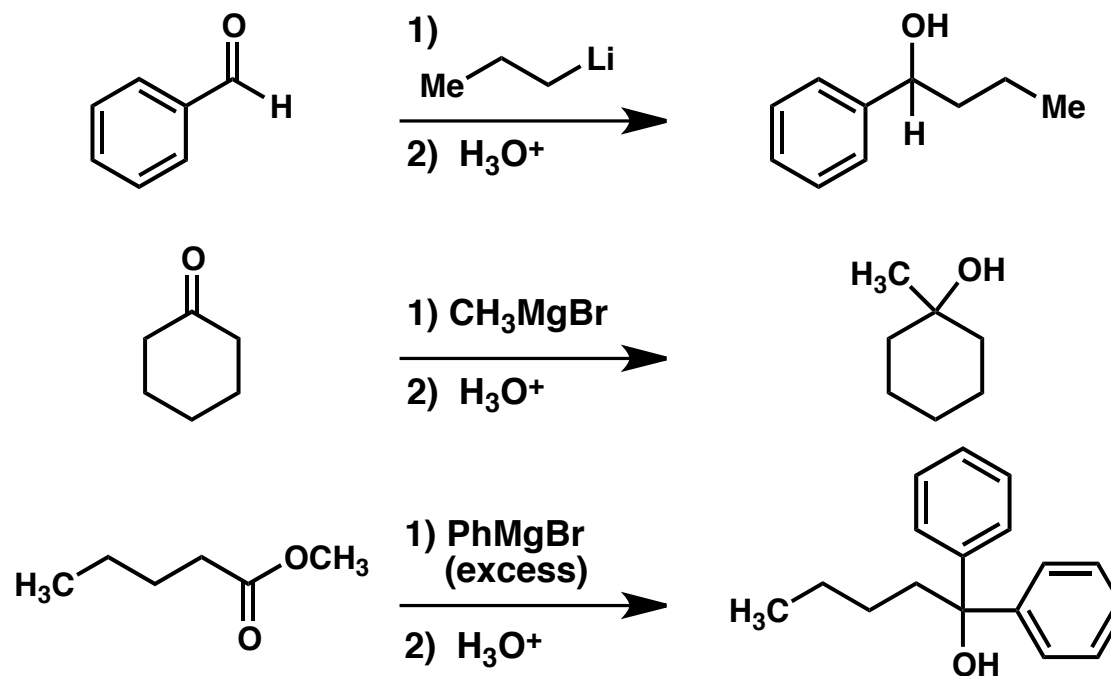


From Last Time

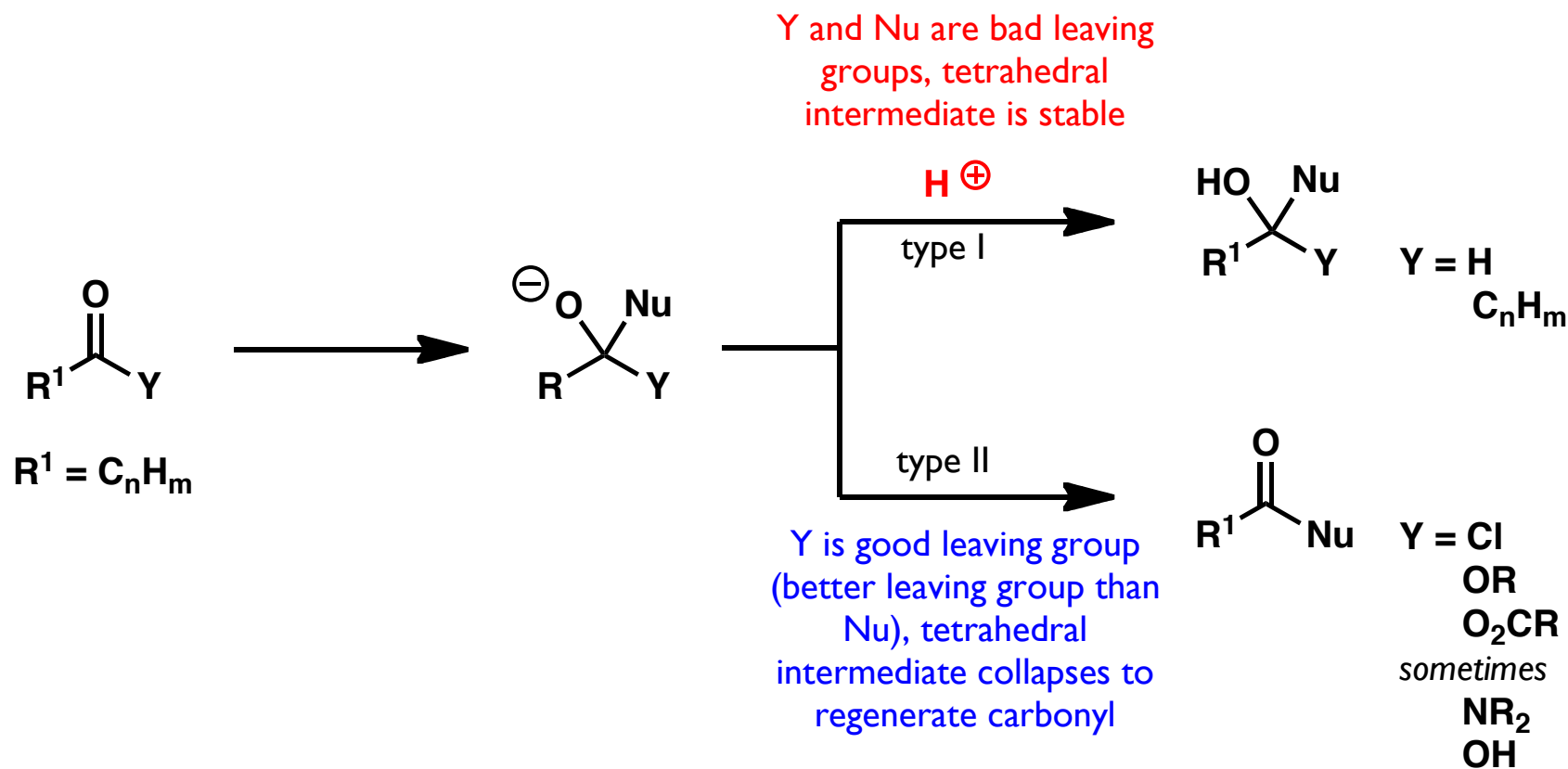
Organometallic reagents: when carbon is bound to electropositive metals (such as Mg or Li), the covalent bond is highly polarized. It reacts as a carbanion, and is both nucleophilic and basic.

- Remember: organometallic reagents are strong bases, and will **deprotonate** acidic protons (particularly O-H, N-H, and S-H bonds).



Divergent Reactivity in Carbonyl Addition Reactions

All carbonyl addition reactions can roughly be divided into two categories:



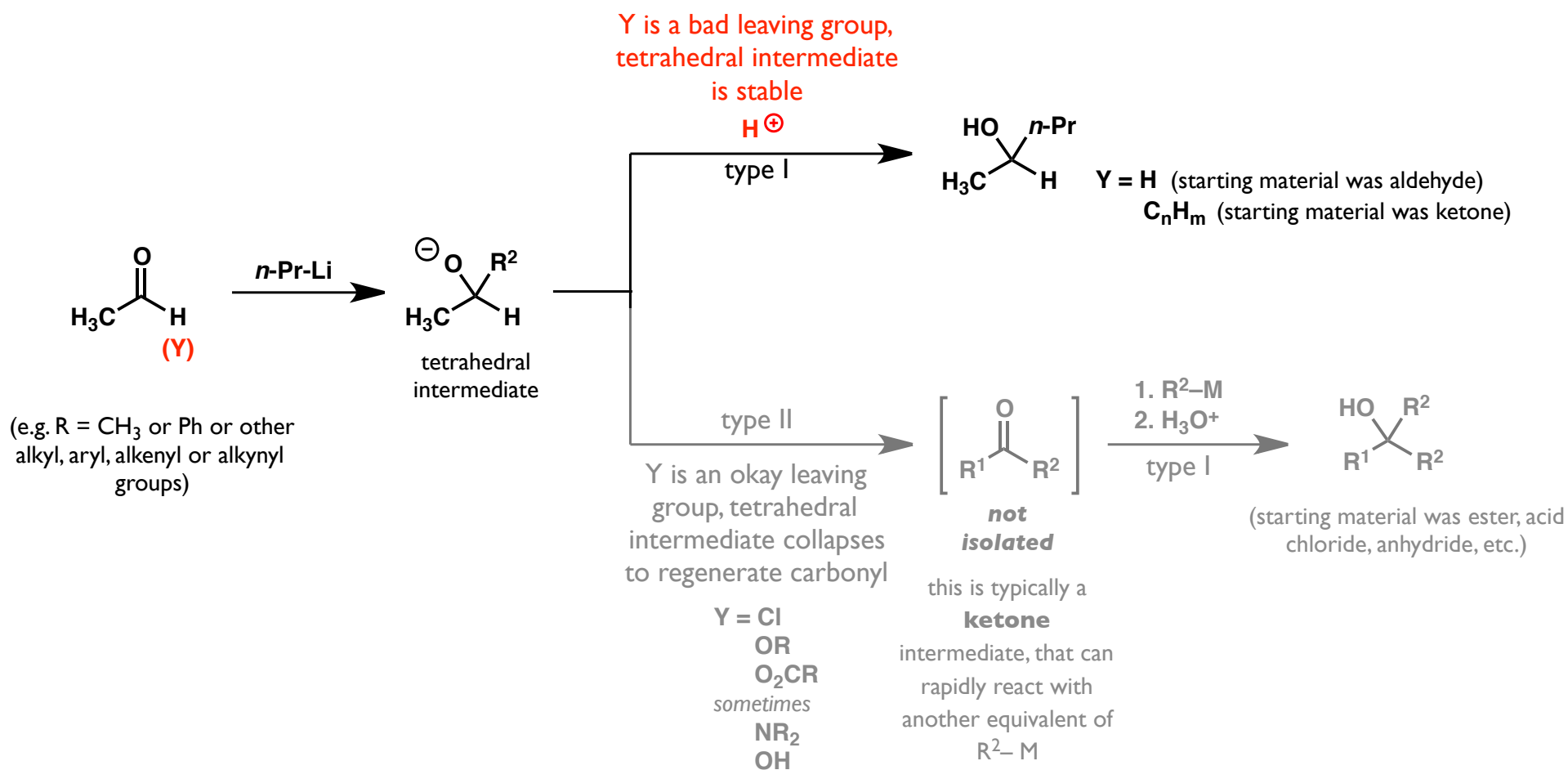
the fate of carbonyl additions depends on *both*:

- the nature of the carbonyl electrophile
- the nature of the nucleophile

Divergent Reactivity in Carbonyl Addition Reactions: Organometallic Nucleophiles

Guide to organometallic reactions

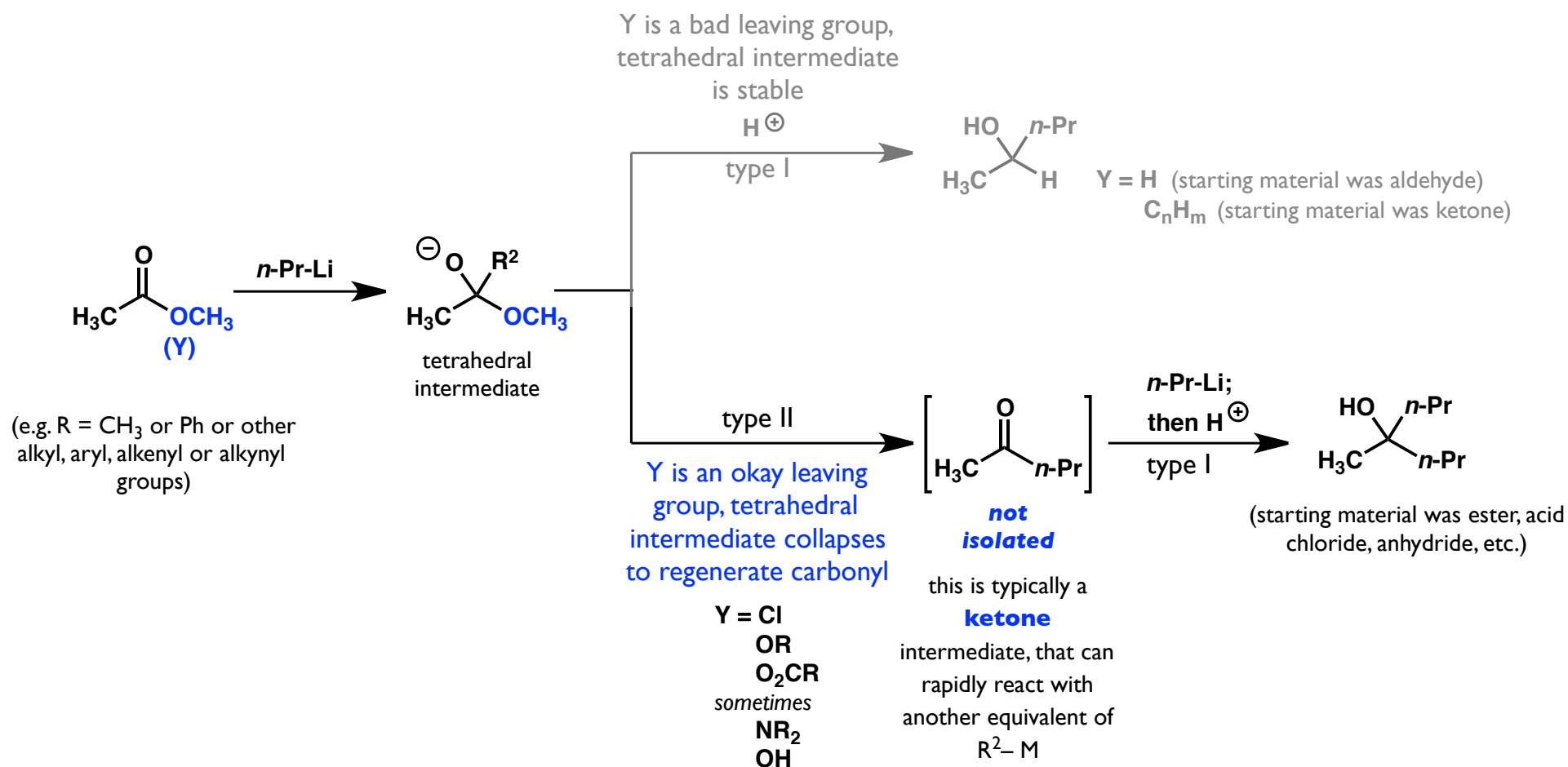
- note: organolithium and Grignard reagents are strong nucleophiles, C-C bond formation is *irreversible*



Divergent Reactivity in Carbonyl Addition Reactions: Organometallic Nucleophiles

Guide to organometallic reactions

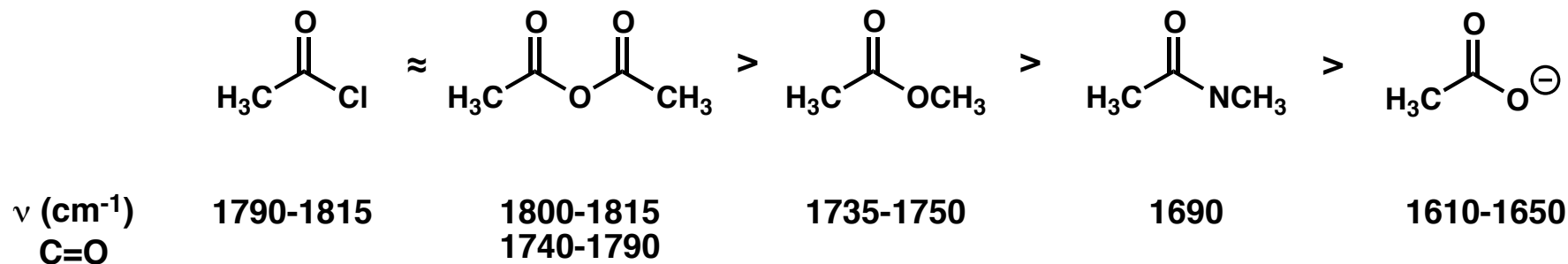
- note: organolithium and Grignard reagents are strong nucleophiles, C-C bond formation is *irreversible*



Follow Up Slide: Reactivity of Carbonyl Compounds

Recall from Lecture 20: substituent effects that influence the electrophilicity of carbonyl compounds

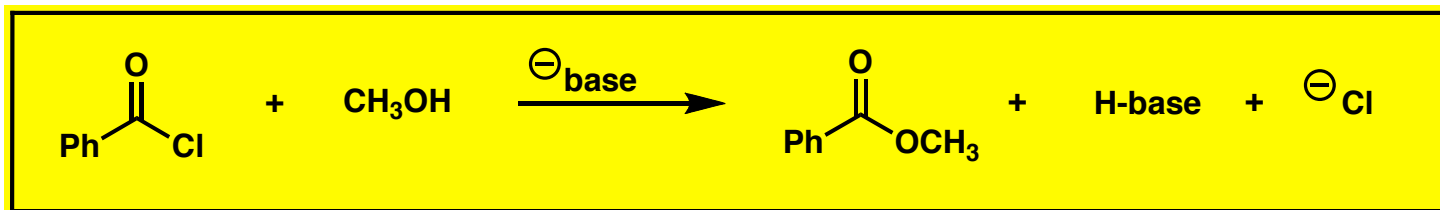
- resonance donation
- inductive effects



Formation of Esters and Amides from Acid Chlorides

Acid chlorides react rapidly with alcohols or amines

- the reaction proceeds by formation of a tetrahedral intermediate



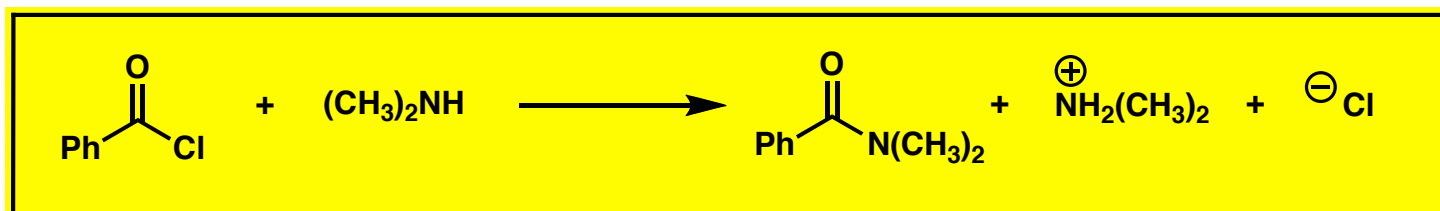
arrow-pushing mechanism:

- weaker nucleophiles (i.e. not organometallics) result in reversible first step
- “addition-elimination” mechanism

Formation of Esters and Amides from Acid Chlorides

Acid chlorides react rapidly with alcohols or amines

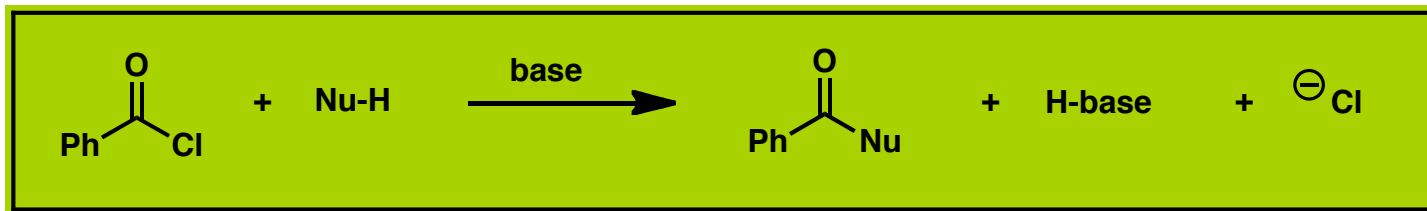
- the reaction proceeds by formation of a tetrahedral intermediate



arrow-pushing mechanism:

- weaker nucleophiles (i.e. not organometallics) result in reversible first step
- “addition-elimination” mechanism

A General Mechanism for Addition of Nucleophiles to Acid Chlorides

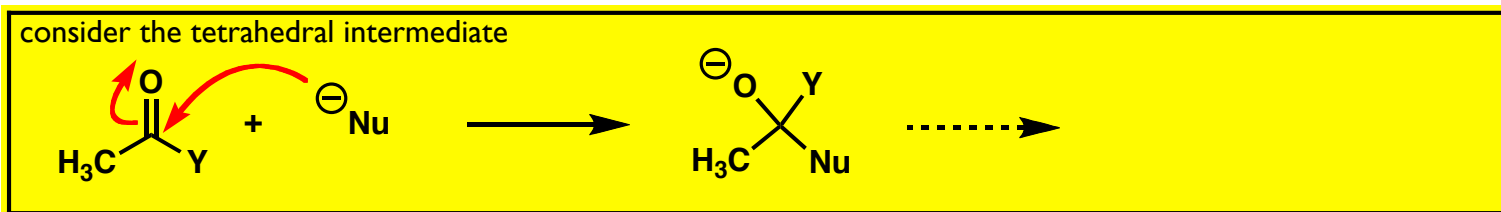


Key points:

- these are “Type II” carbonyl addition reactions
- initial addition of nucleophile is reversible
- proceeds through a “tetrahedral intermediate”
- the better “leaving group” is eliminated

What other carboxylic acids undergo addition/elimination reactions?

The Hierarchy of Carboxylic Acid Derivatives

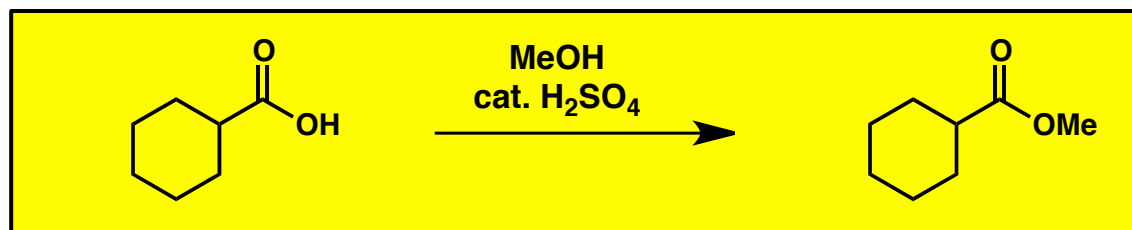


Lets consider some additional carboxylic acid derivatives:

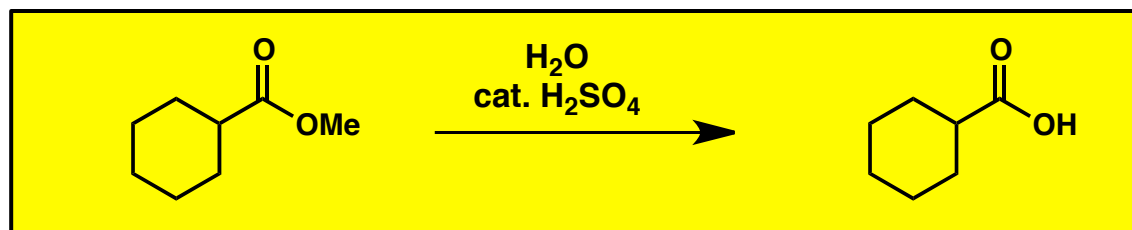
carboxylic acid derivative	leaving group	pK _{aH}
<chem>CC(=O)Cl</chem>		
<chem>CC(=O)OC(=O)C</chem>		
<chem>CC(=O)OC</chem>		
<chem>CC(=O)NC</chem>		

- electrophilicity and leaving group ability follow approximately the same trend

Acid Catalyzes the Formation of Esters from Carboxylic Acids



Acid also Catalyzes the Formation of Carboxylic Acids from Esters

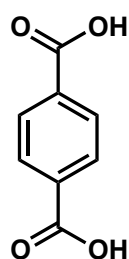


You Now Know How to Make Polyester

"terephthalic acid"

p-phthalic acid

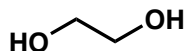
benzene-1,4-dicarboxylic acid



"ethylene glycol"

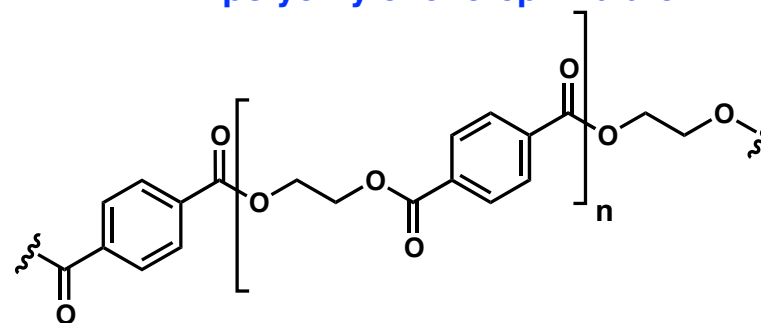
1,2-ethanediol

+



$-2n \text{ H}_2\text{O}$

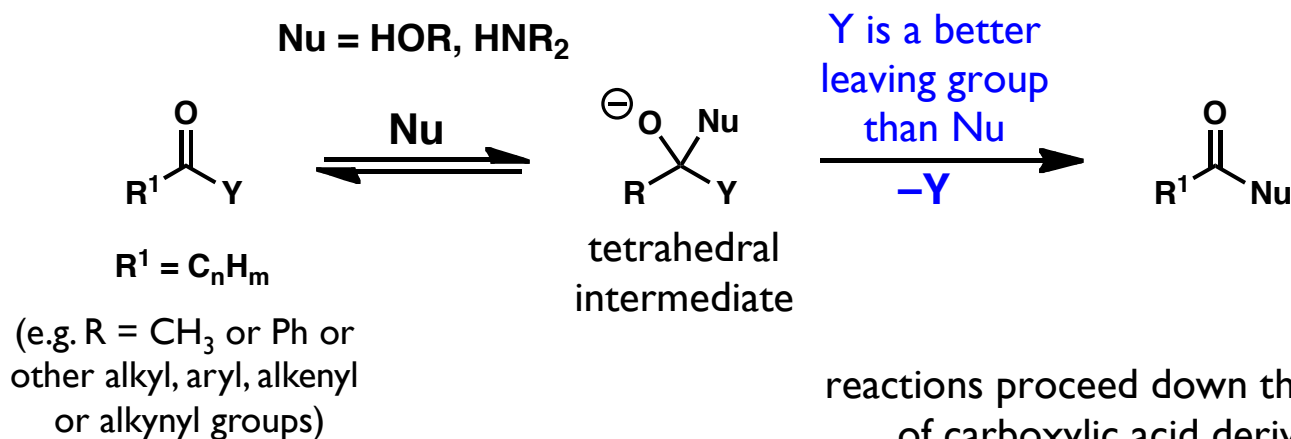
cat. H^+



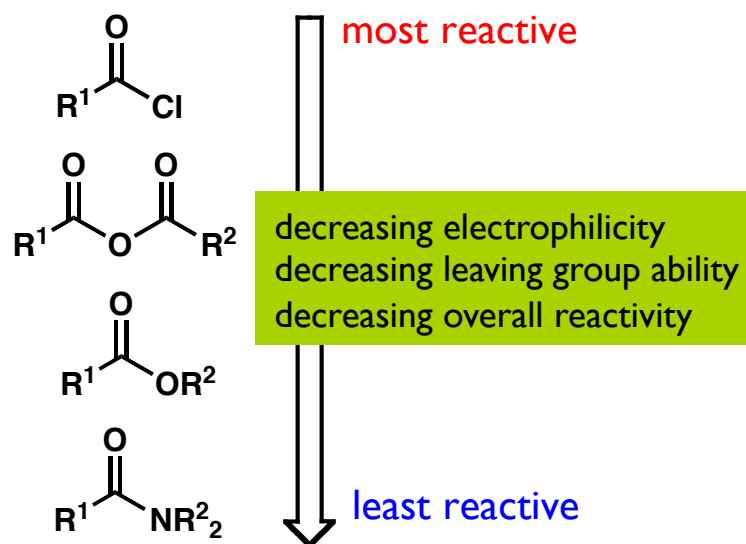
Recap: Nucleophilic *Substitution* at the Carbonyl

Guide to addition/elimination reactions

- note: HOR, HNR₂ are relatively weak nucleophiles



reactions proceed down the hierarchy of carboxylic acid derivatives



Must meet the following 3 conditions for reaction to occur:

- Y must be a better leaving group than Nu (otherwise the reverse reaction will dominate)
- Nu must be nucleophilic enough to attack R¹C(O)Y
- R¹C(O)Y must be electrophilic enough to react with Nu