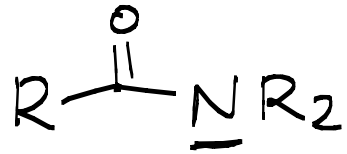
Carboxylic Acids & Derivatives (Ch 17 + 18)

Note Title 4/17/2014

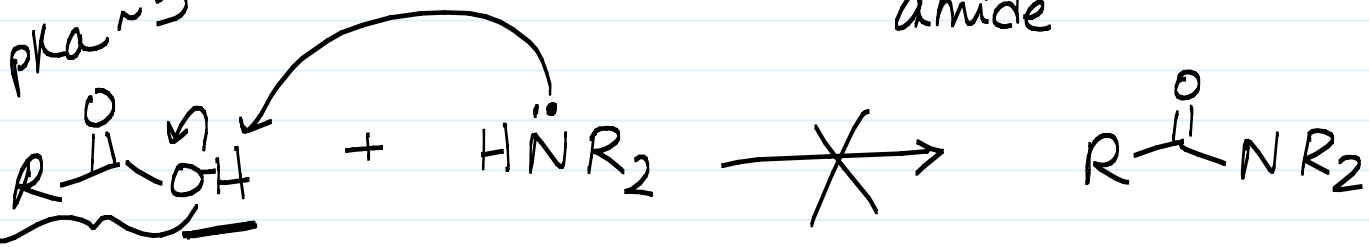
Announcement: Get Midterm 1 after class.

Amide Formation

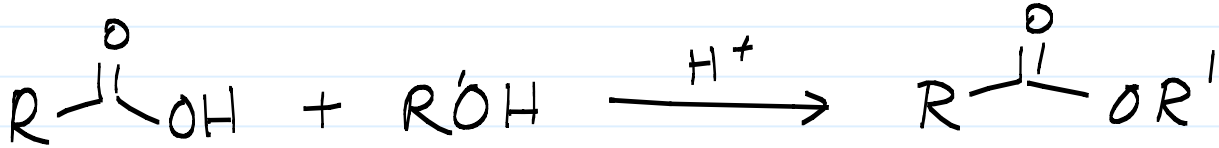


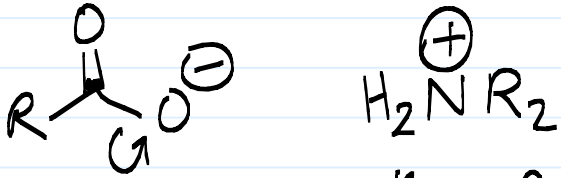
amide

pKa ~ 5



Compare to

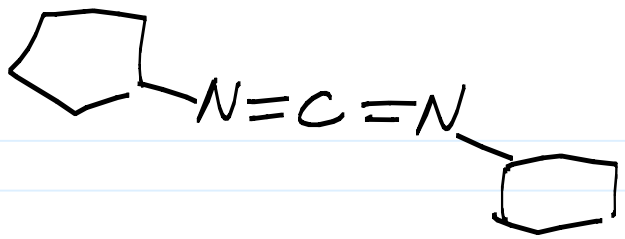




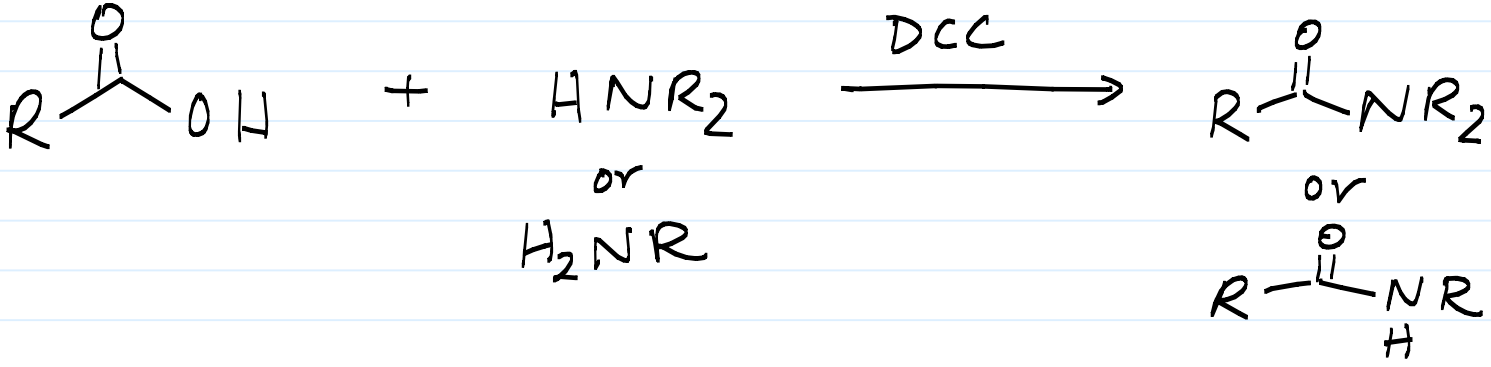
pKa = 9

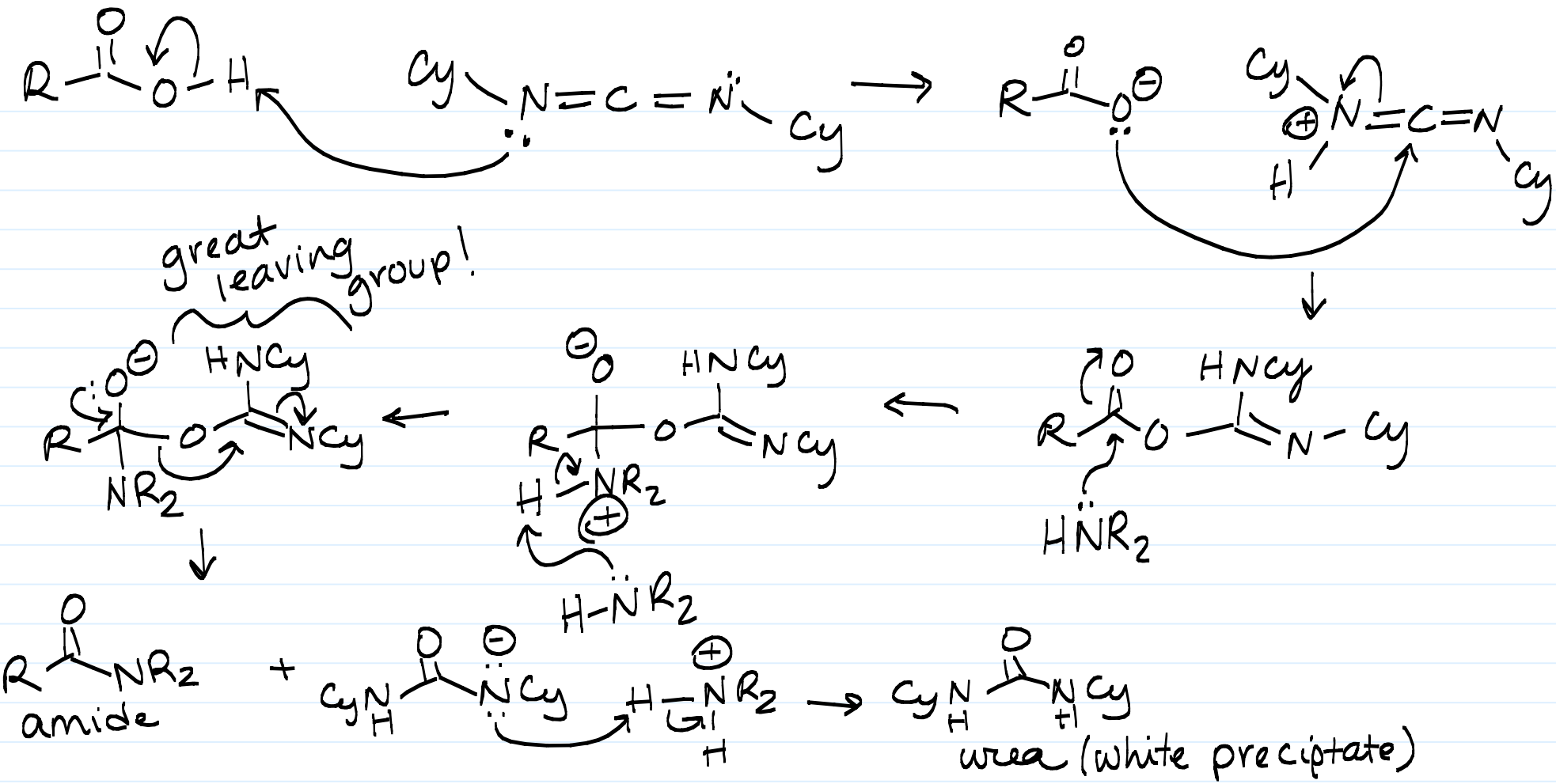
$O^{2\ominus}$ ← HORRIBLE LEAVING GROUP!!

Dicyclohexylcarbodiimide DCC

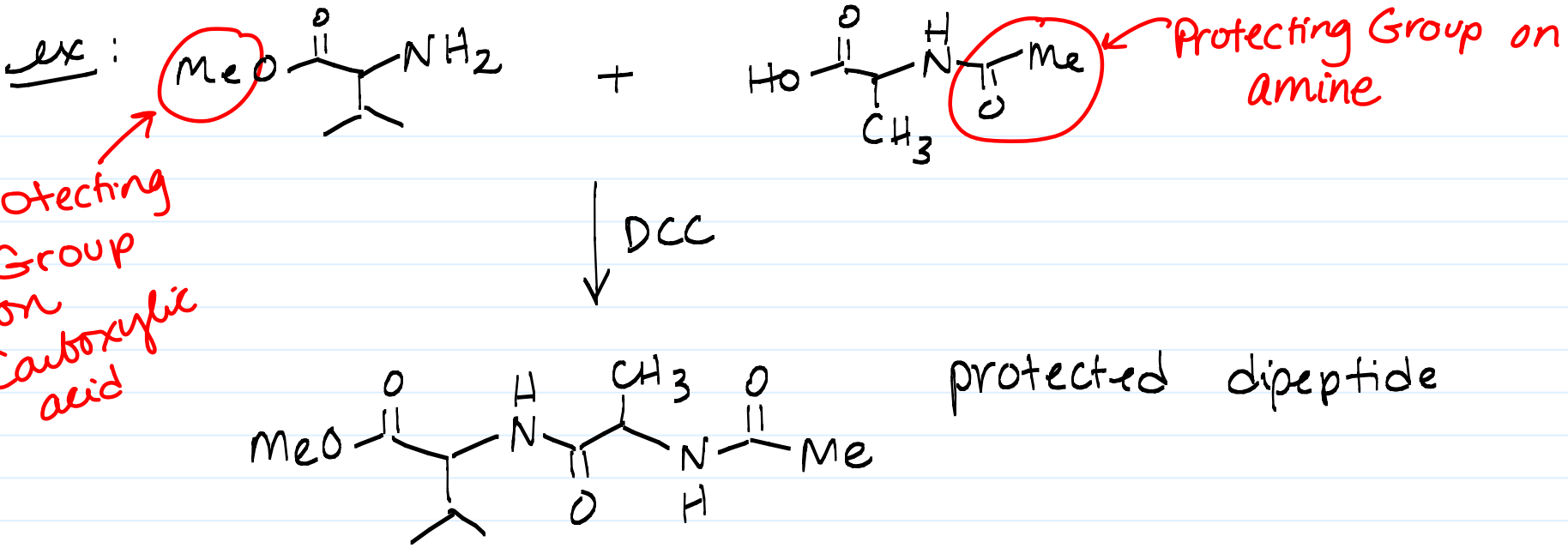


DCC Coupling to Form Amides




great leaving group!
amide
urea (white precipitate)

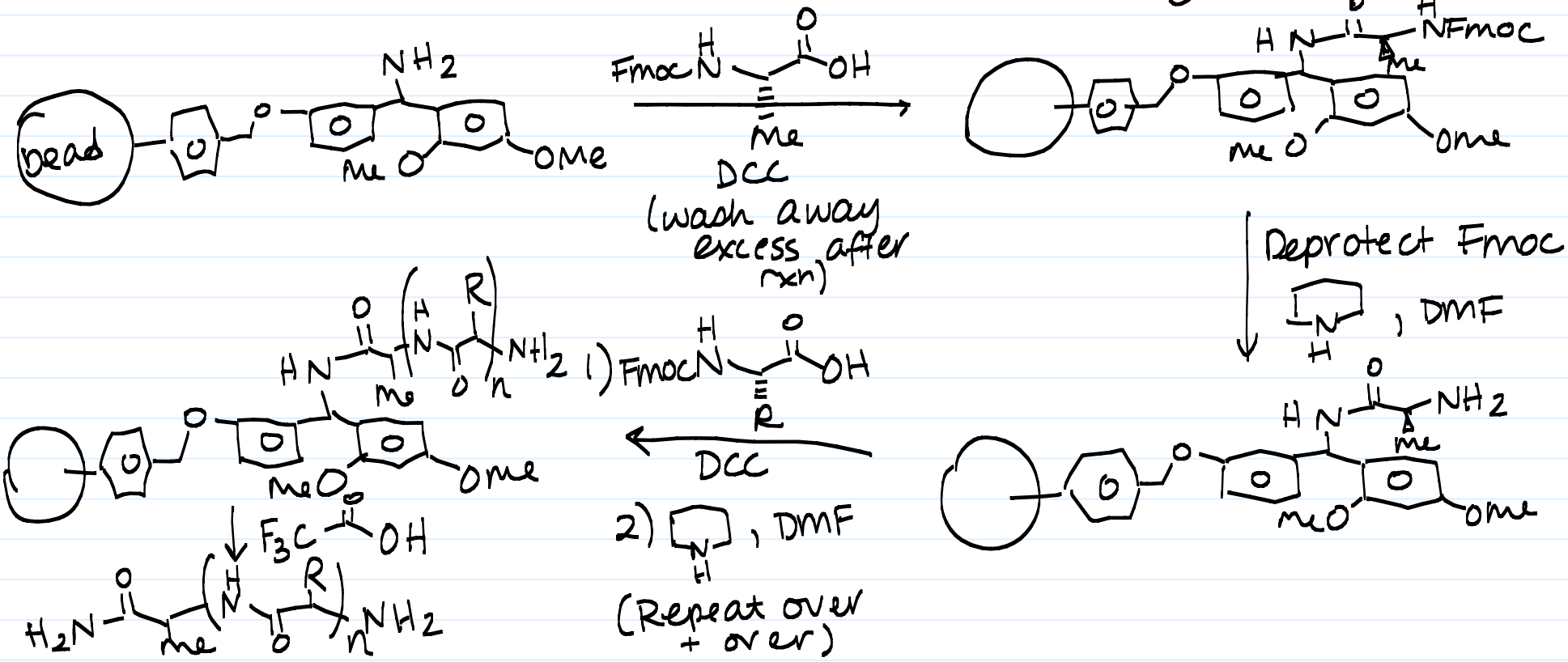
ex:

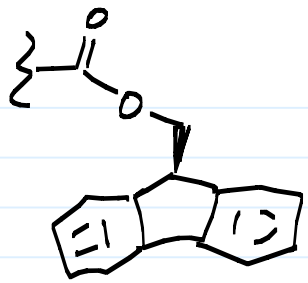


protected dipeptide

DCC couplings are efficient enough that you can do Solid Phase Peptide Synthesis (SPPS)... and a machine can even do it for you!!

Solid Phase Peptide Synthesis (SPPS) - Pioneered by Bruce Merrifield

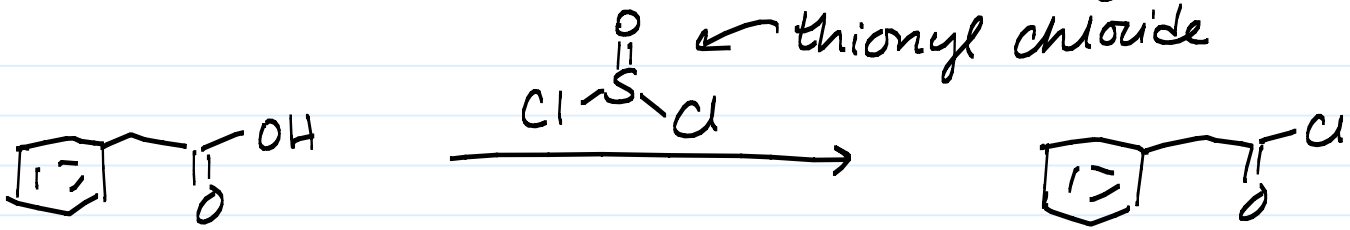


Fmoc = 

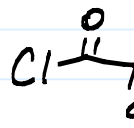
Note: $n \leq 70$. Making longer peptides with this technology is problematic... yields are too low for each step.

SPPS transformed the way that we make peptides... Changes what we can make + the types of questions we can ask.

Formation of Acid Chlorides (or Acyl chlorides)



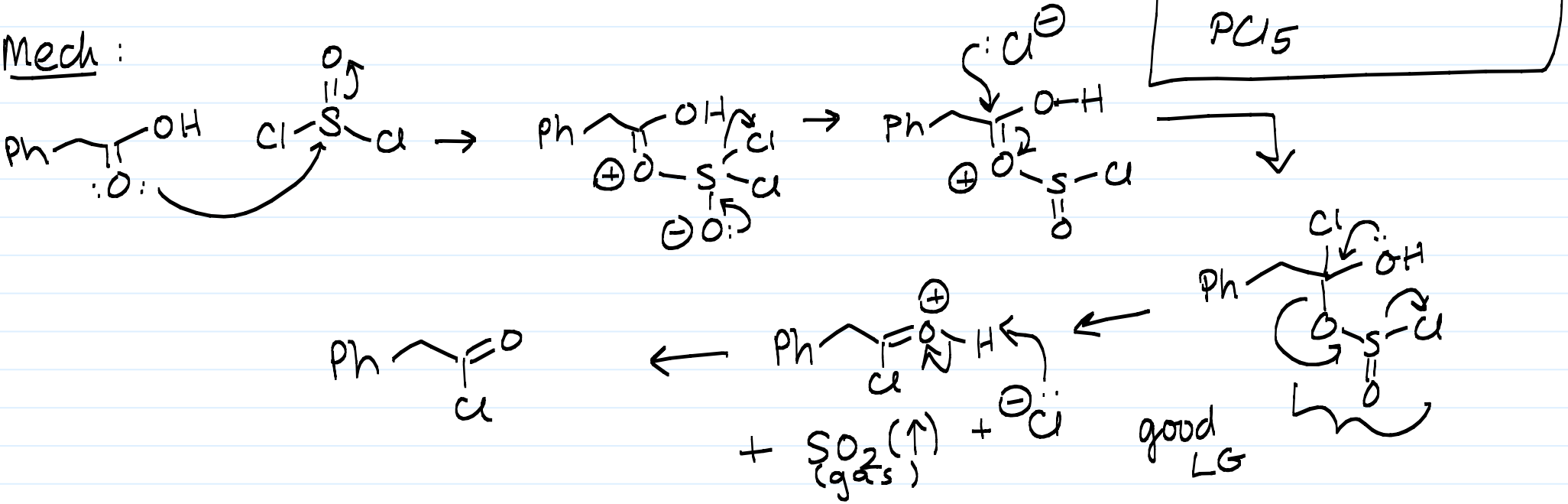
Other reagents you can use:



(oxalyl chloride)

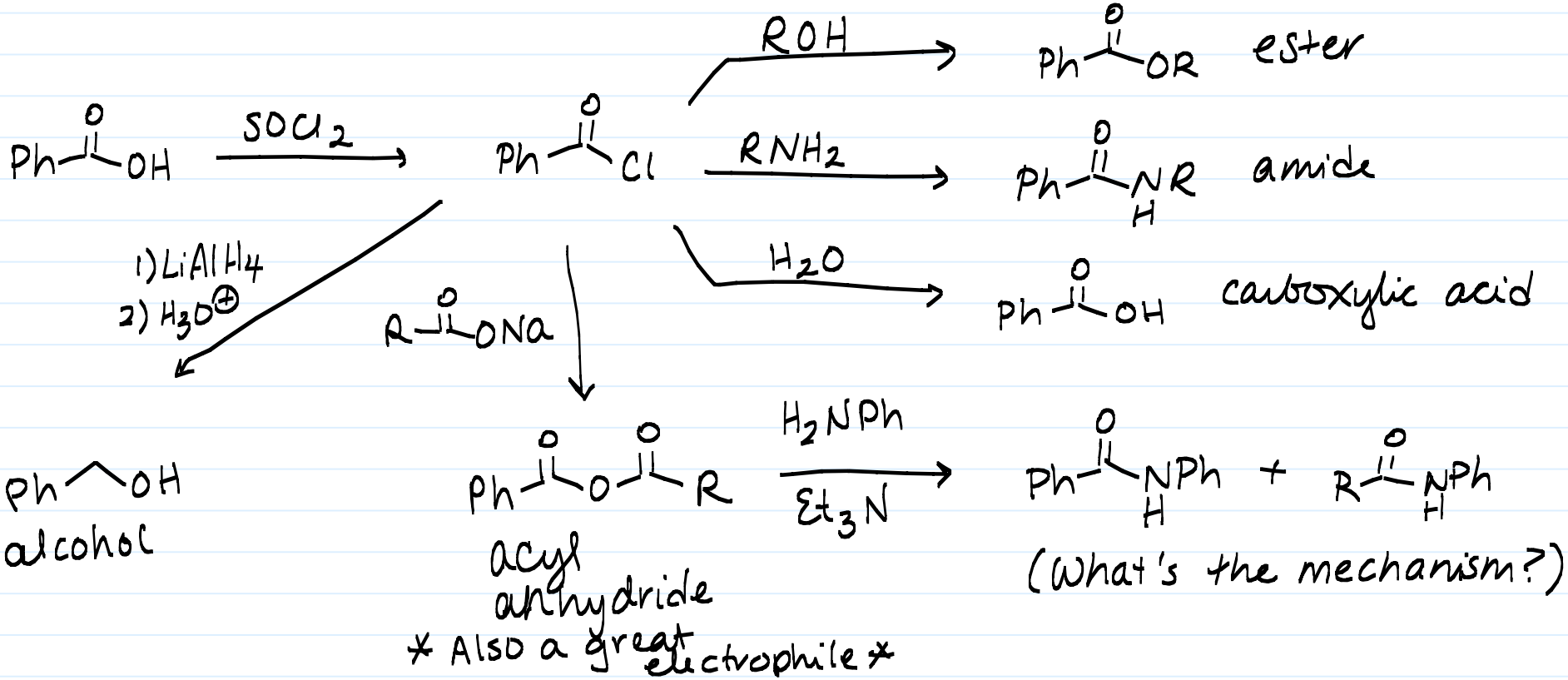
PCl_5

Mech:

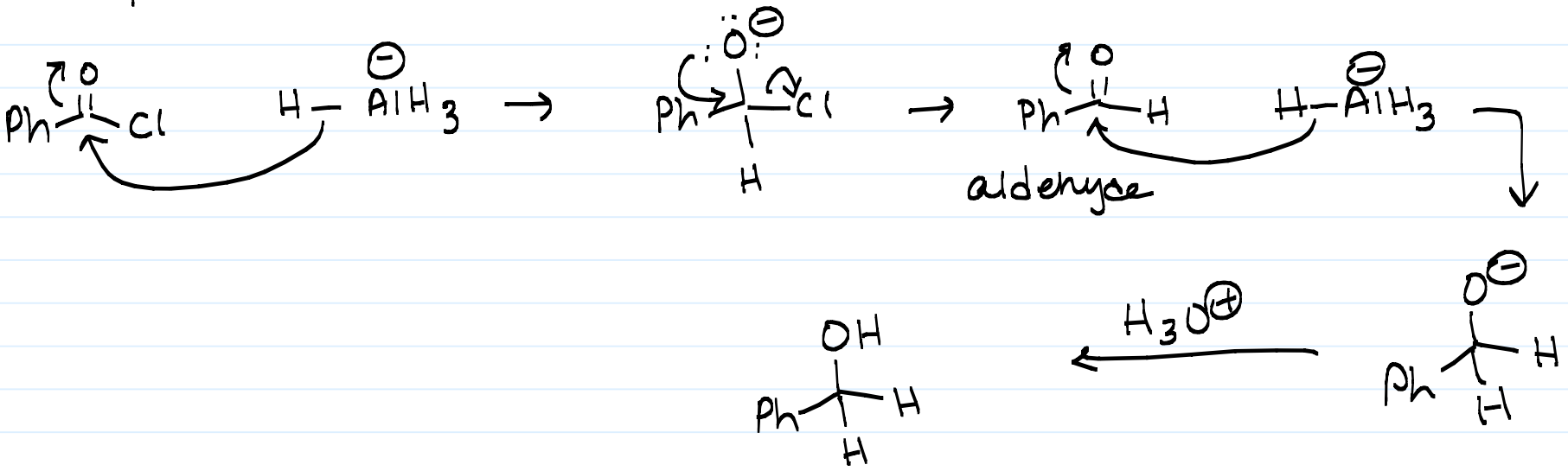


Reactions of Acid Chlorides

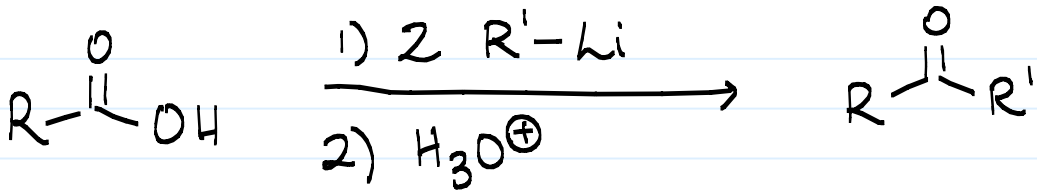
Recall: Acid chlorides in Electrophilic Aromatic Substitution Rxns.



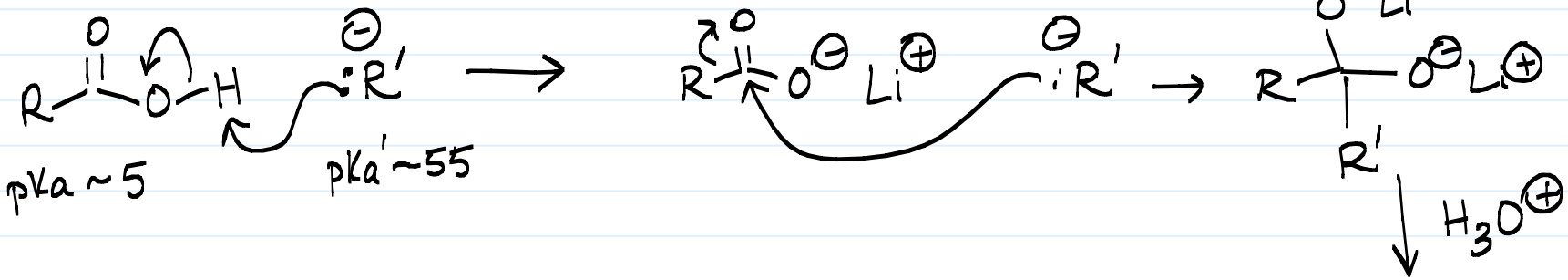
Mech of $LiAlH_4$ Rxn:

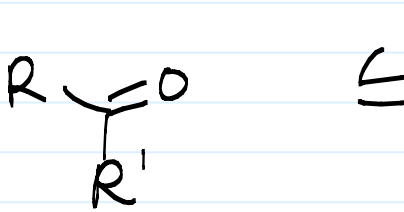


Reaction of Carboxylic Acids w/ RLi

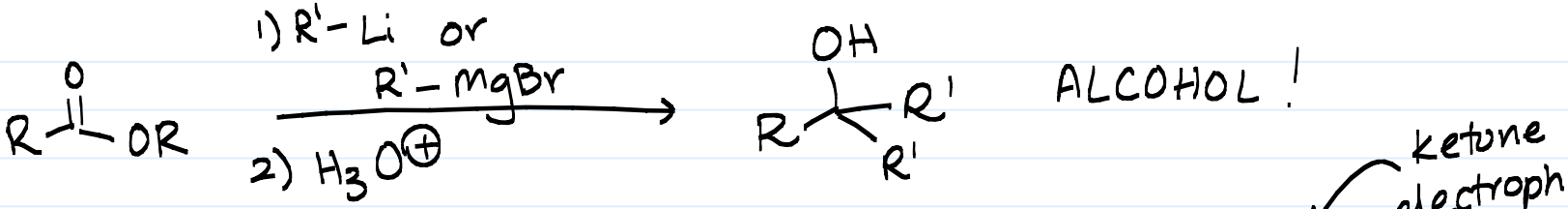


Mech:

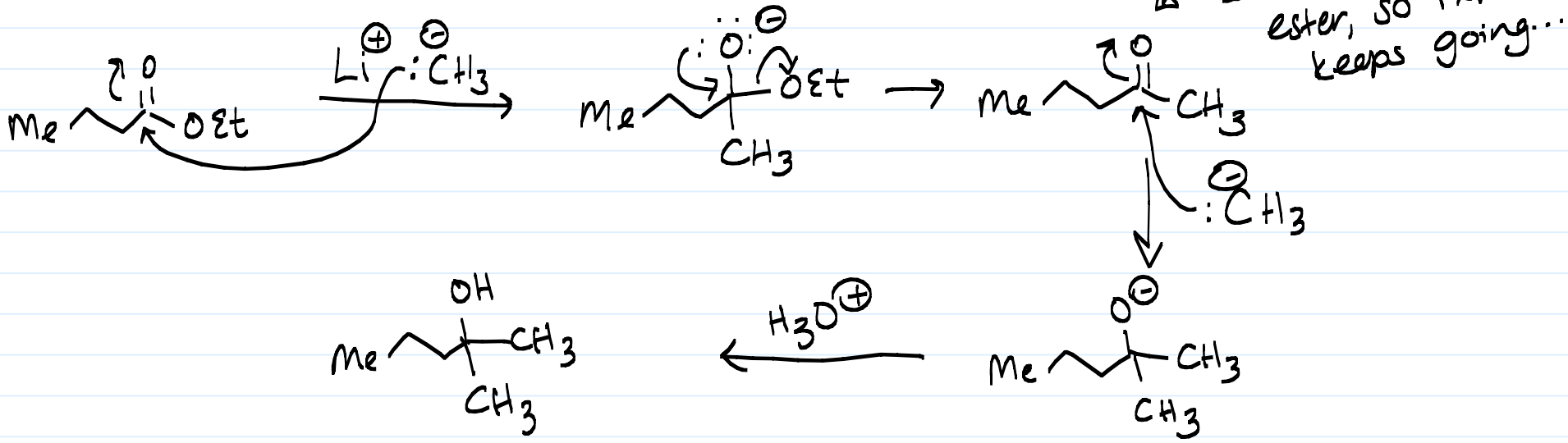




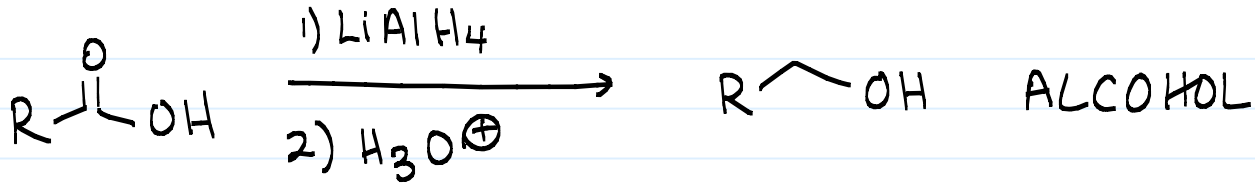
You can also add R'-Li to esters, but you get a different product...



ex:



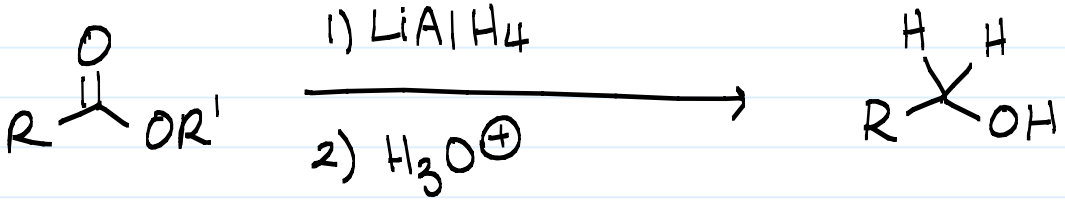
Rxns of Carboxylic Acids w/ $LiAlH_4$



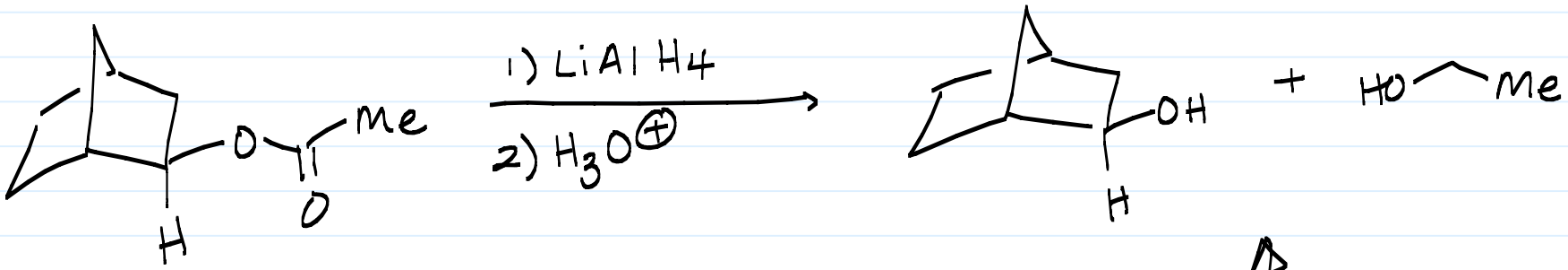
Mech is similar to rxns w/ RLi, but not fully known.
See p. 858 for our best guess.

Can also add $LiAlH_4$ to esters...

Esters + $LiAlH_4$



ex:



* Practice drawing the mechanism of this rxn *