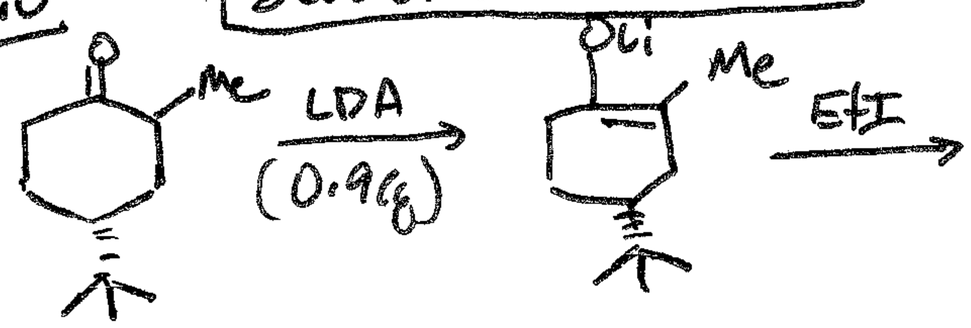
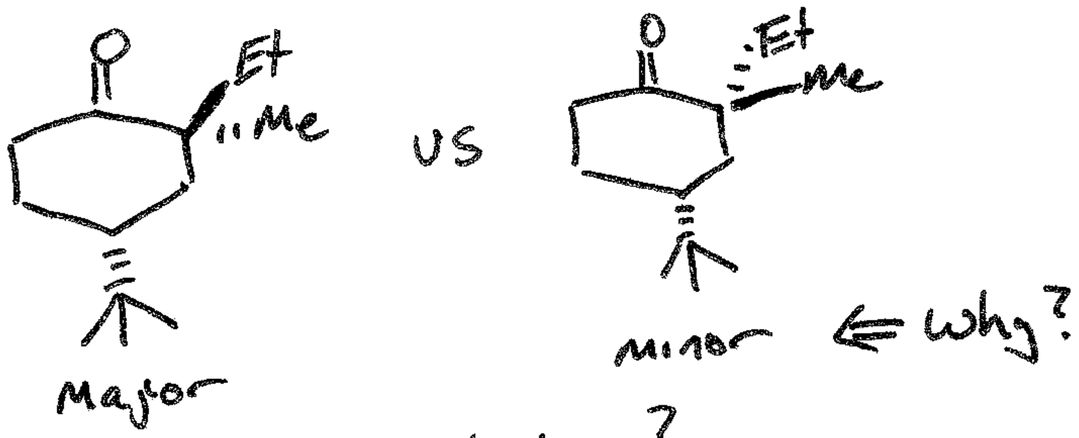
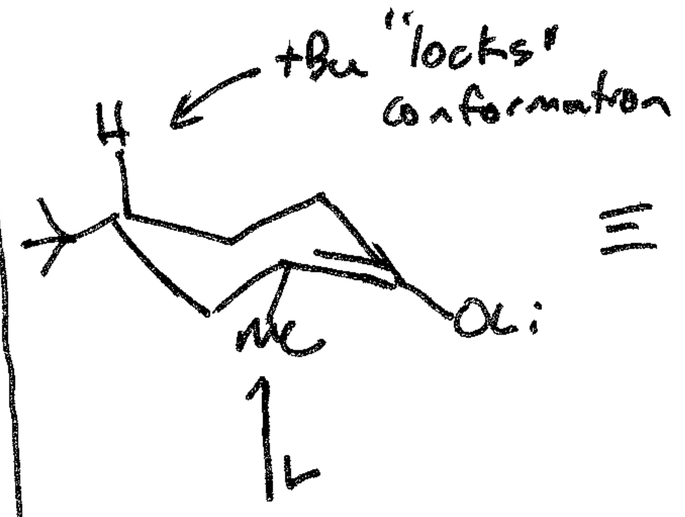
# Enolate Alkylation PART 2: stereochem

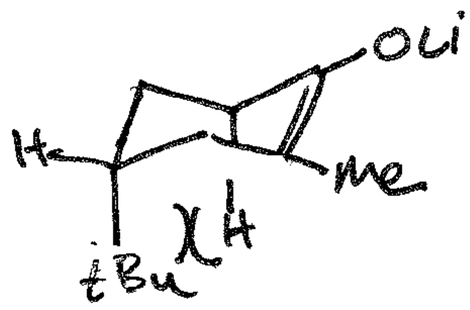
## cyclic — Substrate control

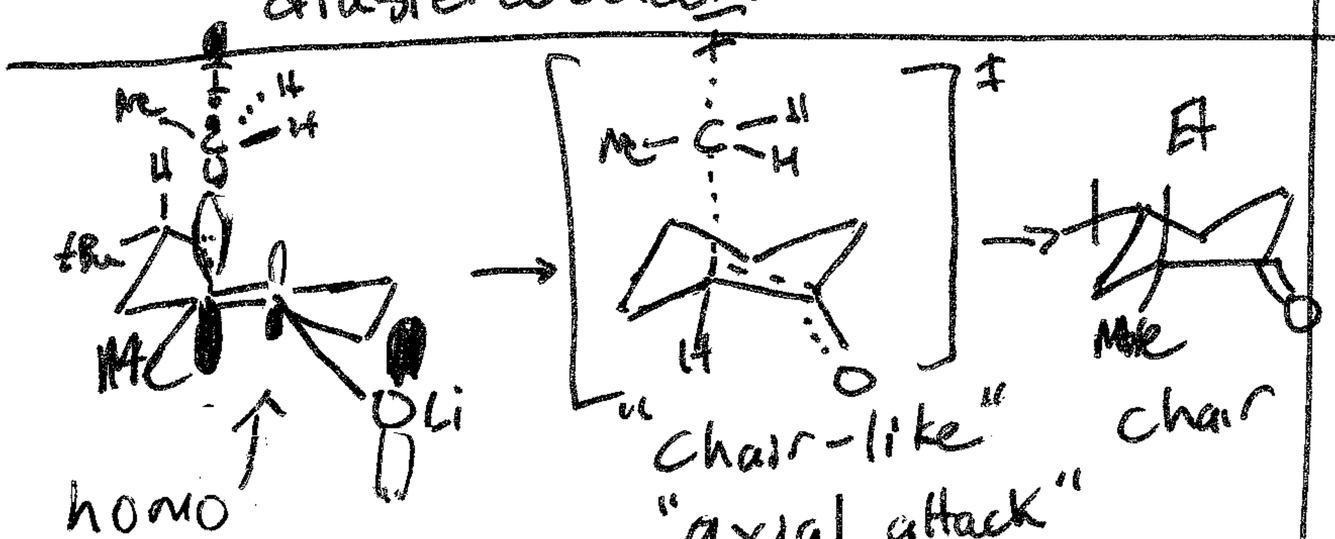


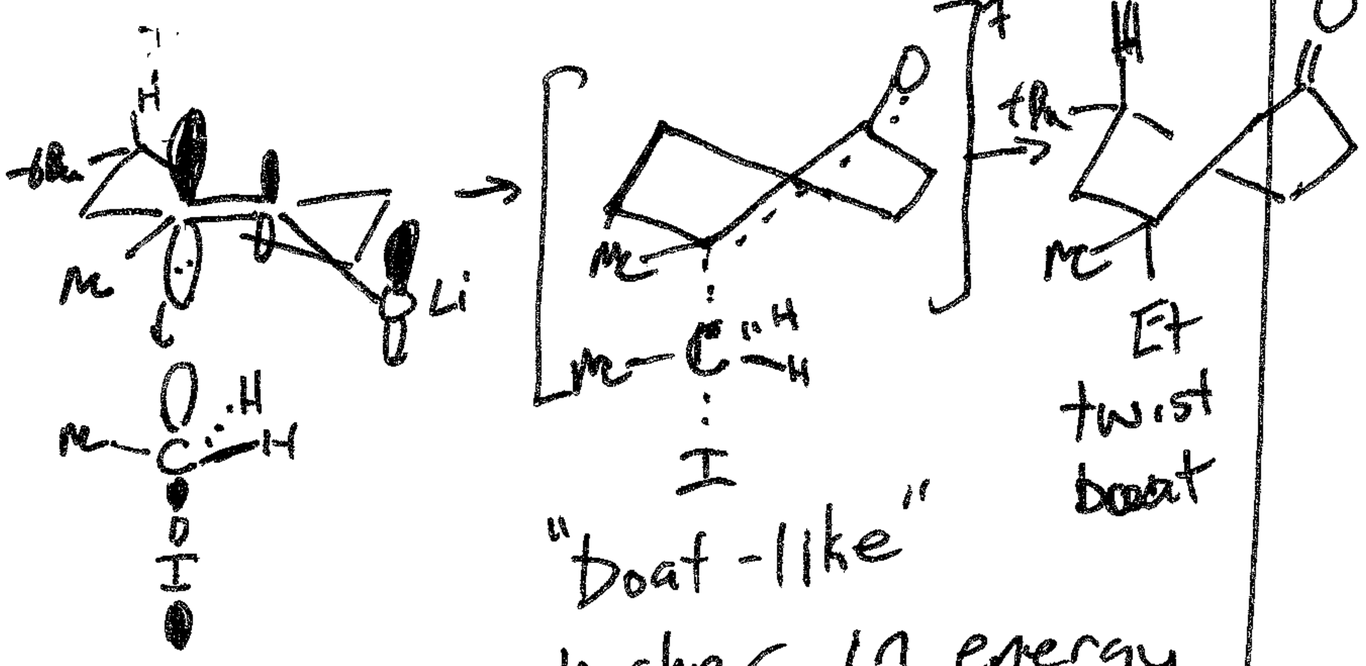




diastereoselection?

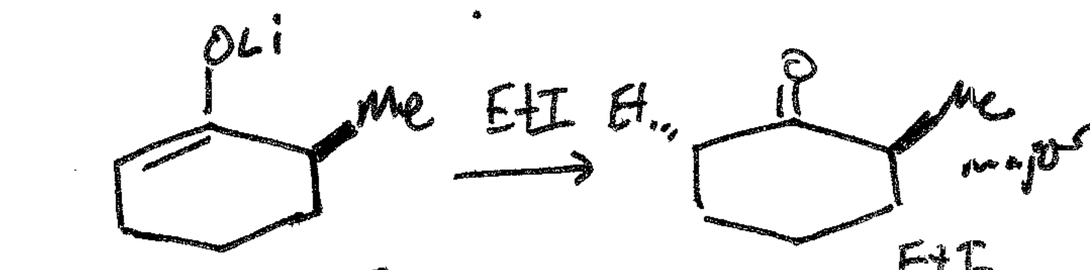


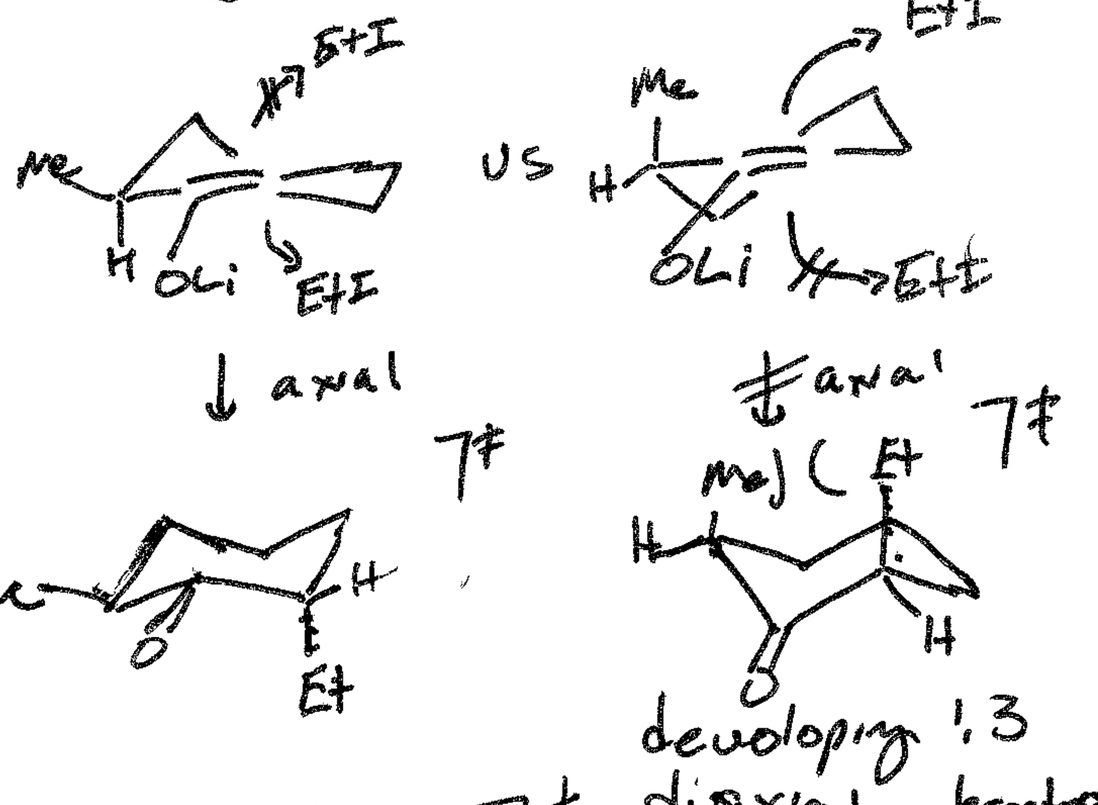



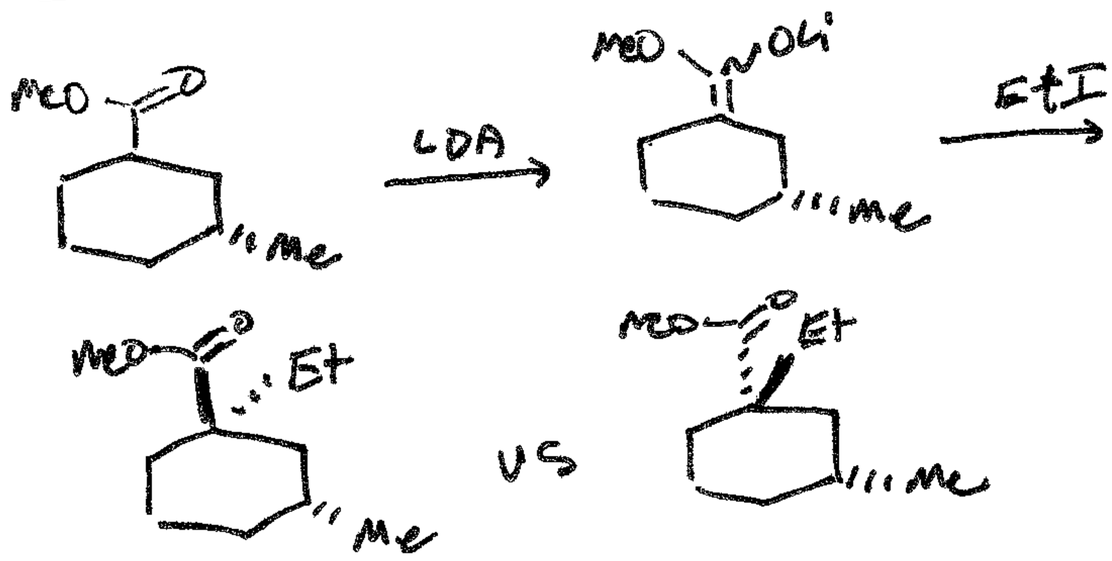




consider rate of steric interactions

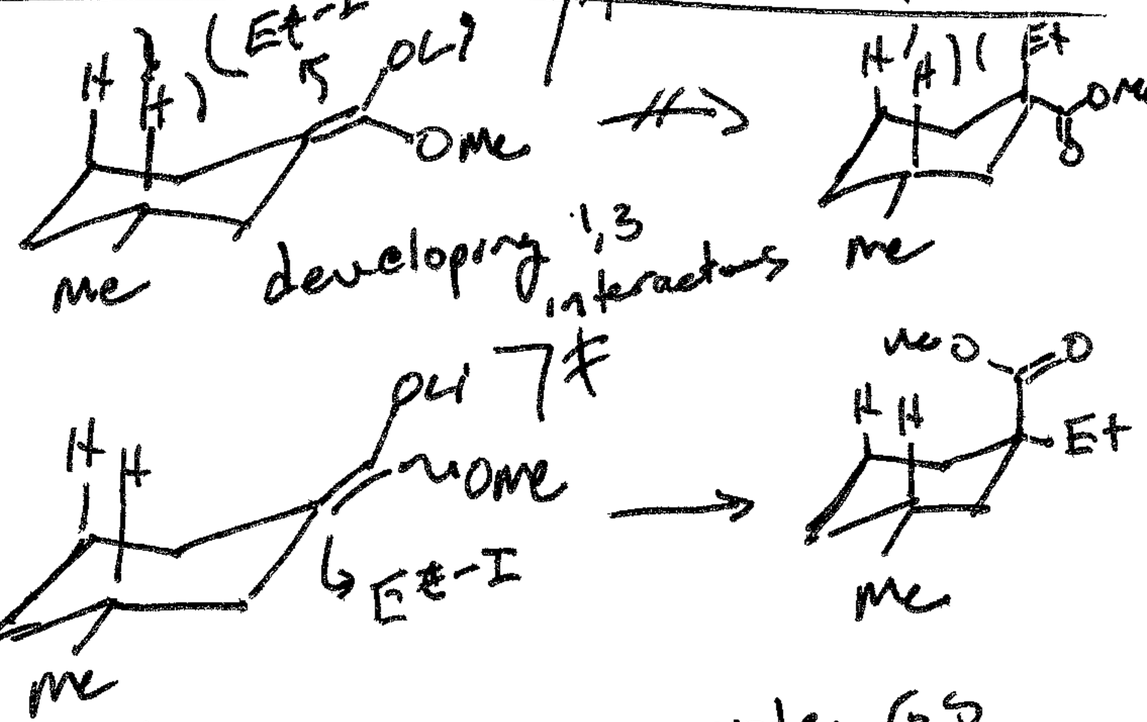



## exocyclic



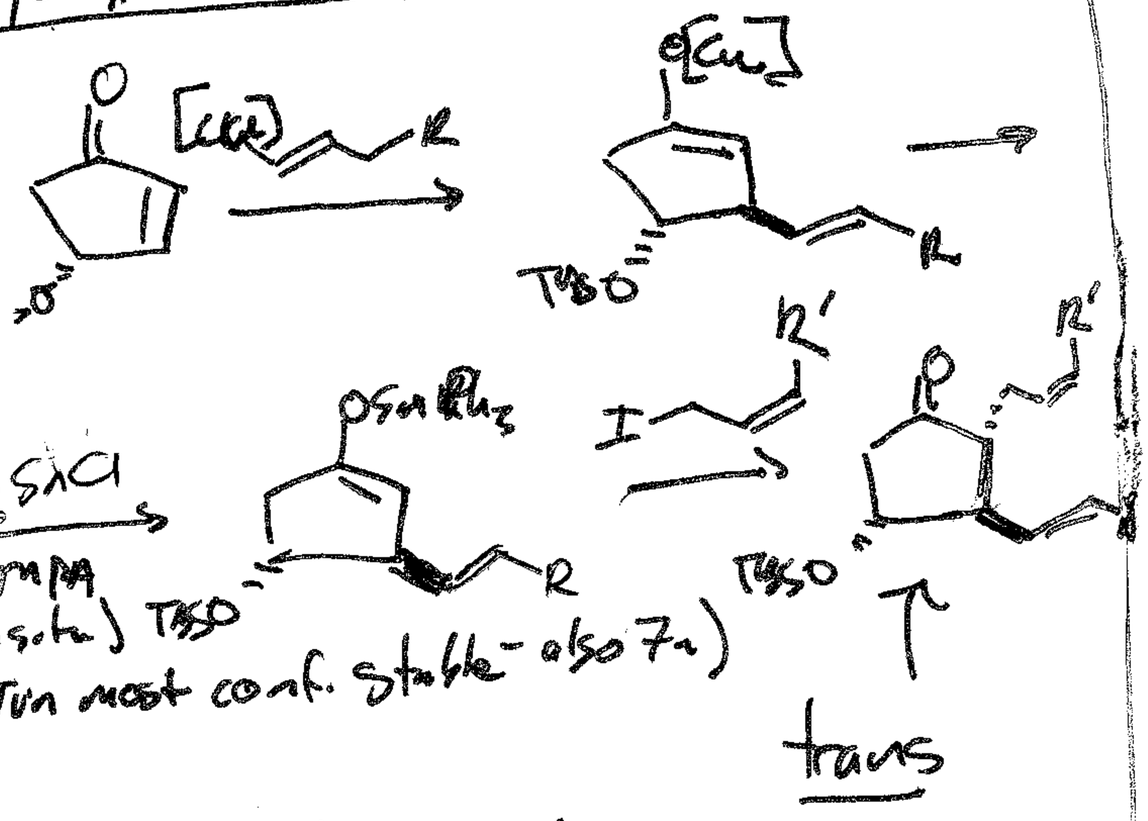

equatorial approach here



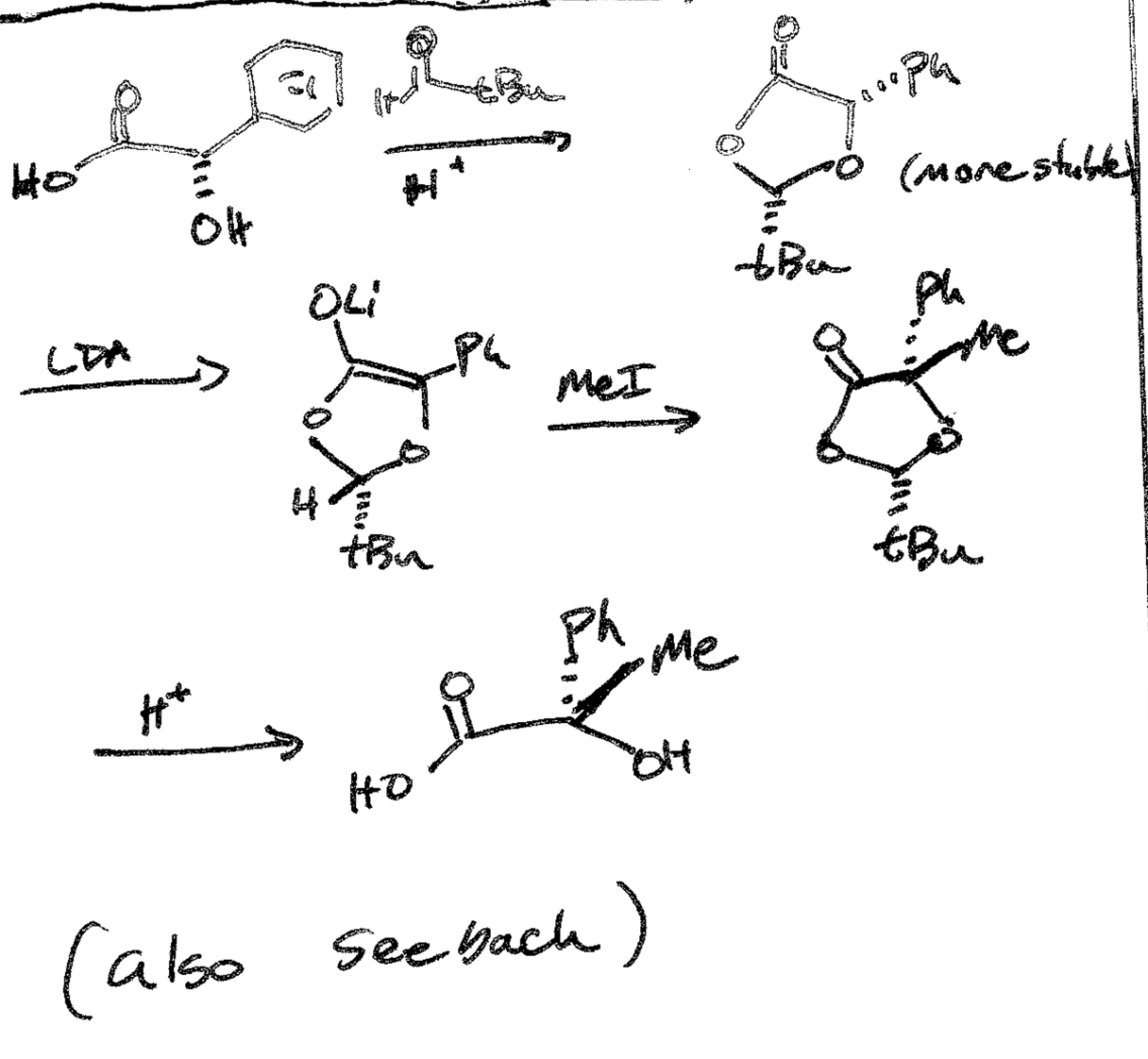

Transition states all that is important!

note GS are ~ same energy!

## Cyclopentanones



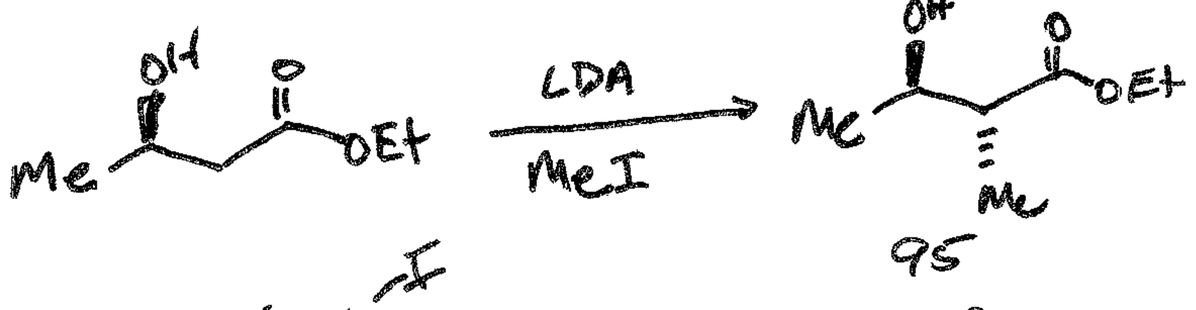

Prostaglandin synthesis
e.g.

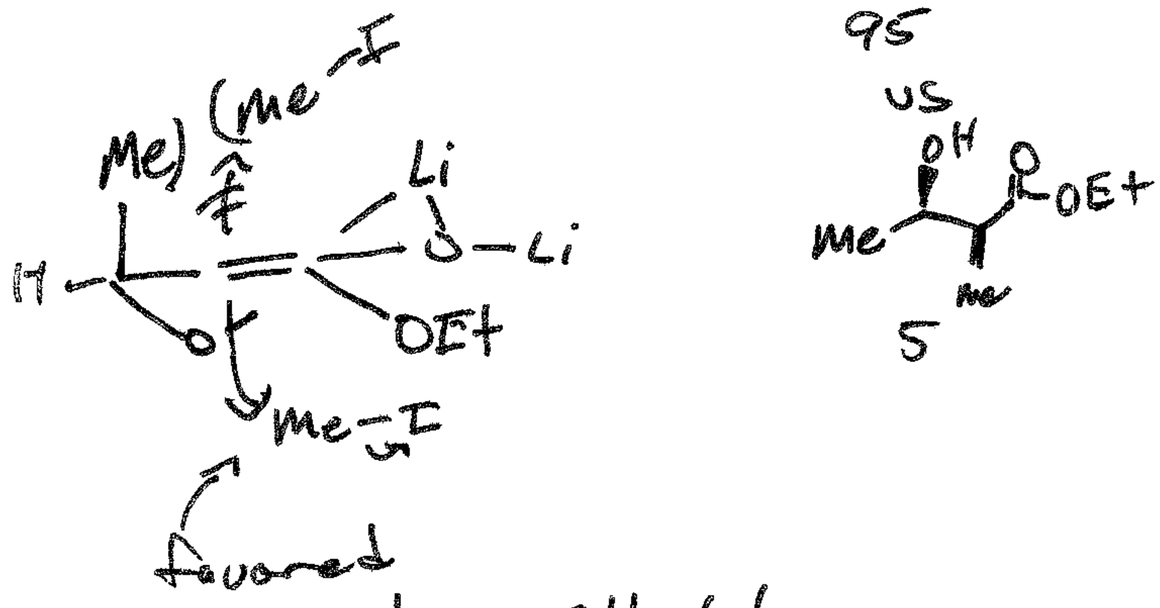



(also Seebach)

## "acyclics"

Note: "anti" aldol product

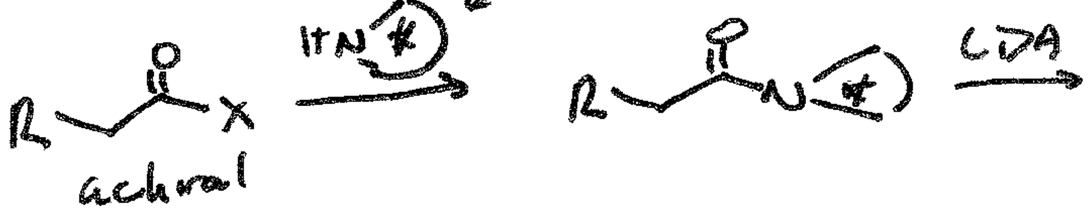



Seebach Frater alkylation

## Chiral Auxiliaries (-CH3 carriers)

General concept:




Most common with amides

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Chiral = has enantiomer

racemic = equal mix of enantiomers

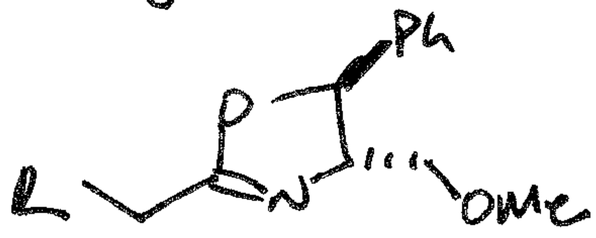
racemic ≠ achiral

$$ee = \left|\frac{R-S}{R+S}\right| \qquad R \text{ & } S = \text{enantiomers}$$

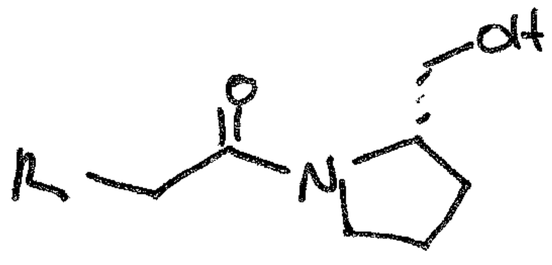
$$de = \left|\frac{D_1-D_2}{D_1+D_2}\right|$$

$D_1$ & $D_2$ = diastereomers

Early Examples




Al Meyers (Acc. Chem Res) 1978, 11, 375

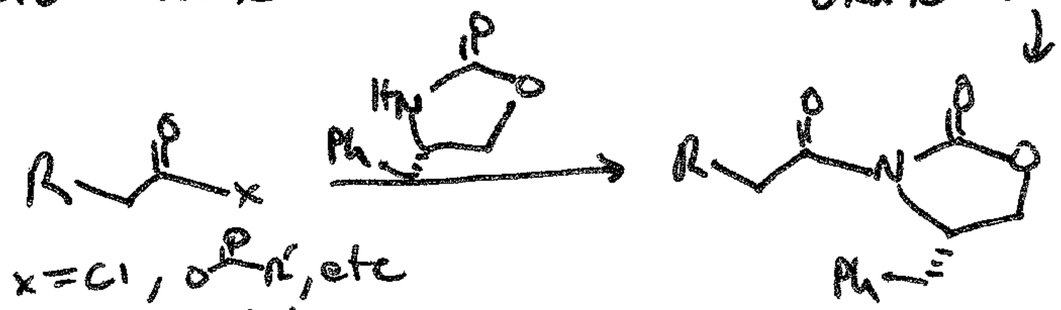


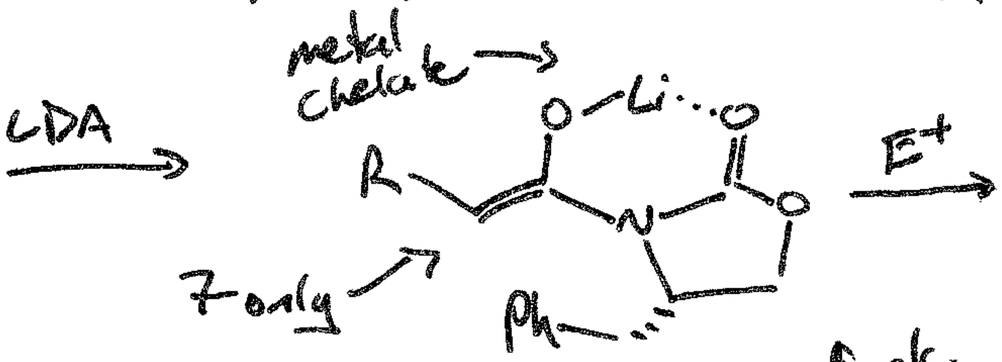

D. Evans TL, 1980, 21, 4233

Sonat JOC, 1980, 45, 3133

Work Horse's

Evan's Oxazolidinones



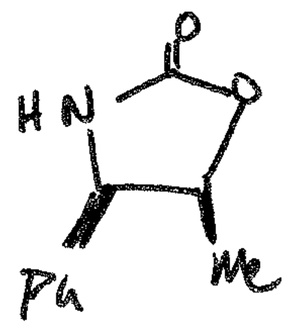


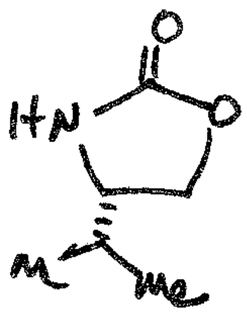
E = MeI, EtI, , 

"hot" electrophiles only

Note: 2nd acyl of oxazolidinone make enolate less reactive

Relate:

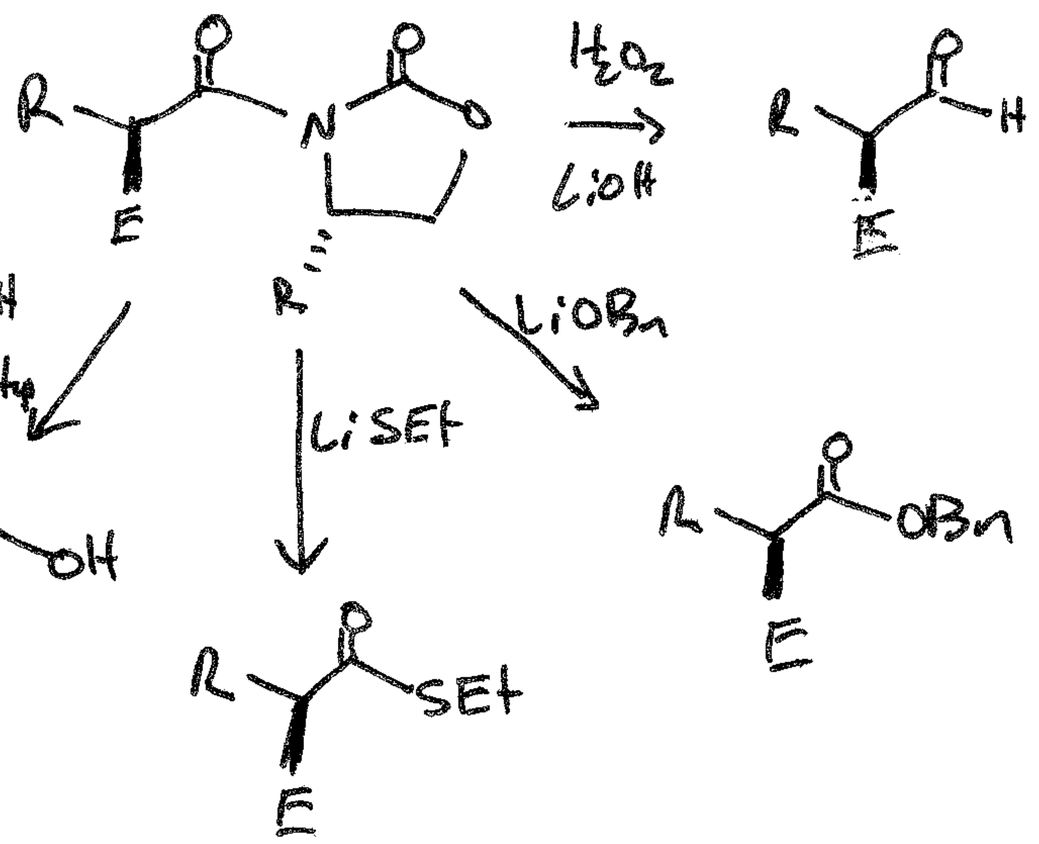




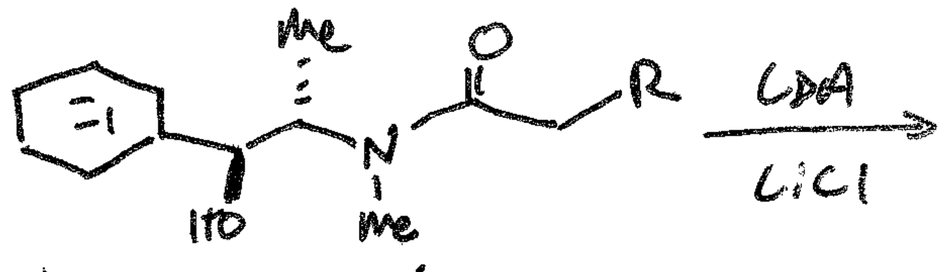
↑ Cheap "pseudo enantiomer"

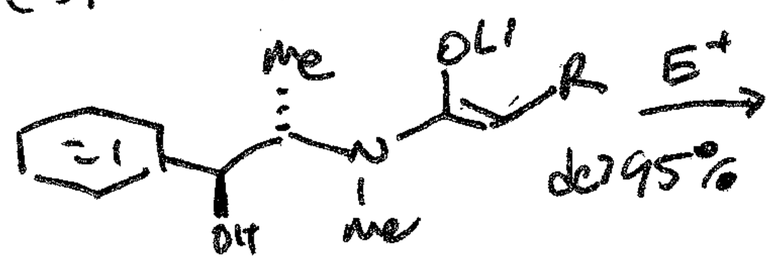
JACS, 1982, 104, 1737

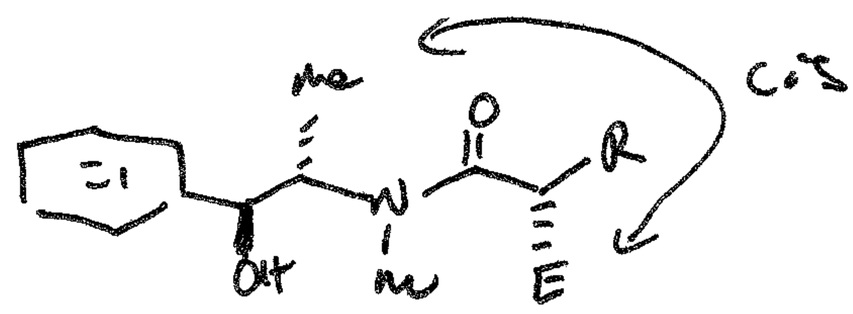
note: other ent. of chiral aux gives other ent. of products!



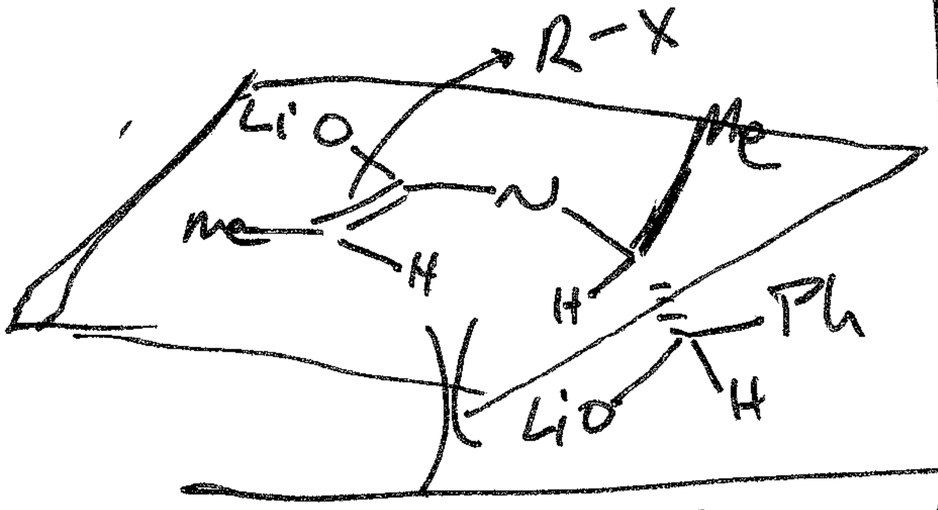

Myers (Andy) JACS, 1994, 116, 9361



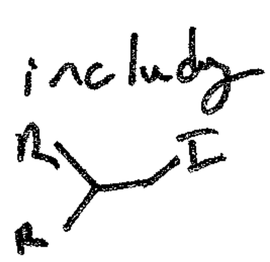




Stereoselection model:



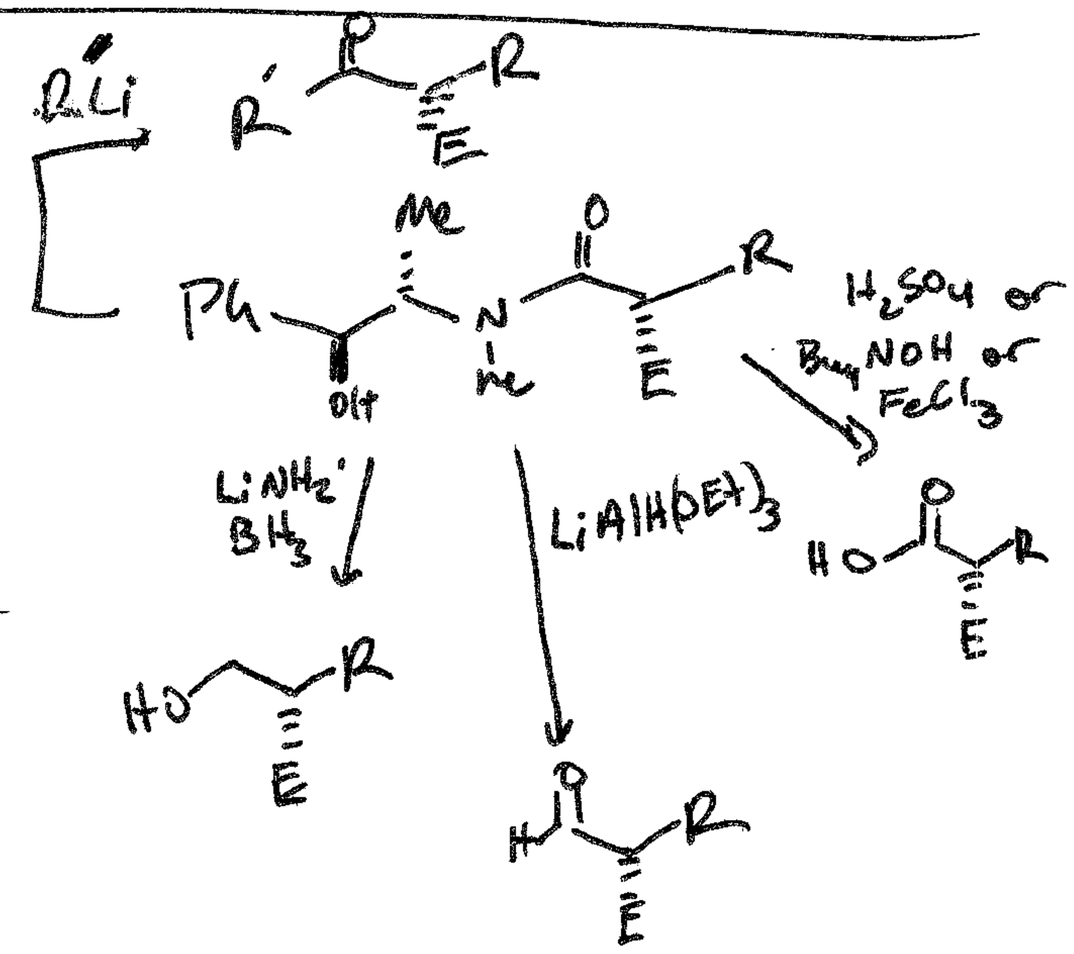

E = lots of 1° things!

including

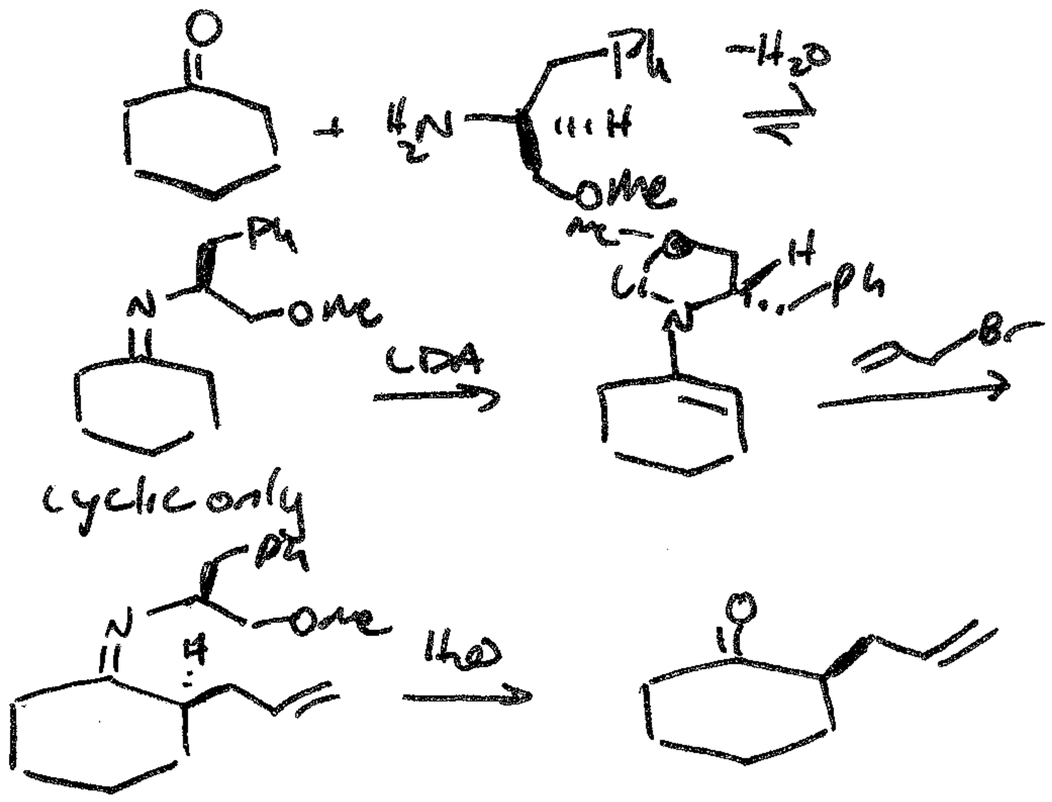


note for  lower face preferred!



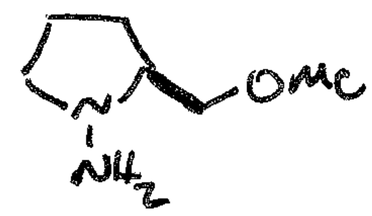


## Ketones — A. Meyers

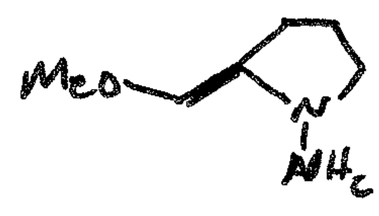



JACS, 1976, 98, 3032

## Ketones, Aldehydes — SAMP/RAMP

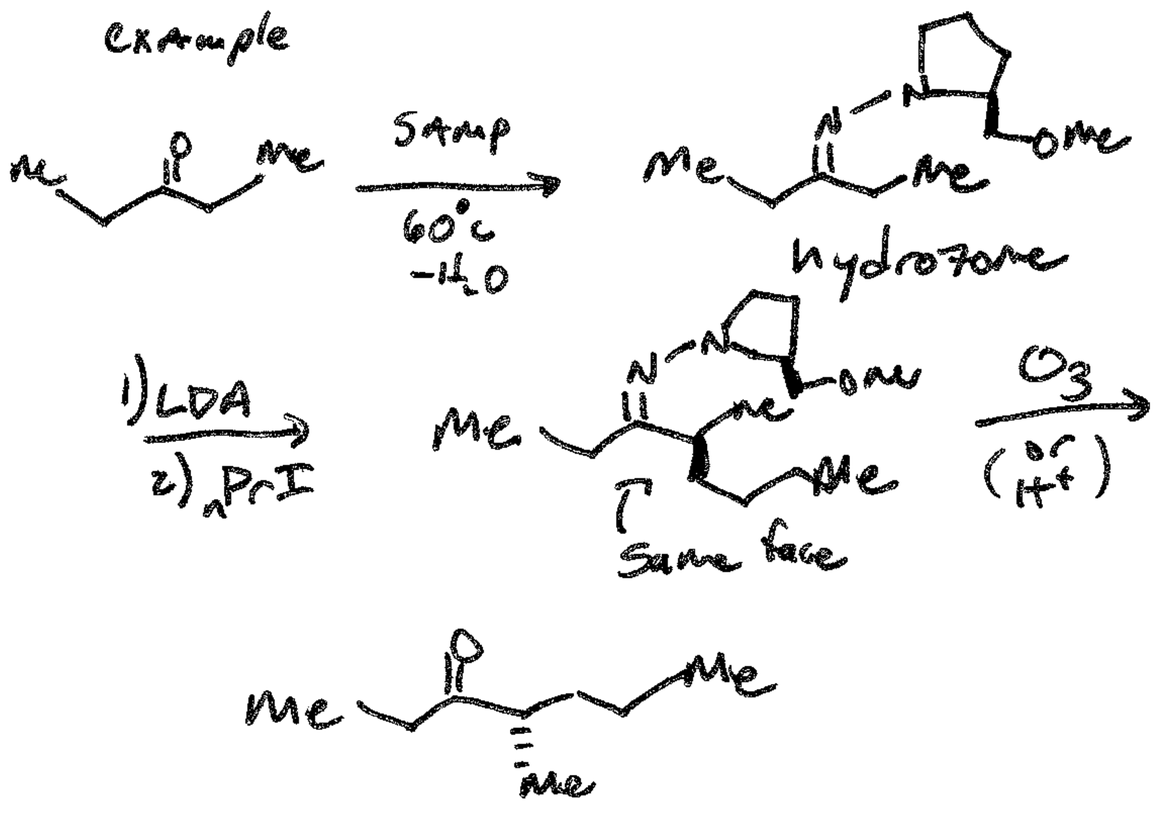



SAMP

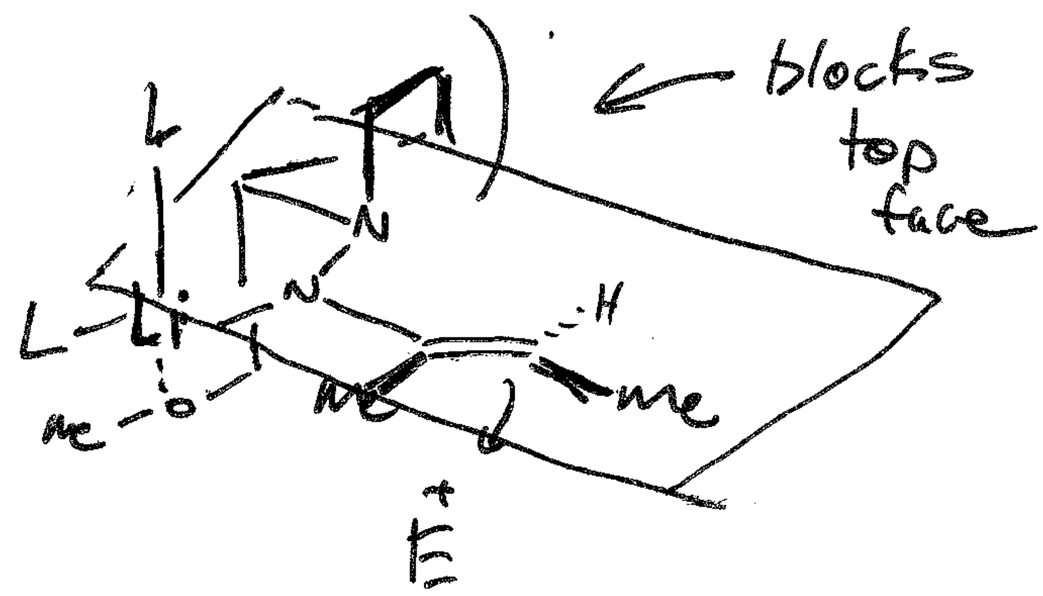



RAMP

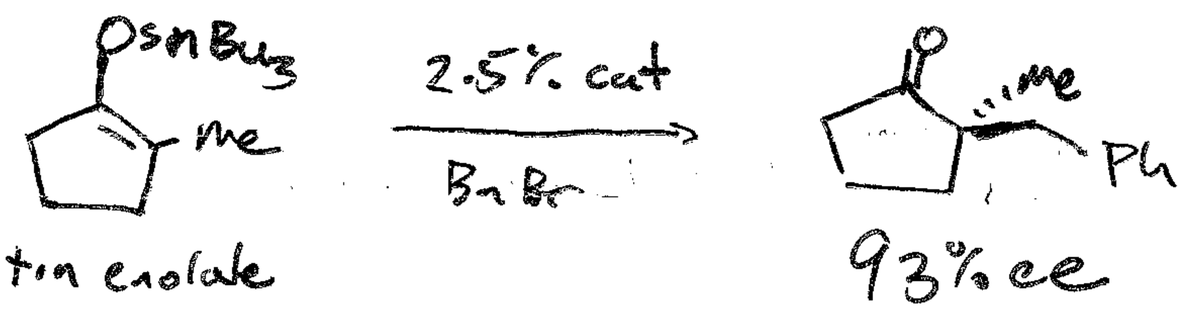
1-Amino-2-methoxymethylpyrrolidine




## Stereoselectron model:



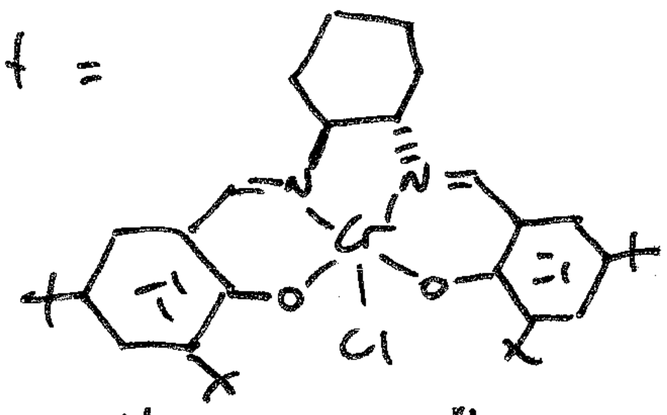

## Enantioselective Enolate Alkylations




tin enolate

93% ee

cat =



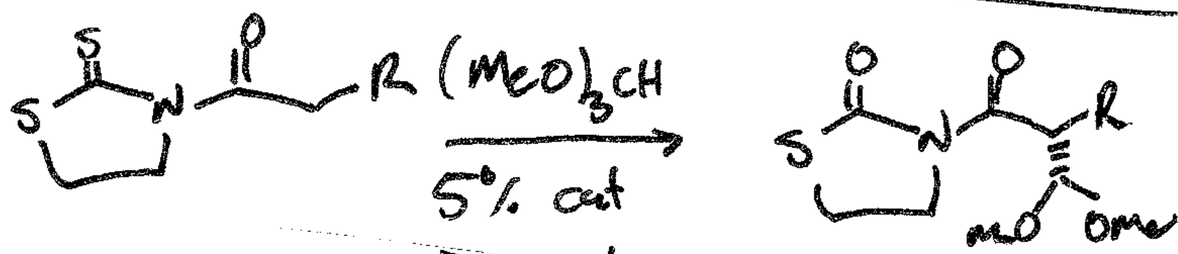

"Cr salen"

R = MeI, BnBr, allyl-X etc

Doyle & Jacobsen

JACS, 2005, 127, 62 / ACIE 2007, 46, 3701

Mech not clear

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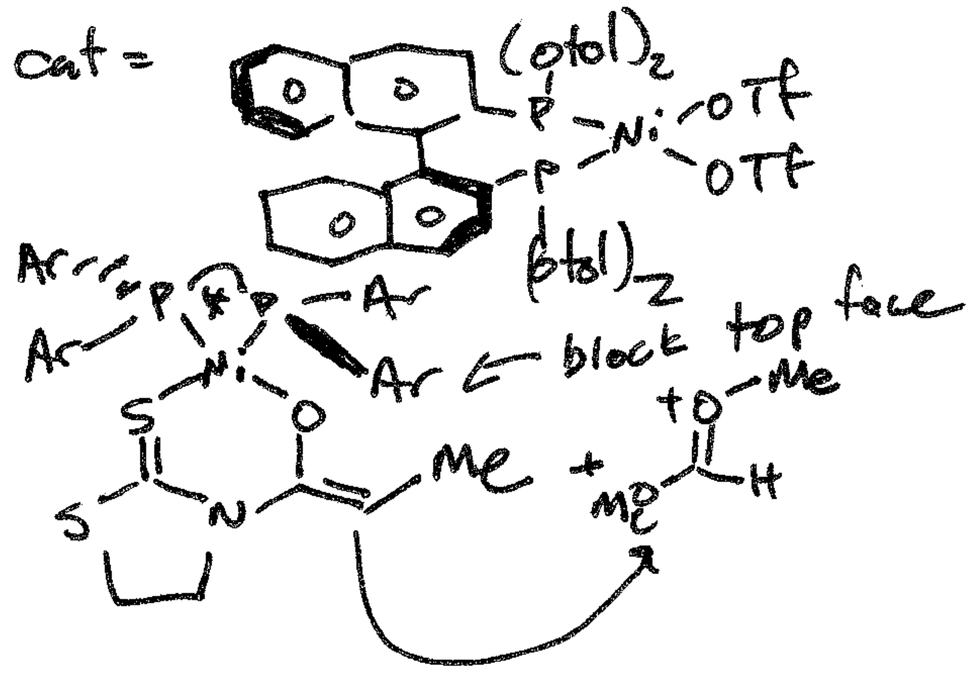


D. Evans JACS, 2005, 127, 10506