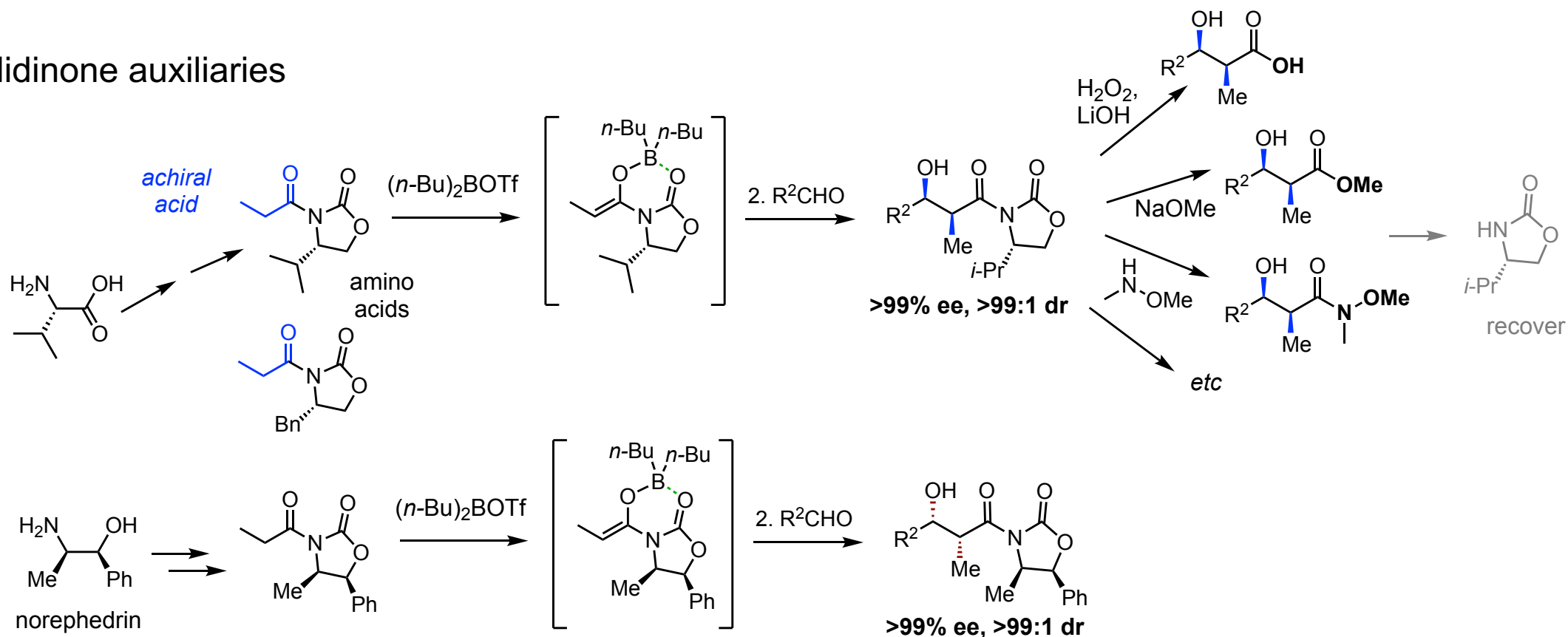


Evans 1981 JACS [doi.org/bshp6p]

“One of the most reliable and predictable reactions in organic synthesis, *and* industrially useful”

3. Chiral Auxiliaries - Evans

Evans Oxazolidinone auxiliaries

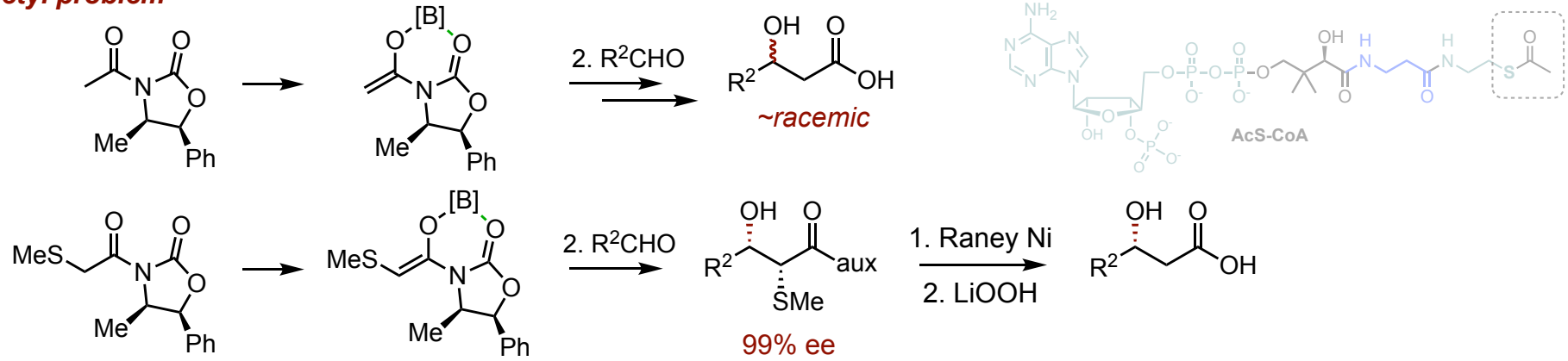


Evans 1981 JACS [doi.org/bsbhp6p]

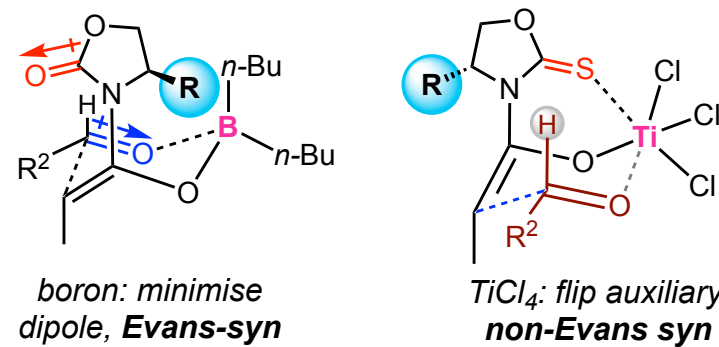
“One of the most reliable and predictable reactions in organic synthesis, *and* industrially useful”

3. Chiral Auxiliaries - Modifications

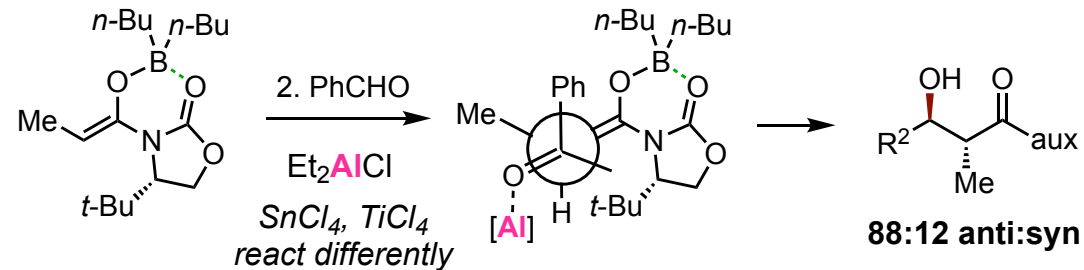
“acetyl problem”



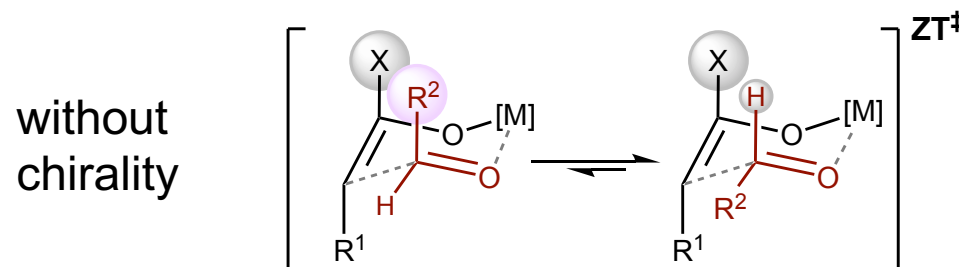
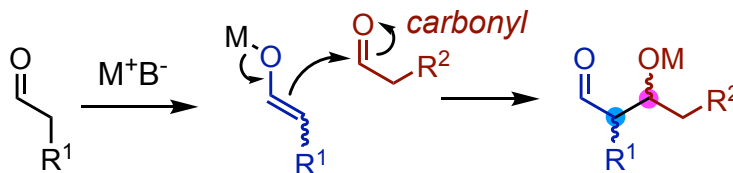
**flip auxiliary:
syn enantiomer**



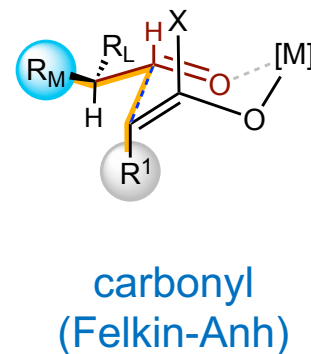
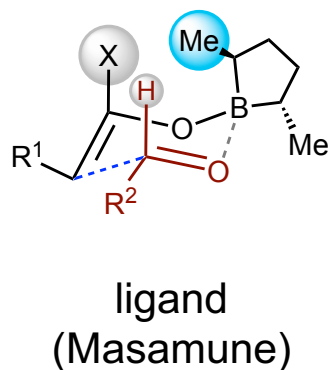
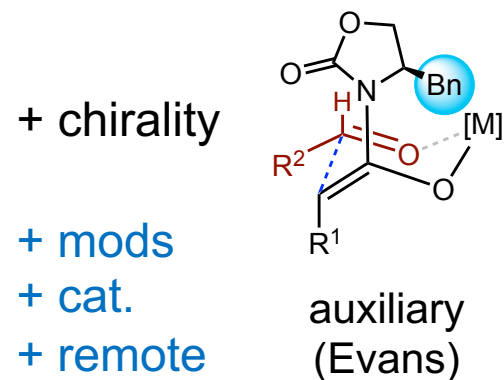
**open TS[‡]:
can get anti**



The Aldol Reaction - Stereoselectivity



syn/anti-diastereoselectivity
from *Z/E*-enolates by *Z-T*[‡]
+ Mukaiyama



**absolute
stereochemistry**

+ biosynthesis
+ total synthesis
+ exercises

Oliver Thorn-Seshold, LMU Munich

Directed Aldol: Mukaiyama 1982, doi.org/d2dkwx; Chiral *syn*-Aldol: Evans 1981, [bshp6p](#); Organocatalytic Aldol: List 2000, [bv7m5f](#)

Modern Aldol: tinyurl.com/aldol-flashback; Carey & Sundberg Part B Ch 2; APOC twitter.com/apocsocial

