

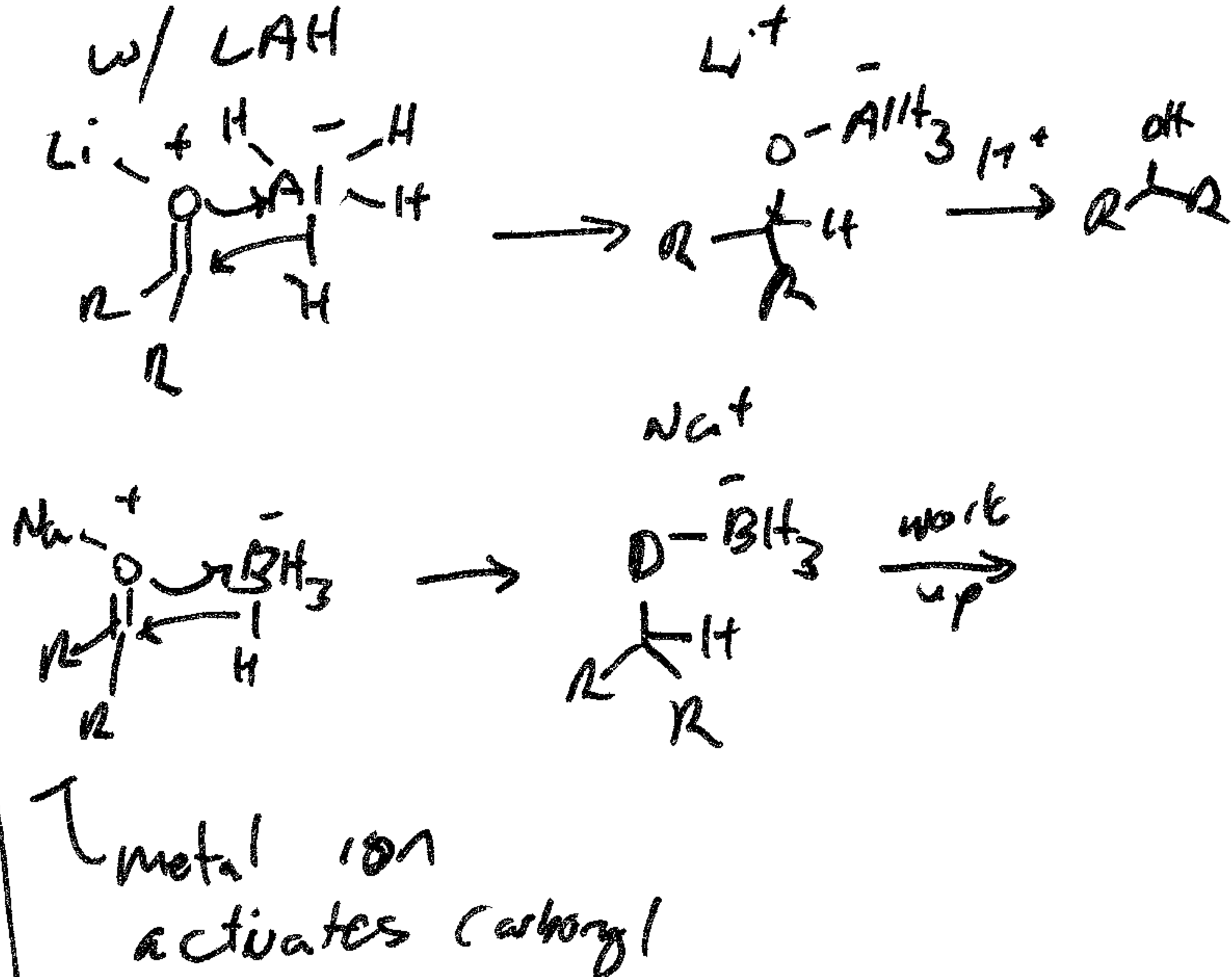
C=X Reduction & Addition (Part 1)

Reductions:

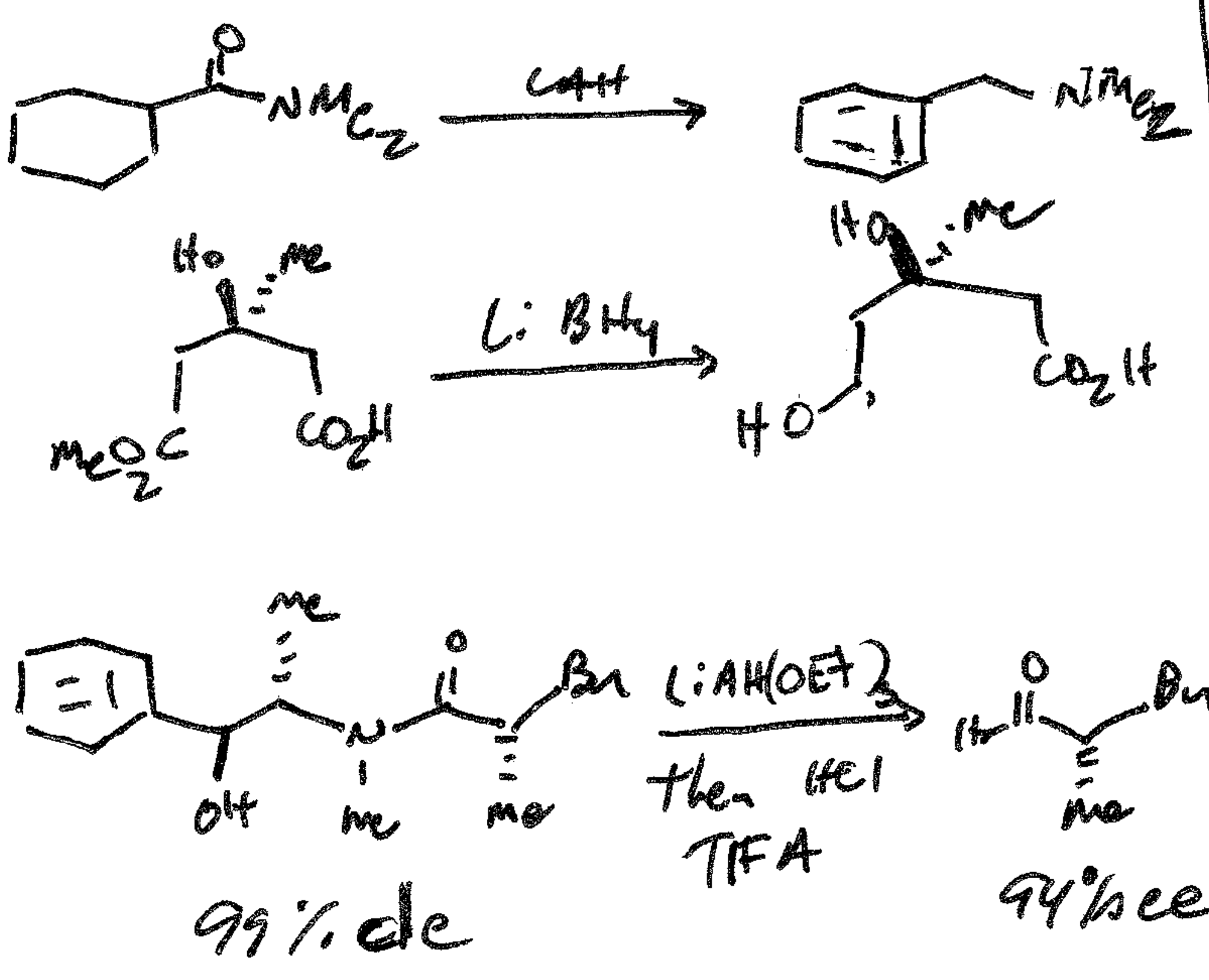
Common $C=C=X$ reducing agents:

$LiAlH_4$, $(iBu)_2AlH$, $NaBH_4$, BH_3 , H_2 , etc... see a Hatched table for common uses of those & other ~~reagents~~ reagents.

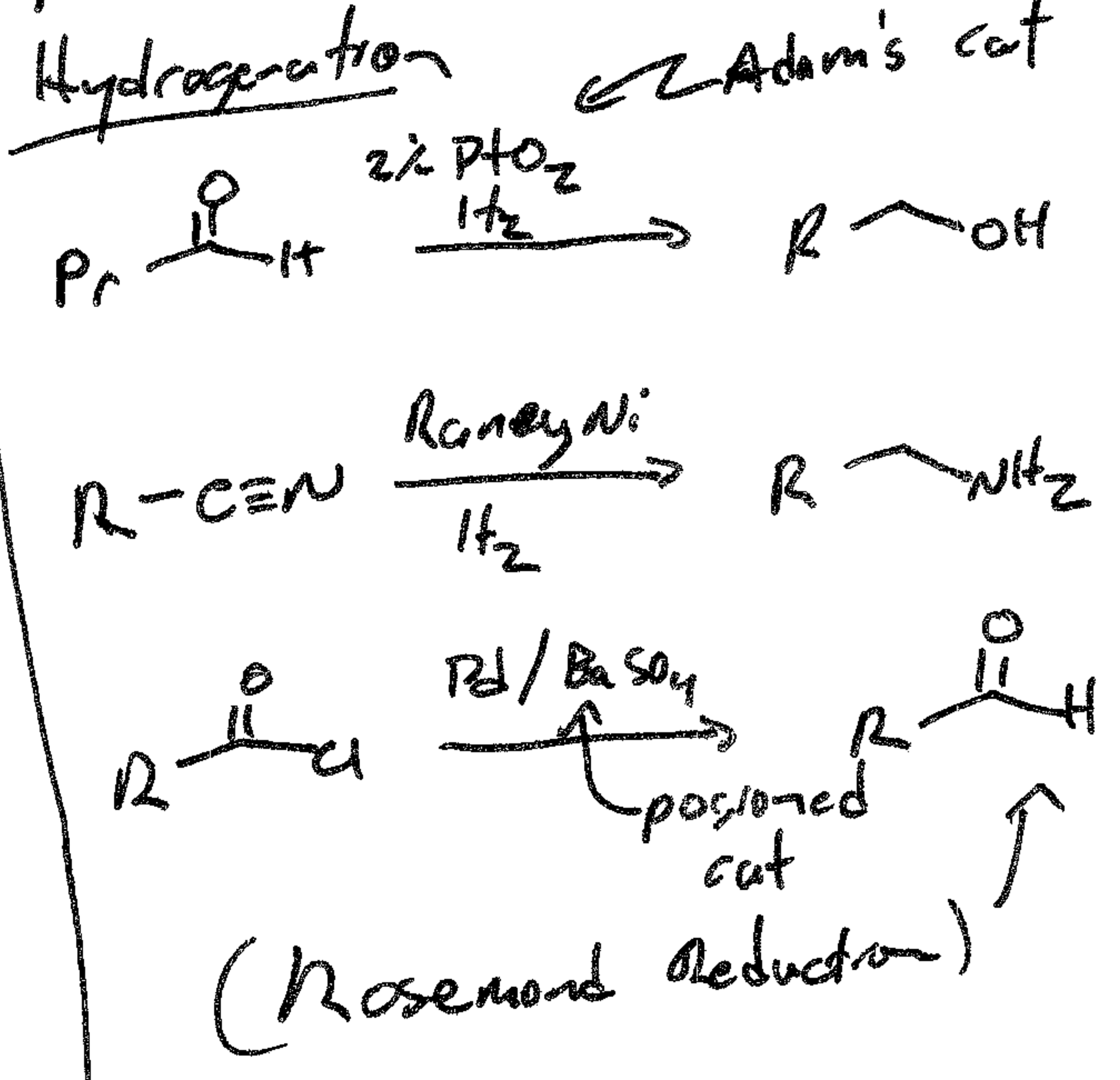
General Mech (Nucleophilic)



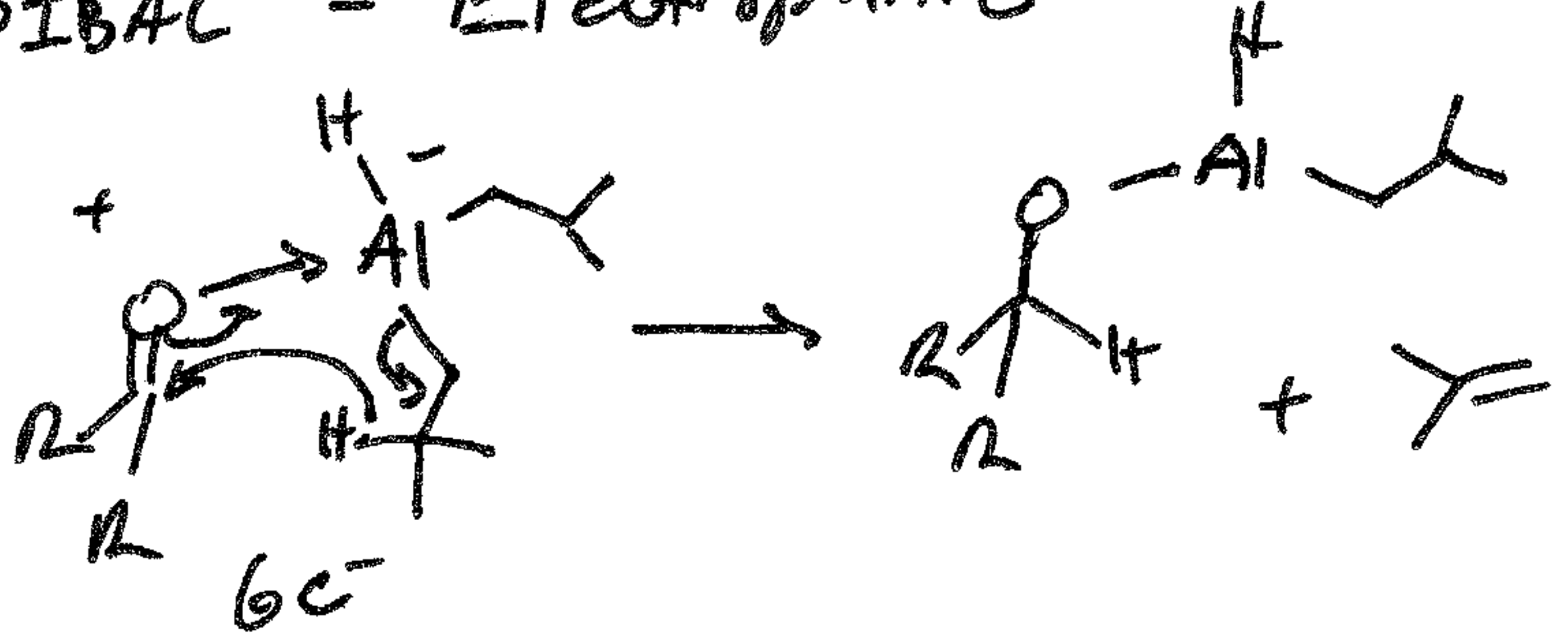
Examples of Nuc. Red (not inclusive)



"Special" Reductions



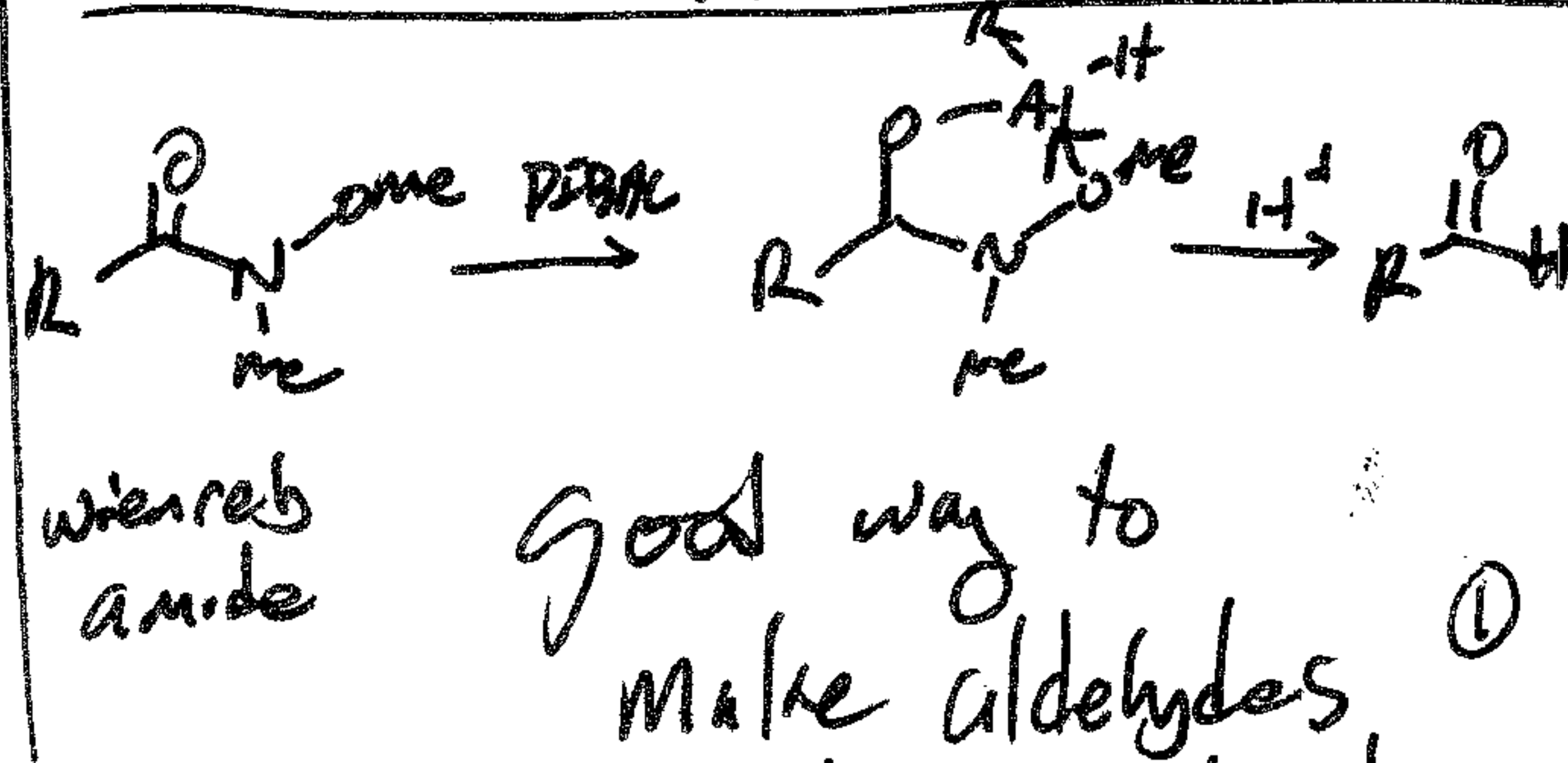
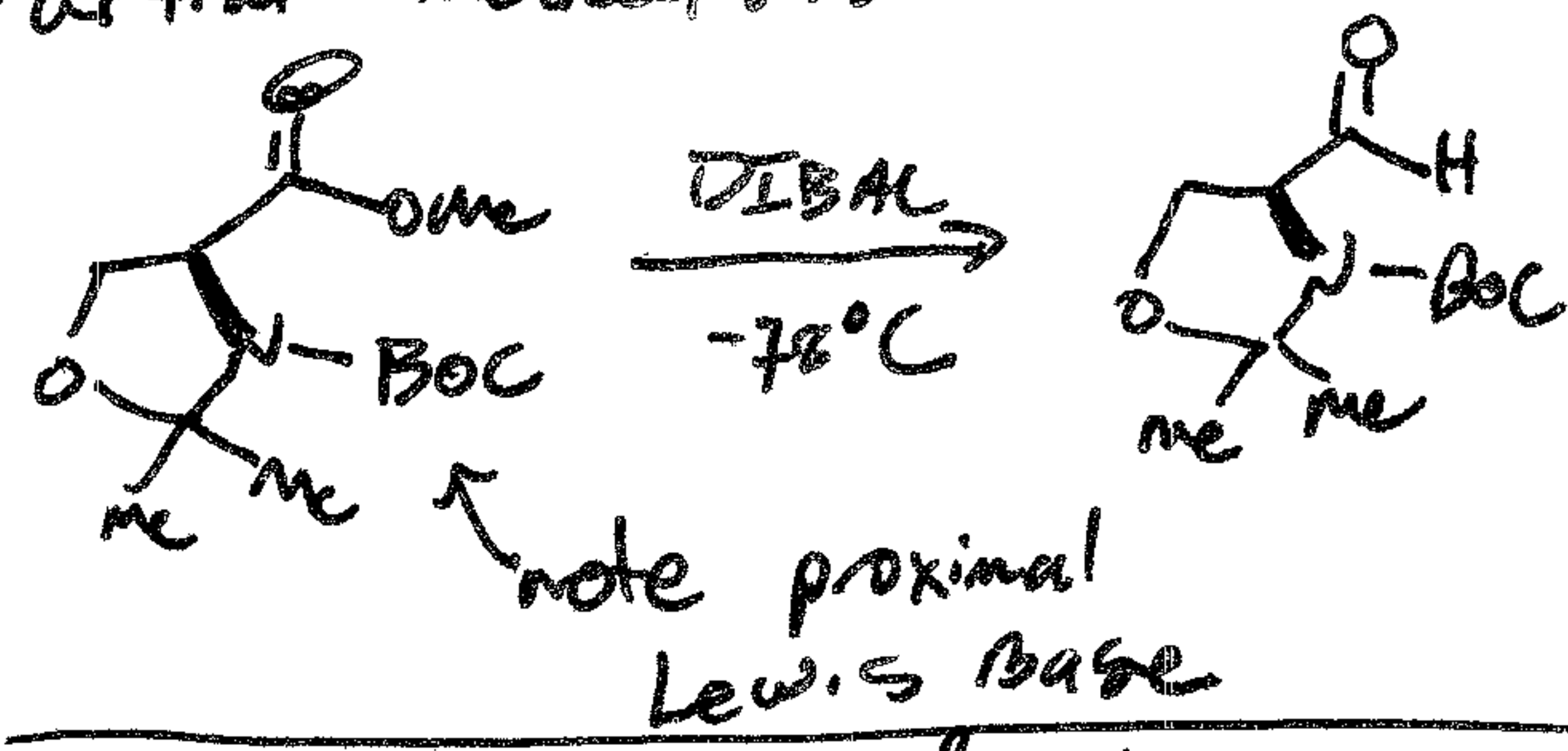
DIBAL - Electrophilic



Note: NOT "H" from Al-H that is the reductant!

3-coordinate Al is electrophilic

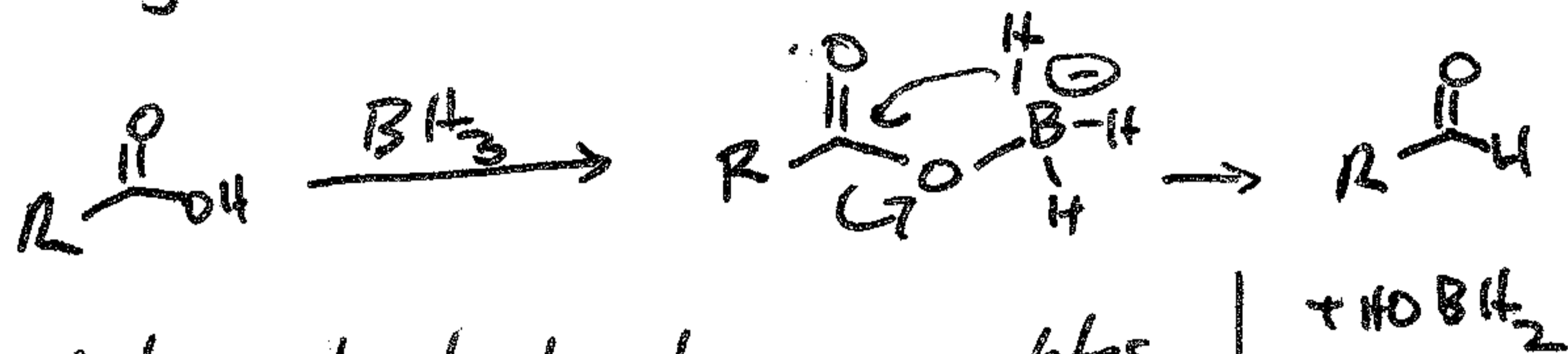
Partial Reductions



Nitriles

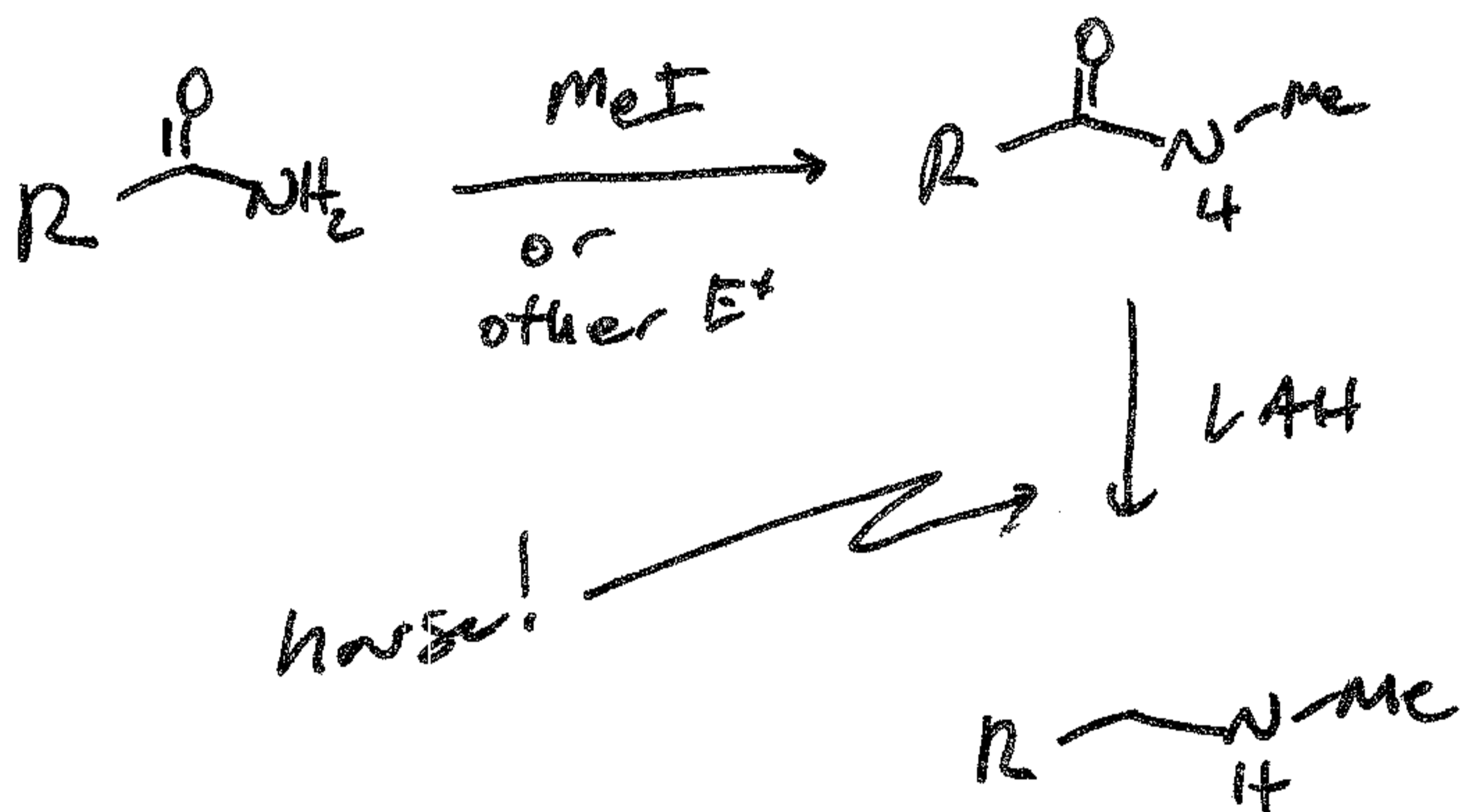


BH₃ (also electrophilic)

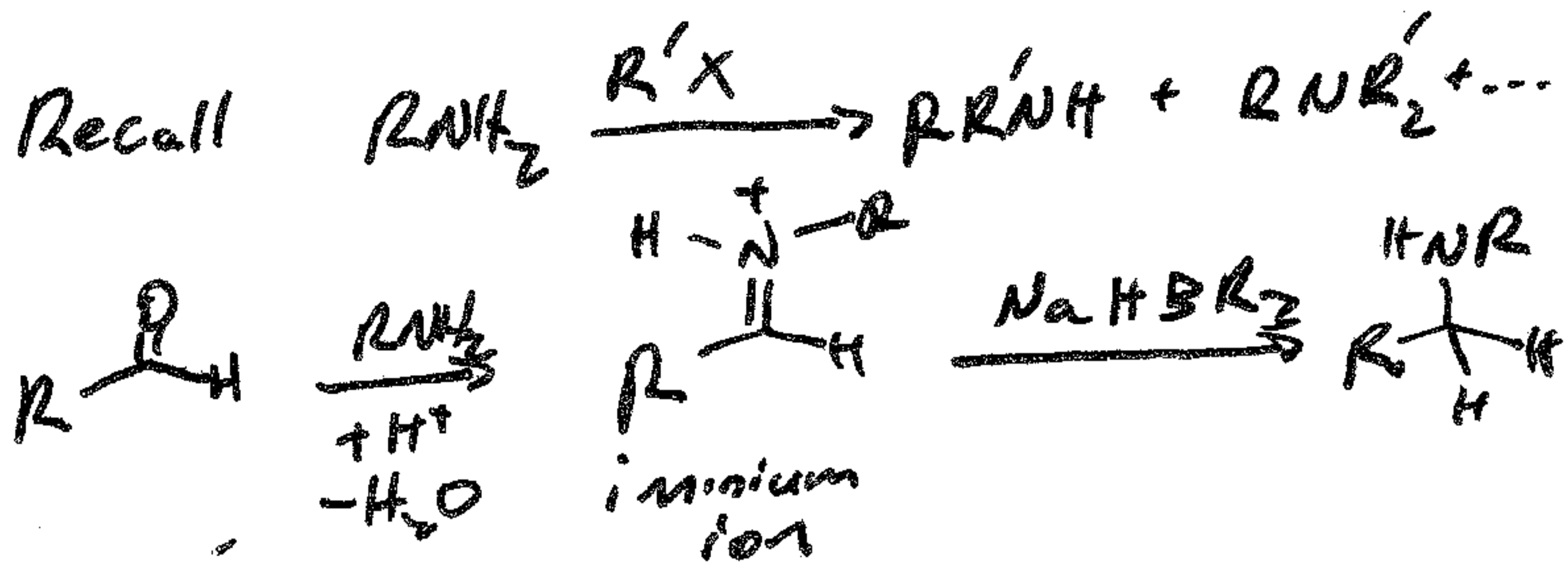


Note: hydroboration completes when alkenes present!

Reductive amination



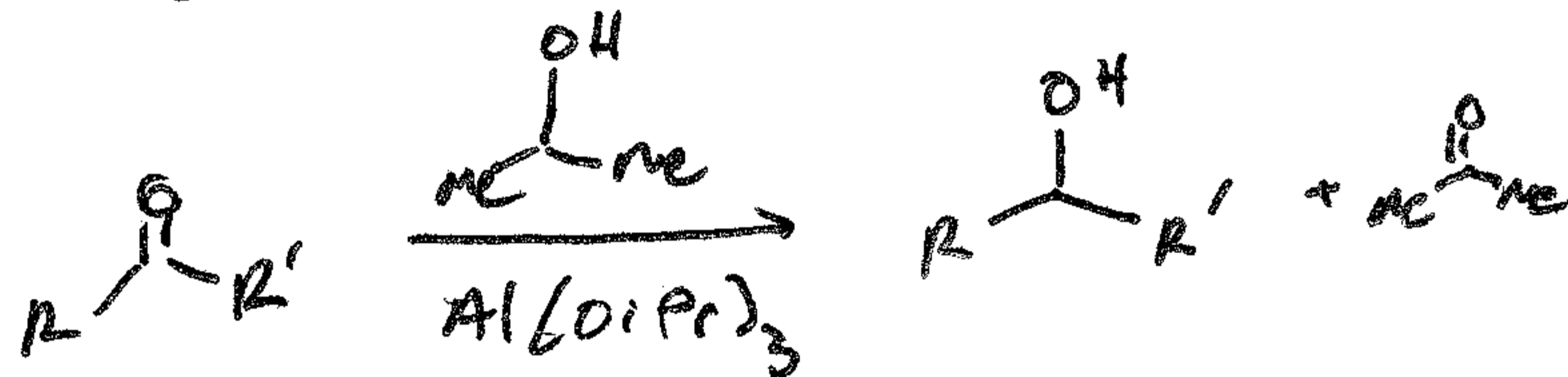
Reductive amination (to make amines)



Red: NaBH₄ cheap
Na(BN)BH₃ or NaBH(OAc)₃ more selective

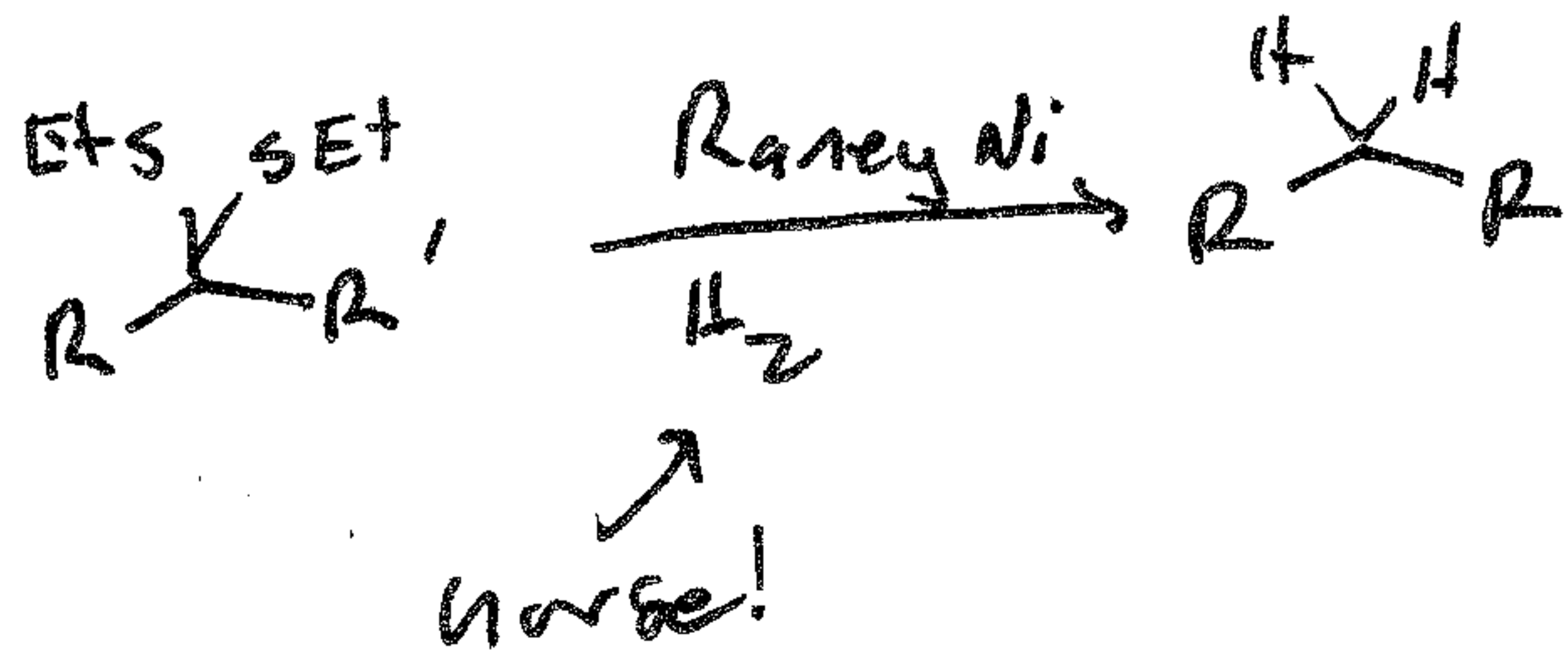
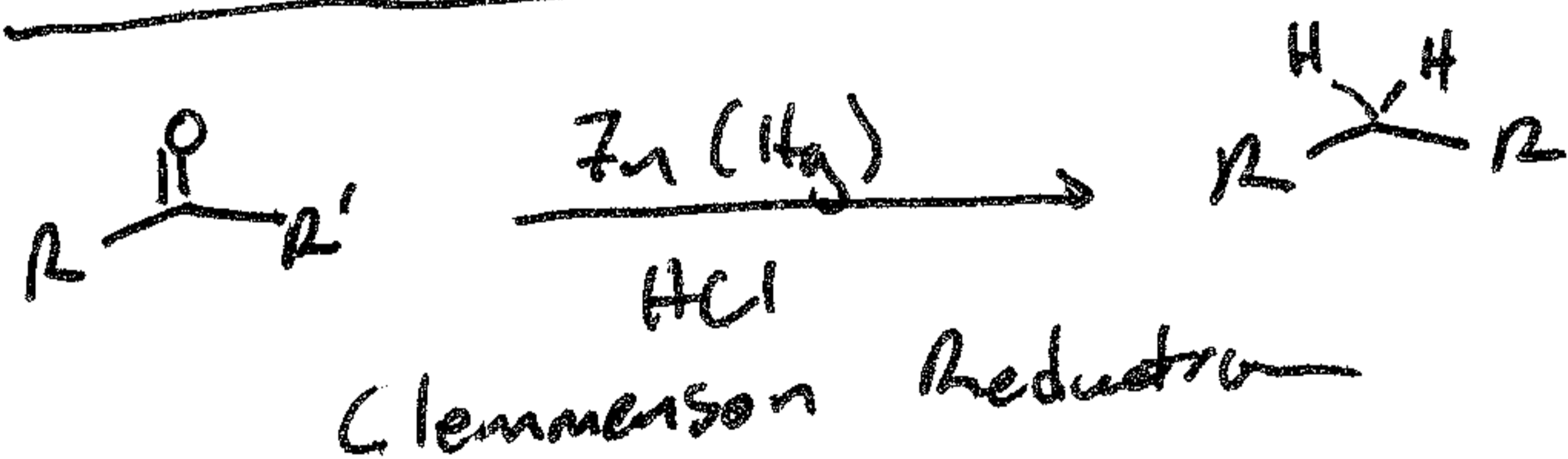
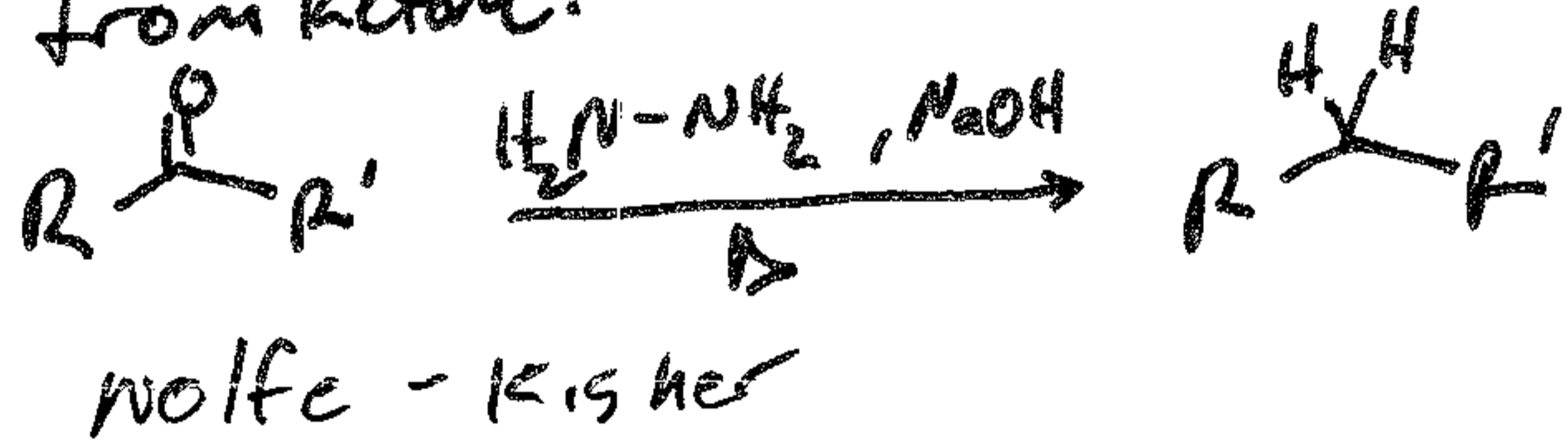
Aldehyde or ketone
amine: 1° or 2°

Recall:

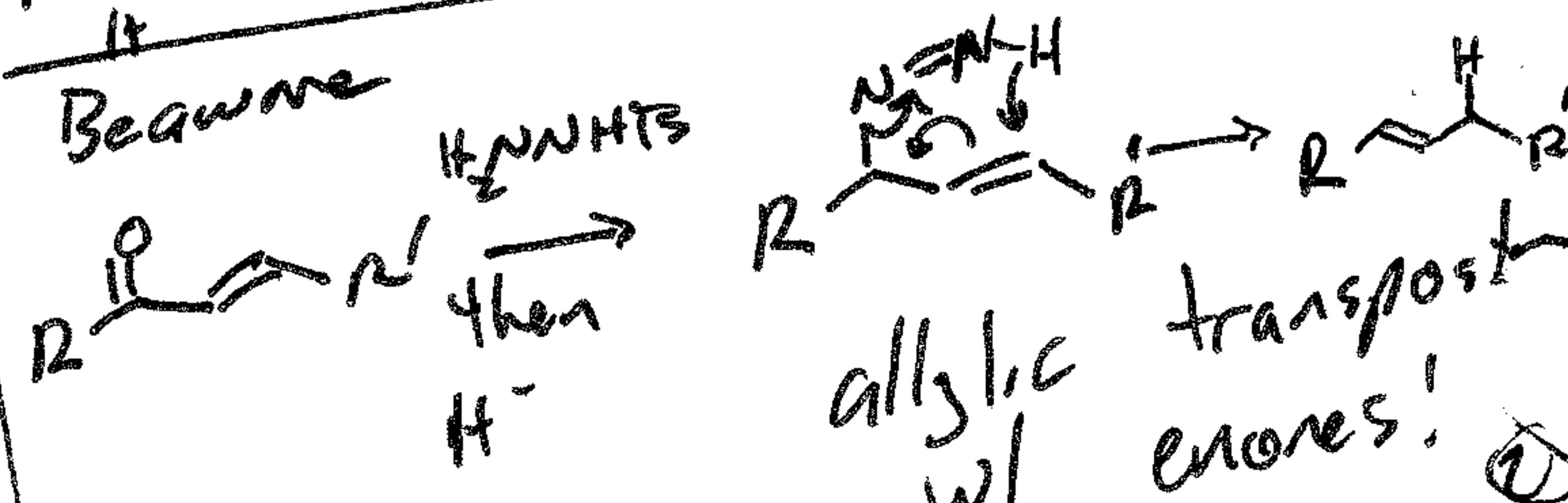
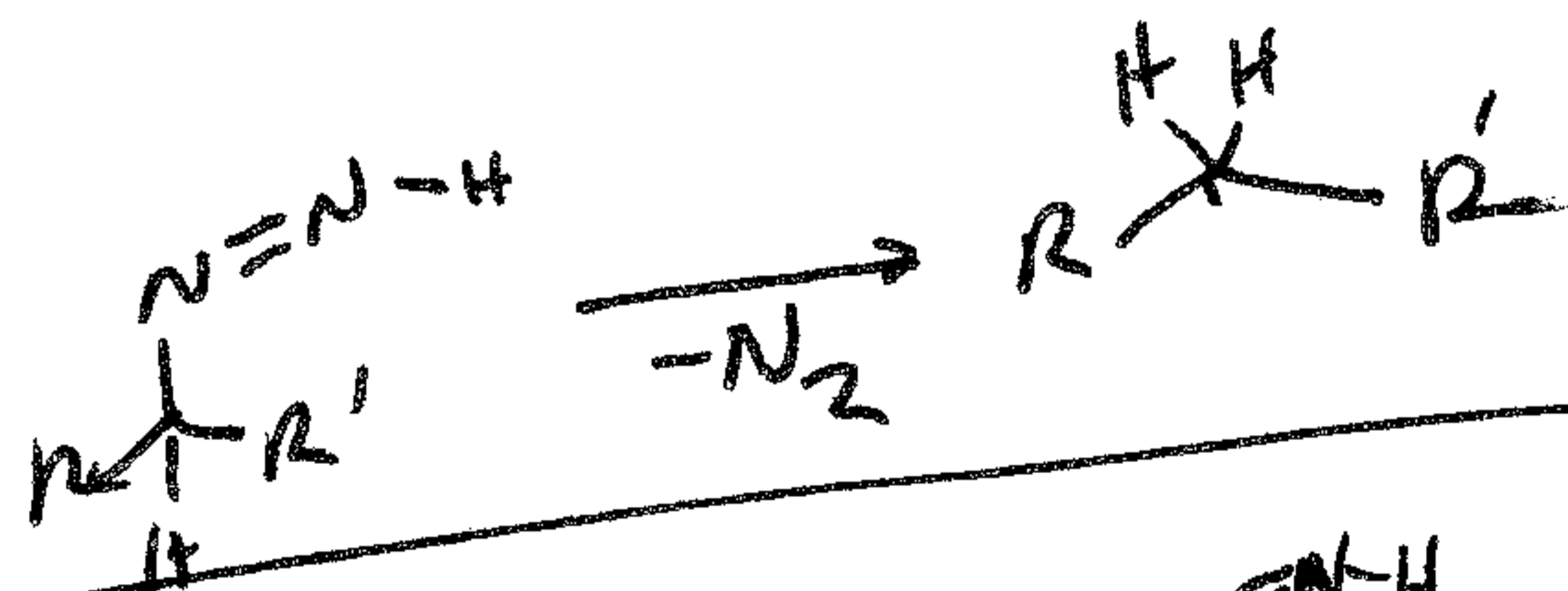
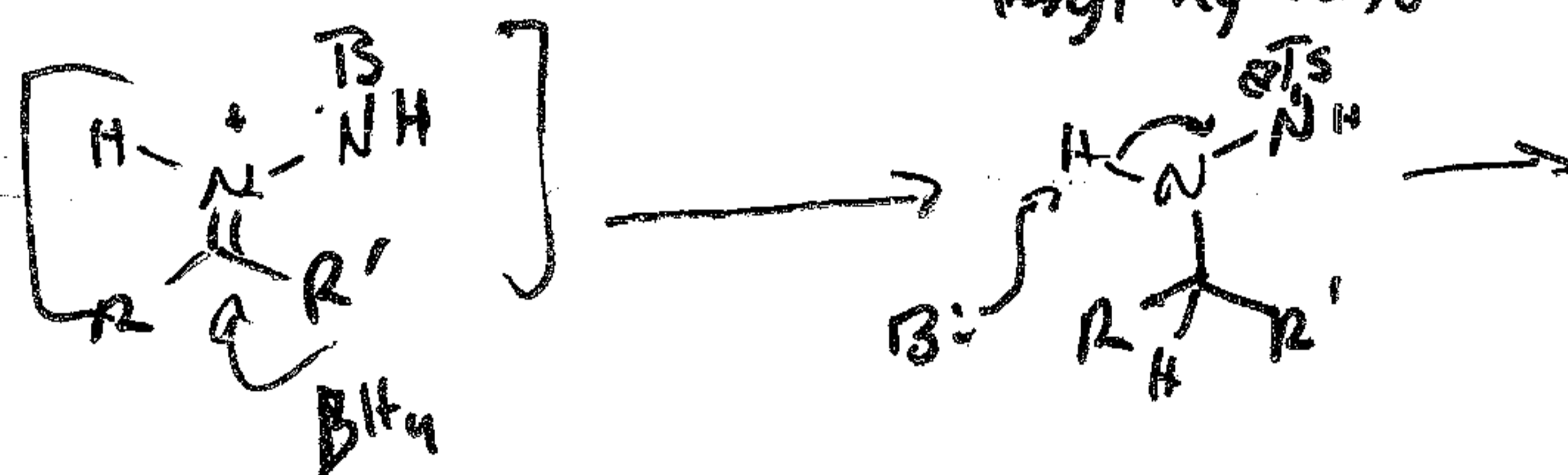
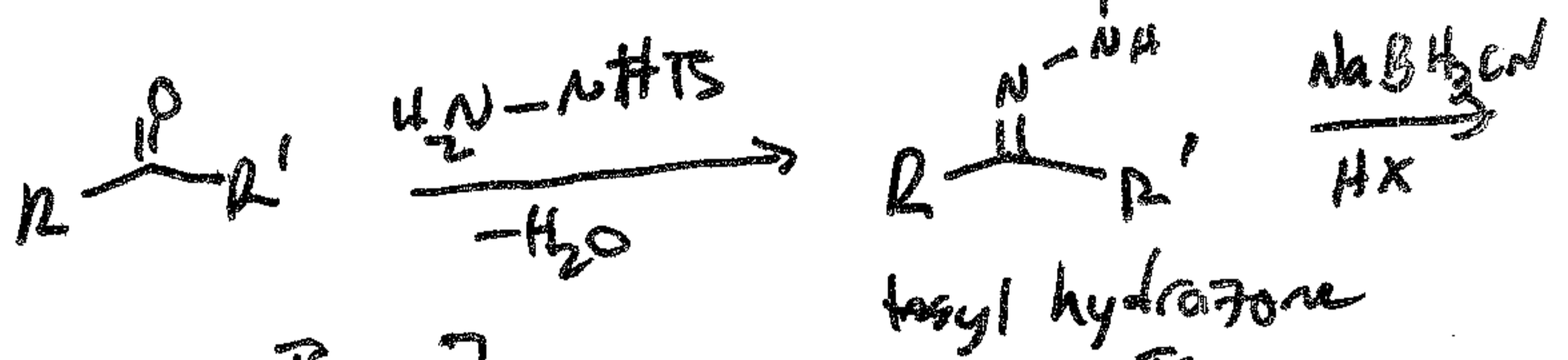


Meerwein-Ponndorf-Verley (MPV) Reduction

Reductions to make alkanes from ketone:

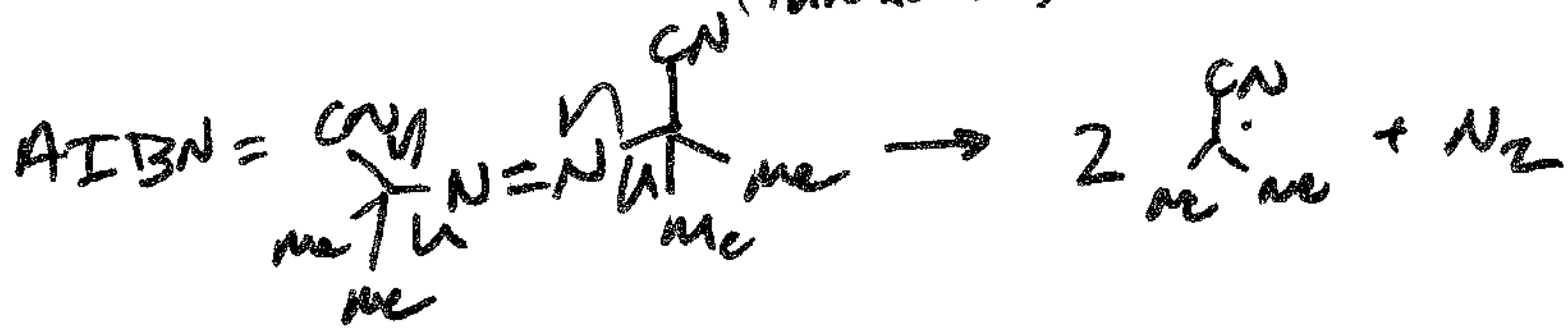
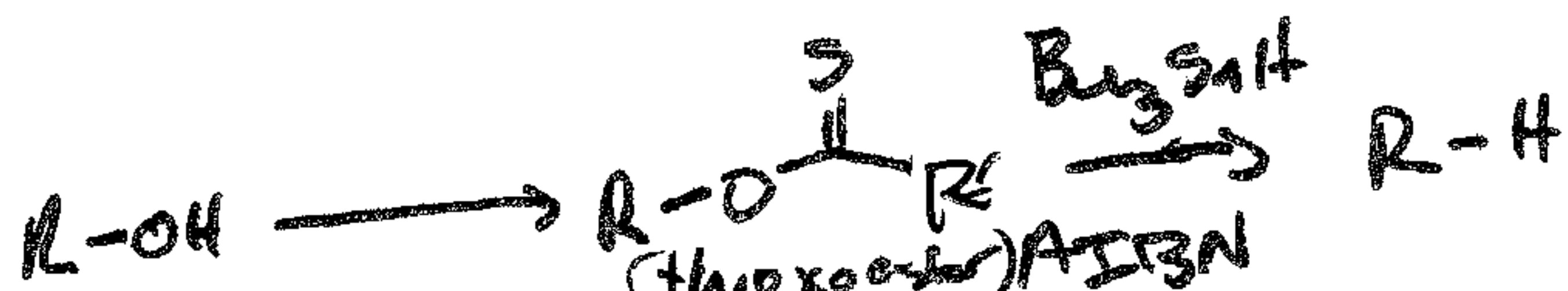


More mild ketone → alkane



Barton Reductions (Radical)

Barton McCombie Deoxygenation

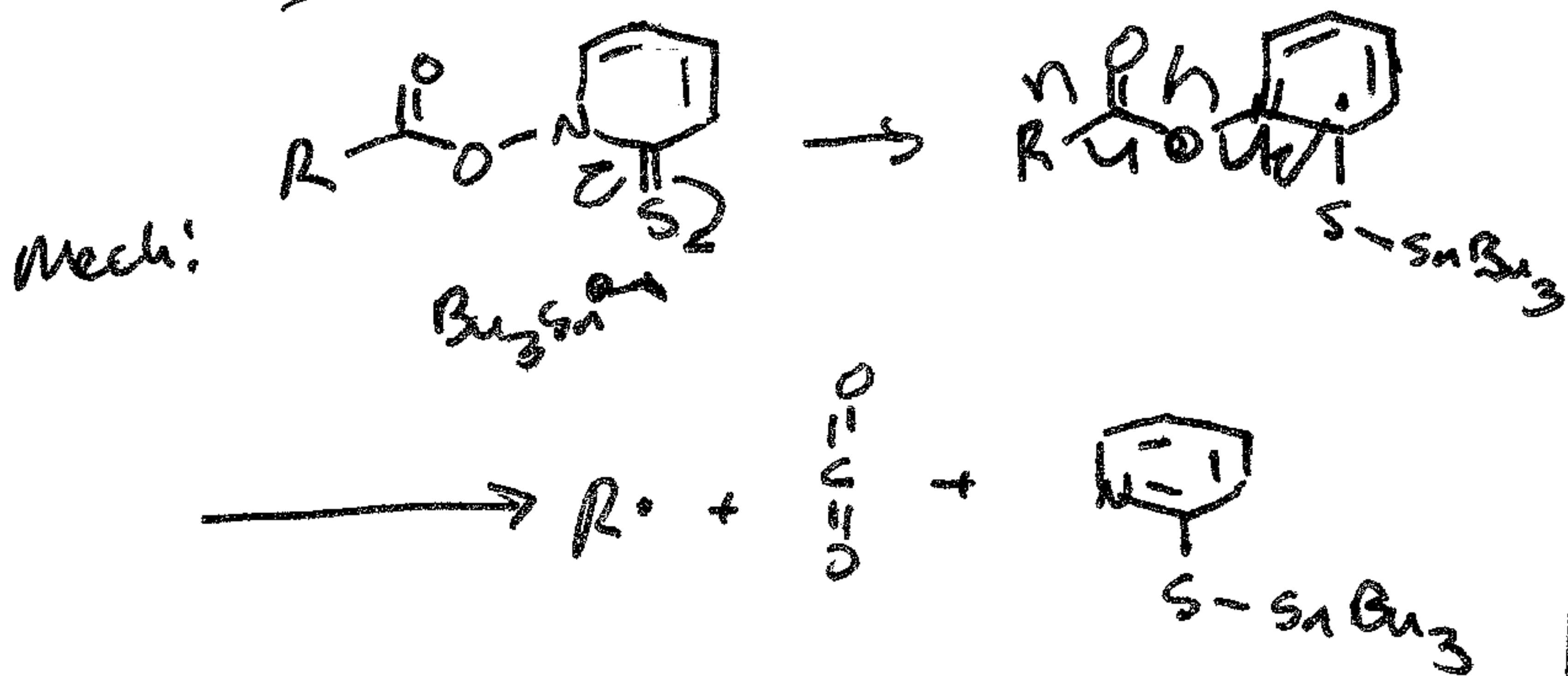
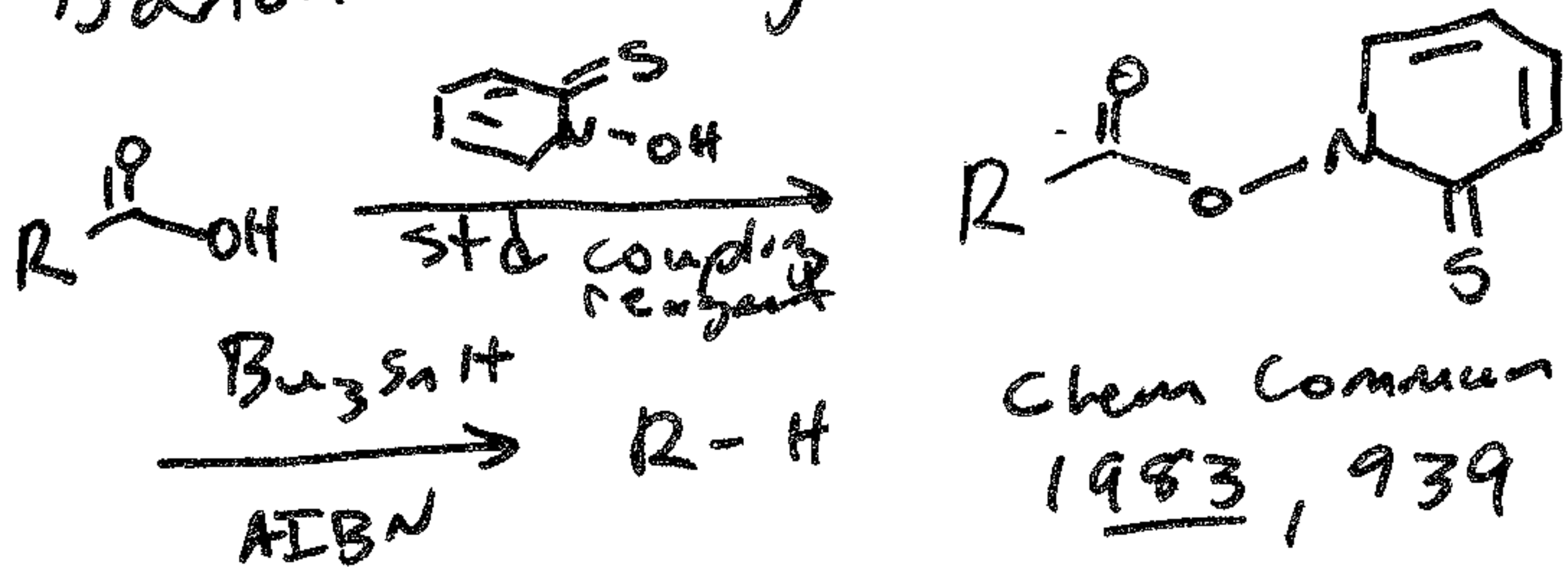


B/m = Perkin Trans I, 1975, 1574

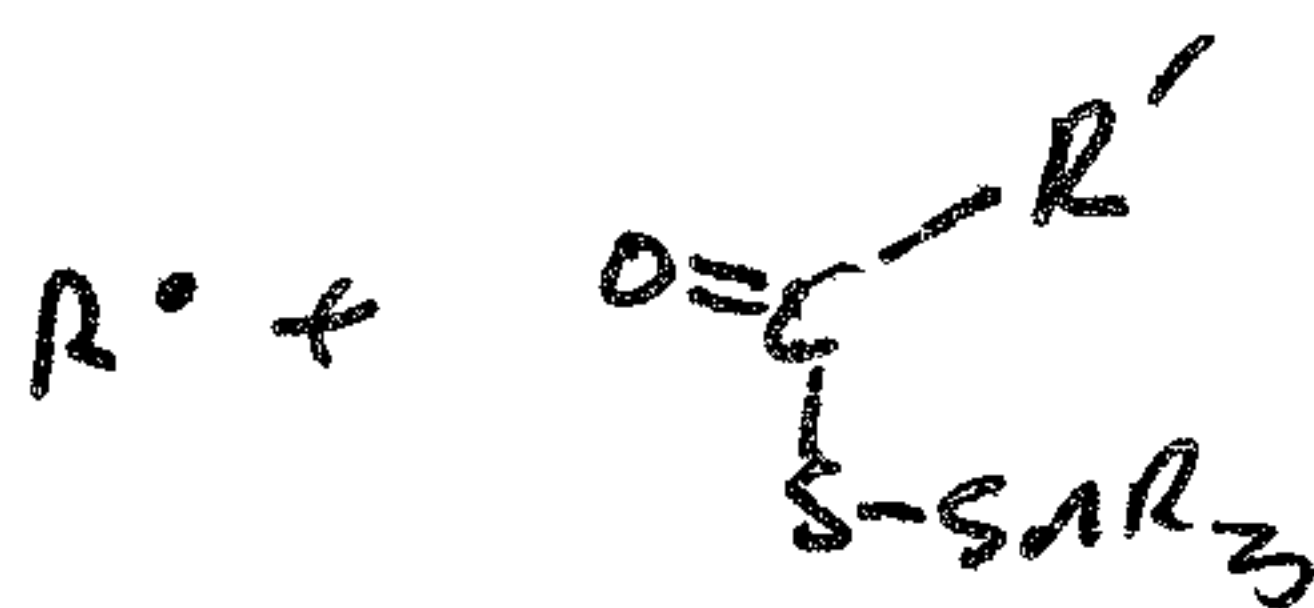
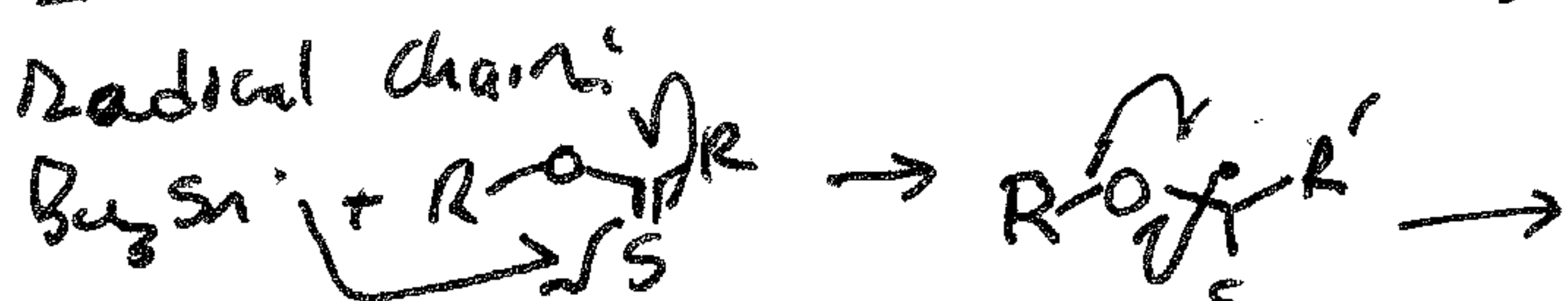
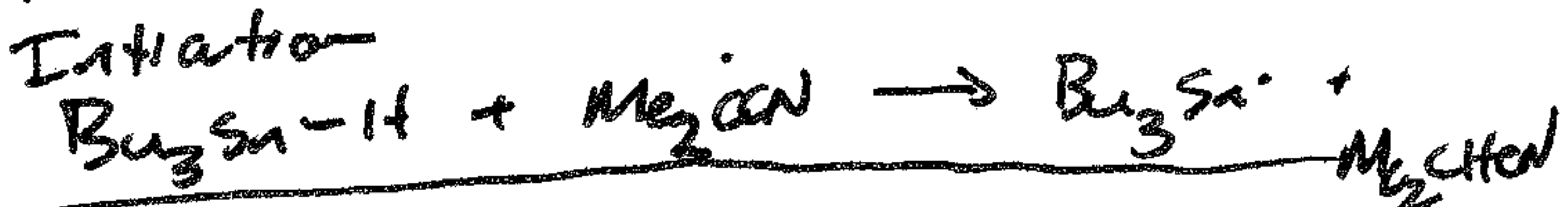
R' = Me, OPh, Imid, etc

cond: NaH, CS₂, MeI or Cl-P(=O)(OR)₂ etc

Barton Decarboxylation



Mech



dehalogenation



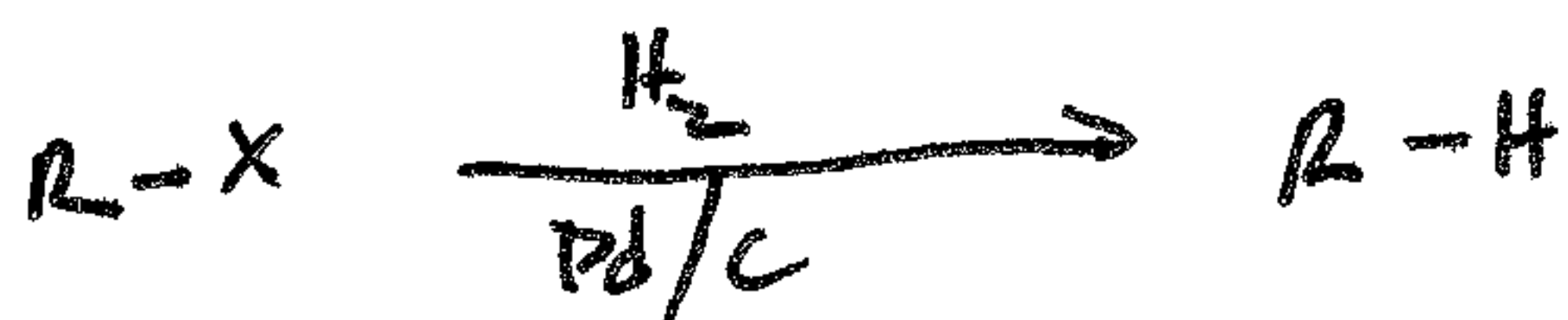
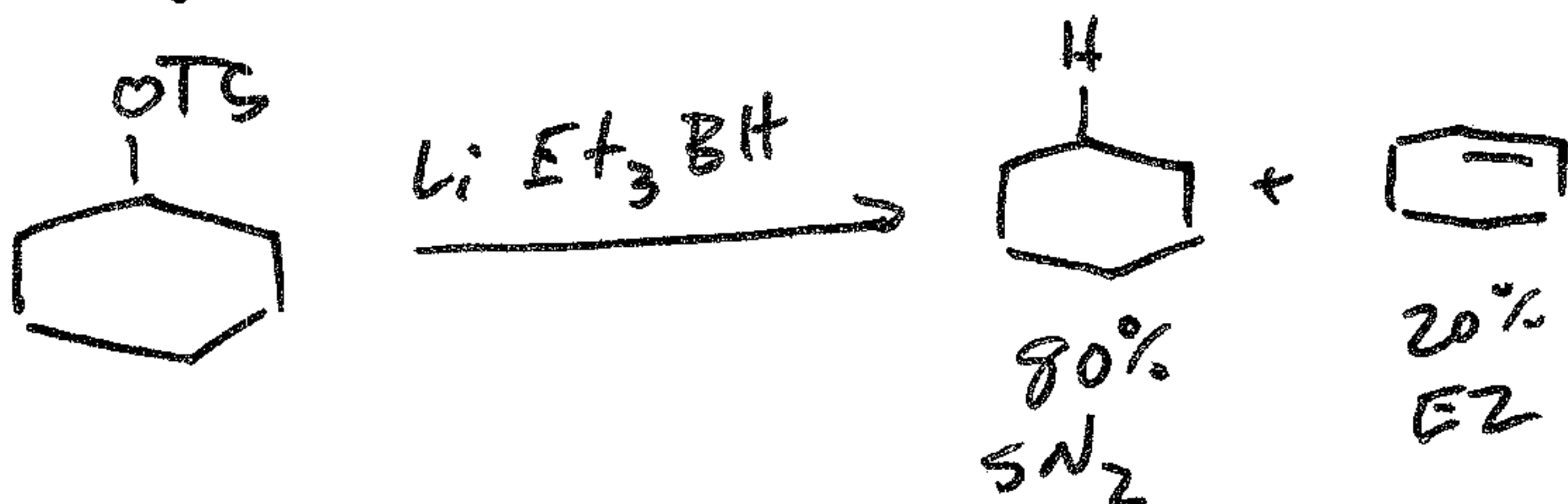
I > Br > Cl

3° > 2° > 1° (radical stability)

Also SmI₂ can be used here

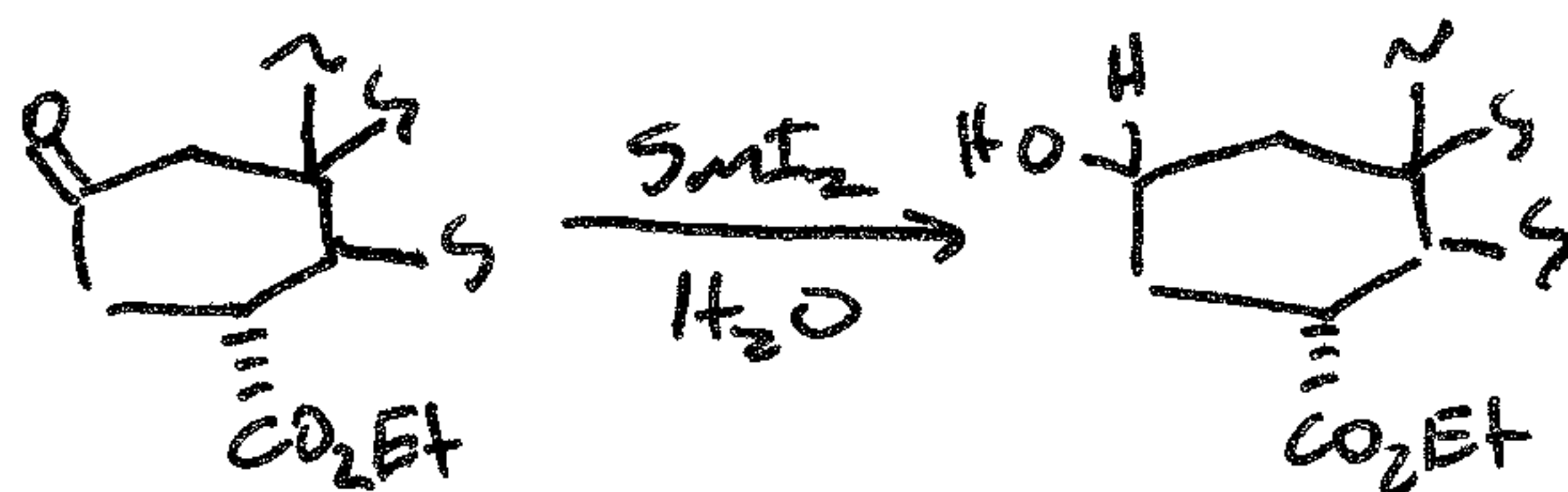
Kayen JACS, 1980, 102, 2693

Alkyl OTs Reduction

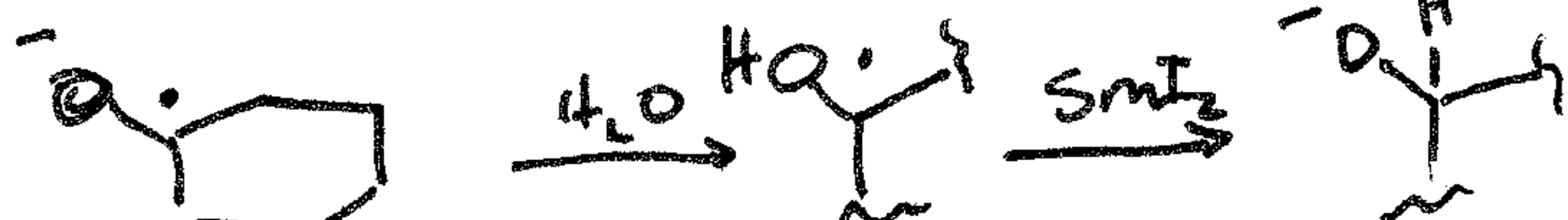


X = I > Br

SmI₂ (single e⁻ donor)



↓ SmI₂



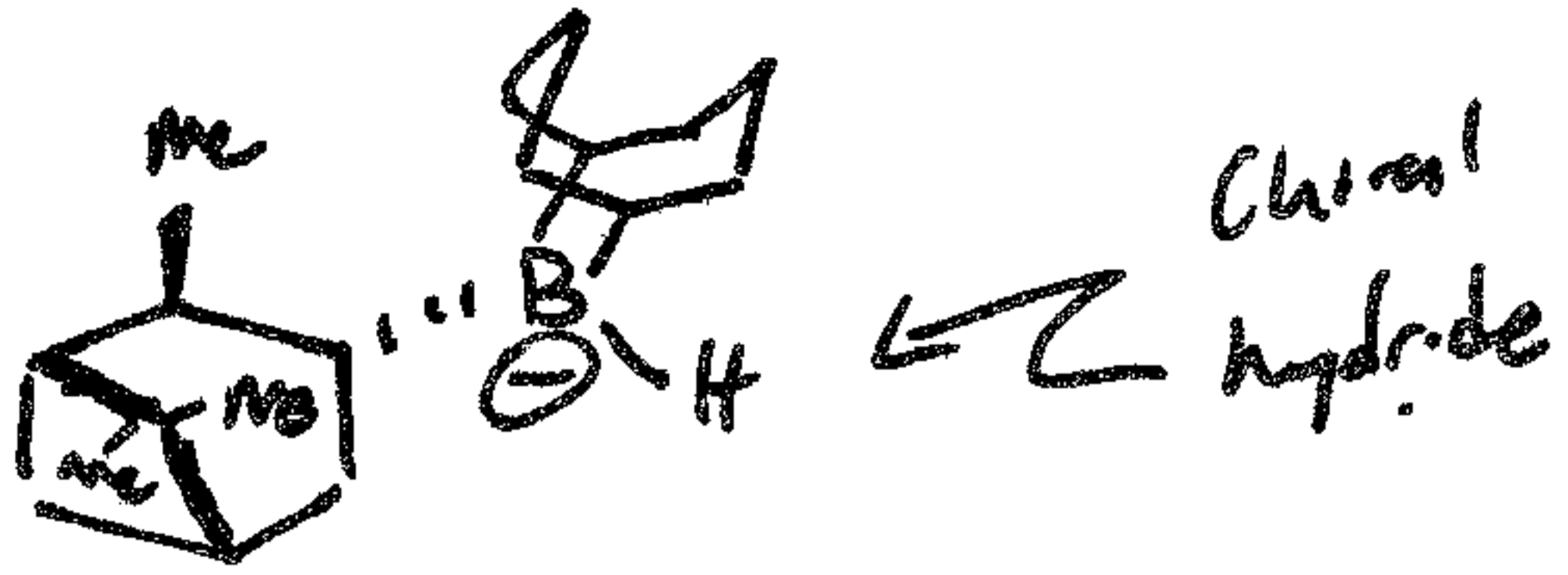
Chem Rev

1992, 92, 29

(malondar)

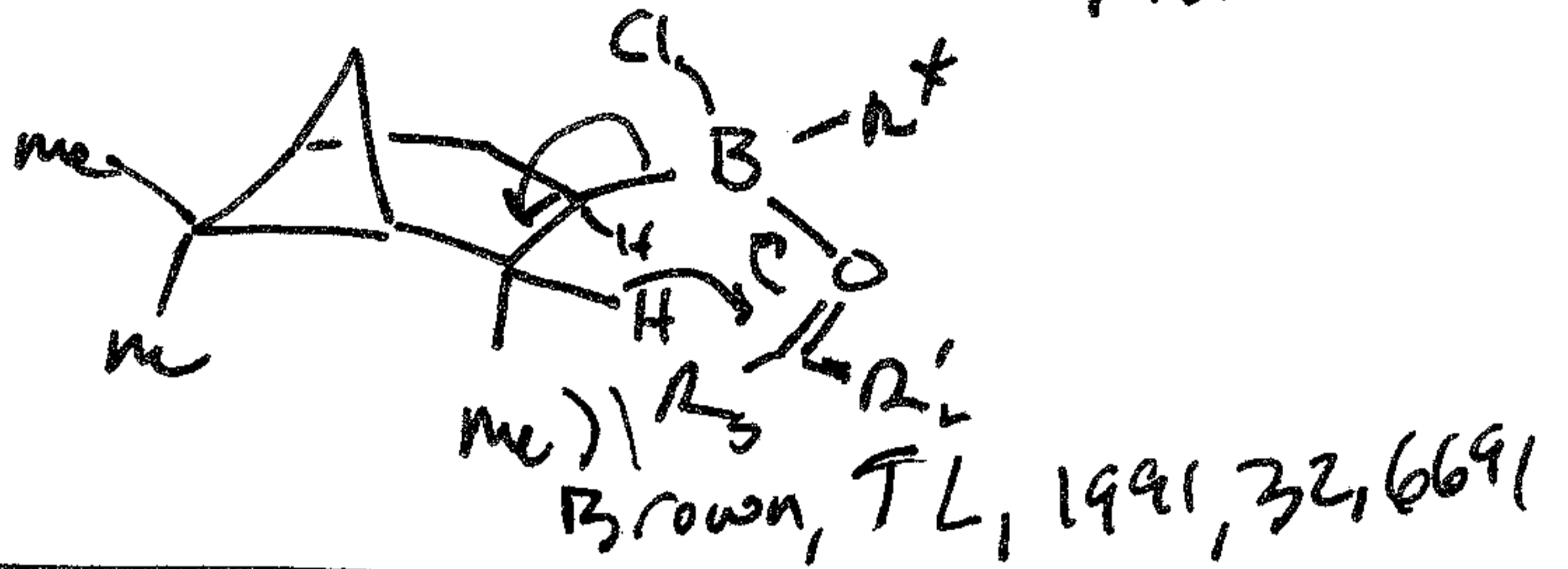
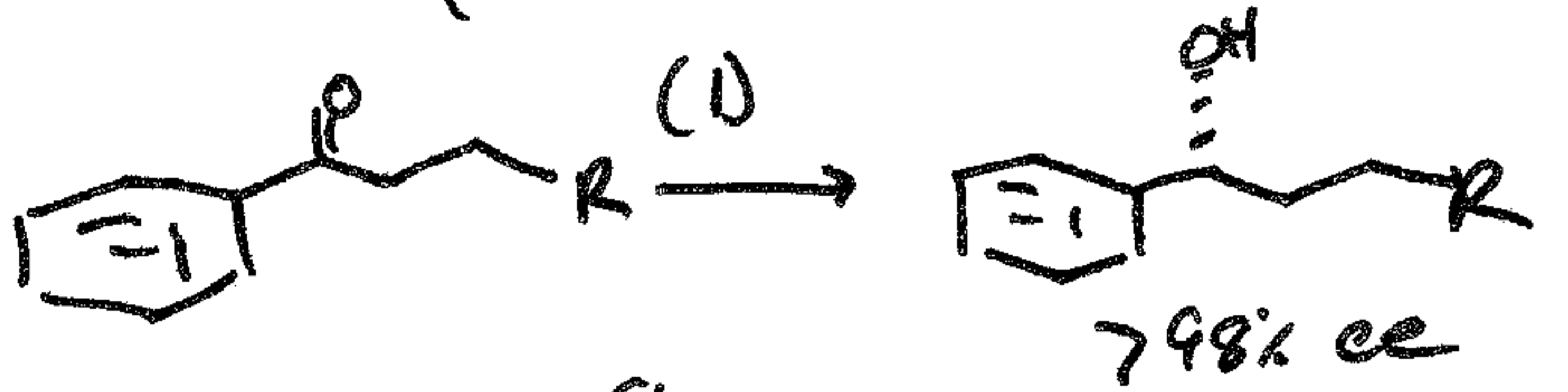
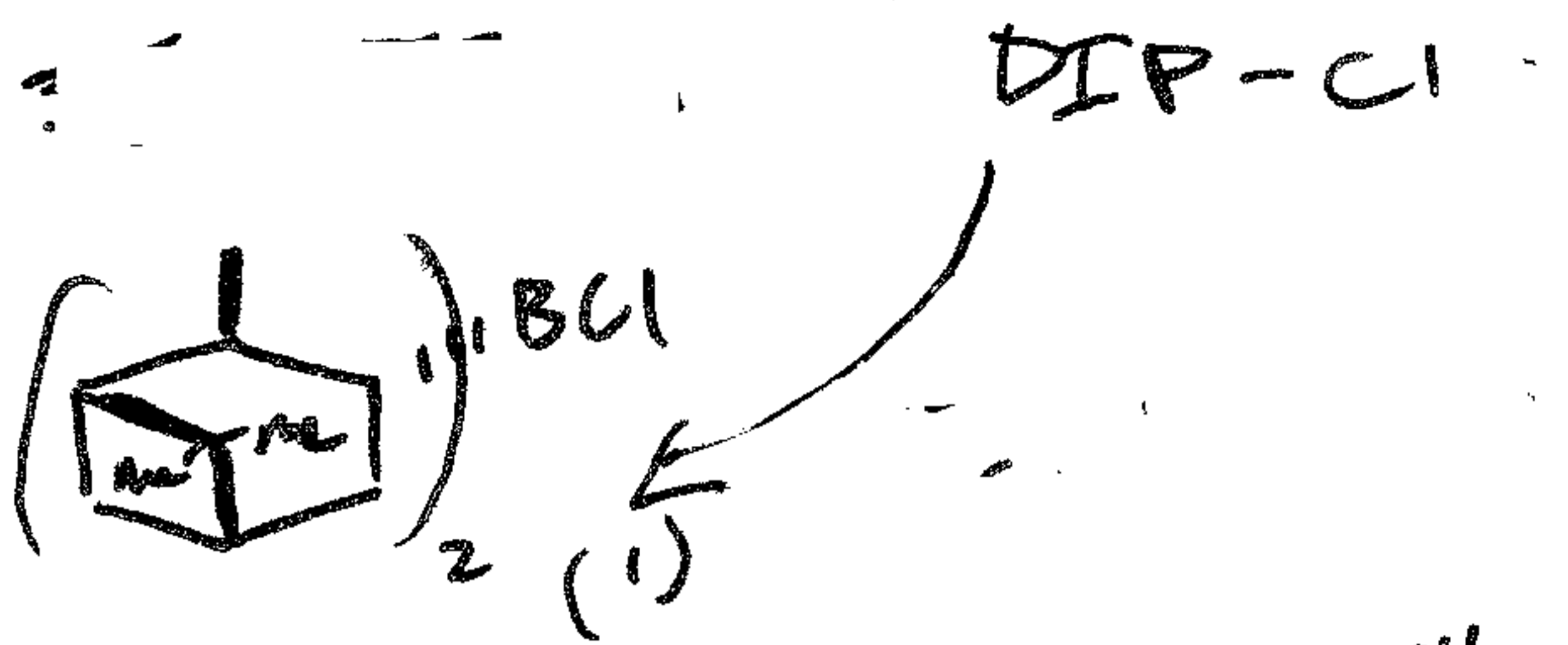
(3)

Misc enantioselective reductions



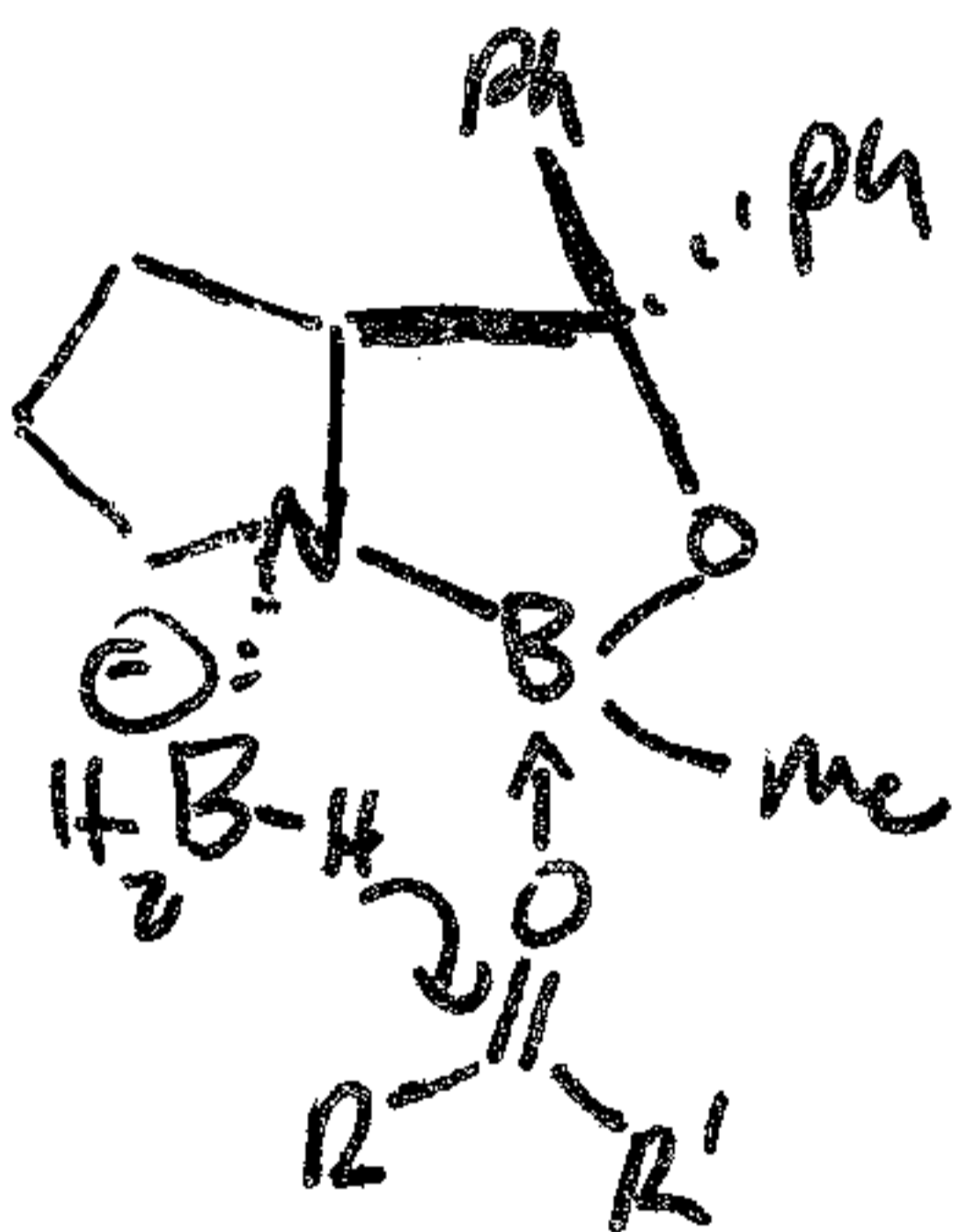
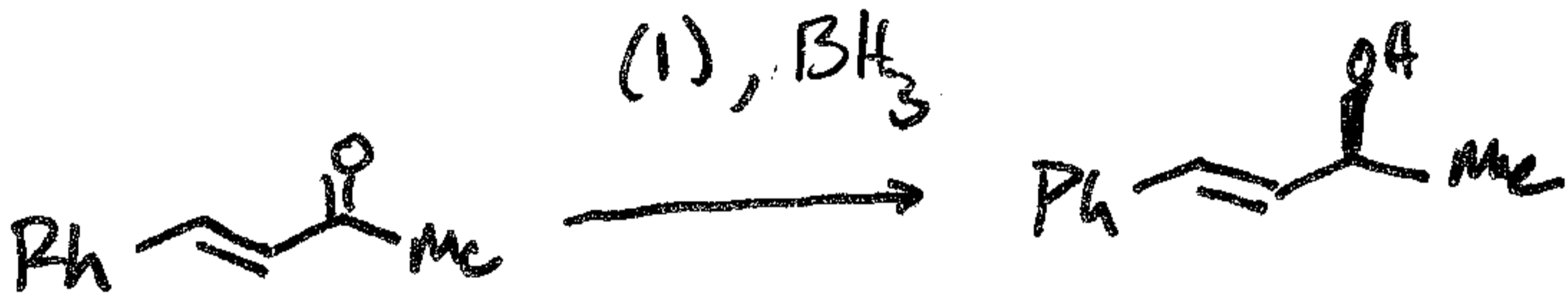
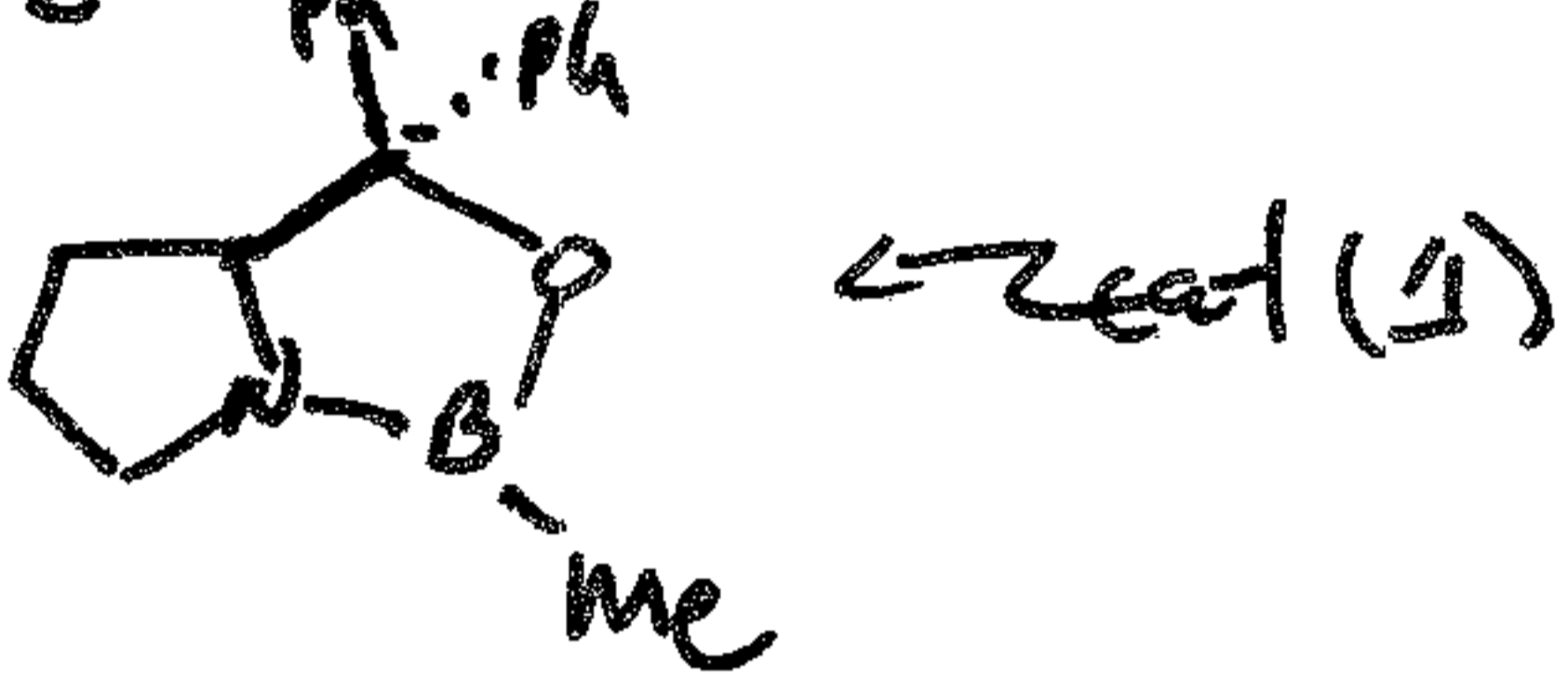
Alpine-borane (Aldrich)

Clem Rev. 1989, 89, 1553

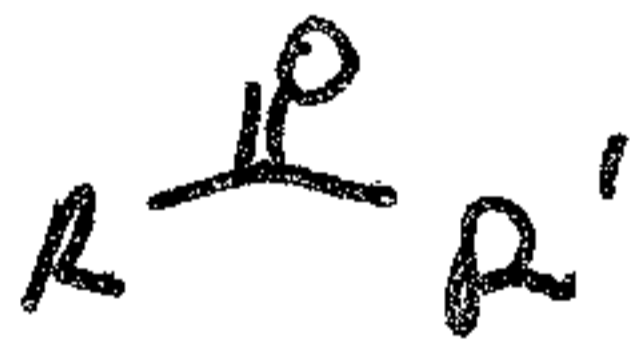


Covey-Bakhi-Shibata (CB7) catalyst

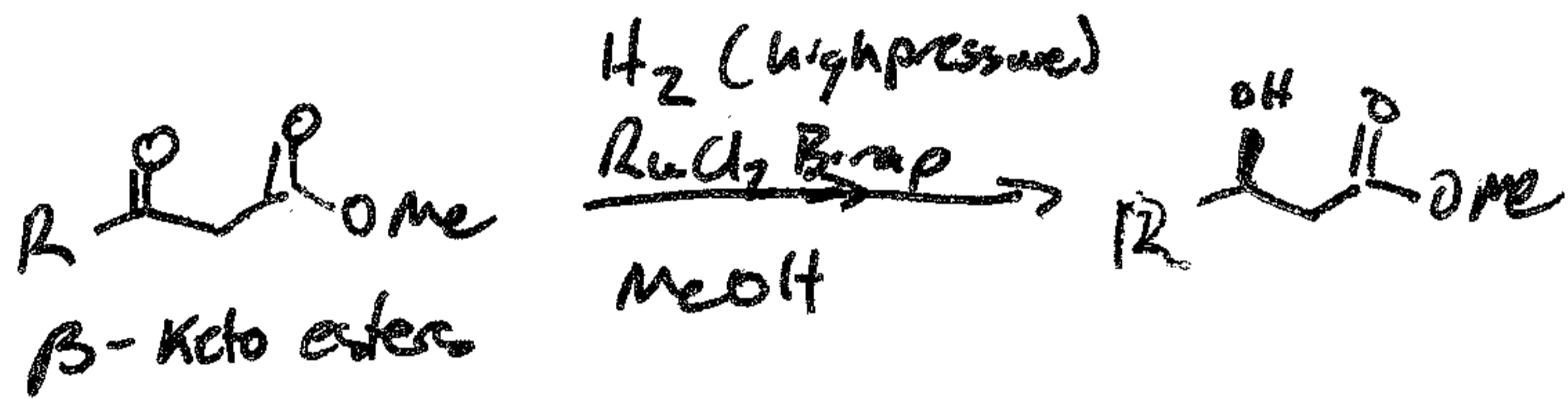
JACS, 1987, 109, 7925



Note primary electronic differentiation between R & R'



Noyori Hydrogenation



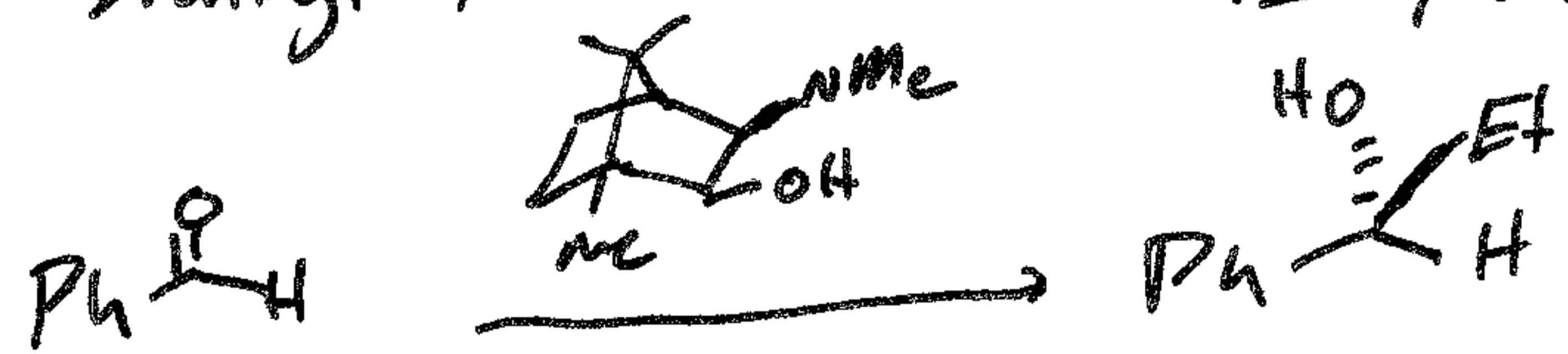
Noyori Acc. Chem Res. 1990, 23, 345

lower pressure variant:

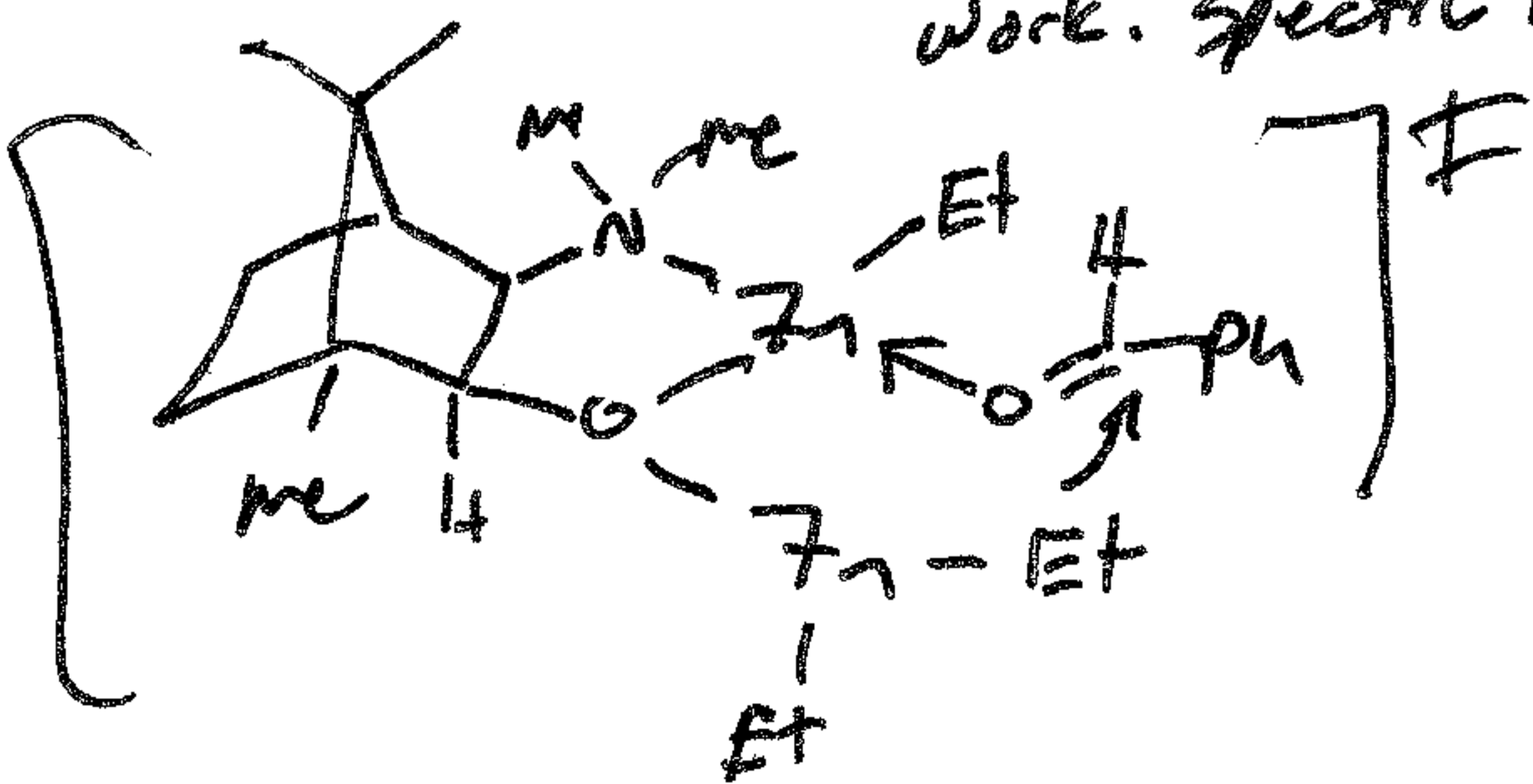
Taber TL, 1991, 32, 4227

Dialkyl Zn additions

EVANS Science 1988, 240, 420



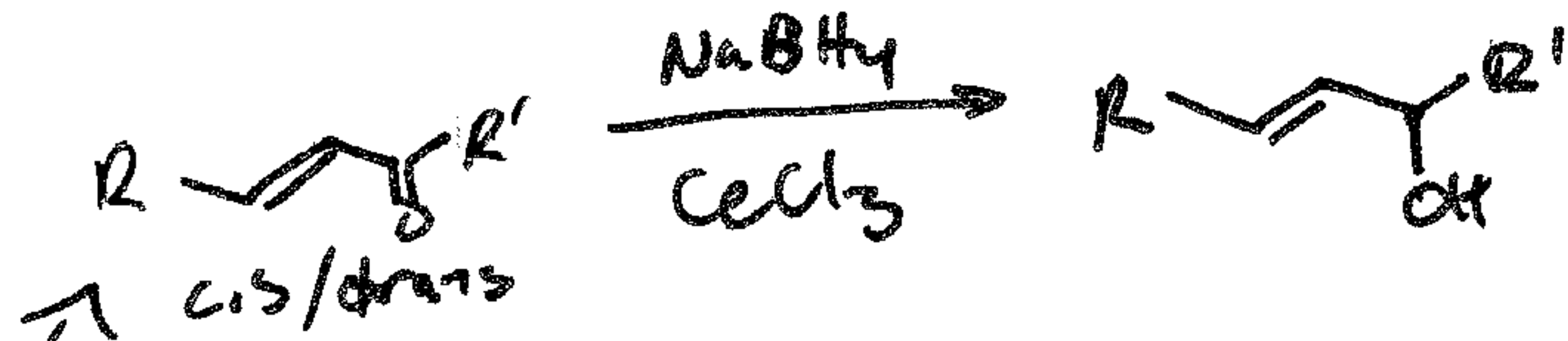
many chiral amino alcohols work. specific to R₂Zn



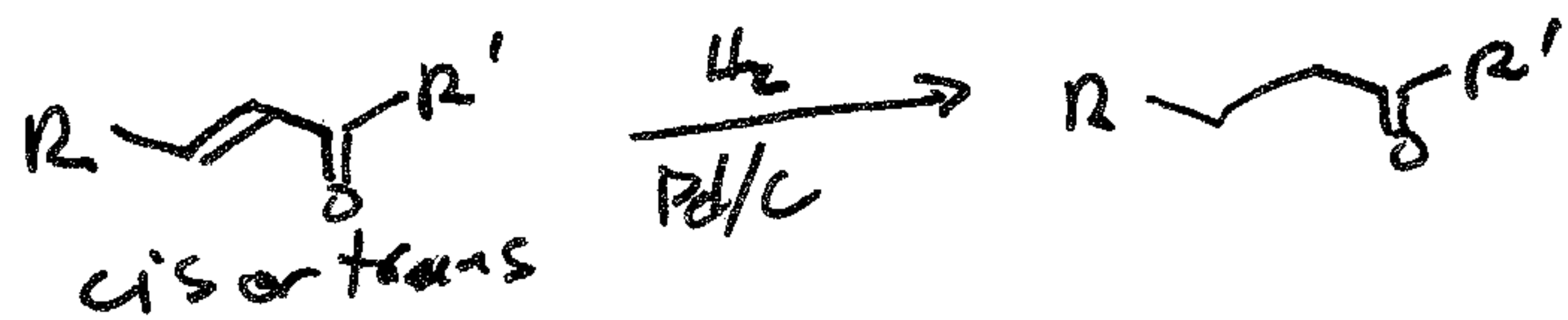
more "C-" additions next week.

Skip

Enones (1,2 vs 1,4)

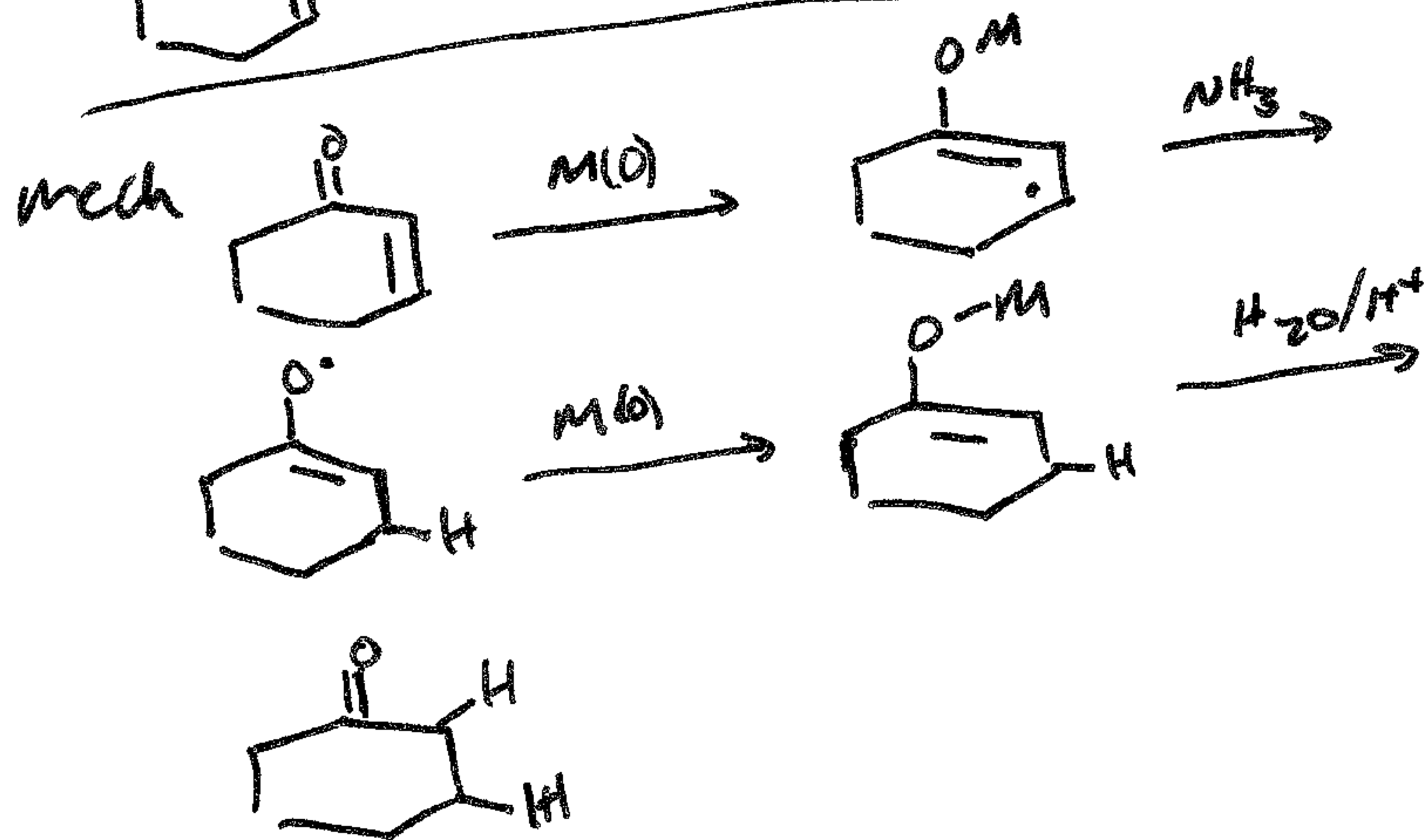
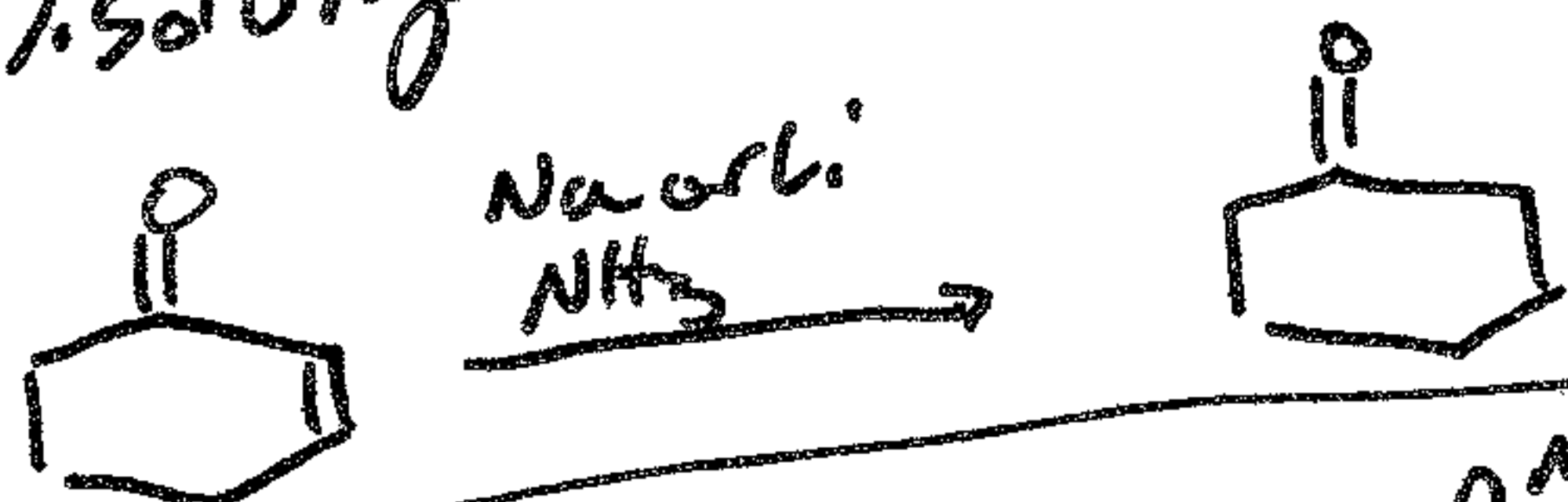


Luuche Reduction
(w/o $CeCl_3$ 1,4 reduction completes)

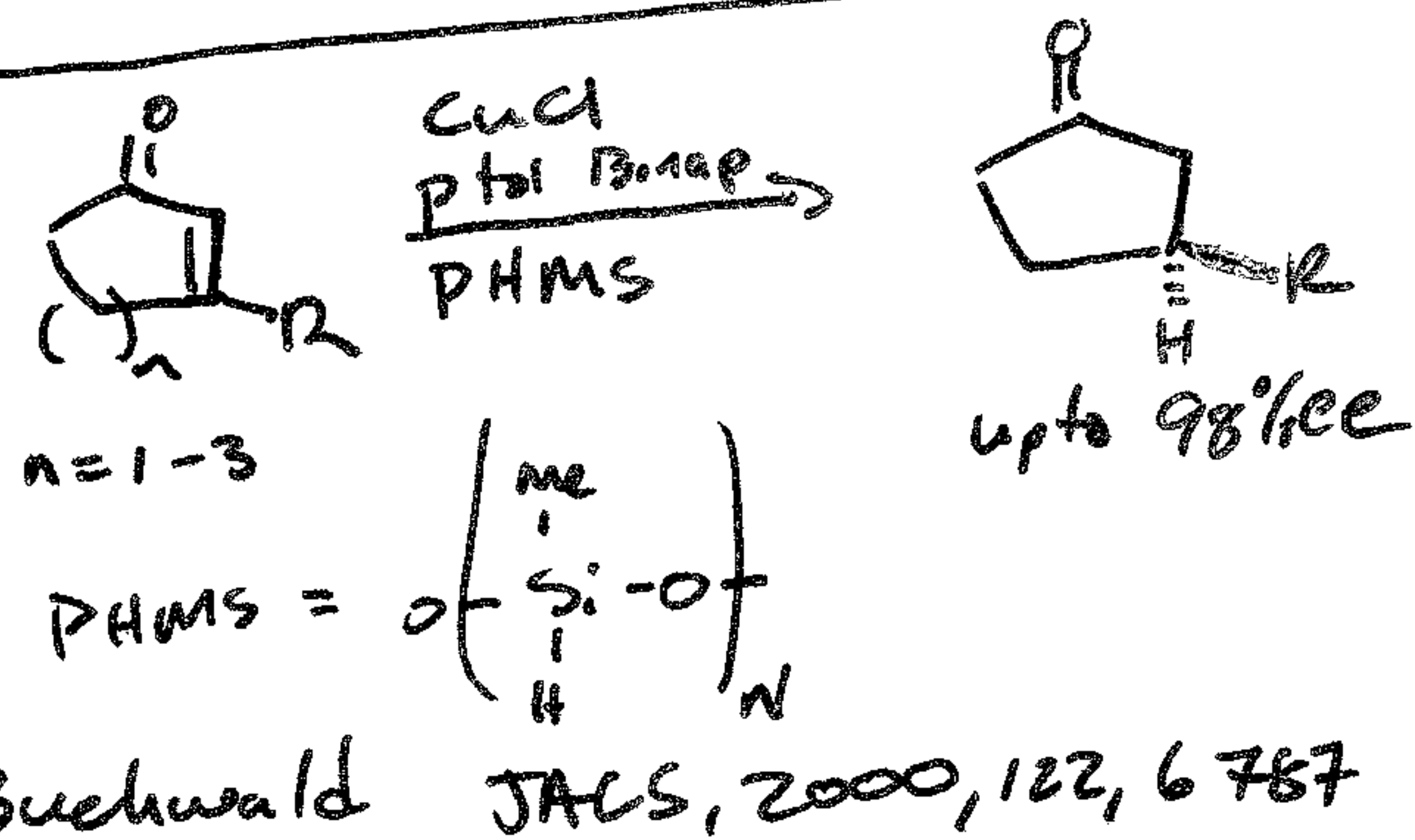
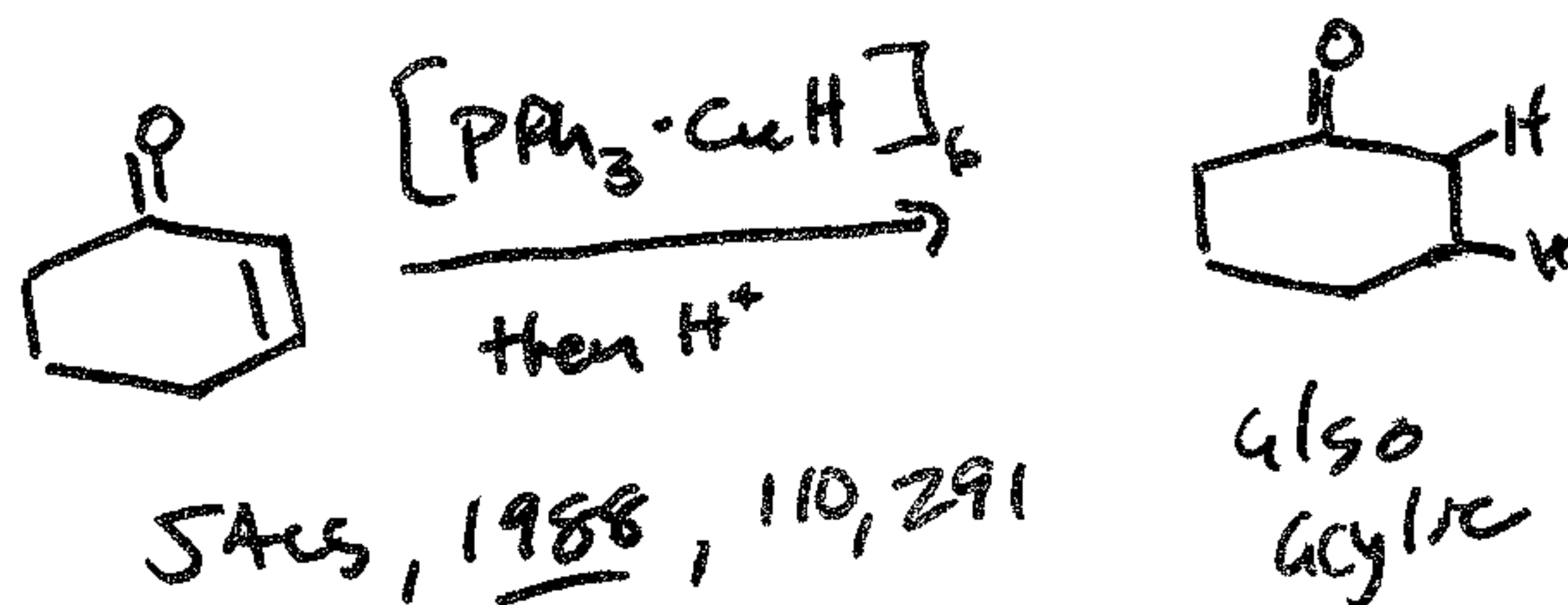


note: hydrogenation of trans and/or electron different alkenes can be slow

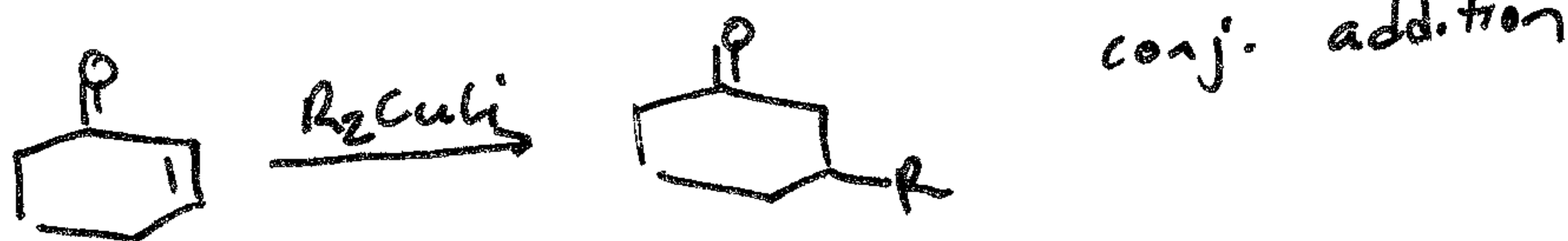
Disolving metal



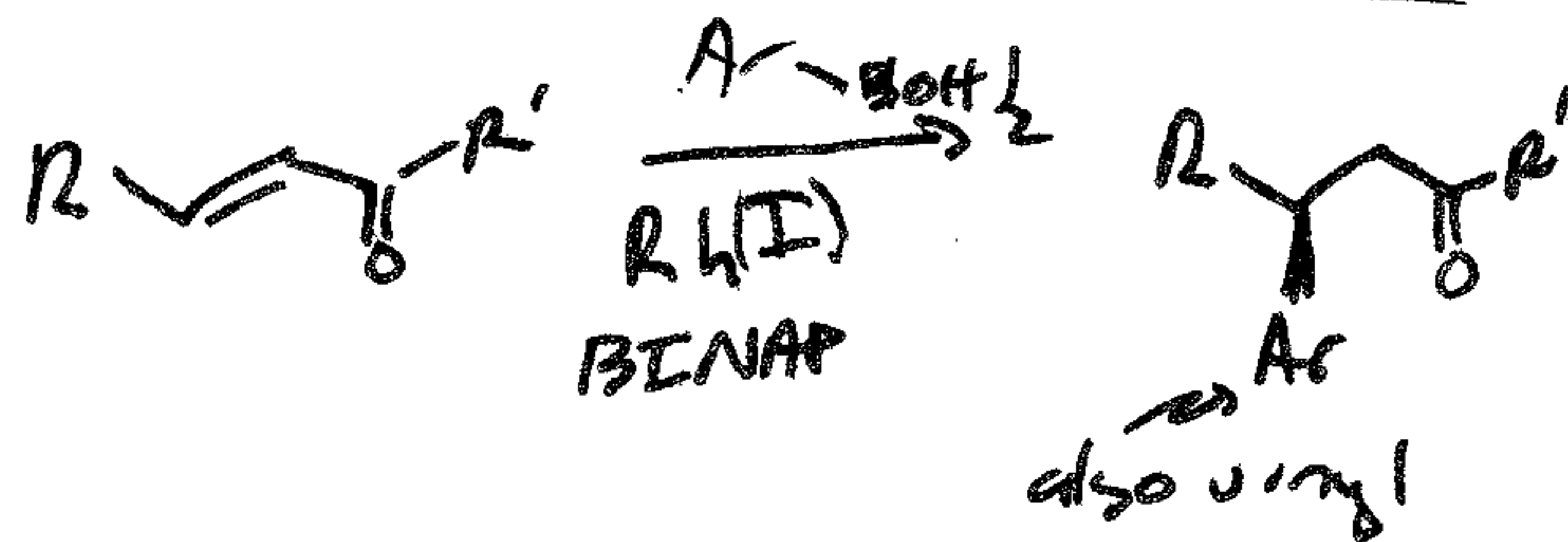
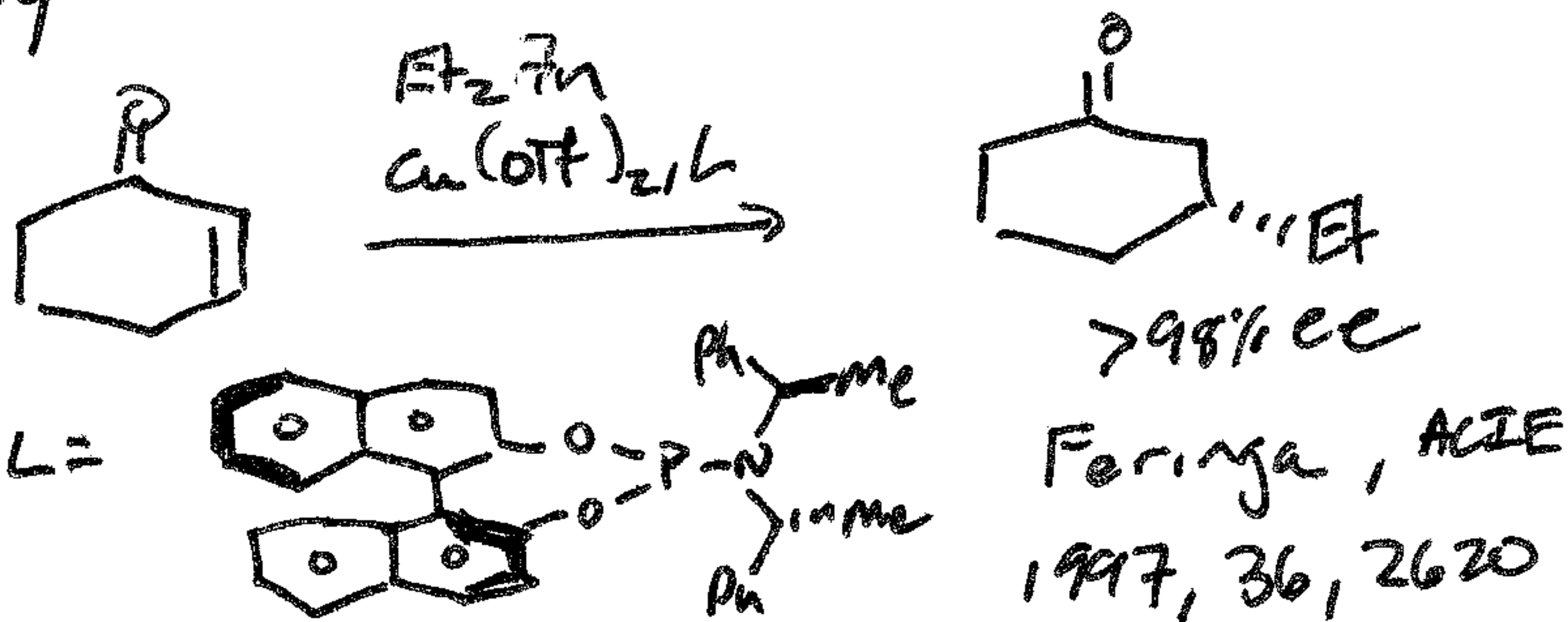
Stryker Reagent



Also for "R" $C\&S$ 8.1/8.7



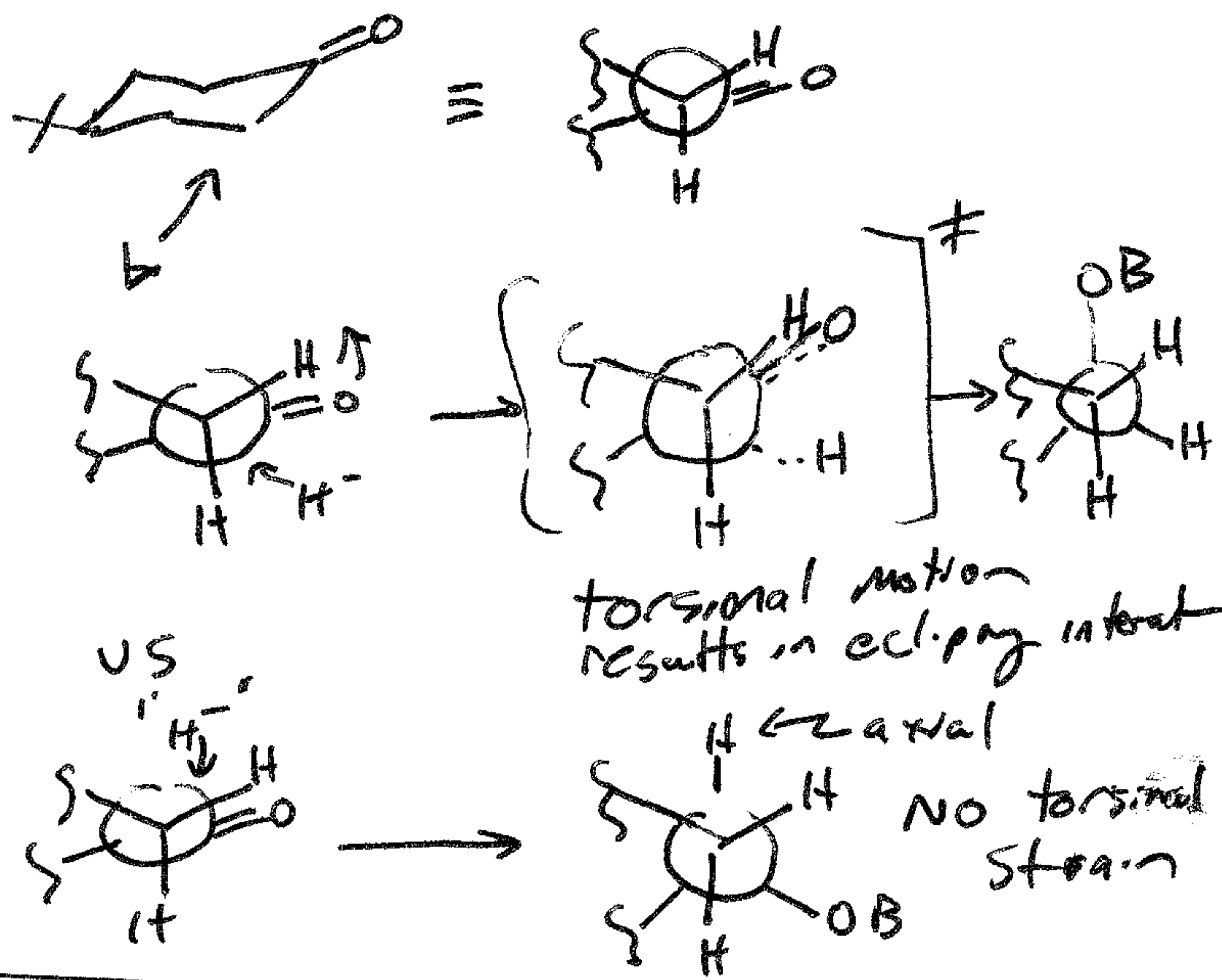
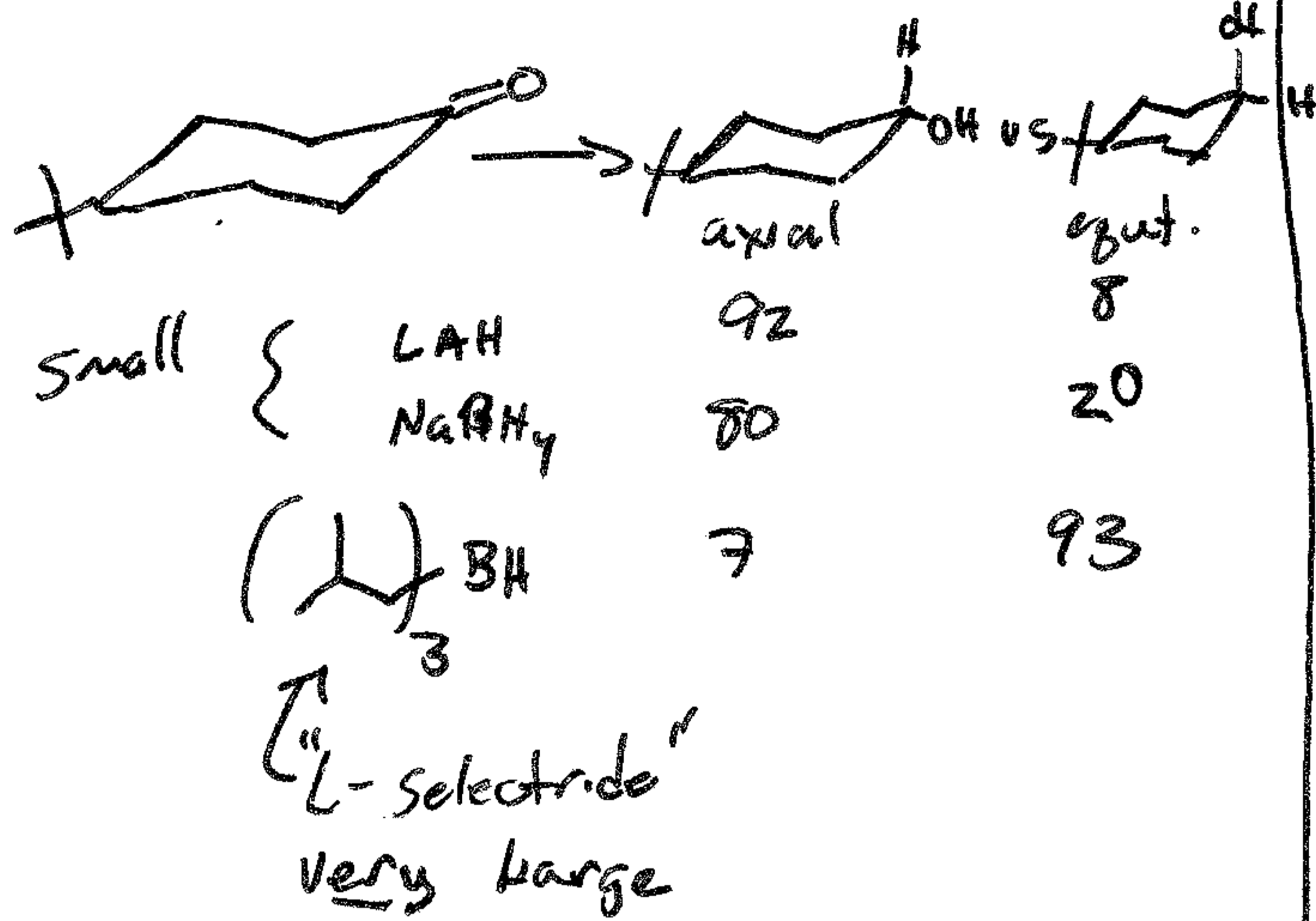
Asy. version also known



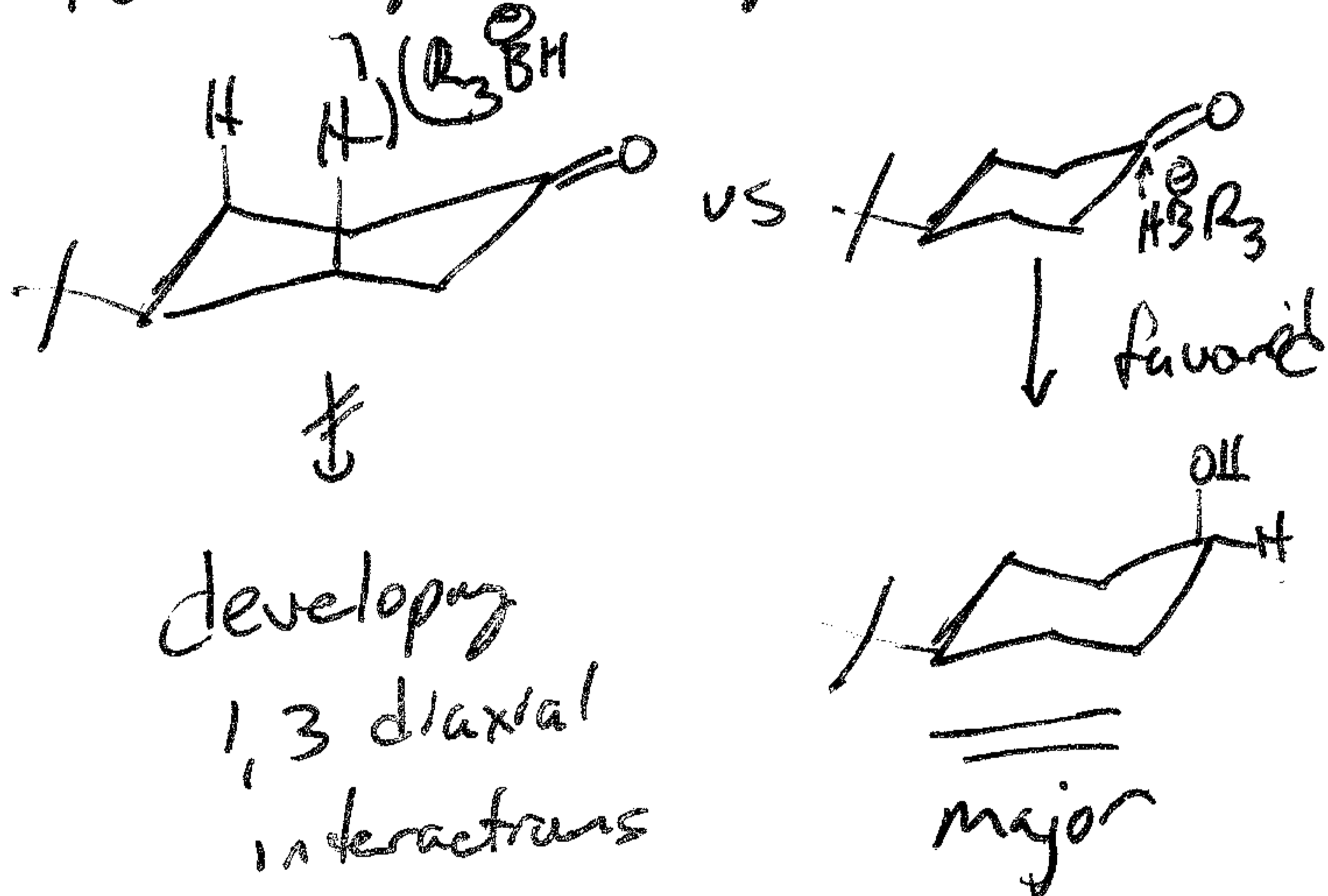
Hayashi Chem Rev 2003, 103, 2829

Diastereoselective Reductions (additions)

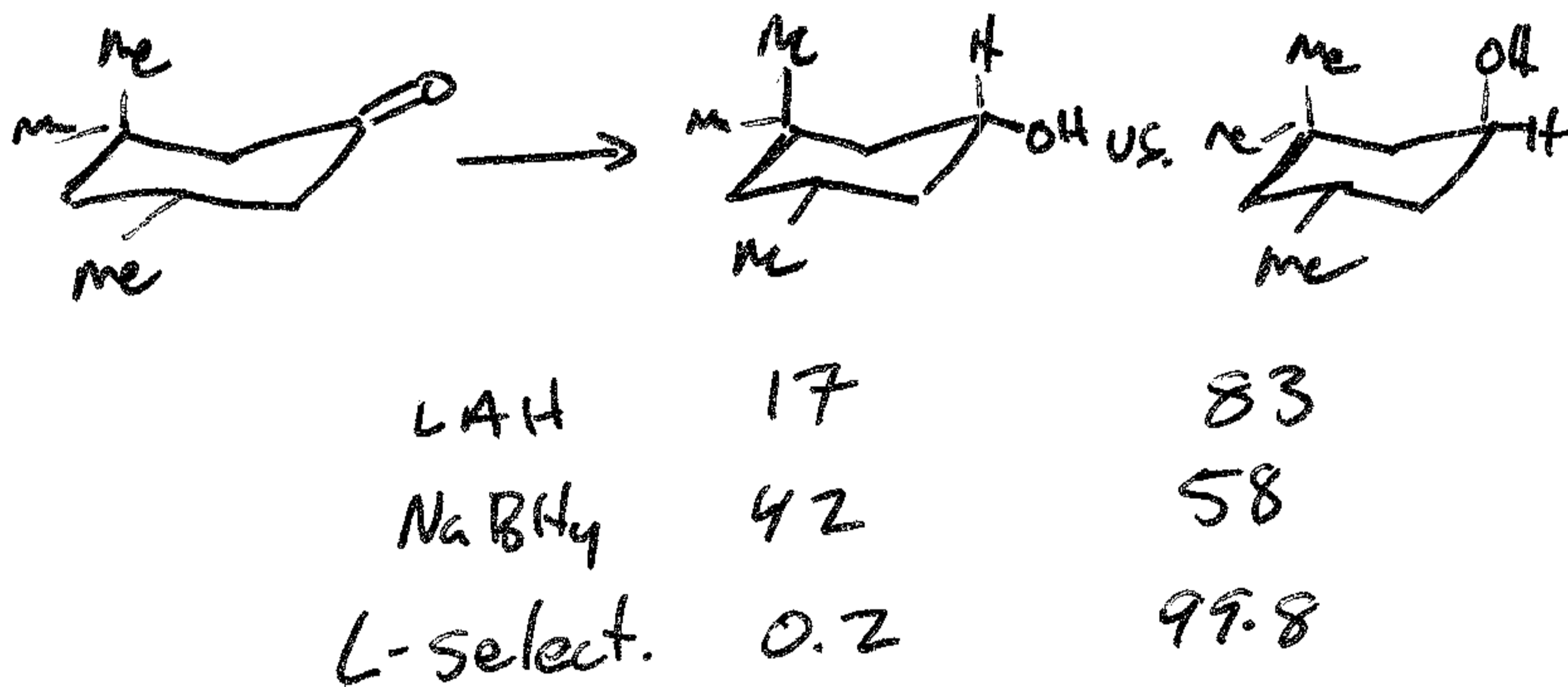
For small Red. Agents



For large Red. Agents

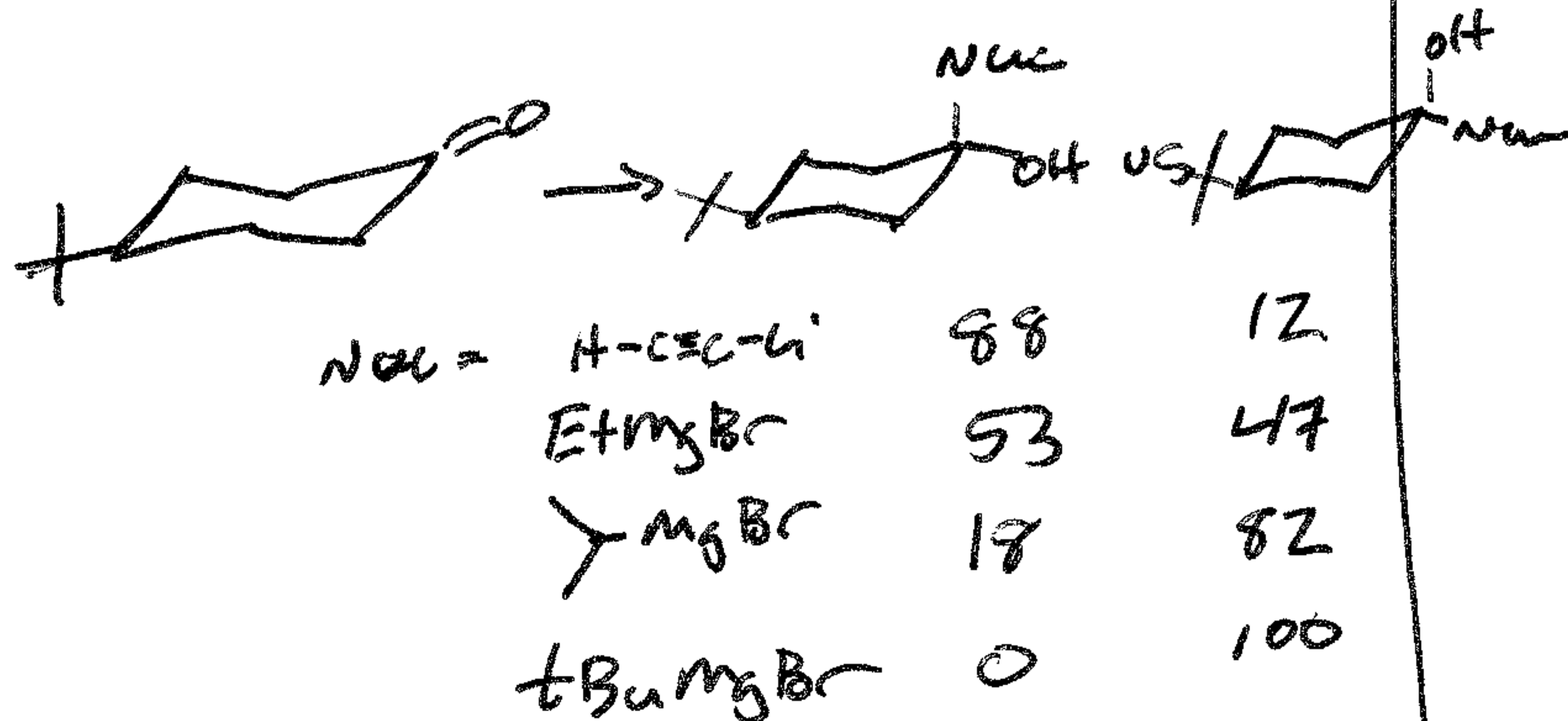


Steric interactions can override

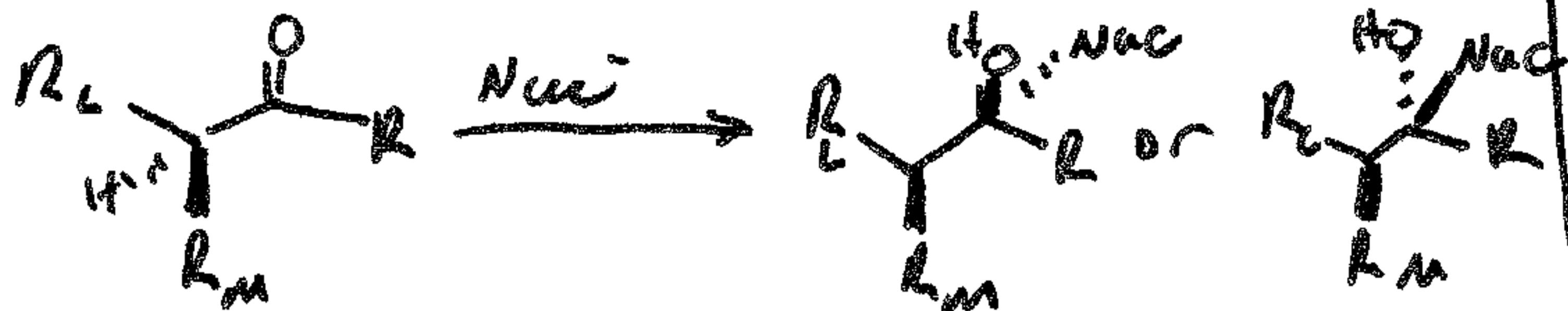


all favor equatorial attach

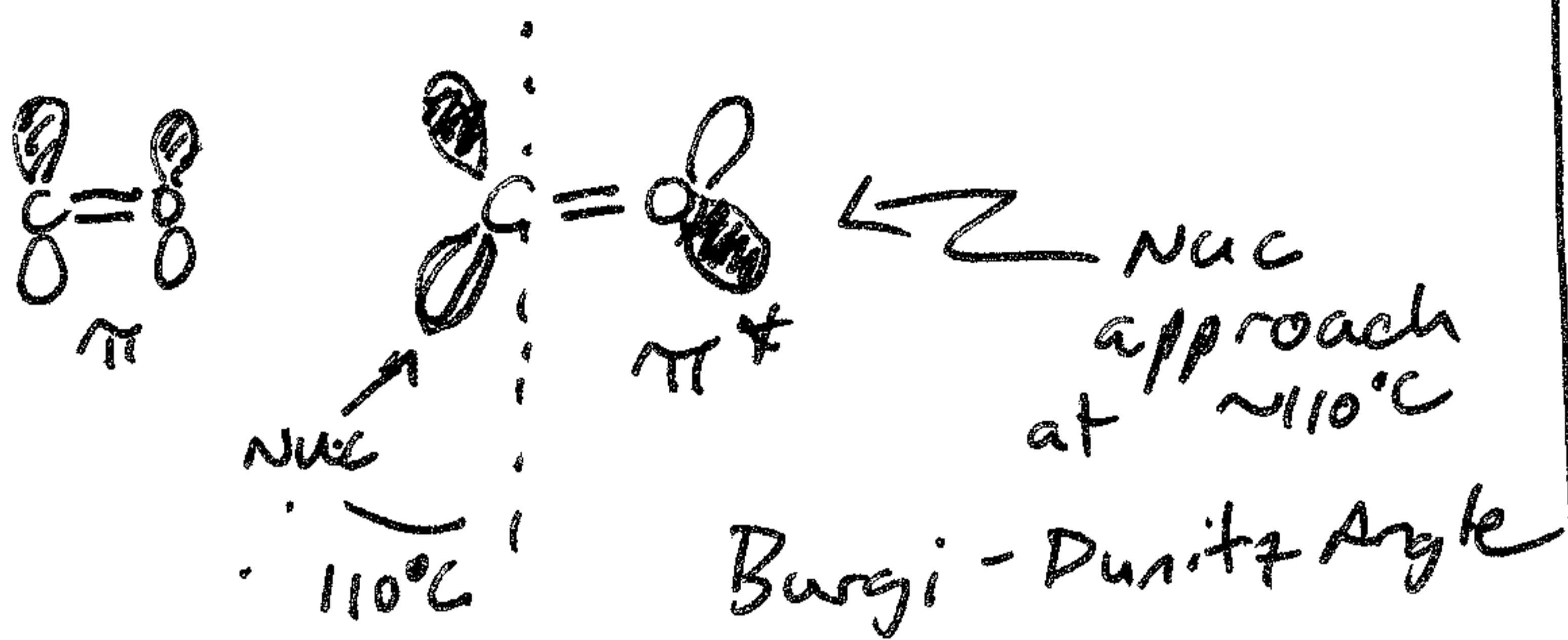
Similar for "C" Nuc's



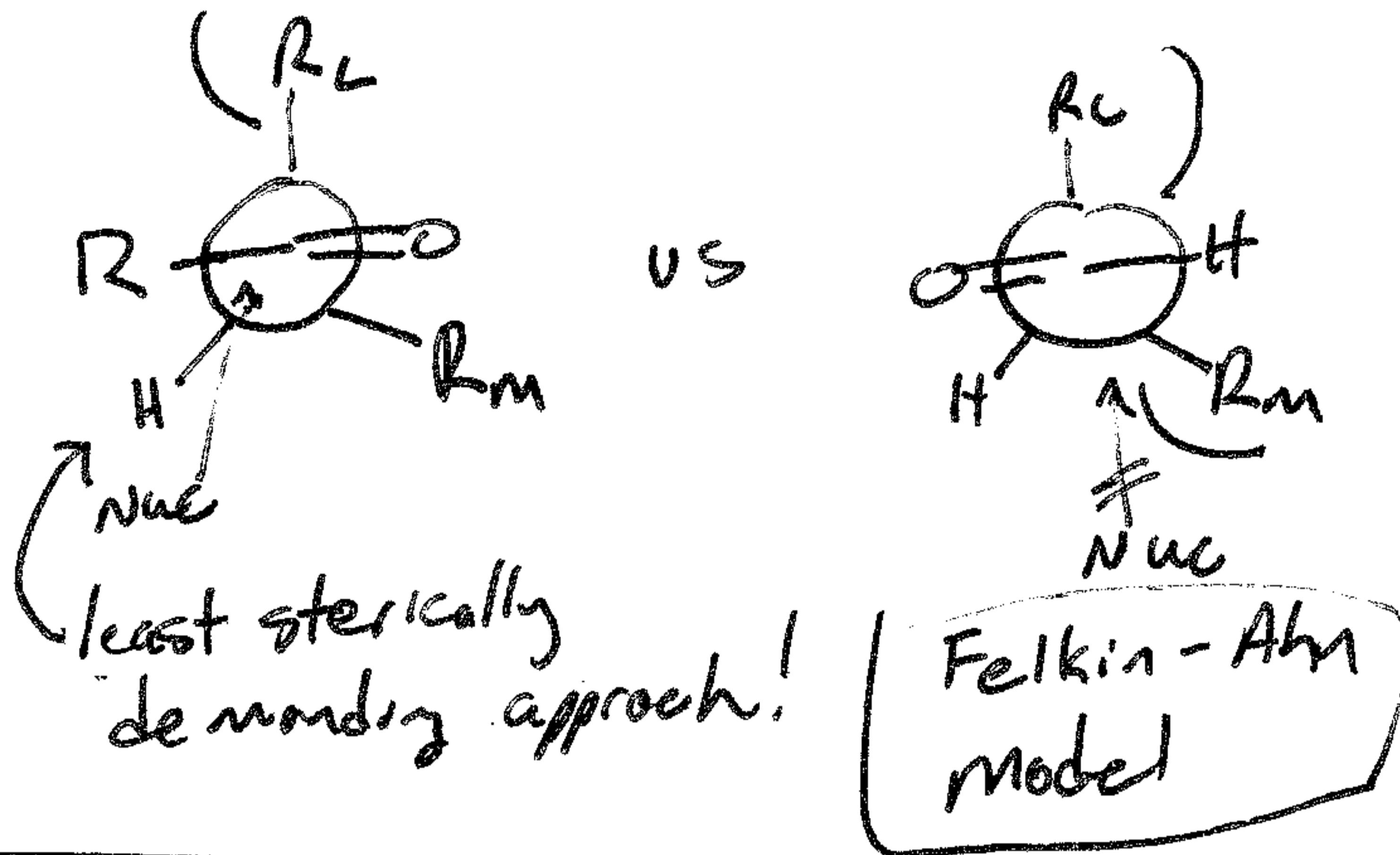
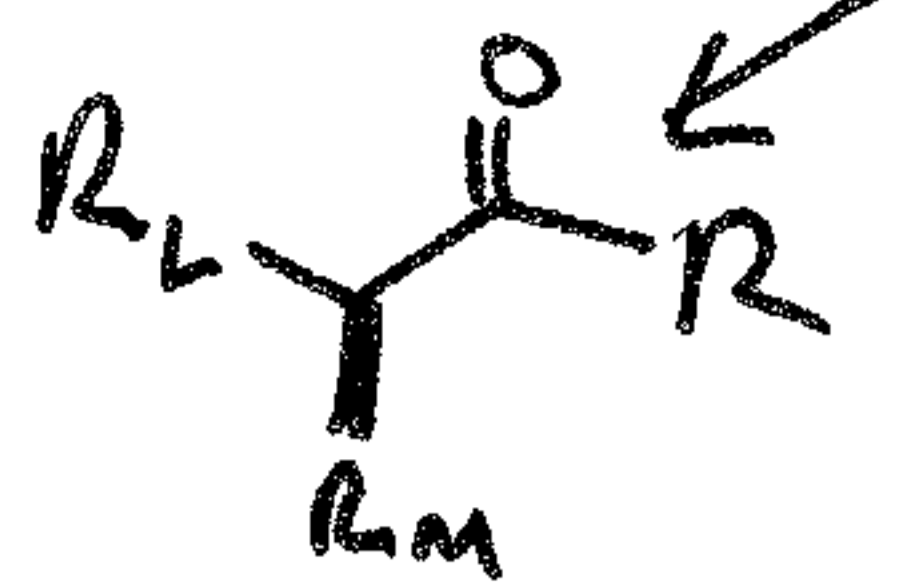
acyclic control



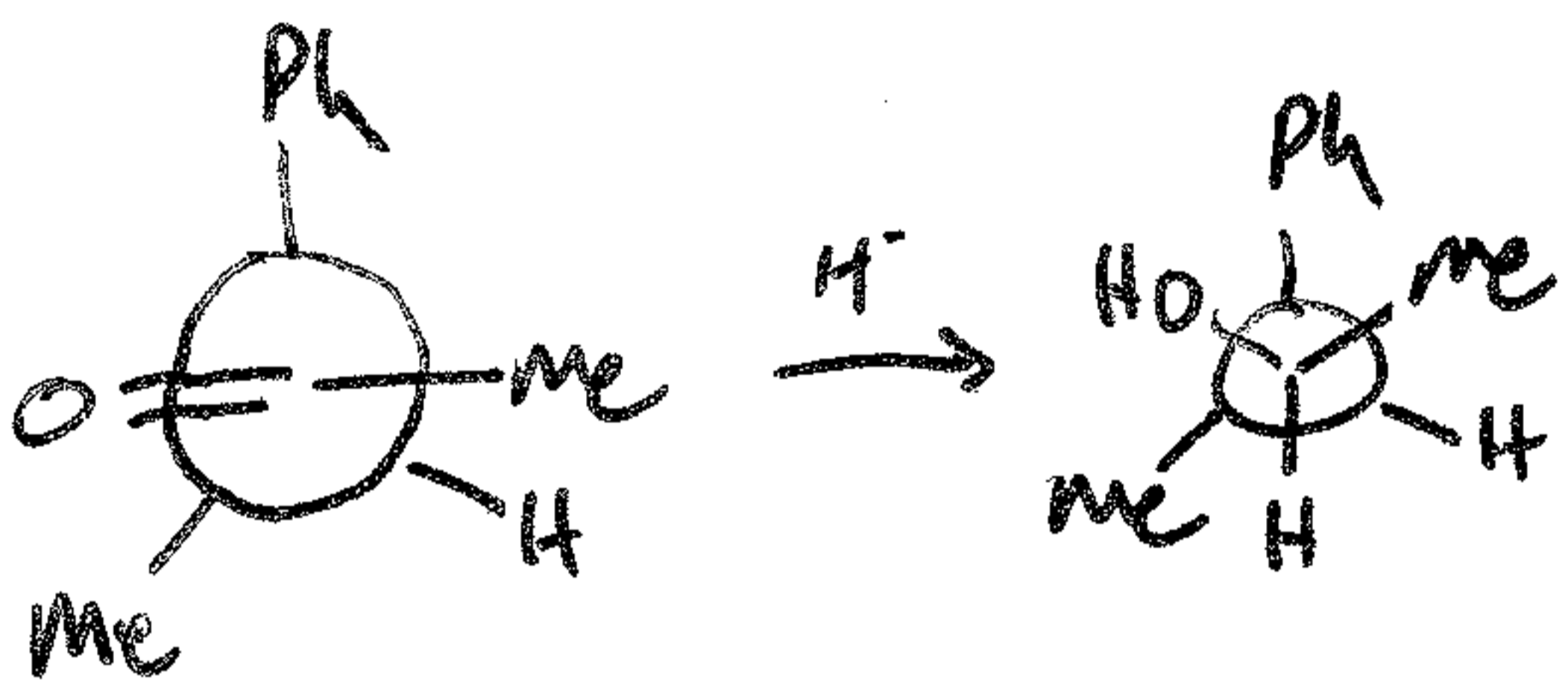
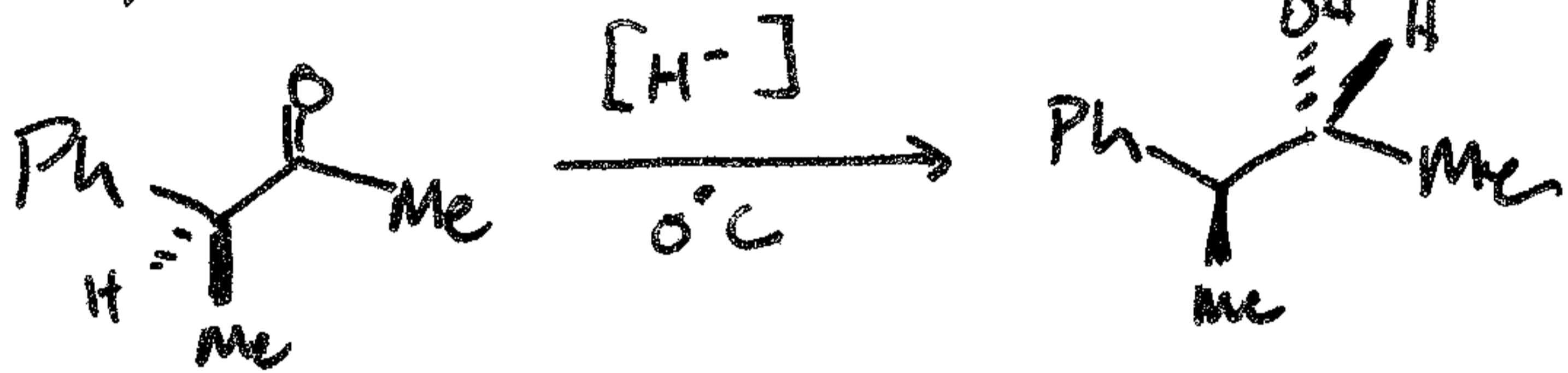
Where does Nuc⁻ approach from (FMO)



consider ¹contranations
Reactive



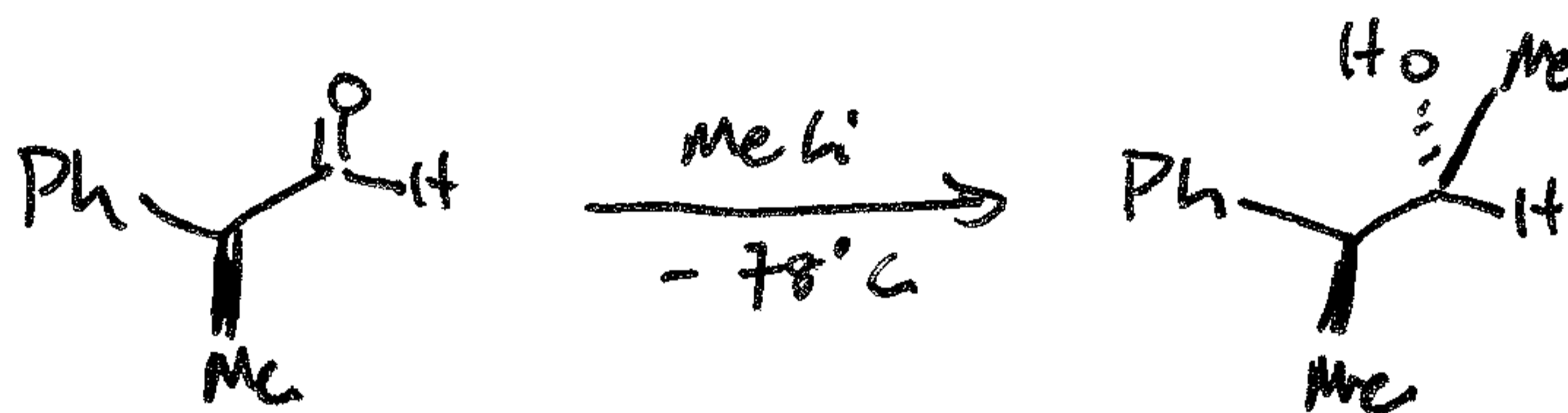
Example



LAH 74:26
L-sel. 99:1

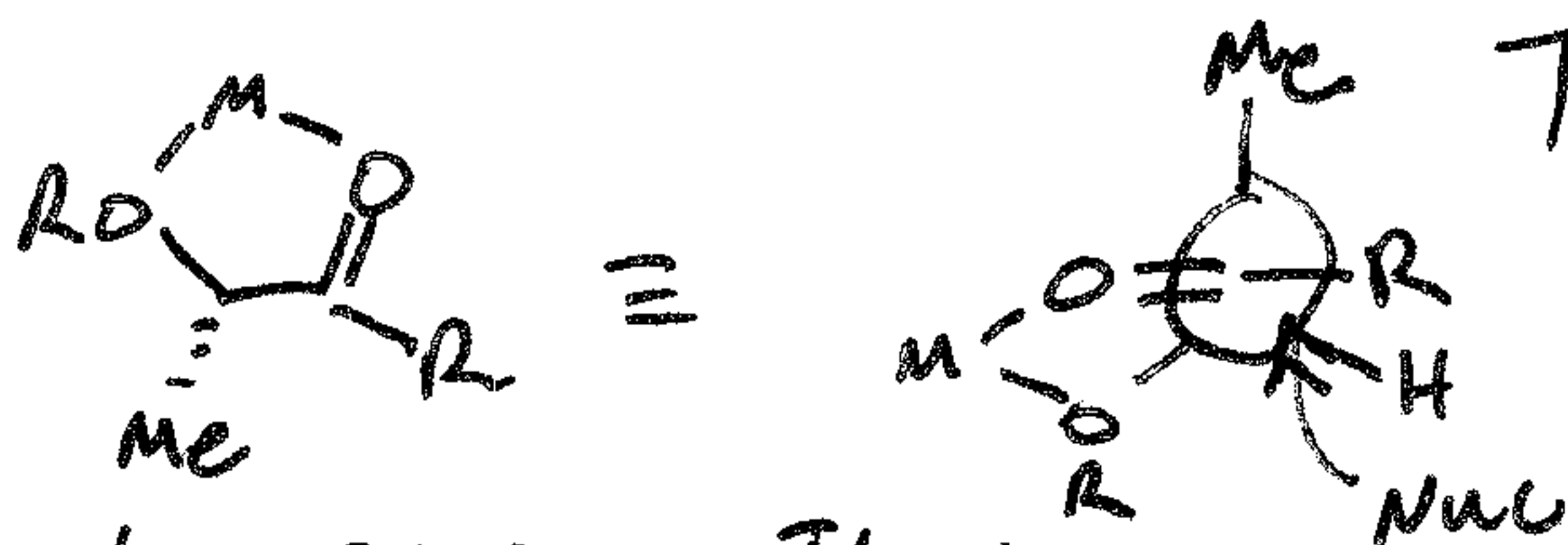
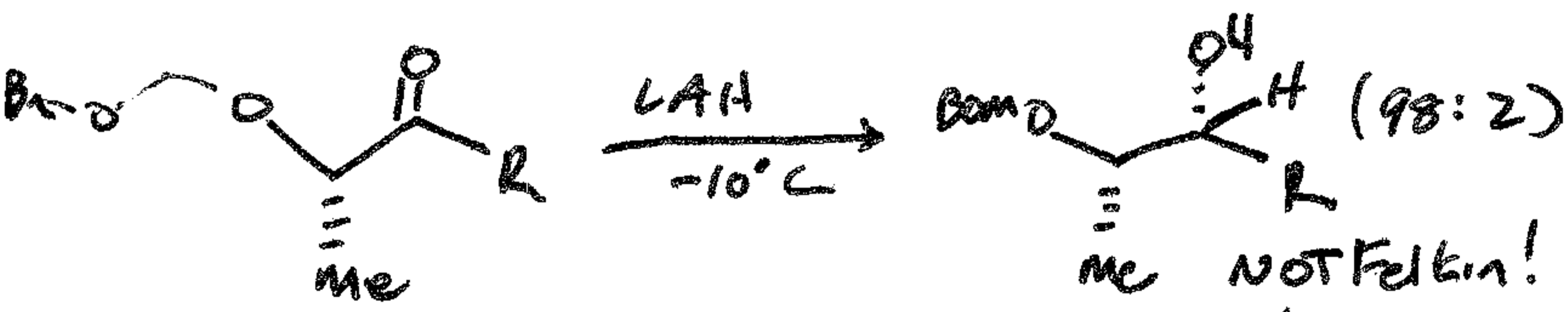
Yamamoto JACS, 1988, 110, 4475

Carbon Nuc's also (much more next week)



Ohno, JACS, 1988, 110, 4826

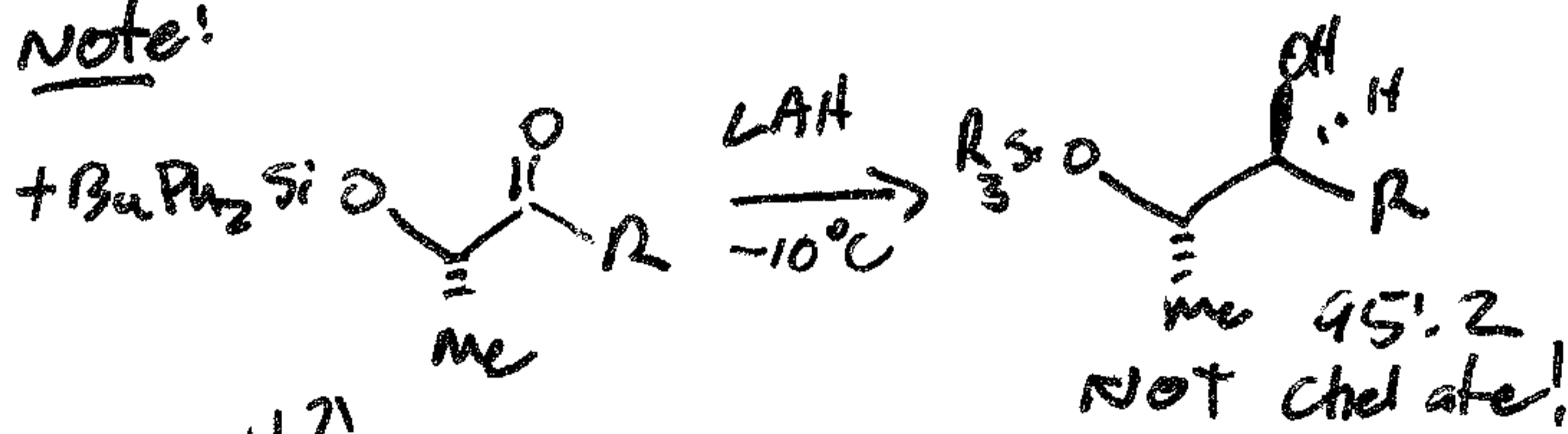
1,2-chelation control



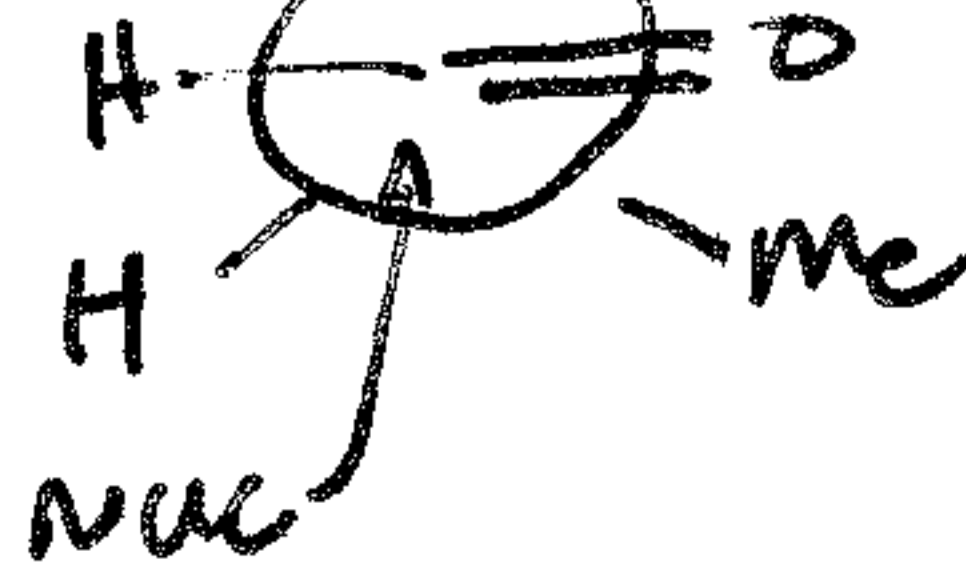
Example Overman TL, 1982, 2355

Review Rectz, Acc. Chem Res, 1993, 26, 462

Note!



trans!!?!
→ OSiR₃ ≠ OSiR₃ not good for chelation

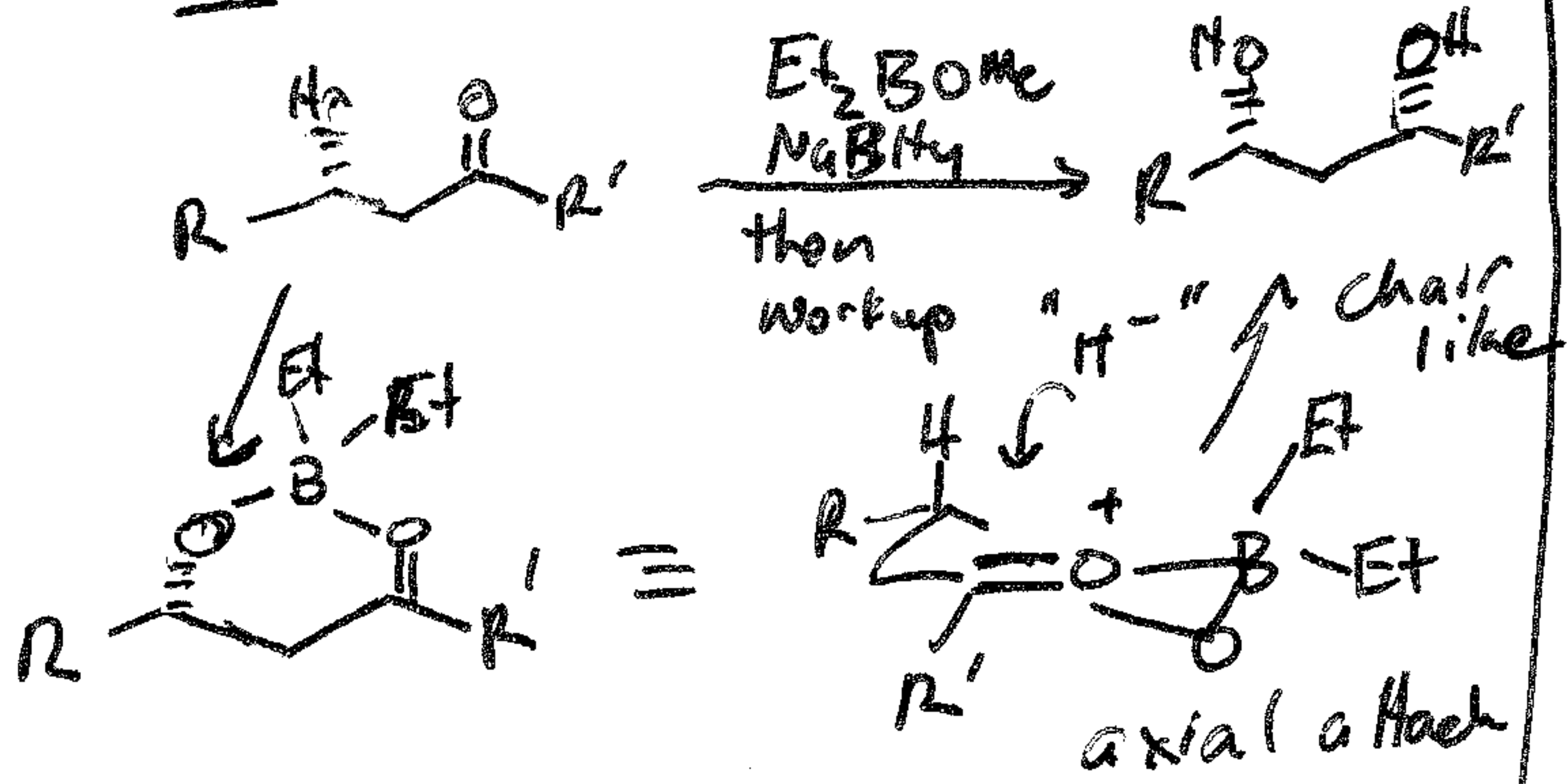


"Polar Felkin-Anh"
β-OSiR₃, Cl, etc

At TS $\sigma_{Nuc-C} \rightarrow \sigma_{C-X}^*$ stabilization of forming bond

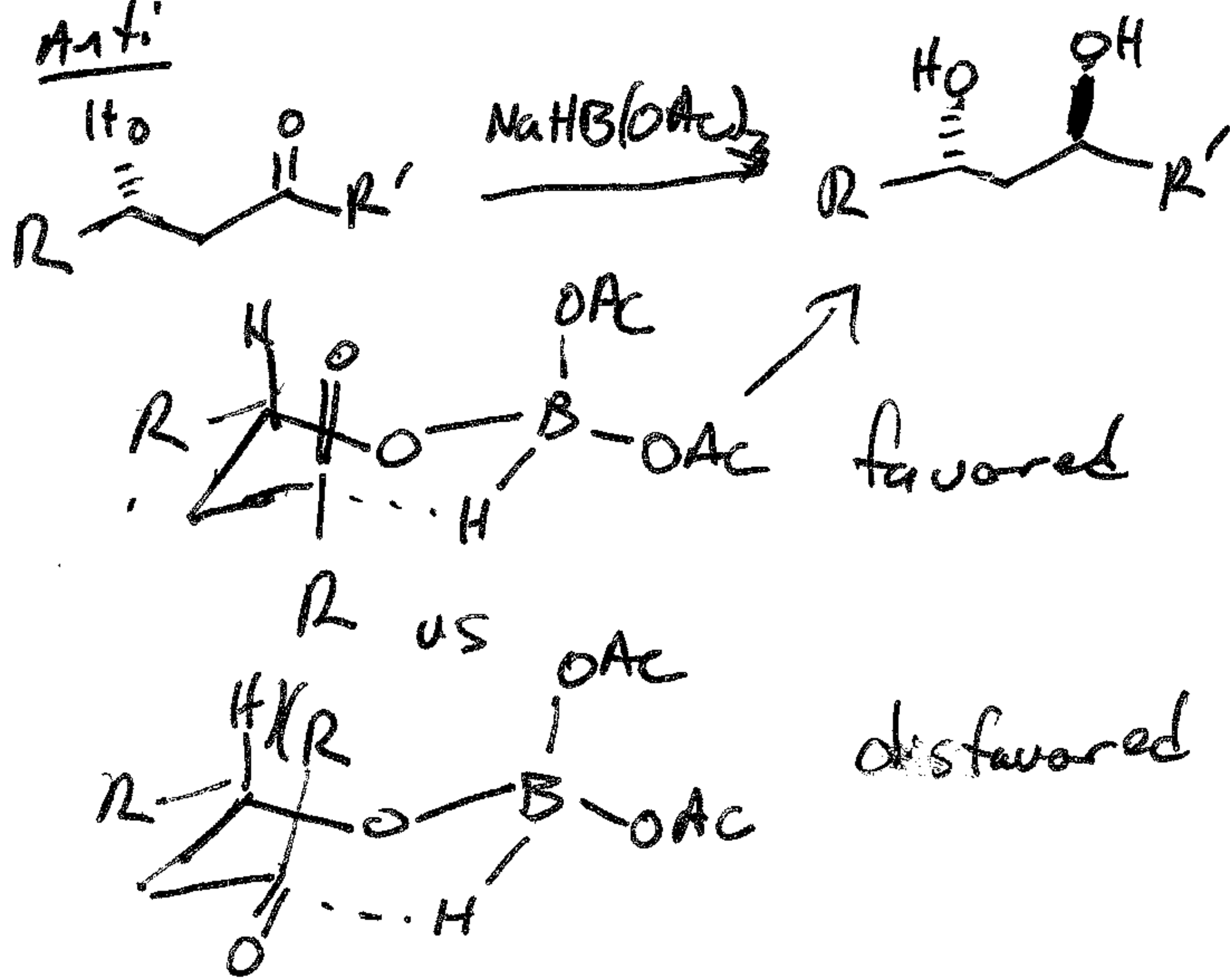
1,3 control

Syn



Narasaka Chem Lett, 1990, 1415

Anti



Evans JACS, 1988, 110, 3560

C=X reductants

| | comment/electrophile | iminium ion | acid chloride | aldehyde/ketone | ester | amide | carboxylate | nitrile |
|---|--|-------------|-----------------|-----------------|-------------|----------------|-------------|-------------|
| LiAlH ₄ (LAH) | Very strong, low solubility in tol | amine | ROH | ROH | ROH | amine | ROH | amine |
| NaAlH ₂ (OCH ₂ CH ₂ OMe) ₂ (Red-Al) | Very strong, soluble | amine | -- | ROH | ROH | amine | ROH | amine |
| LiAlH(OEt) ₃ | Weaker than LAH | -- | -- | -- | alcohol | RHO (3° amide) | -- | RHO |
| NaAlH(OtBu) ₃ | Weaker yet | amine | slow to ROH | -- | slow to ROH | slow to amine | -- | -- |
| NaBH ₄ | Moderate | amine | ROH | ROH | n/r | n/r | -- | -- |
| LiBH ₄ | More reactive than Na verison | amine | -- | ROH | ROH | -- | -- | -- |
| NaBH(OAc) ₃ | Weaker than NaBH ₄ , more selective | amine | -- | ROH | ROH | -- | slow to ROH | -- |
| NaCNBH ₃ | even more so | amine | -- | slow to ROH | n/r | slow to ROH | -- | -- |
| LiBHET ₃ (Super-Hydride) | Very strong reductant | -- | -- | slow to ROH | n/r | n/r | -- | -- |
| (iBu) ₂ AlH (DIBAL or DIBAL-H) | electrophilic | -- | ROH | ROH | ROH | RHO (3° amide) | -- | likely red. |
| BH ₃ •L (L = THF or DMS) or B ₂ H ₆ | electrophilic | -- | ROH | ROH | ROH or RHO | amine or RHO | ROH | RHO |
| H ₂ / cat | hydrogenation | -- | -- | ROH | slow to ROH | slow to amine | ROH (fast) | -- |
| | | amine | ROH or aldehyde | ROH | ROH | amine | -- | amine |

-- = not product or not commonly used combination
n/r = no reaction, ROH = alcohol, RHO = aldehyde

Adapted from Carey and Sunburg, 5th Ed.