

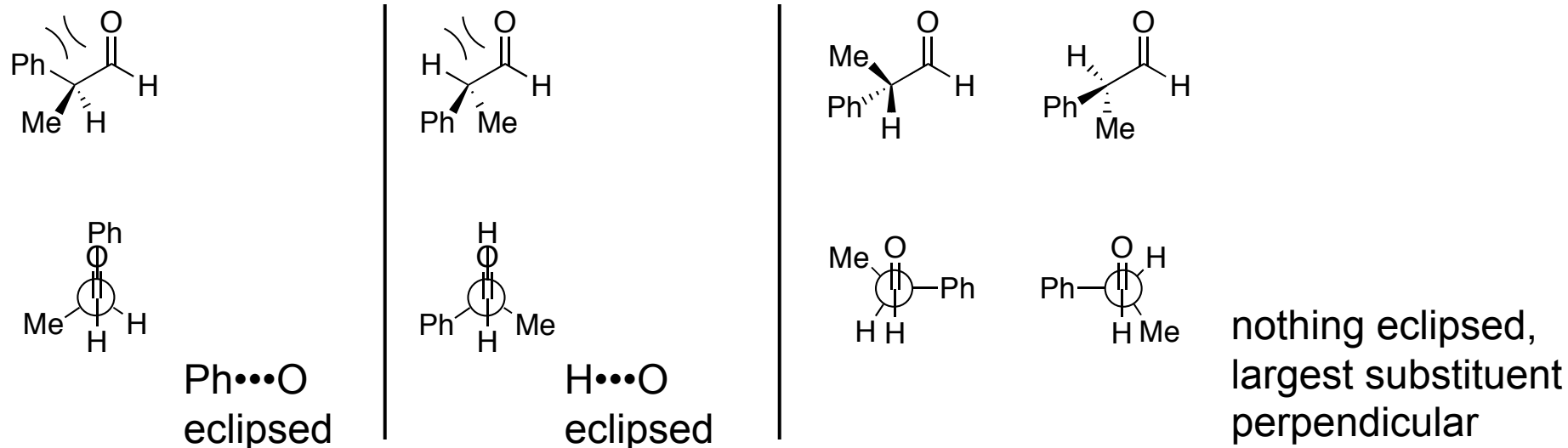
Chapter 34 — Diastereoselectivity

- The Felkin-Ahn model for carbonyl conformations and diastereoselective nucleophilic attack
- The effect of electronegative atoms on carbonyl conformation
- Carbonyl chelation and stereoselectivity

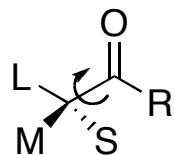
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- The aldol reaction's chair-like transition state and stereoselective formation of *syn* and *anti* isomers
 - Selective production of *cis* and *trans* enolates of ketones

 - *Stereospecificity vs. stereoselectivity (and a pre-midterm review of reactions)*

The conformations of acyclic carbonyls

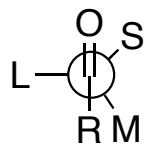
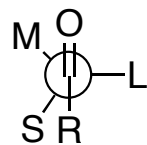


The Felkin-Ahn model for carbonyl conformations

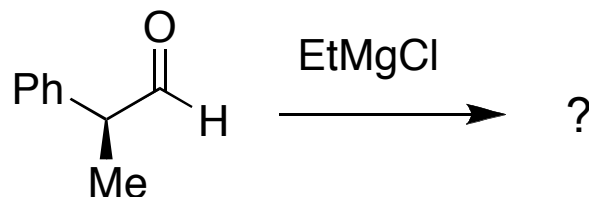


Alpha-substituted carbonyls assume conformations that:

- 1) avoid all eclipsed interactions
- 2) have the largest substituent perpendicular to the plane of the carbonyl

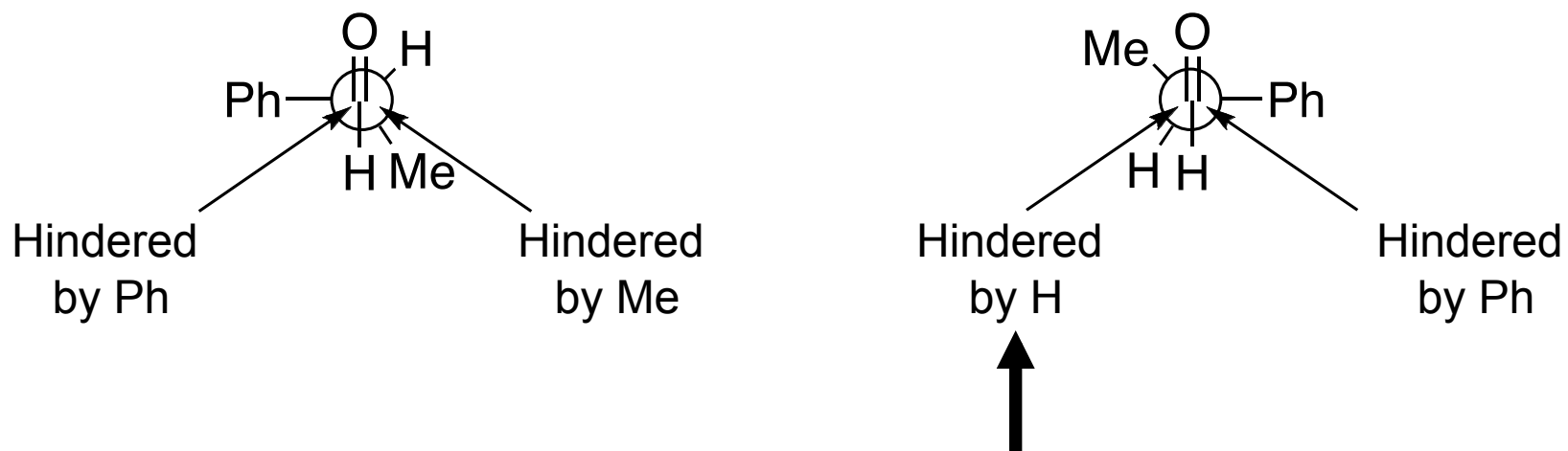


Nucleophilic attack on a Felkin-Ahn conformation 1.



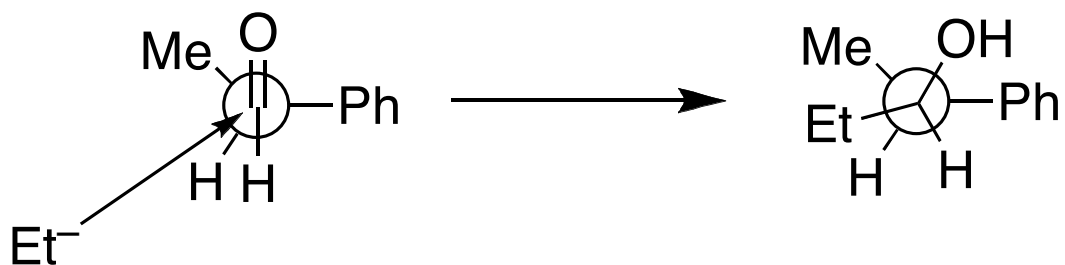
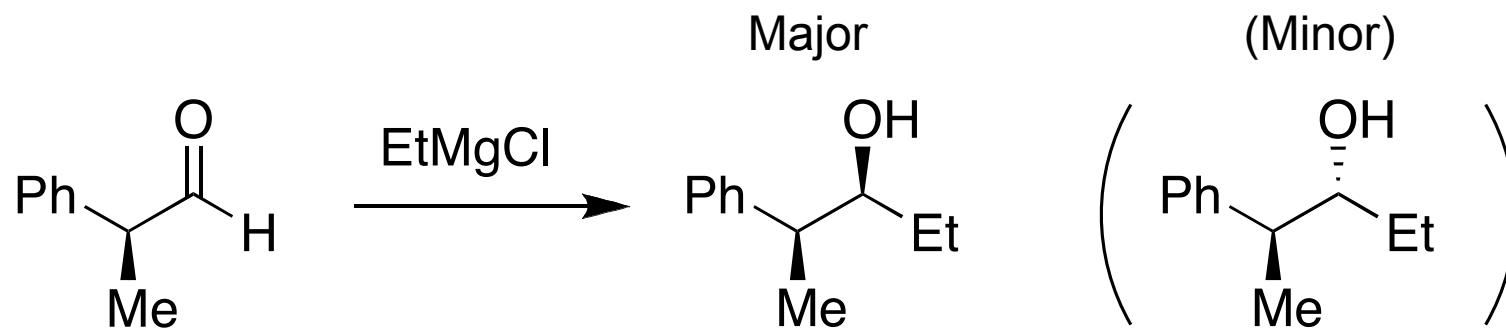
The most stable conformation will be attacked by the nucleophile from the least hindered trajectory. What trajectory...?

...remember Bürgi and Dunitz!

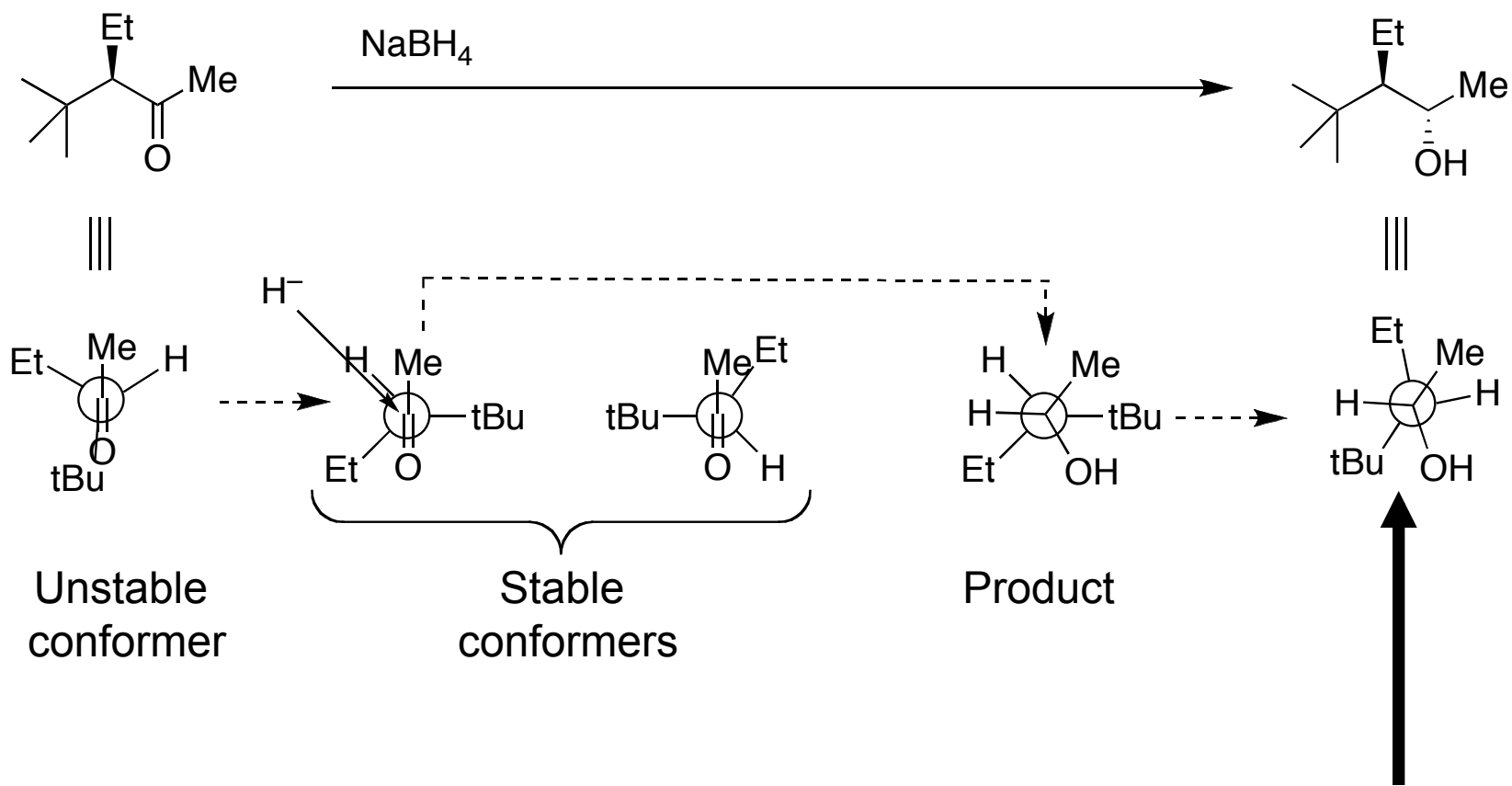


This is the easiest approach for the nucleophile

Nucleophilic attack on a Felkin-Ahn conformation 2.

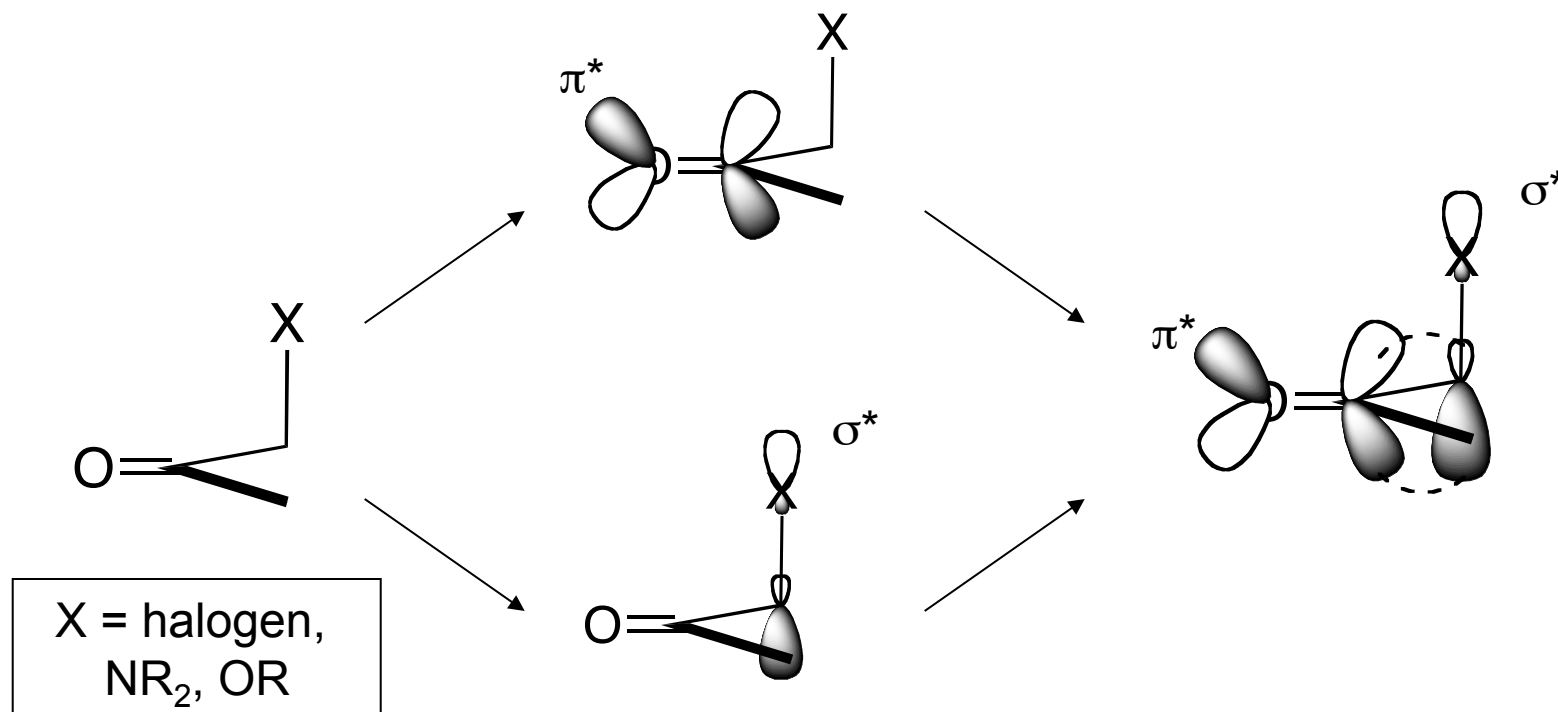


Another example



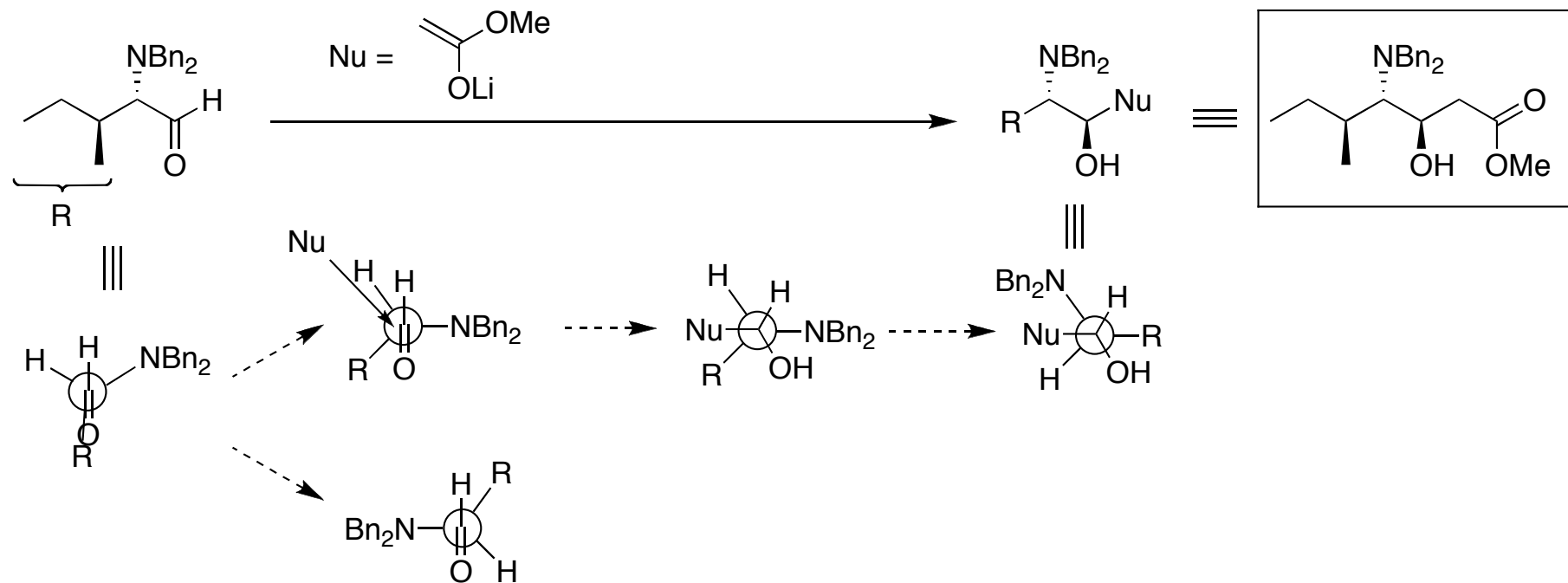
Redrawing the product Newman projection into a Newman projection with the main substituents (Me, tBu in this case) opposite to each other often makes it easier to translate back into a normal zig-zag structure

Electronegative α -substituents occupy the perpendicular position because of $\sigma^*-\pi^*$ alignment



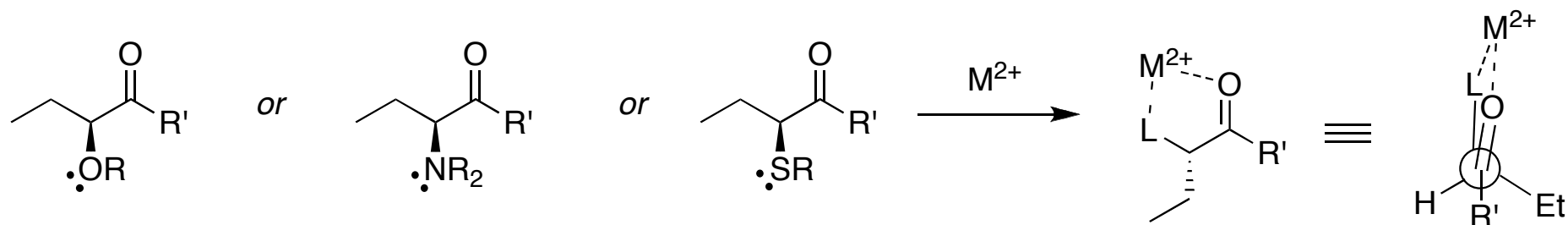
EWG have low-energy σ^* orbitals that can conjugate to the neighbouring carbonyl π^* orbital ONLY when the alignment is right (i.e. only when the EWG is perpendicular to the carbonyl plane)

Electronegative α -substituents occupy the perpendicular position: example



Homework: Check which product would have formed if you put "R" in the perpendicular position instead of NBn_2

Chelation-controlled carbonyl conformations



Alpha substituents with lone pairs can coordinate divalent (or higher valency) metal ions together with the carbonyl lone pairs.

The chelation ring becomes the dominant factor in determining the conformation, and gives VERY high selectivity for nucleophilic attack.

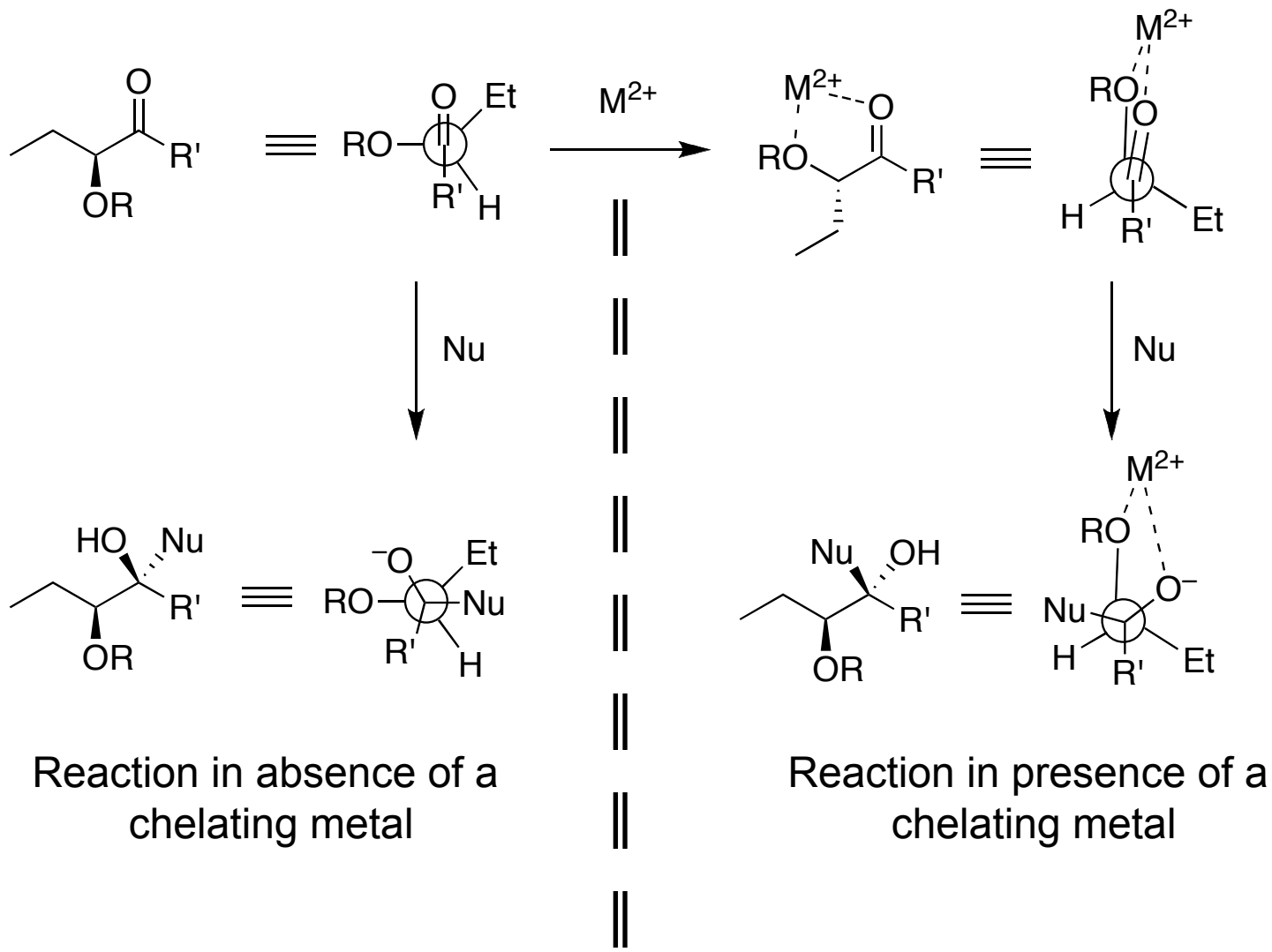
Common chelating metals:

Zn²⁺, Cu²⁺, Ti⁴⁺, Ce³⁺, Mg²⁺ (MgCl⁺ is not as good)

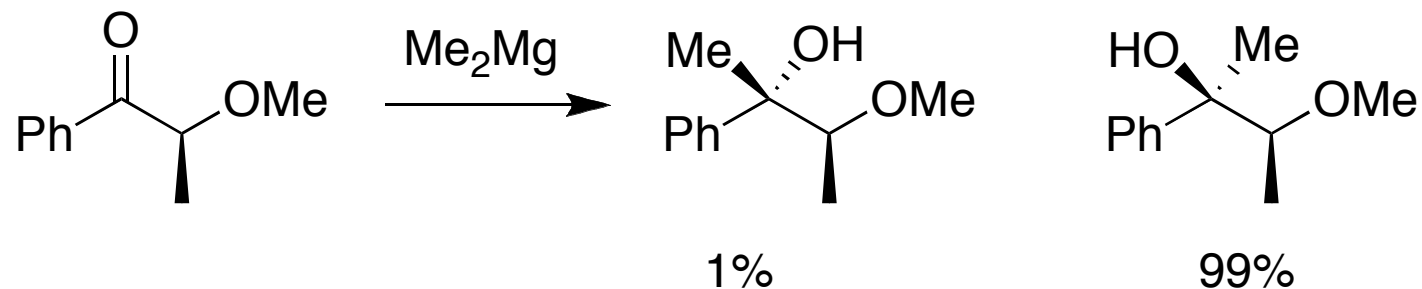
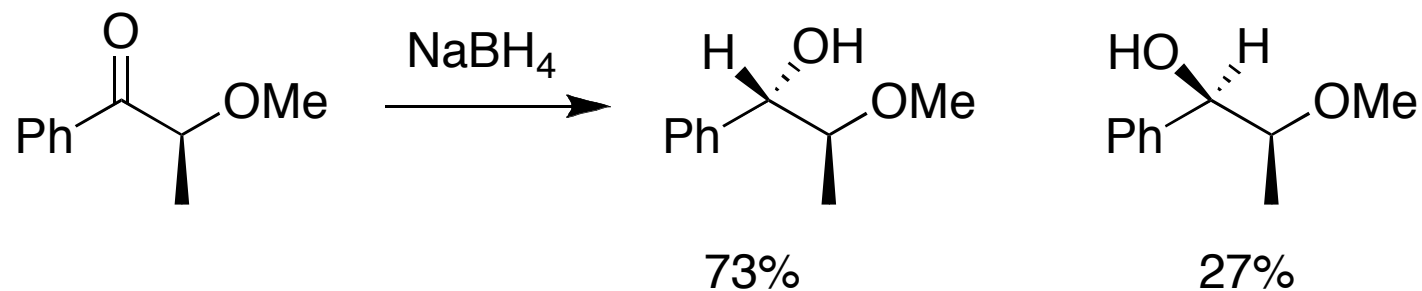
Non-chelating metals:

Li⁺, Na⁺, K⁺.

Chelation control can reverse selectivity

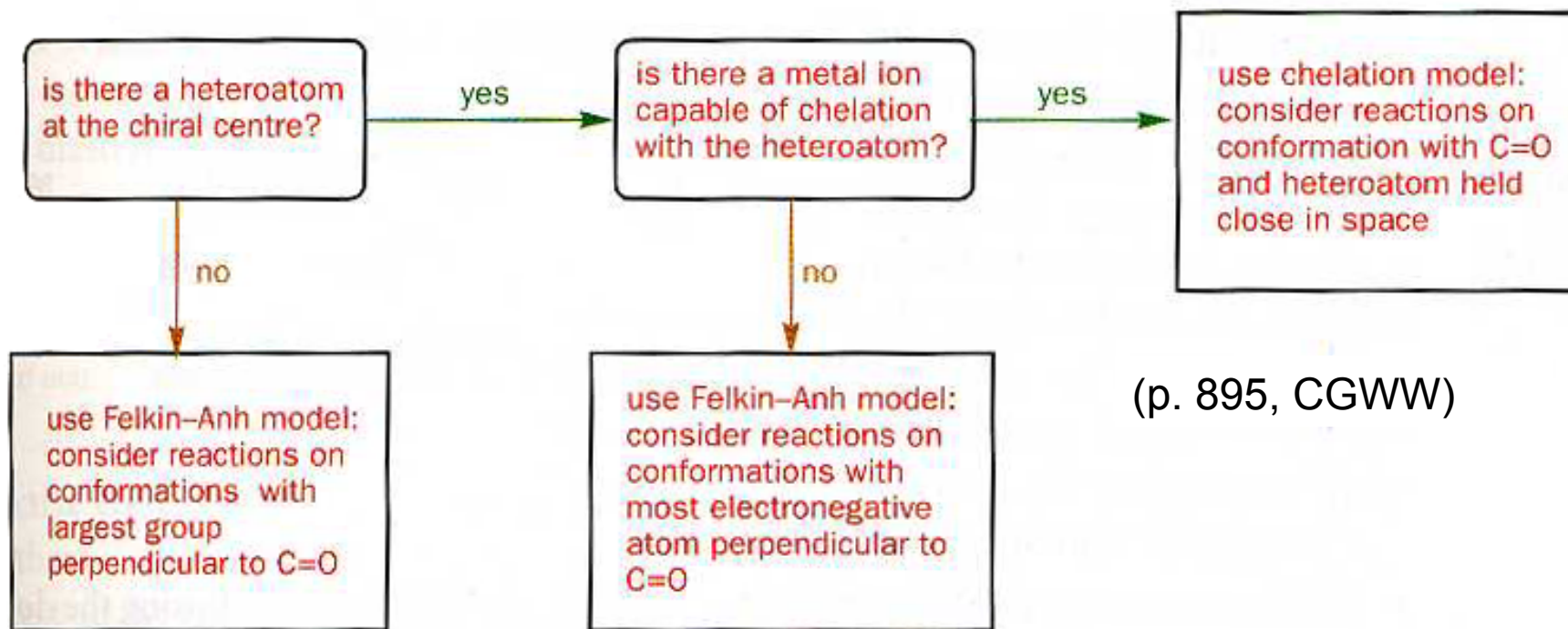


Chelation control can reverse selectivity: example



Work these problems to make sure you can predict the right products

Attack on α -substituted carbonyls: summary

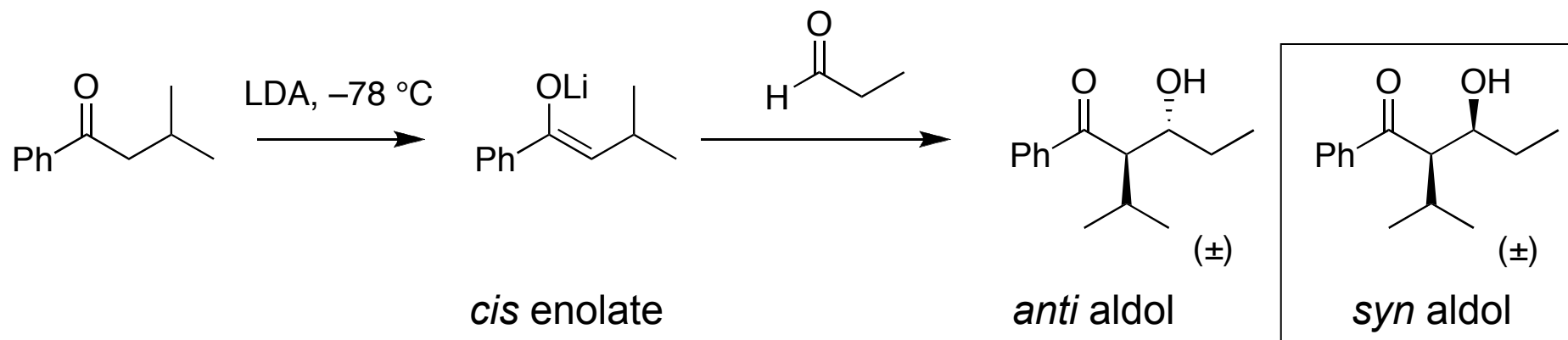
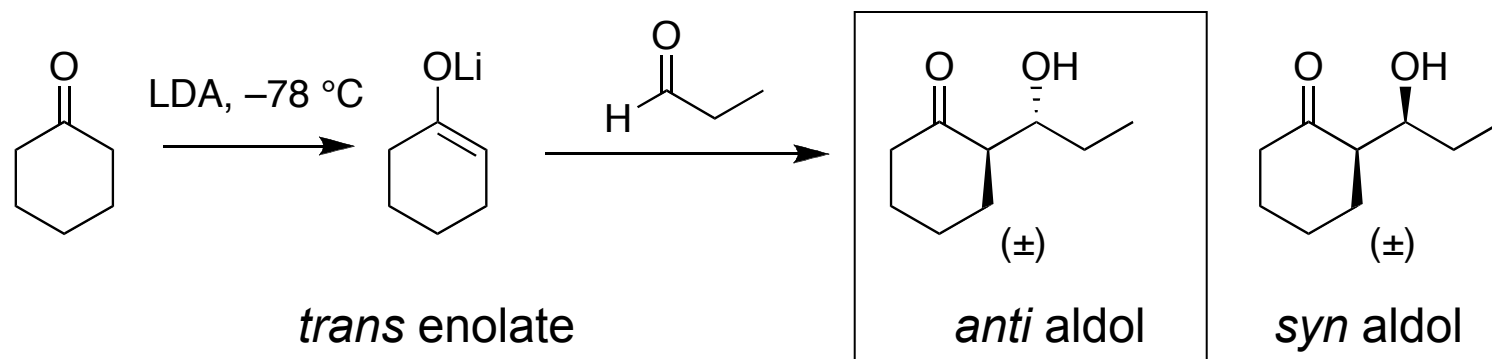


(p. 895, CGWW)

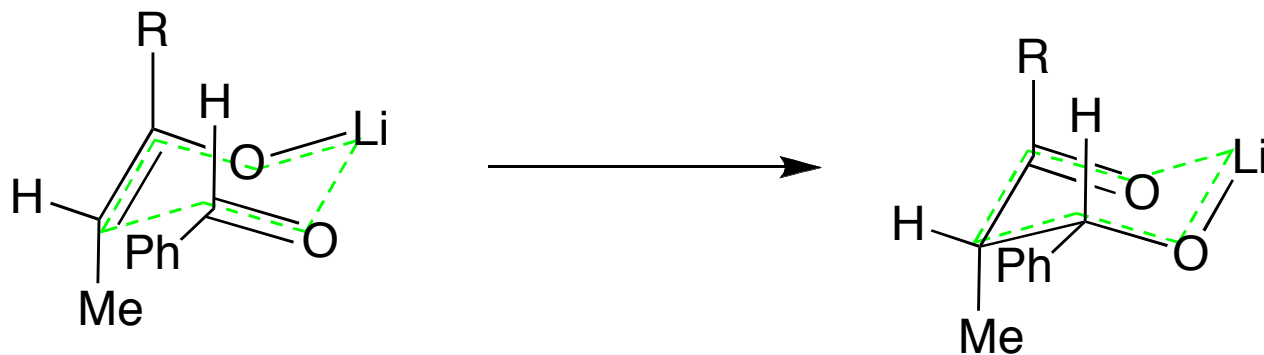
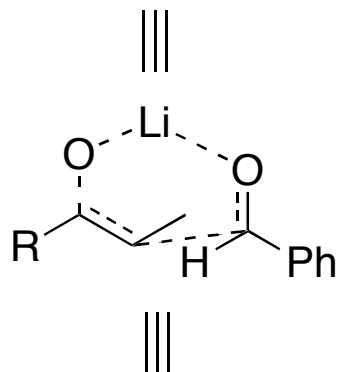
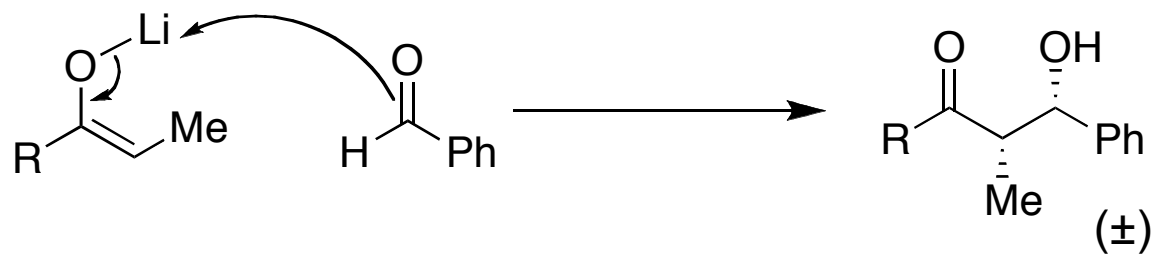
Your choices for predicting the reactive conformation:

1. Normal Felkin-Ahn model (No α -heteroatoms)
2. Electronegative heteroatom perpendicular
3. Electronegative heteroatom chelated and in the plane of the carbonyl

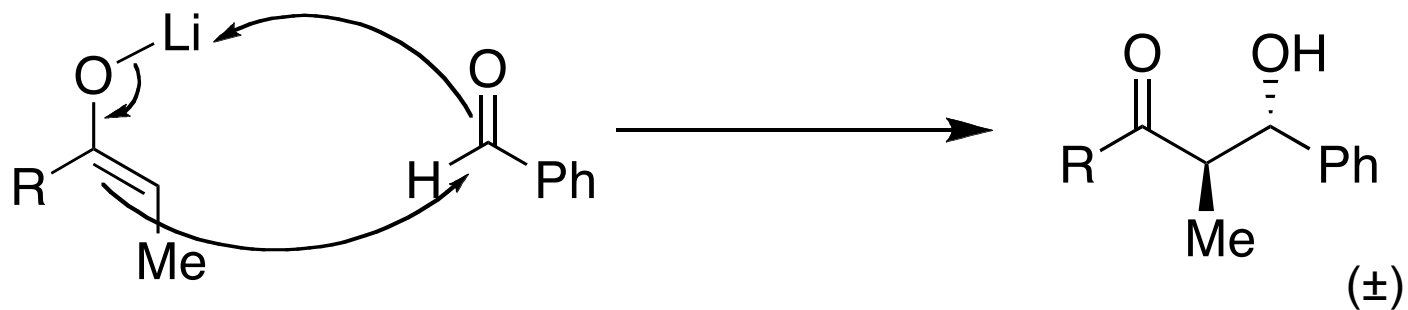
***Aldol reactions are stereoselective!!!
(so no more wiggly bonds)***



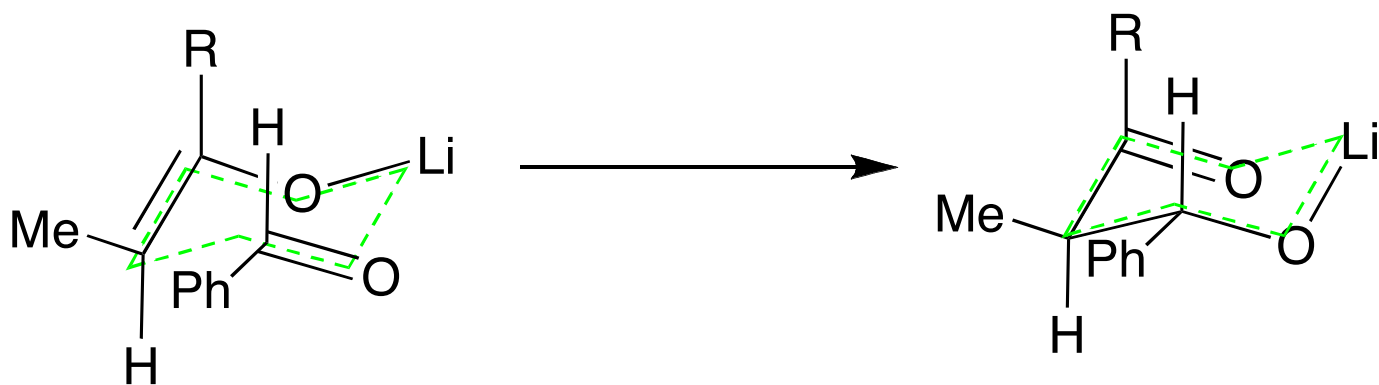
Explaining cis-enolate—syn-aldol product selectivity using a cyclic chair-like T.S.



Explaining trans-enolate—anti-aldol product selectivity using a chair-like T.S.

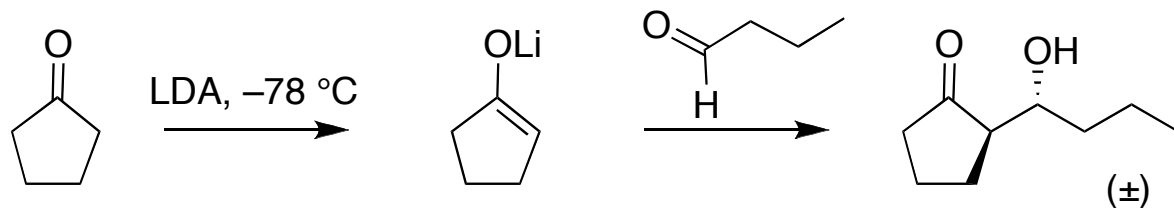


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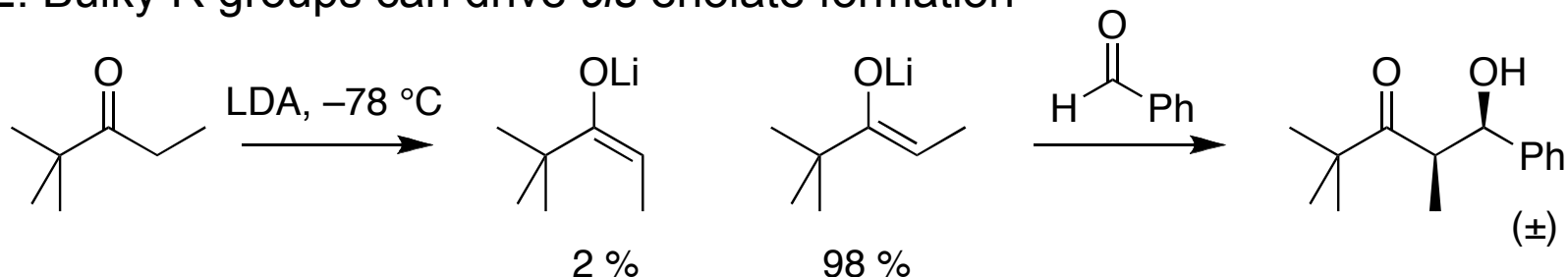


Selective production of cis and trans ketone enolates

1. Cyclic ketones must make *trans* enolates



2. Bulky R groups can drive *cis* enolate formation



3. Treatment with bulky boron reagents that attach to the enolate oxygen atom drives formation of a *trans* boron enolate

