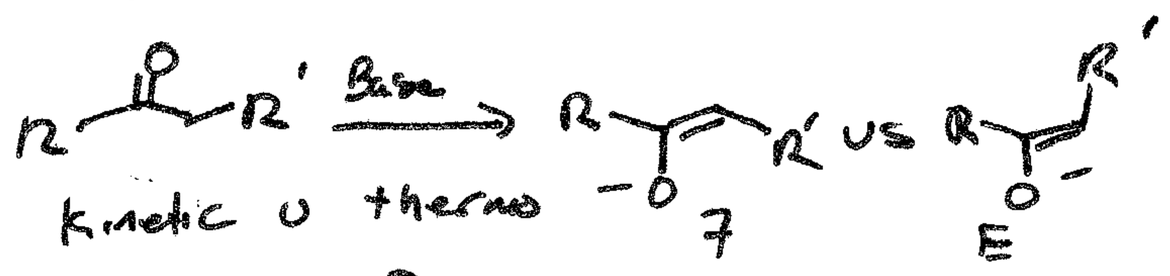
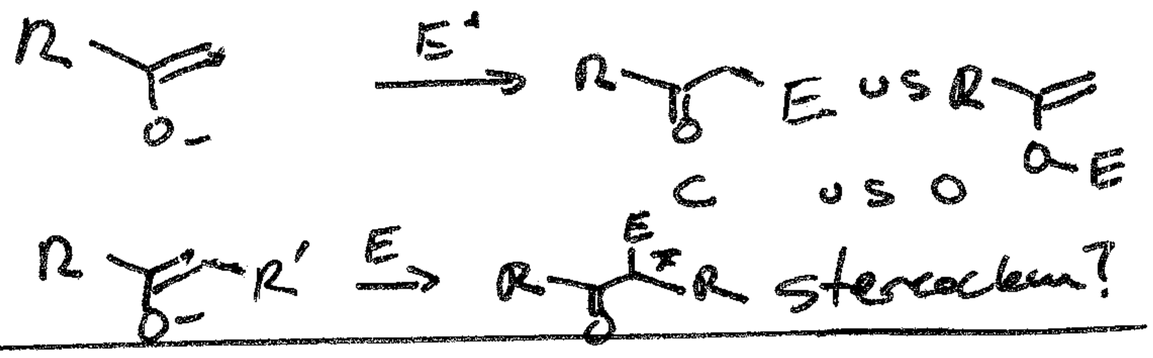
Enolate chemistry Part 2

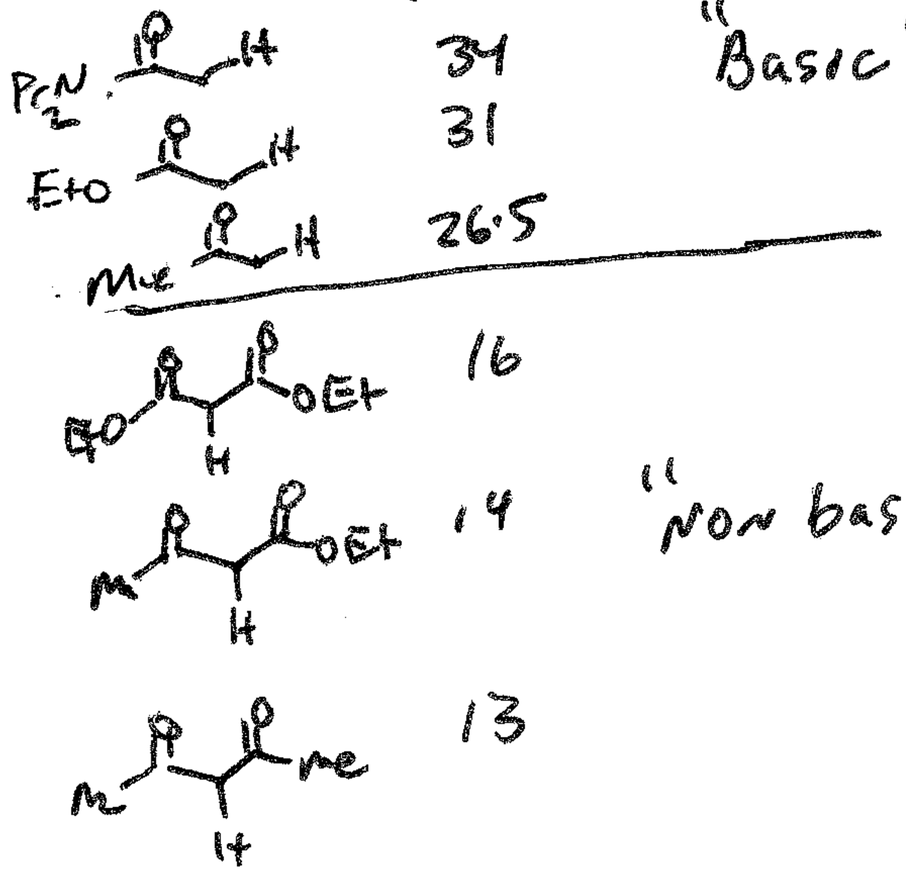
Most simple

Very complex consider

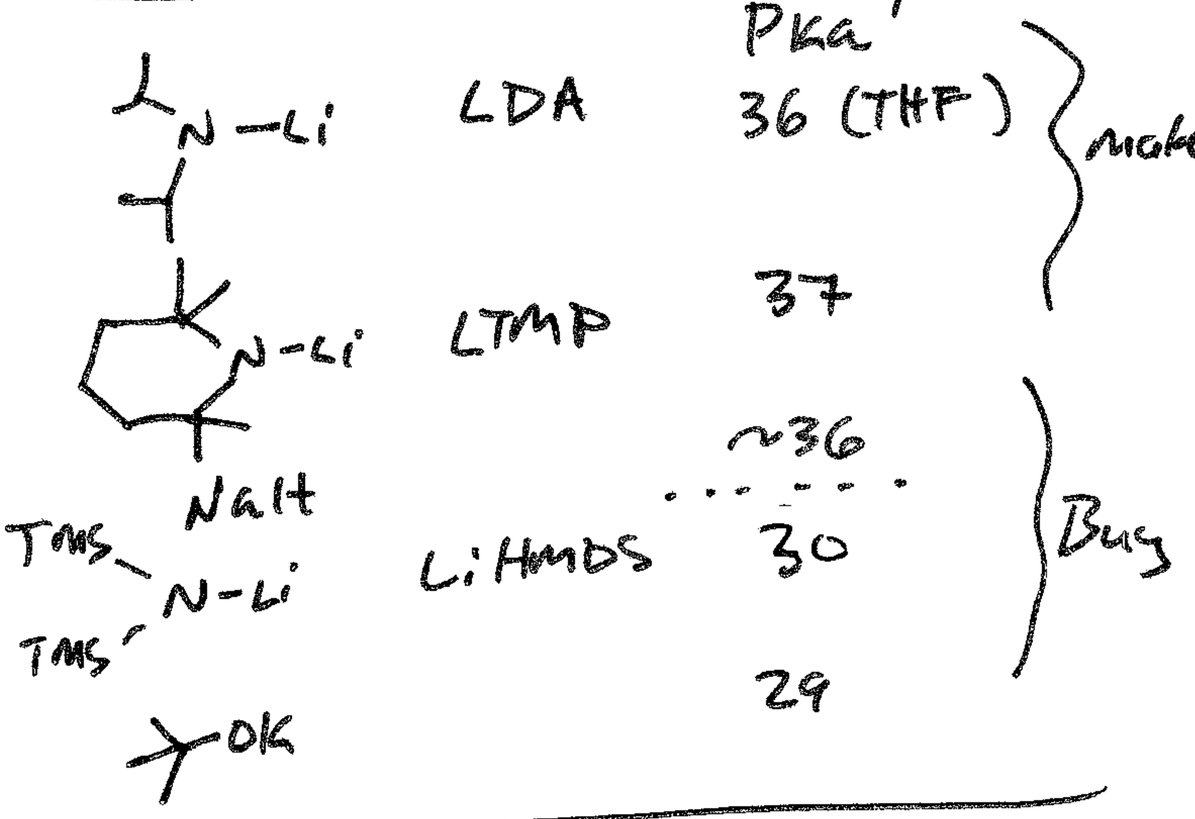




Pka's First

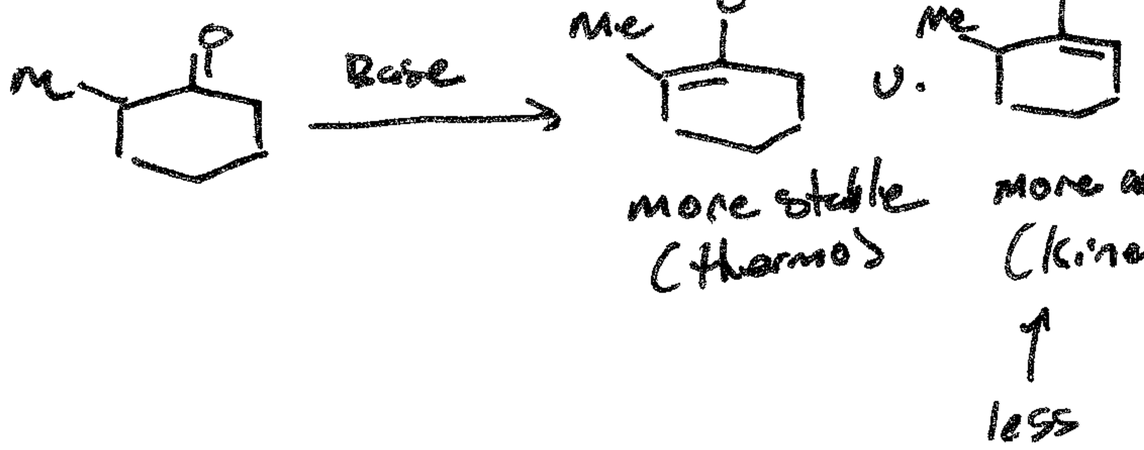


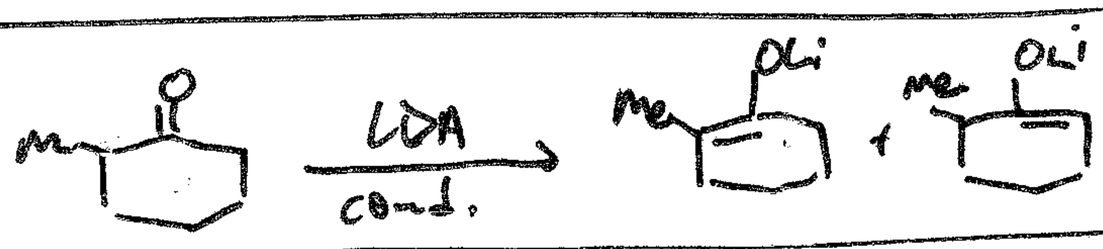
Bases



$R_2NH \xrightarrow{BuLi} R_2NLi$

Kinetic vs thermodynamic

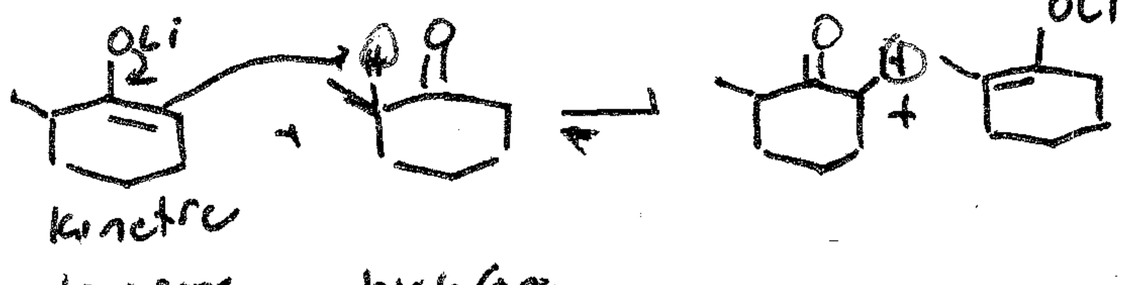




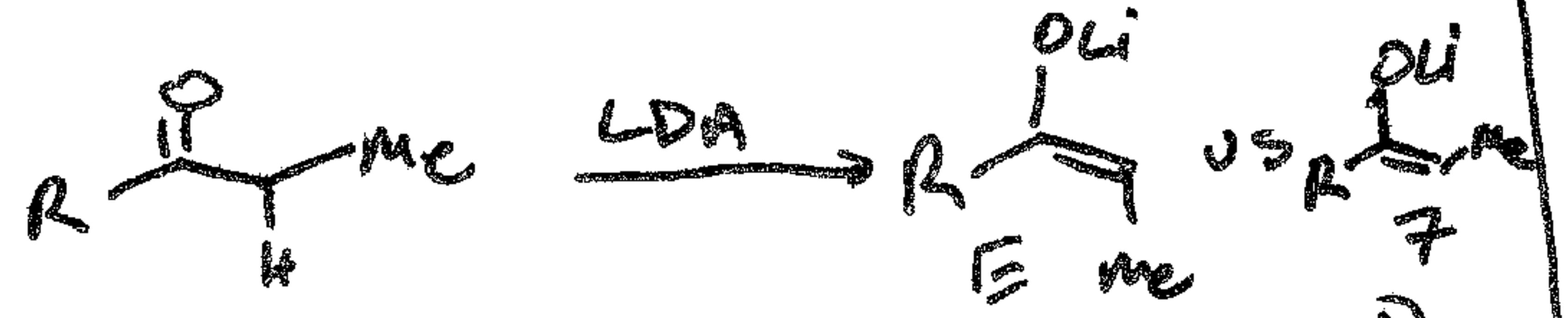
Slow add ketone to LDA — minor / major — "inverse addition"

Slow add LDA to ketone — major / minor

"After first dep" in pool of ketone



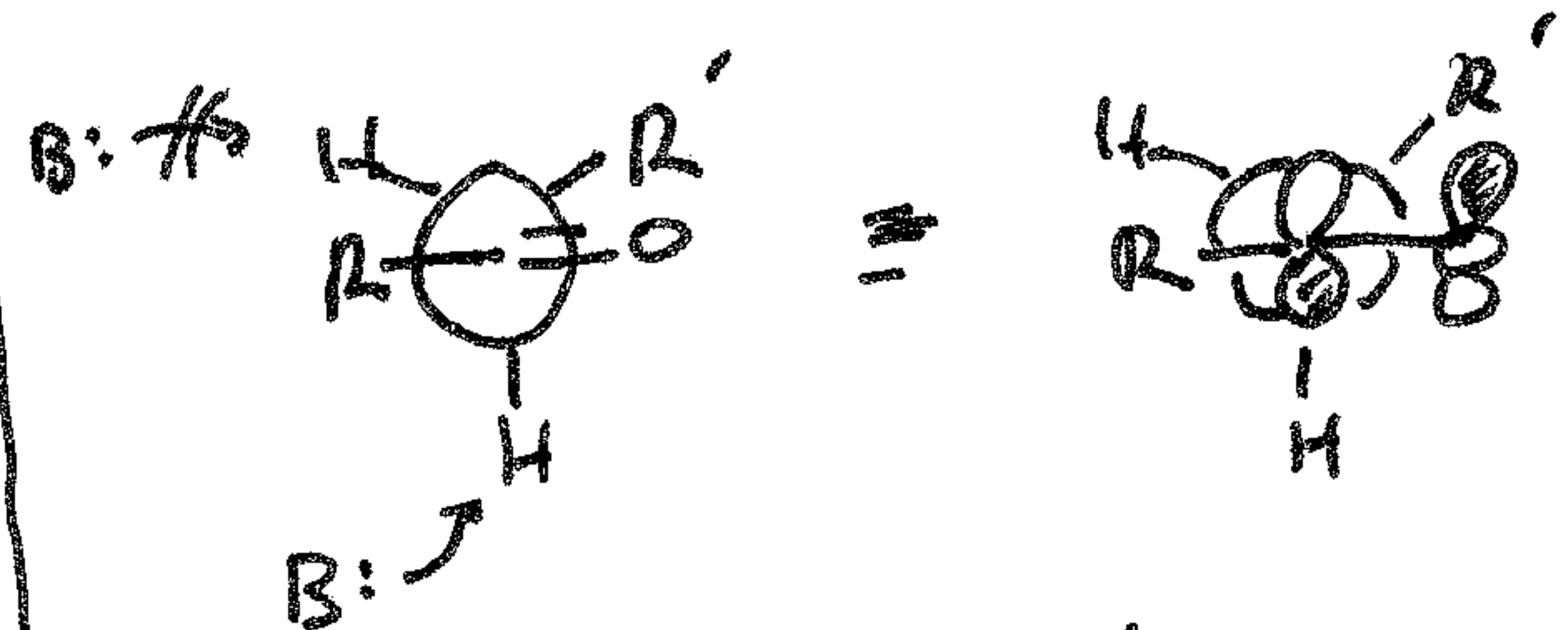
E vs Z (kinetic)



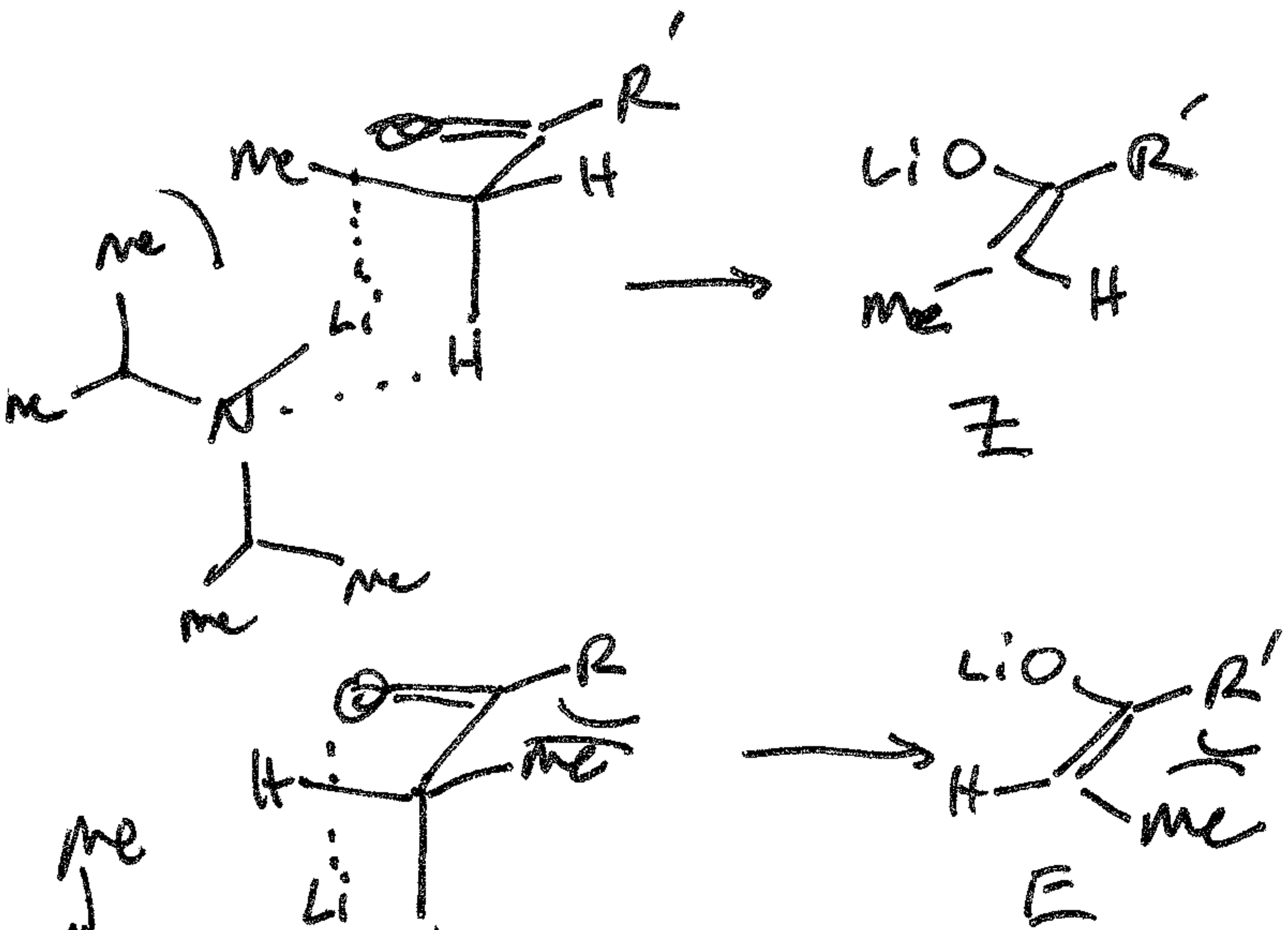
R	E/Z (THF)	E/Z (HMPA)
MeO	95/5	12/88
Et	70/30	8/92
tBu	0/100	—
NEt$_2$	0/100	—

Heathcock JOC, 1980, 45, 1066

Note cyclic always E!



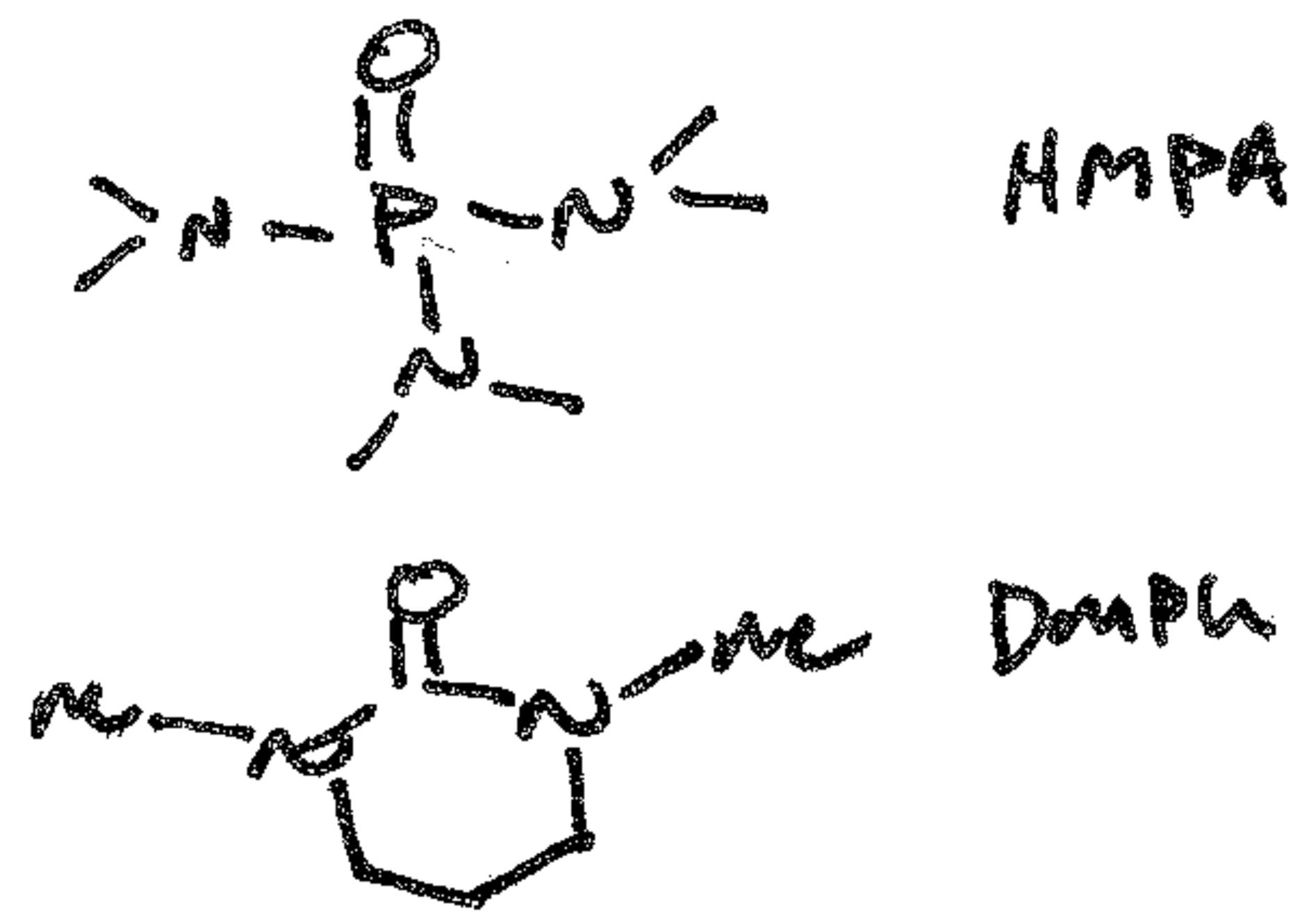
$\sigma_{CH} \rightarrow \pi^*_{CO}$ Required!



A 1,3 strain

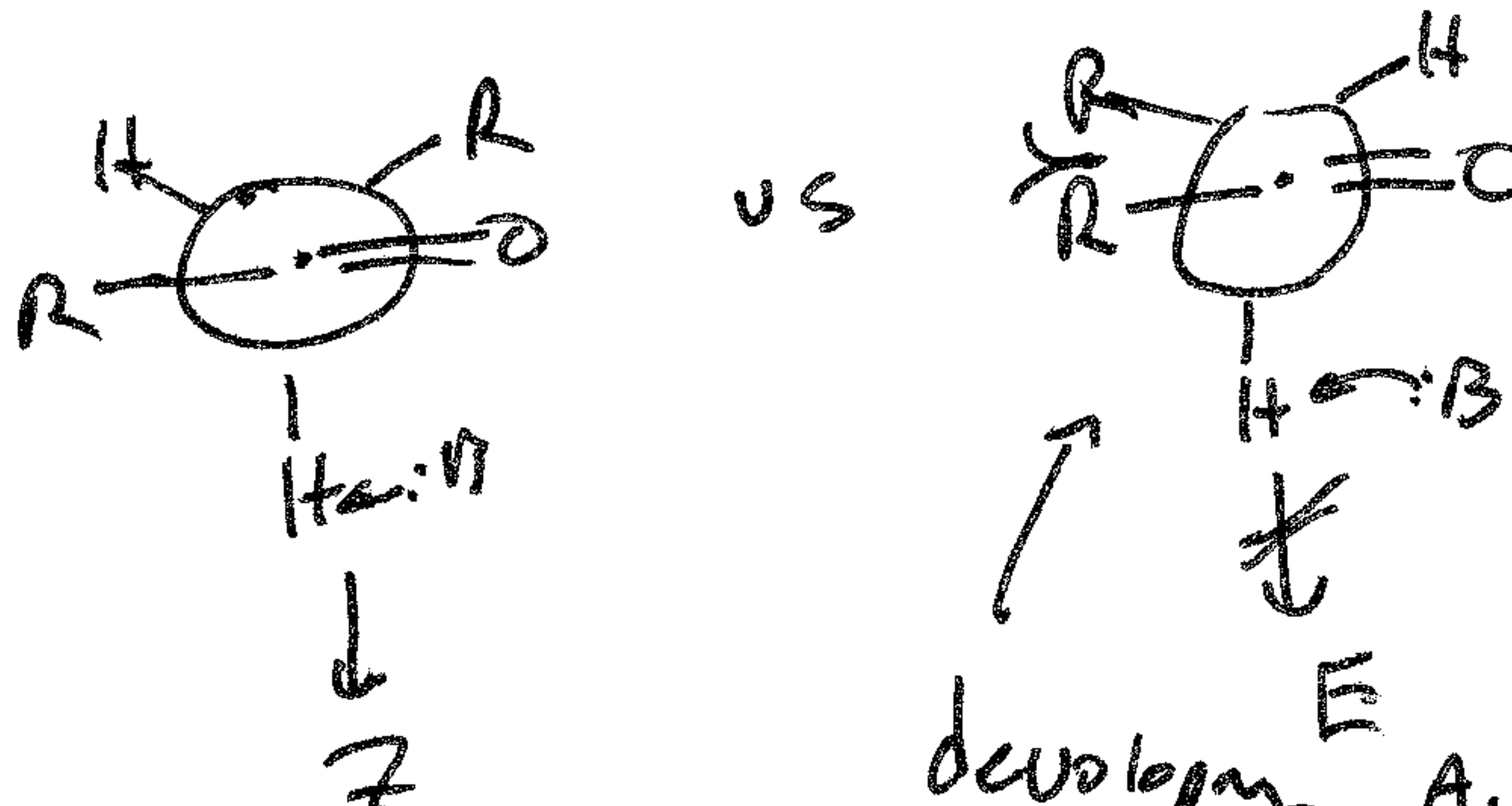
Ireland Model

HMPA?



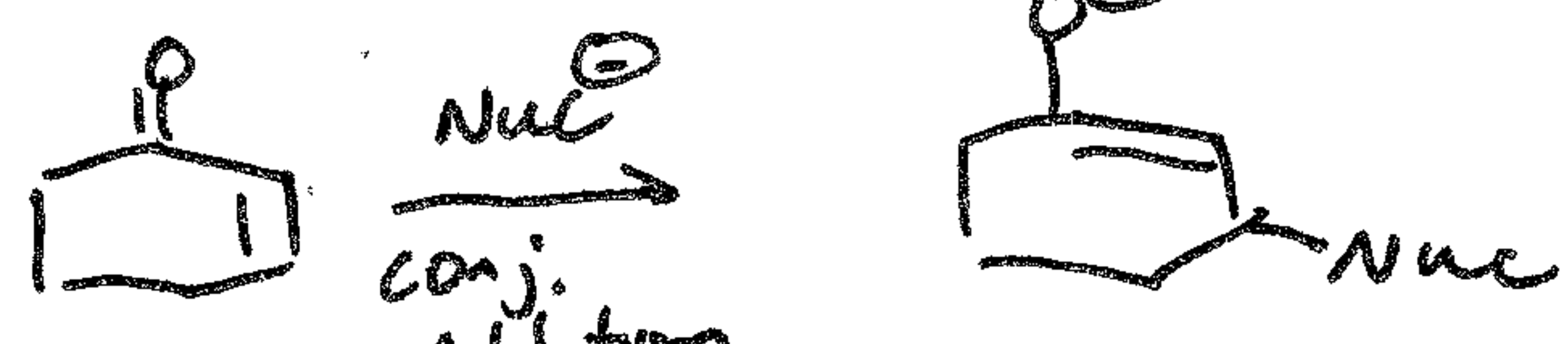
additives modulate reactivity

more reactive & can not coordinate ketone

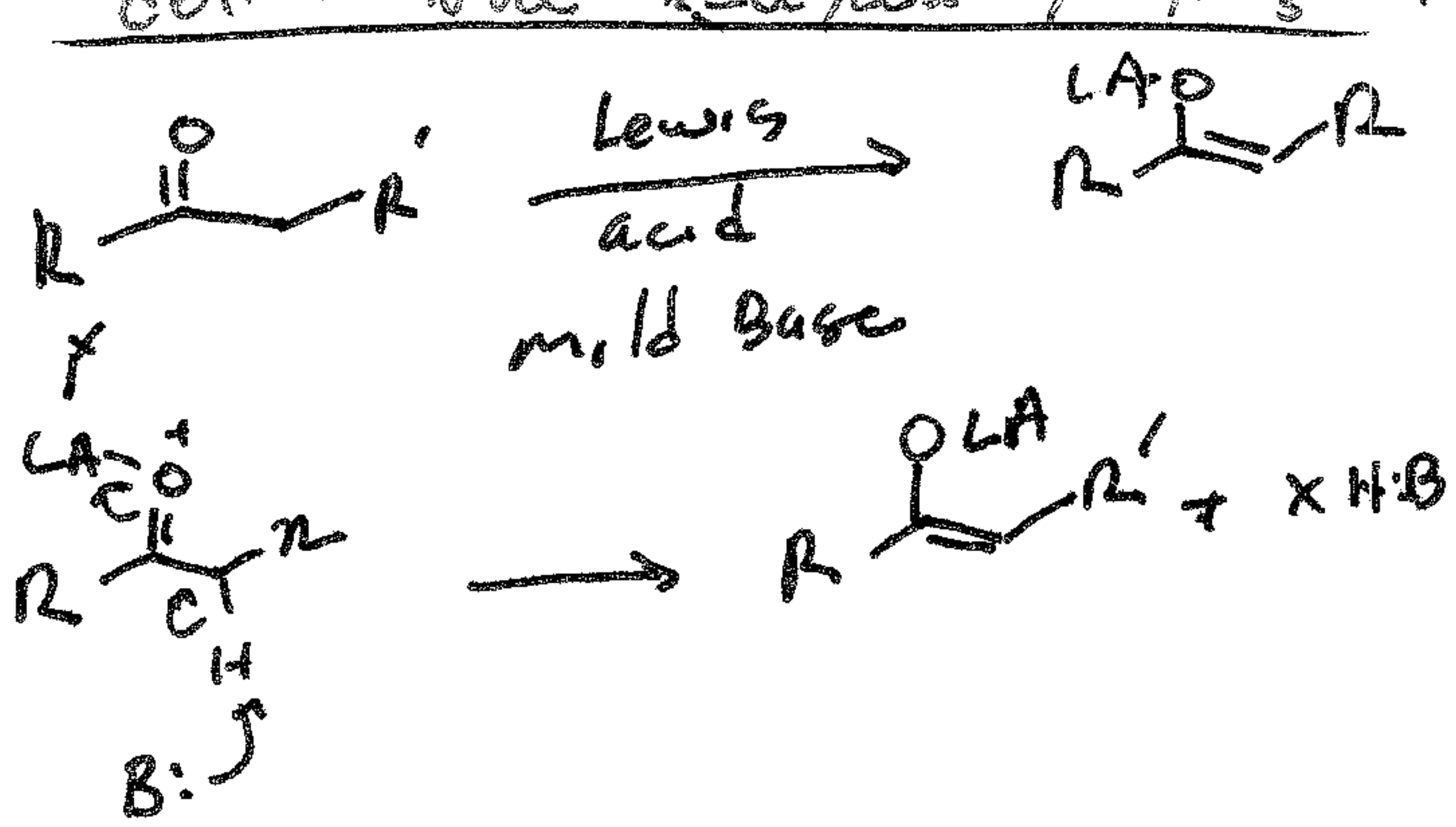


developing A1,3 in transition state

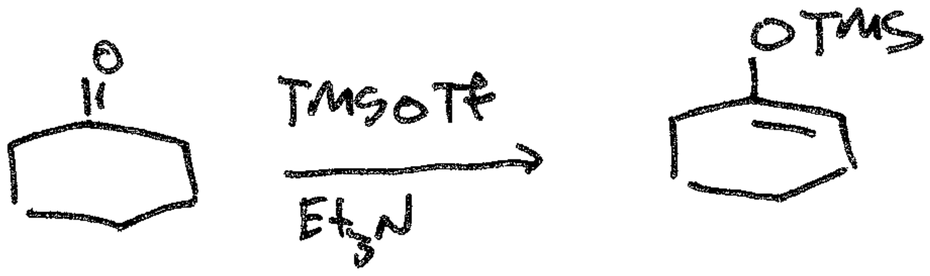
Other methods to make Enolates



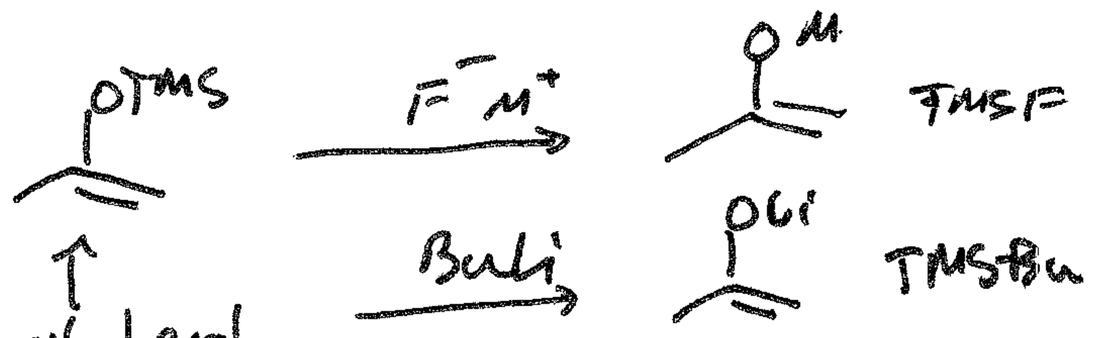
define Nuc⁻ R$_2$Cu⁻, LCu-H, Li/NH$_3$ = "H⁻"



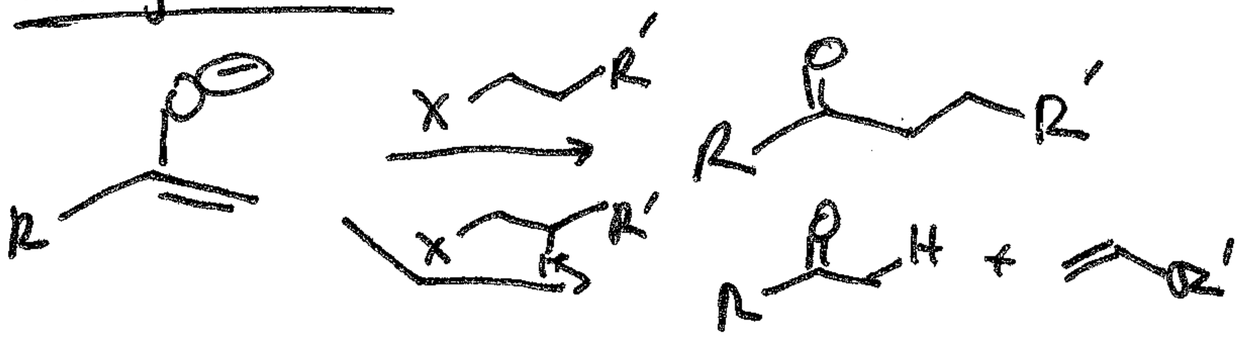
Examples



Masked enolates



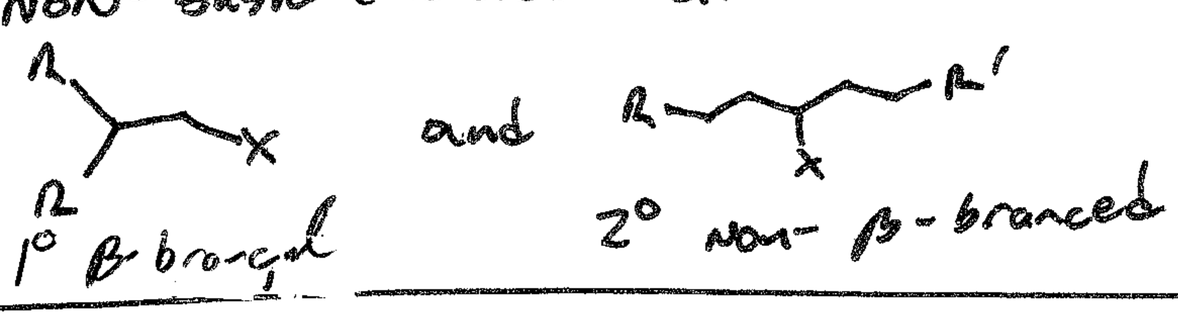
Alkylations



More basic : more E2

'Basic enolates': Rx can be MeI, Ph—x, =—x, RO—x or R—x ← not β-branched

"non-basic enolates" all of above



C vs O alkylation

Soft

R—x > R(=O)—x > R3Si—x

C — mainly — O

Soft

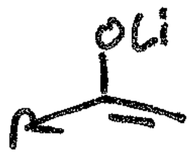
R—I > R—Br > R—OTs > R—Cl

Hard

> ROSO2OR

Solvent in O vs C

Alcohols & Ethers favor C-alkylation



← strong O-Li bond

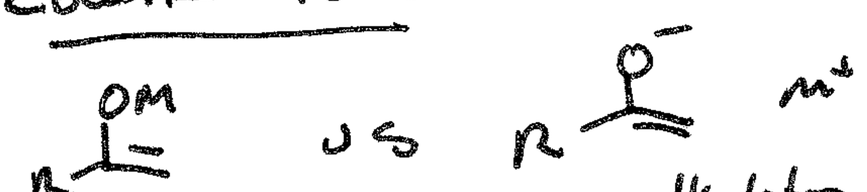
V. polar aprotic's favor O-alkylation

DMF, 

"NMP", DMSO, HMPA, etc

more 

Counter ions

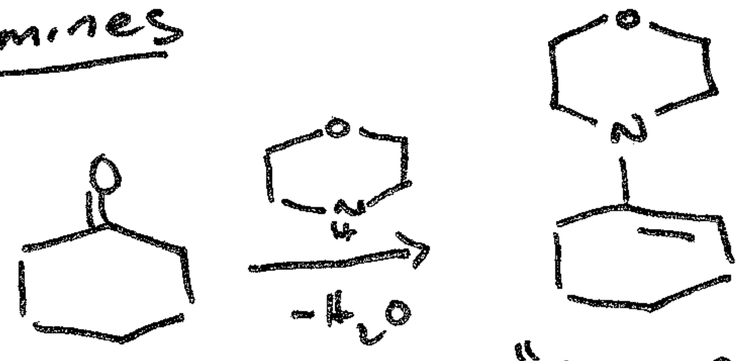


C

$Li^+ > Na^+ > K^+ > Cs^+ > R_4N^+$

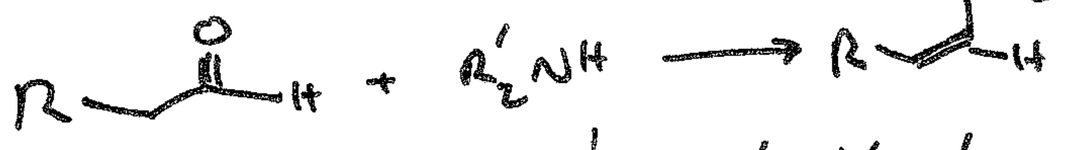
↑ strongest O-M bond overlap

Enamines

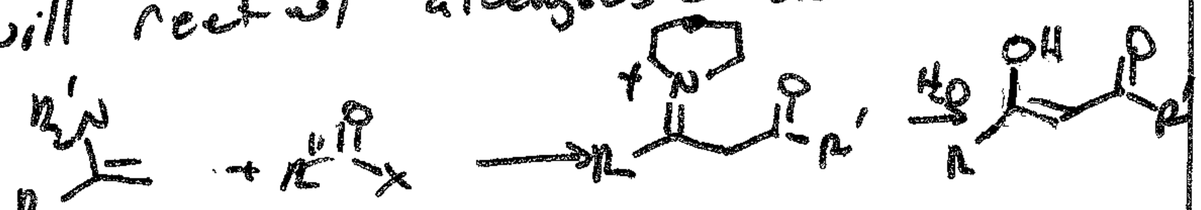


Stork JACS 1963, 85, 207

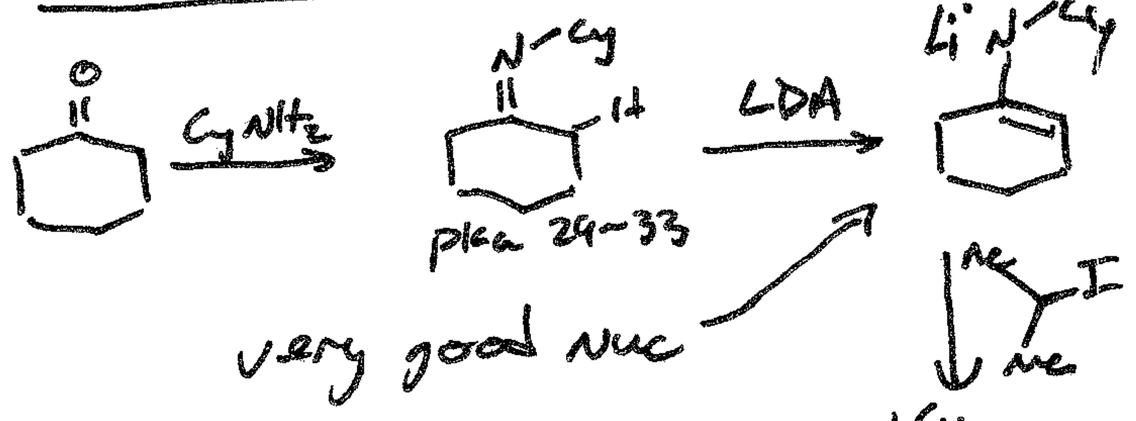
"enamine" More reactive than enol



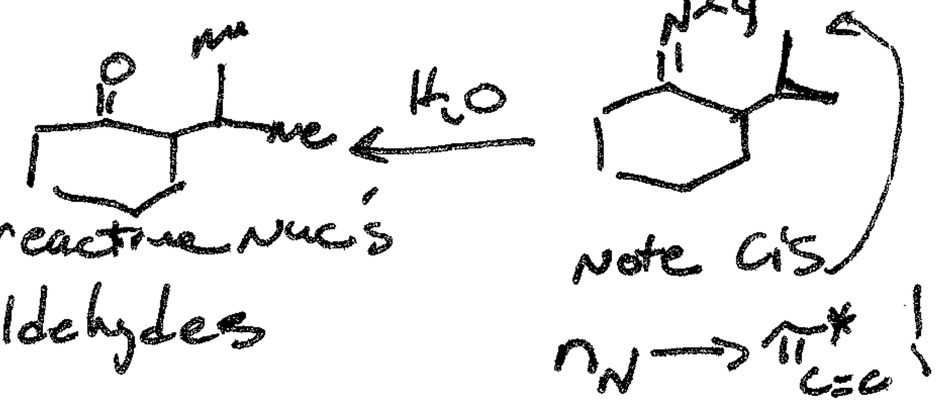
Will react w/ aldehydes & acid chloride



Metallocene amines



very good Nuc



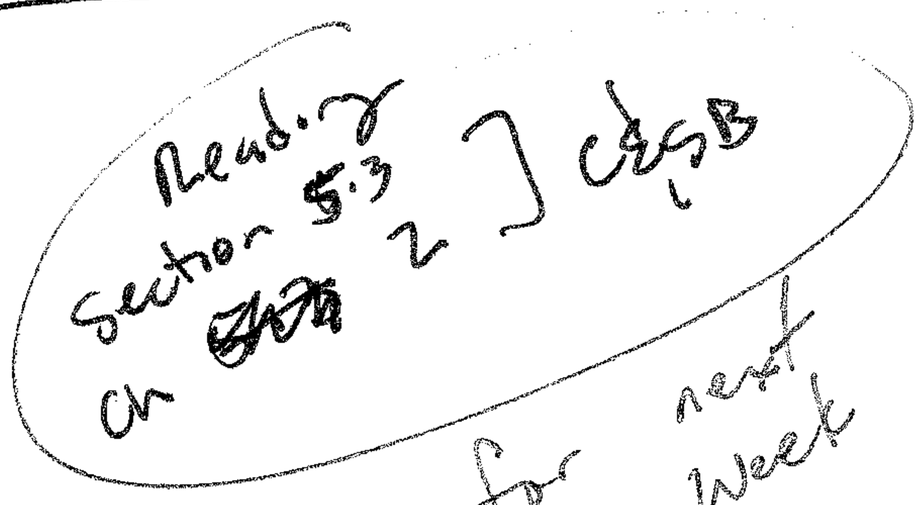
*less reactive Nuc's

*aldehydes

Note C's

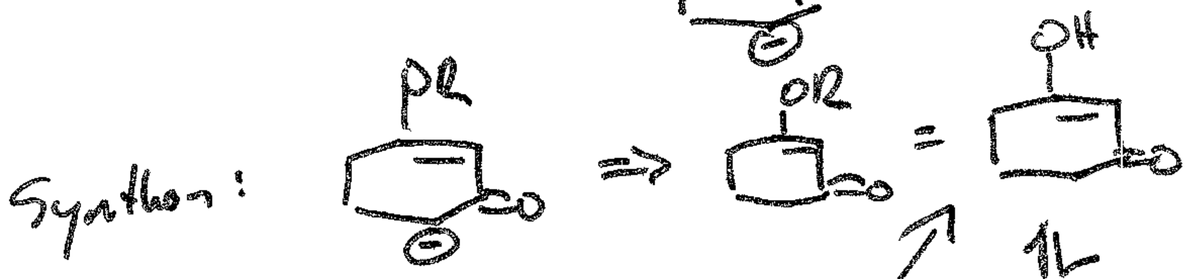
$\pi_N \rightarrow \pi^*_{C=O}$!

Stork JACS, 1963, 85, 2178



Stork-Danheiser

Synthon:



Note: Danheiser was an undergrad in Stork's lab!