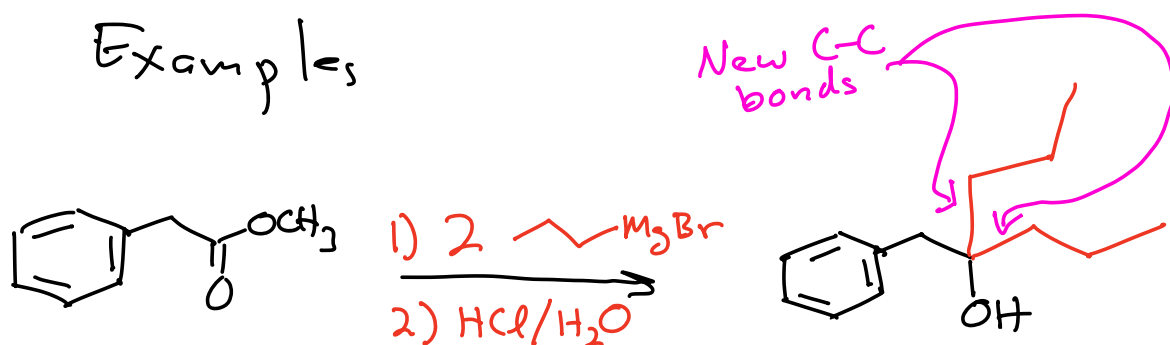
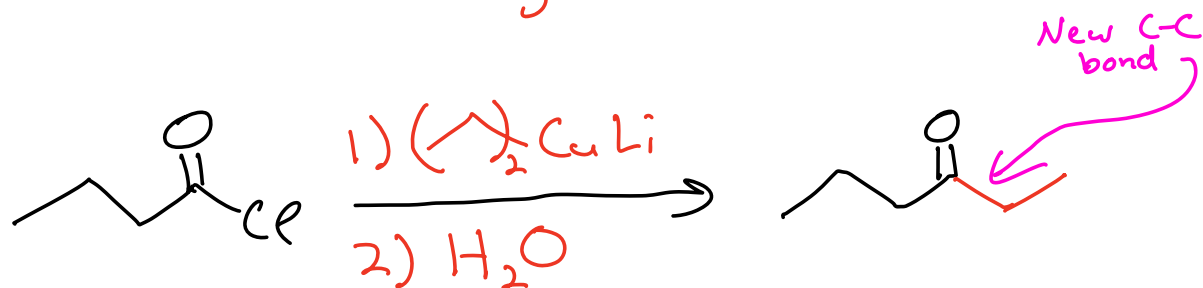


## Examples



Great new reaction  $\rightarrow$  Not responsible for the mechanism

$\rightarrow$  Reacting an acid chloride with a Gilman reagent to give a ketone



KRE  $\rightarrow$  A new C-C bond next to the C=O of a ketone

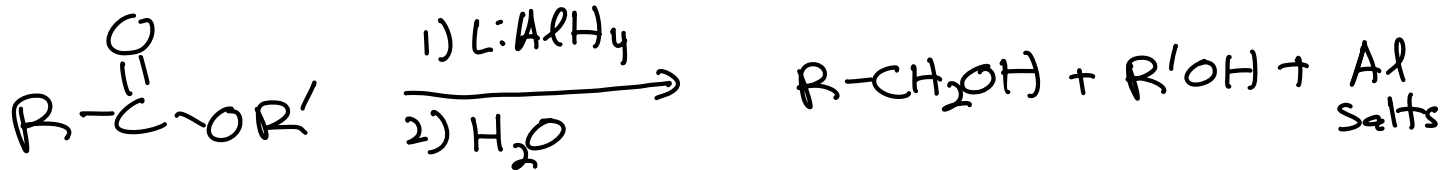


Warning → These two reactions are specific → DO NOT "mix and match"

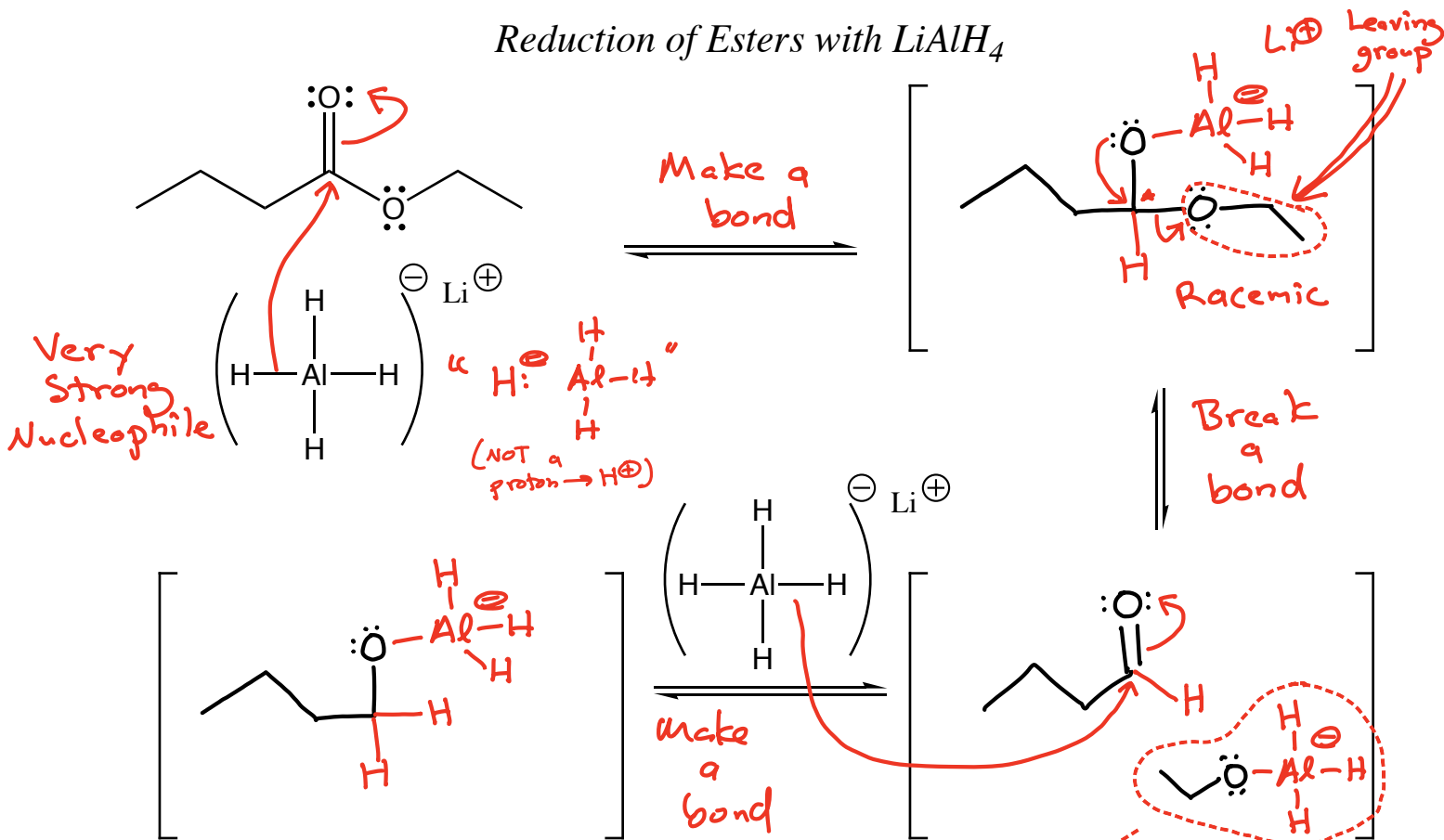
Grignard + Ester → Alcohol

Gilman + Acid Chloride → Ketone

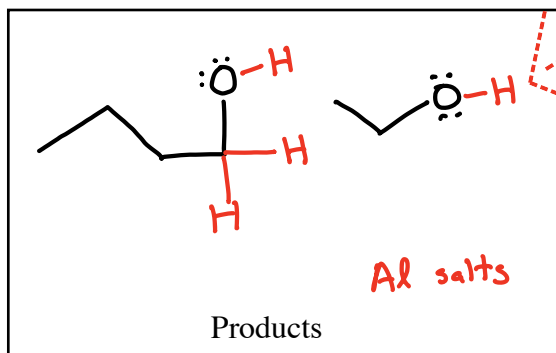
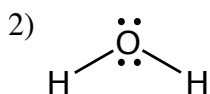
~~Grignard + Acid Chloride  
or  
Gilman + Ester~~



Reduction of Esters with  $LiAlH_4$



Chemist Opens Flask

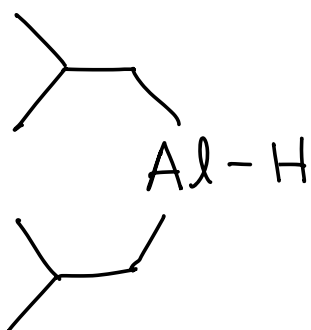


Just keeping track of this product

KRE → converts an ester into two alcohols → breaks C-O bond

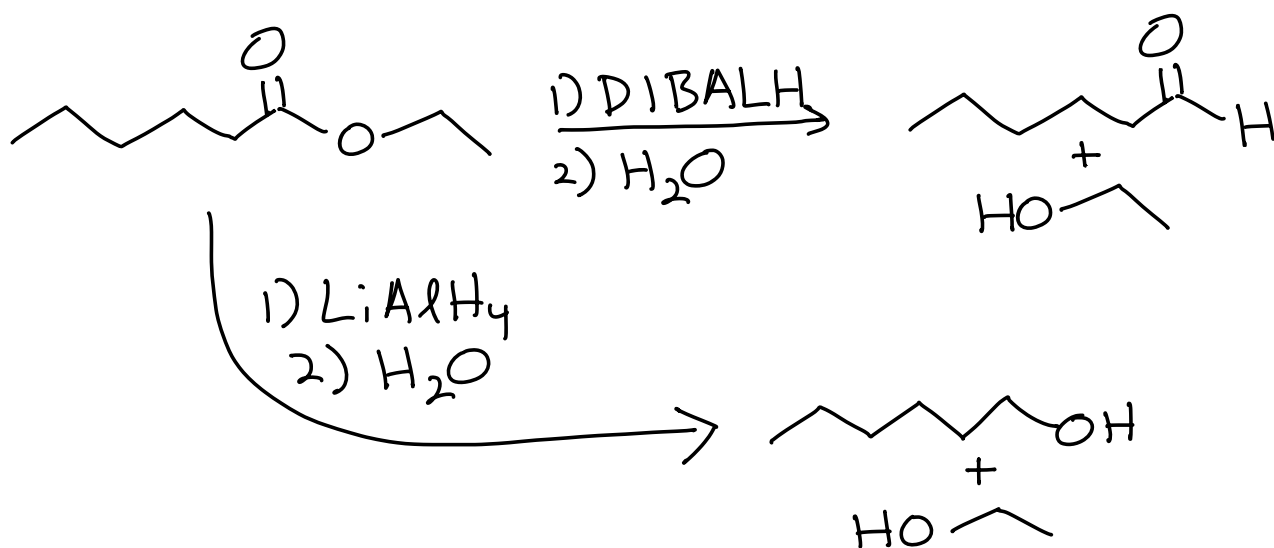
Note the extreme similarities between these last two mechanisms!

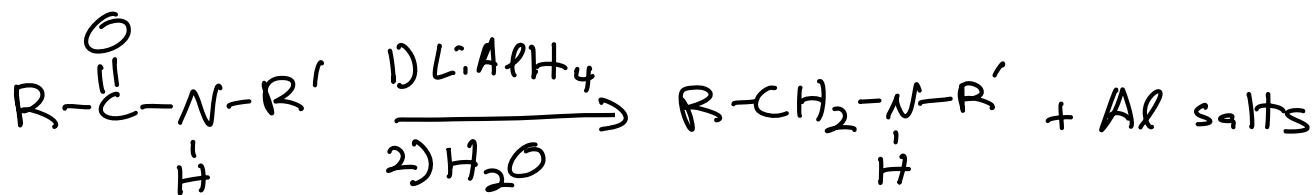
Note: An aldehyde is produced as an intermediate when esters react with  $\text{LiAlH}_4$



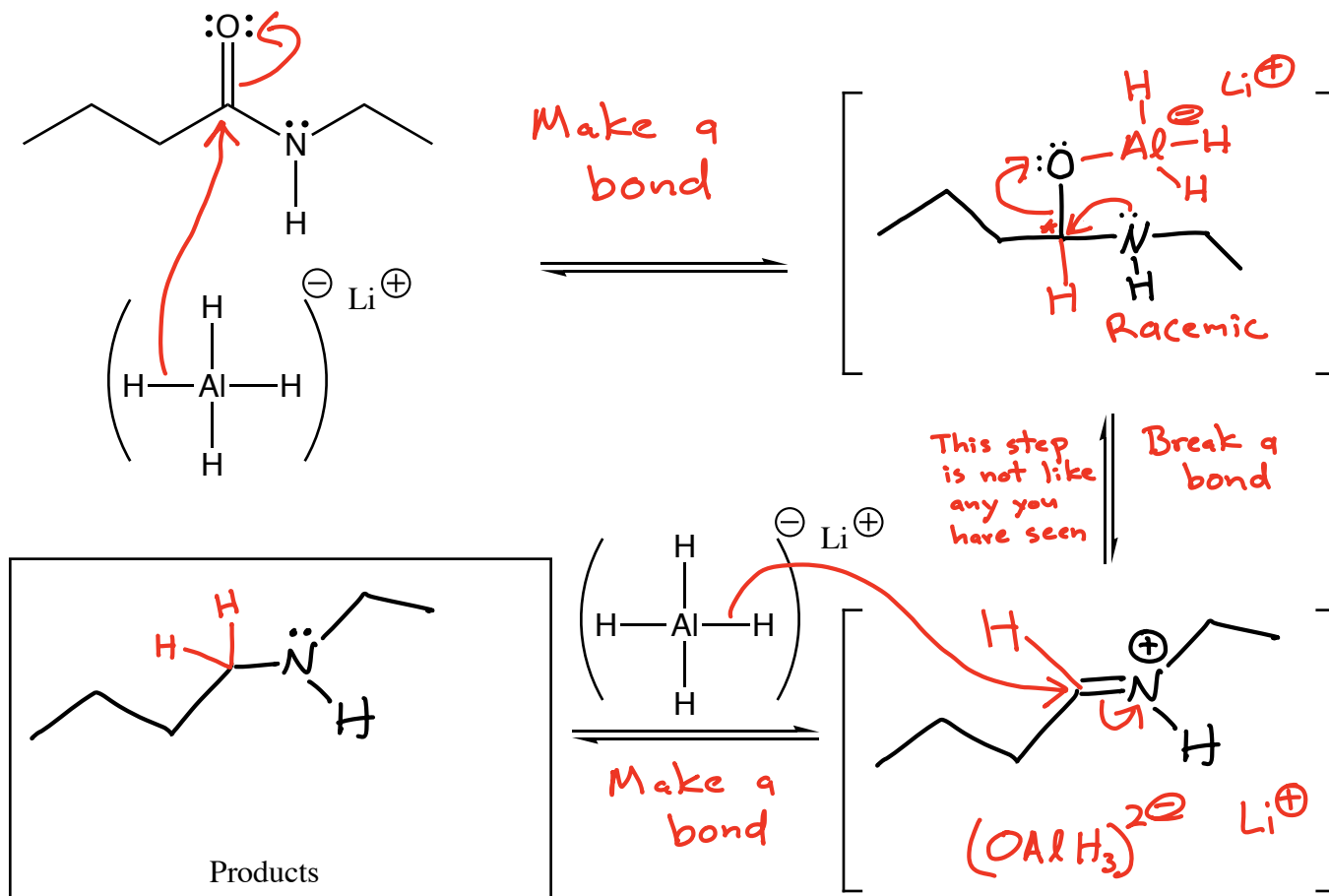
Diisobutylaluminum hydride  
DIBALH

Reaction stops  
at the aldehyde!

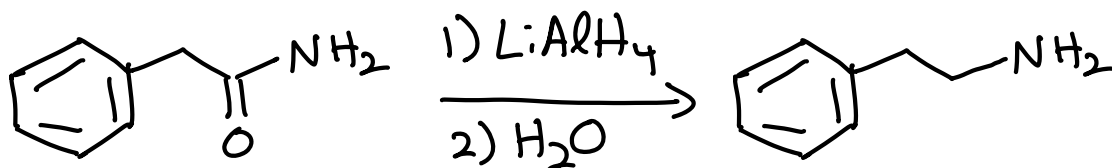




Reduction of Amides with  $LiAlH_4$



Note: In this reaction the chemist opens the flask and adds water in a second step that quenches any excess  $LiAlH_4$ . Therefore, you need a second step to add water when using this reaction in synthesis even though it is not shown in the mechanism above.





	Acid Chloride	Anhydride	Ester	Amide
	$R-\overset{\text{O}}{\parallel}{C}-Cl$	$R-\overset{\text{O}}{\parallel}{C}-O-\overset{\text{O}}{\parallel}{C}-R$	$R-\overset{\text{O}}{\parallel}{C}-O-R'$	$R-\overset{\text{O}}{\parallel}{C}-\underset{\text{R}''}{\text{N}}-R'$
Leaving Group	$:\ddot{Cl}:^{\ominus}$	$^{\ominus}:\ddot{O}:\overset{\text{O}}{\parallel}{C}-R$	$^{\ominus}:\ddot{O}-R'$	$^{\ominus}:\ddot{N}-R'$ $\text{R}''$
Conjugate Acid	$H-Cl$	$HO-\overset{\text{O}}{\parallel}{C}-R$	$H-O-R'$	$H-\underset{\text{R}''}{\text{N}}-R'$
pK <sub>a</sub>	-7	3-5	16	38

← Anion Stability

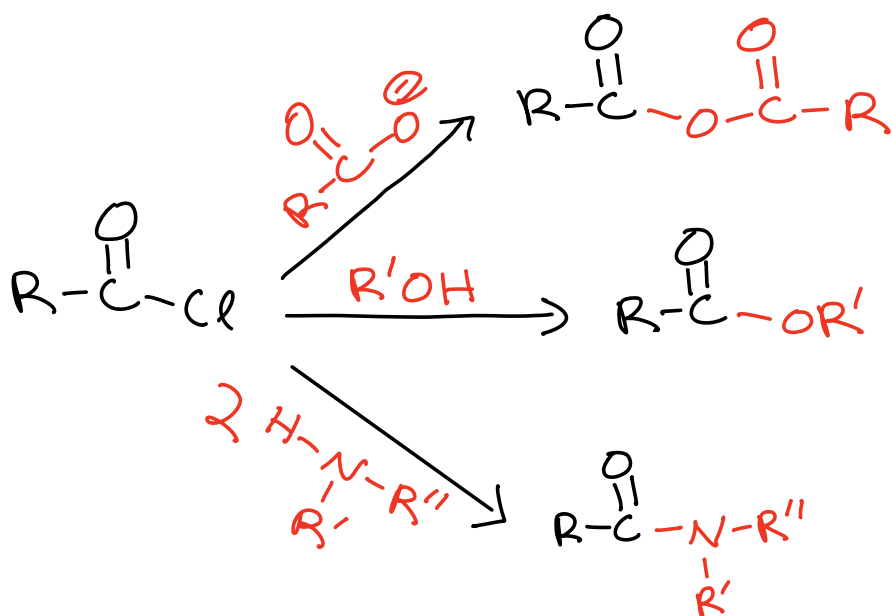
← Better Leaving Group Ability

← Reactivity of Carboxylic Acid Derivative

Think of carboxylic acid derivatives  
 $\Rightarrow$  C=O with a leaving group attached

Here is the big rule → You can make any of the less reactive carboxylic acid derivatives from any of the more reactive carboxylic acid derivatives using the appropriate nucleophiles

Note: Acid chlorides and anhydrides spontaneously react with nucleophiles at room temperature, esters usually need some heat.

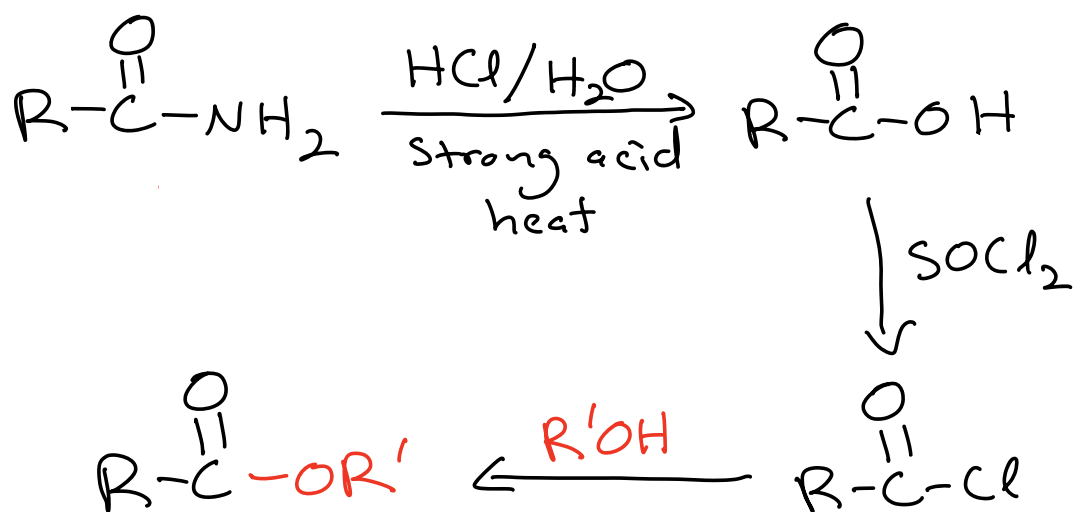






However: You can make a less stable carboxylic acid derivative from a more stable carboxylic acid derivative, but only if you:

- 1) You hydrolyze the carboxylic acid derivative to the carboxylic acid
- 2) You react the carboxylic acid derivative with  $\text{SOCl}_2$  to make an acid chloride



Interconversion of Carboxylic Acid Derivatives

