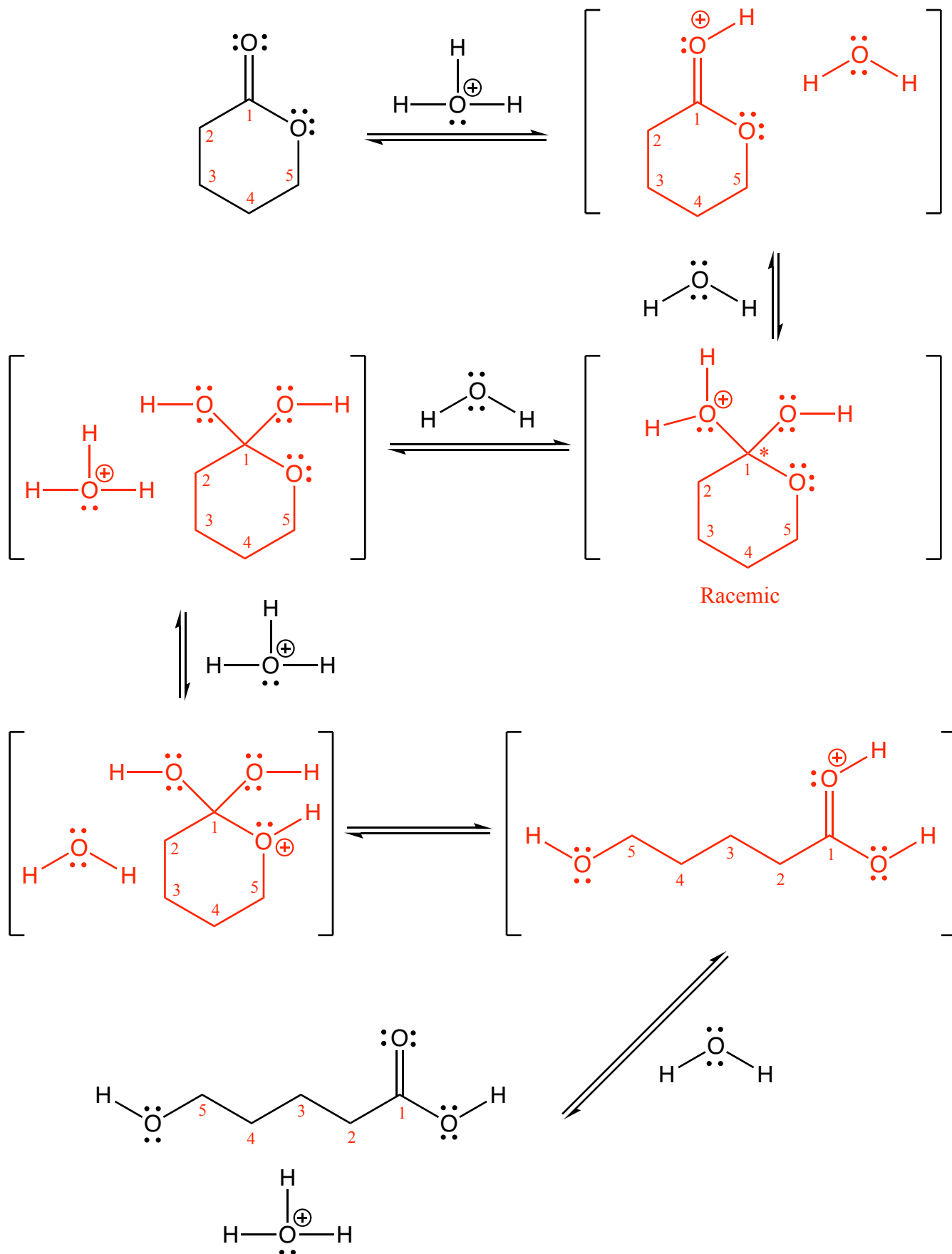
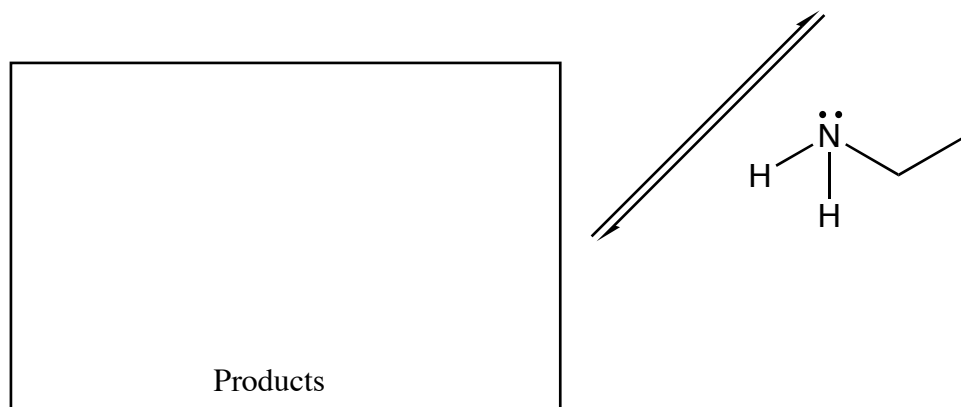
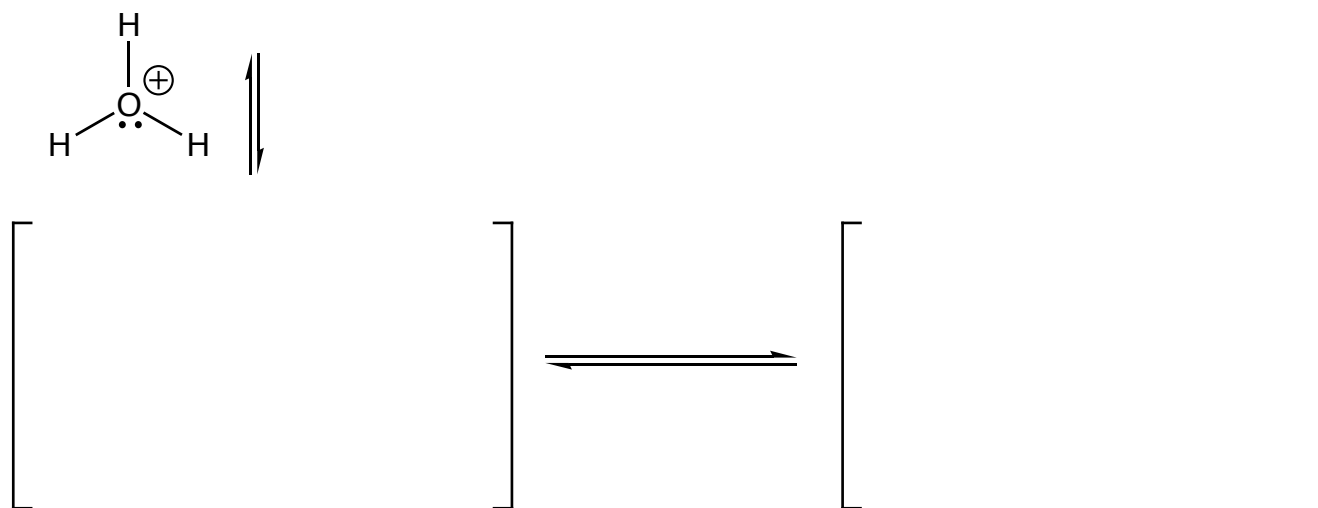
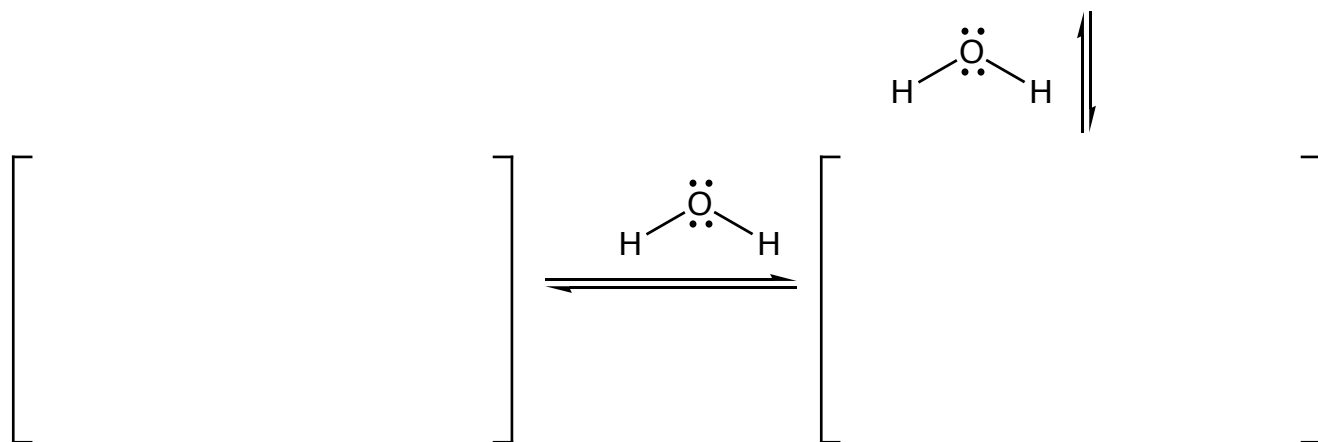
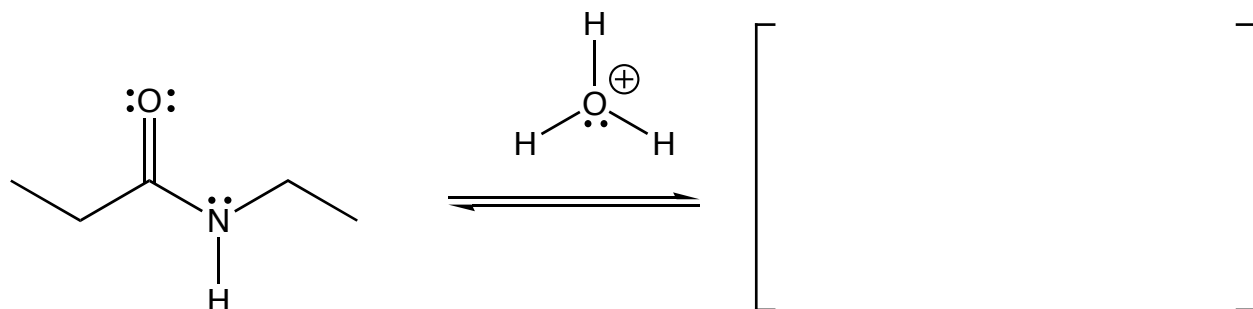
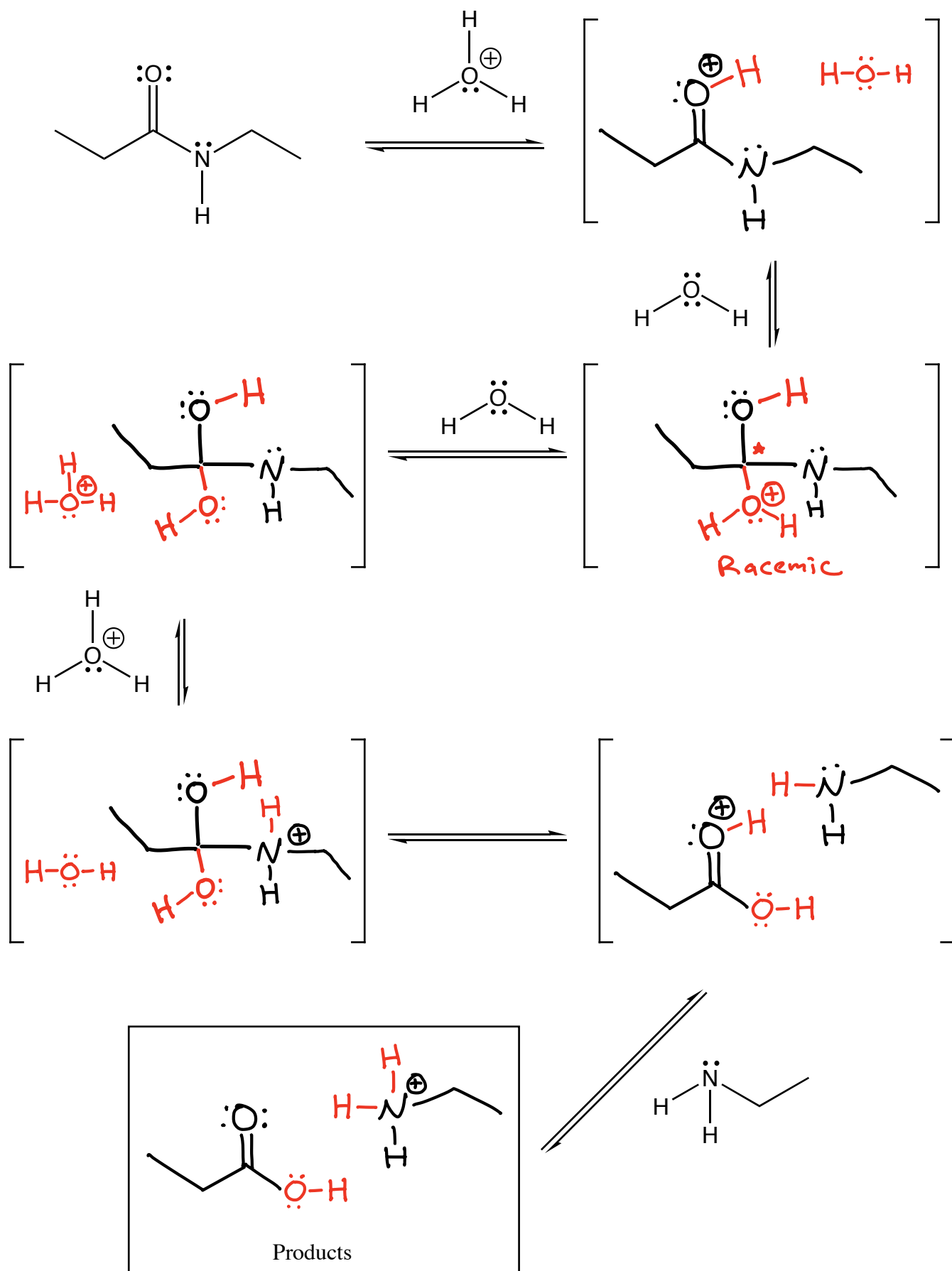
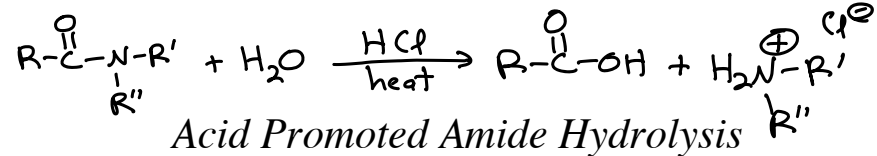


Microscopic Reversibility: Acid Catalyzed Ester Hydrolysis-Fischer Esterification

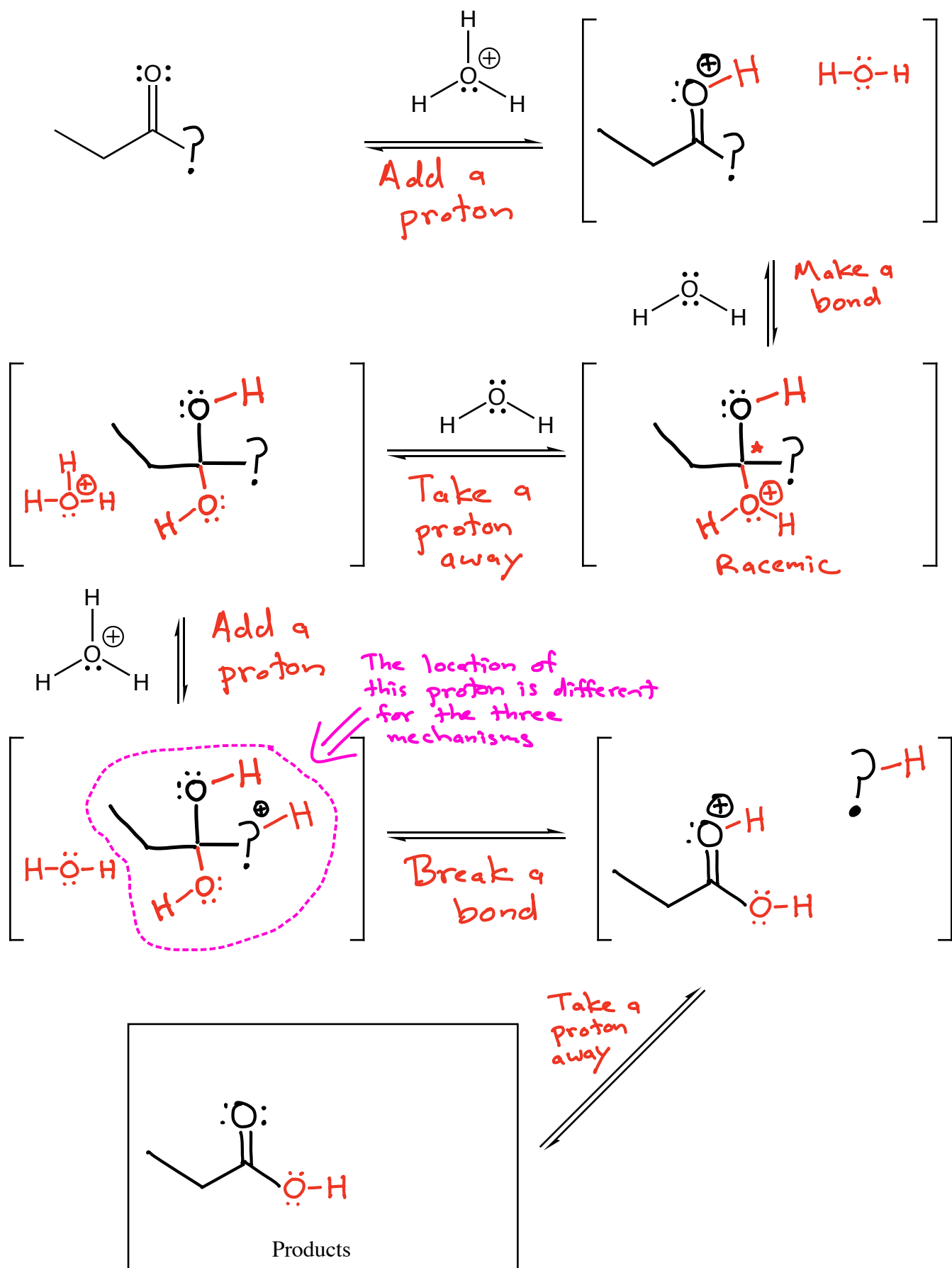


Acid Promoted Amide Hydrolysis

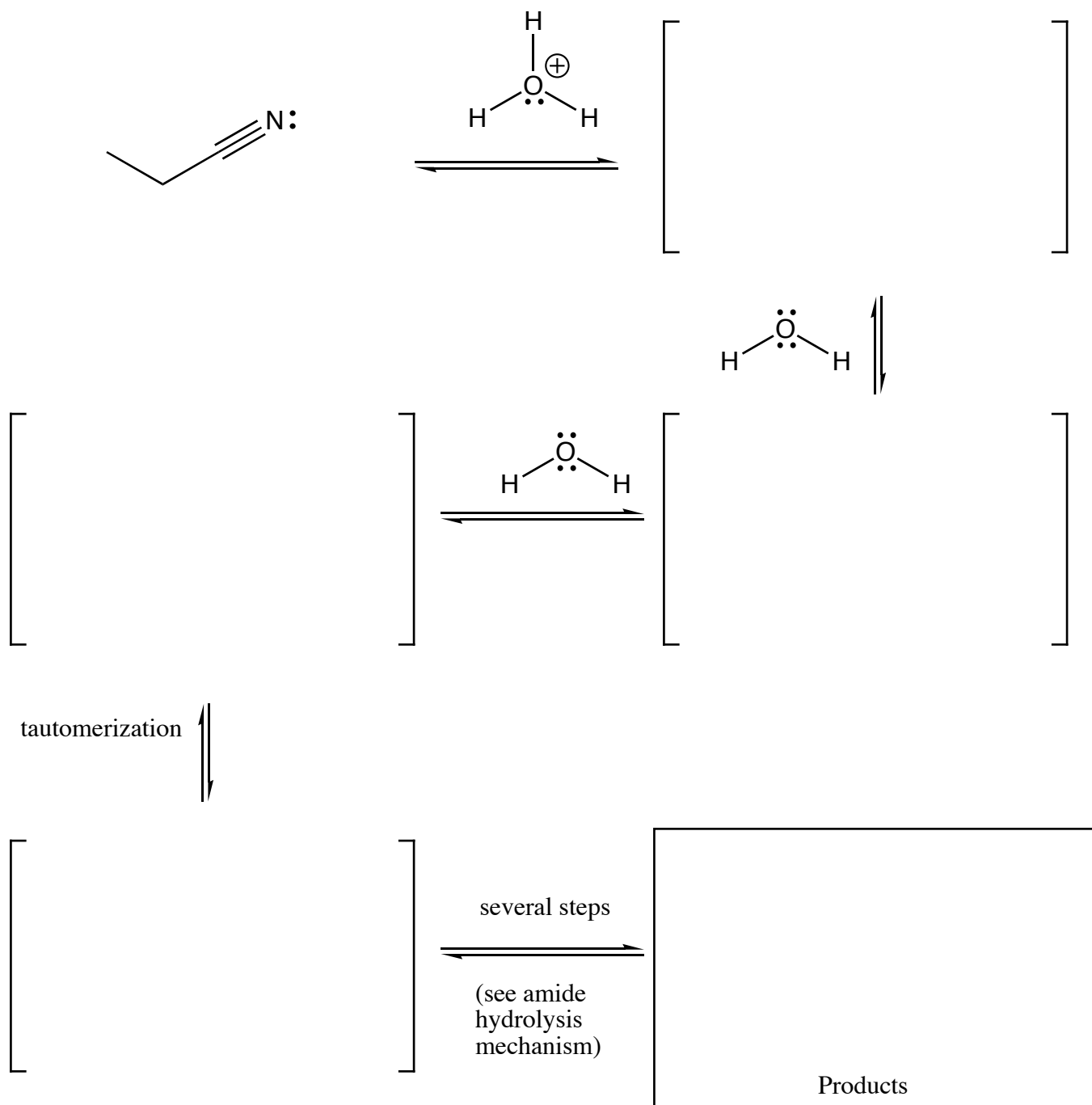




The following mechanism applies to which reaction we have seen?

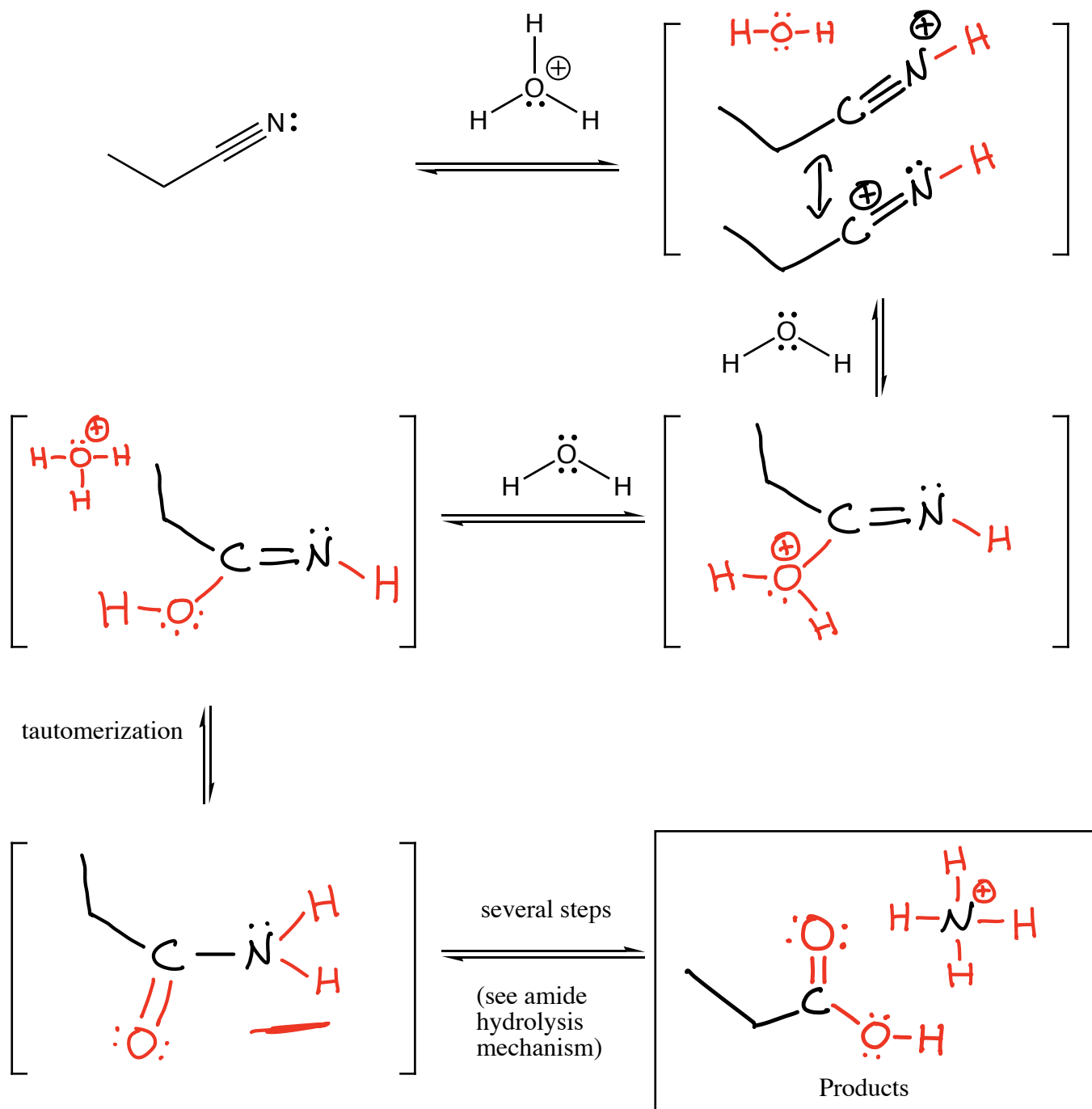


Acid Promoted Nitrile Hydrolysis

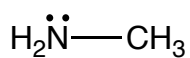
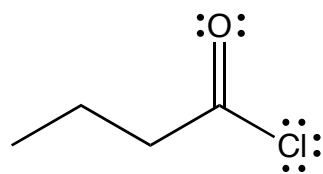




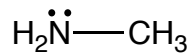
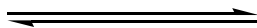
Acid Promoted Nitrile Hydrolysis



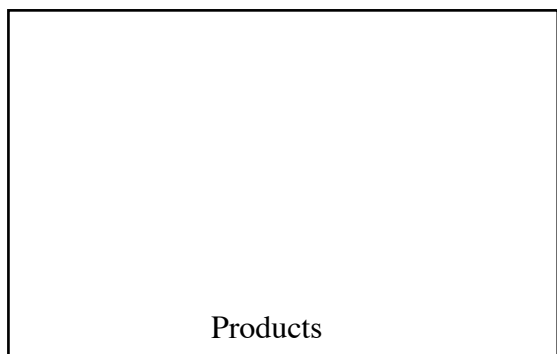
Acid Chlorides Reacting with Amines

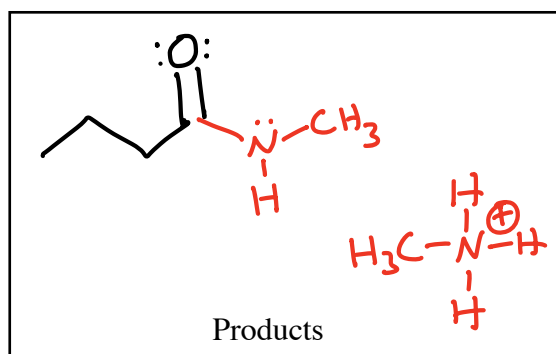
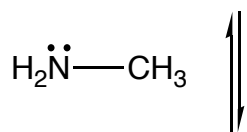
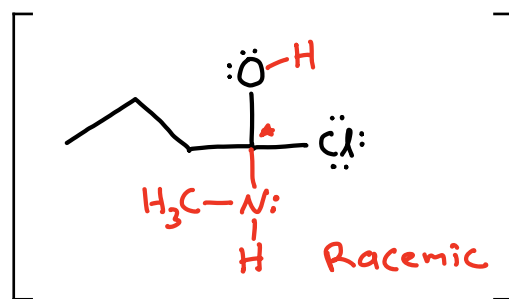
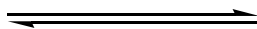
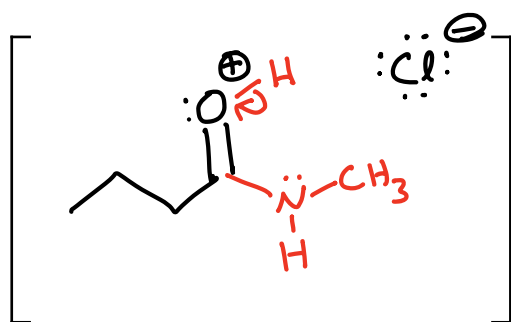
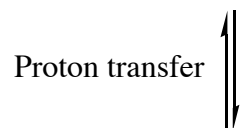
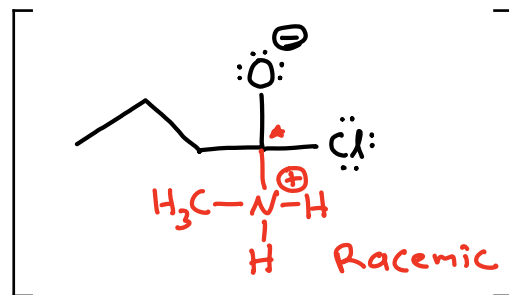
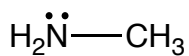
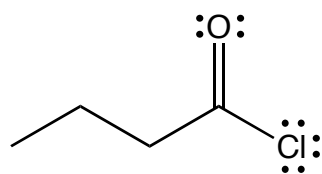
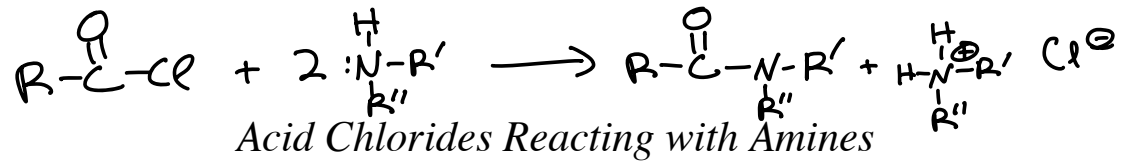


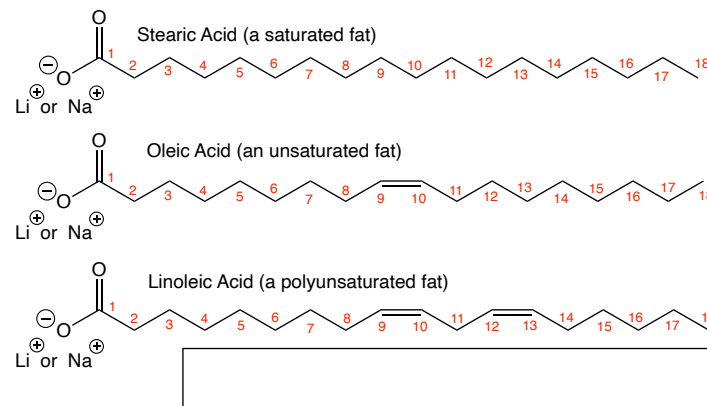
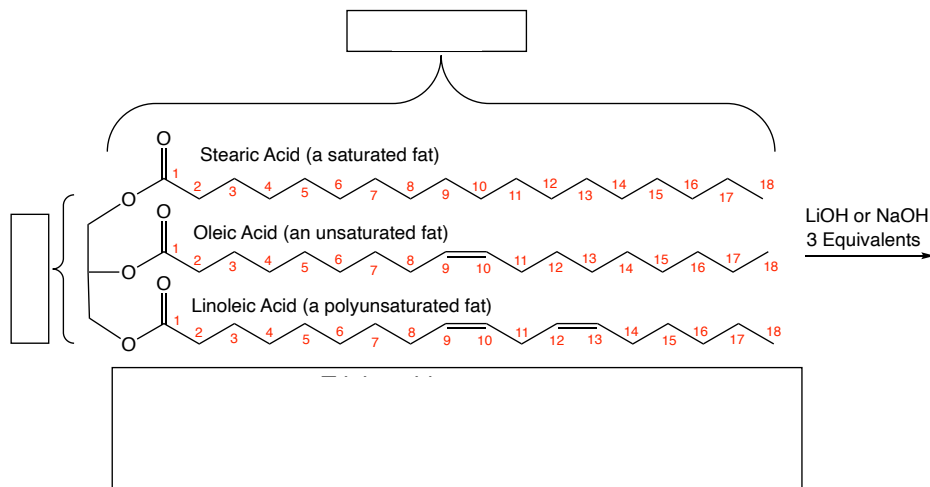
Proton transfer



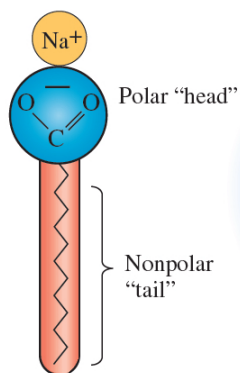
Products



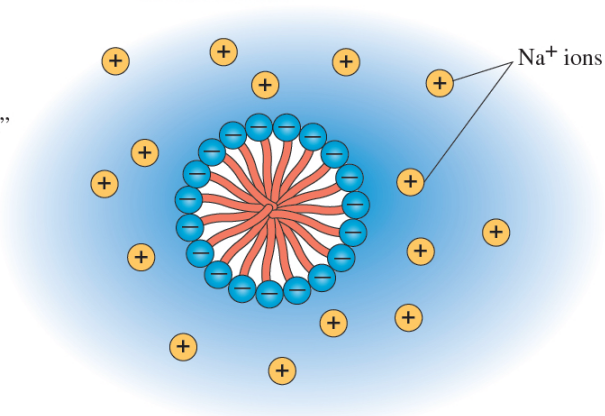




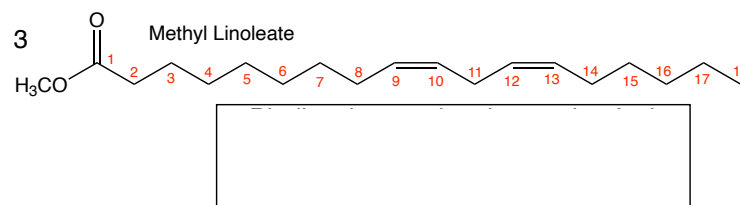
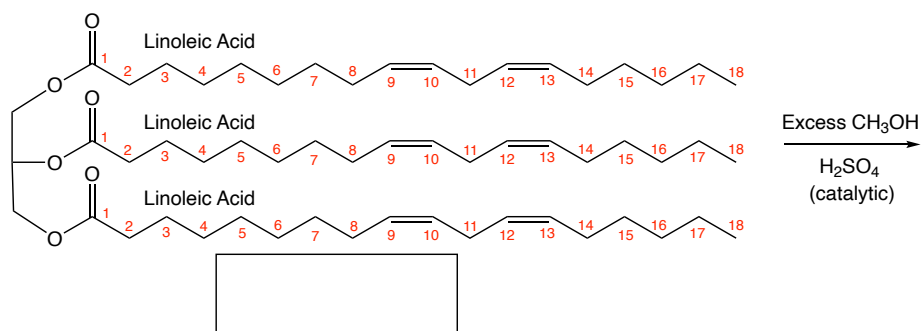
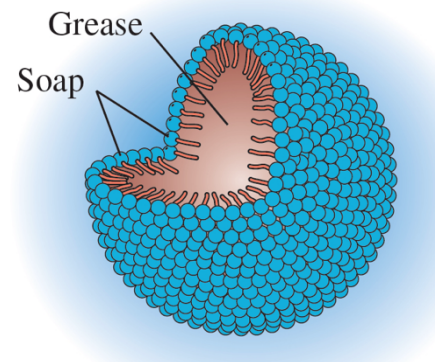
(a) A soap



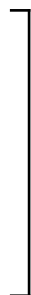
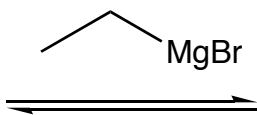
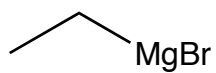
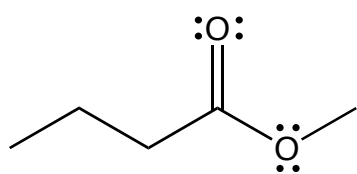
(b) Cross section of a soap micelle in water



Soap micelle with "dissolved" grease

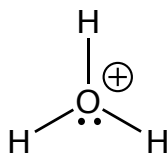


Grignard Reacting with Esters

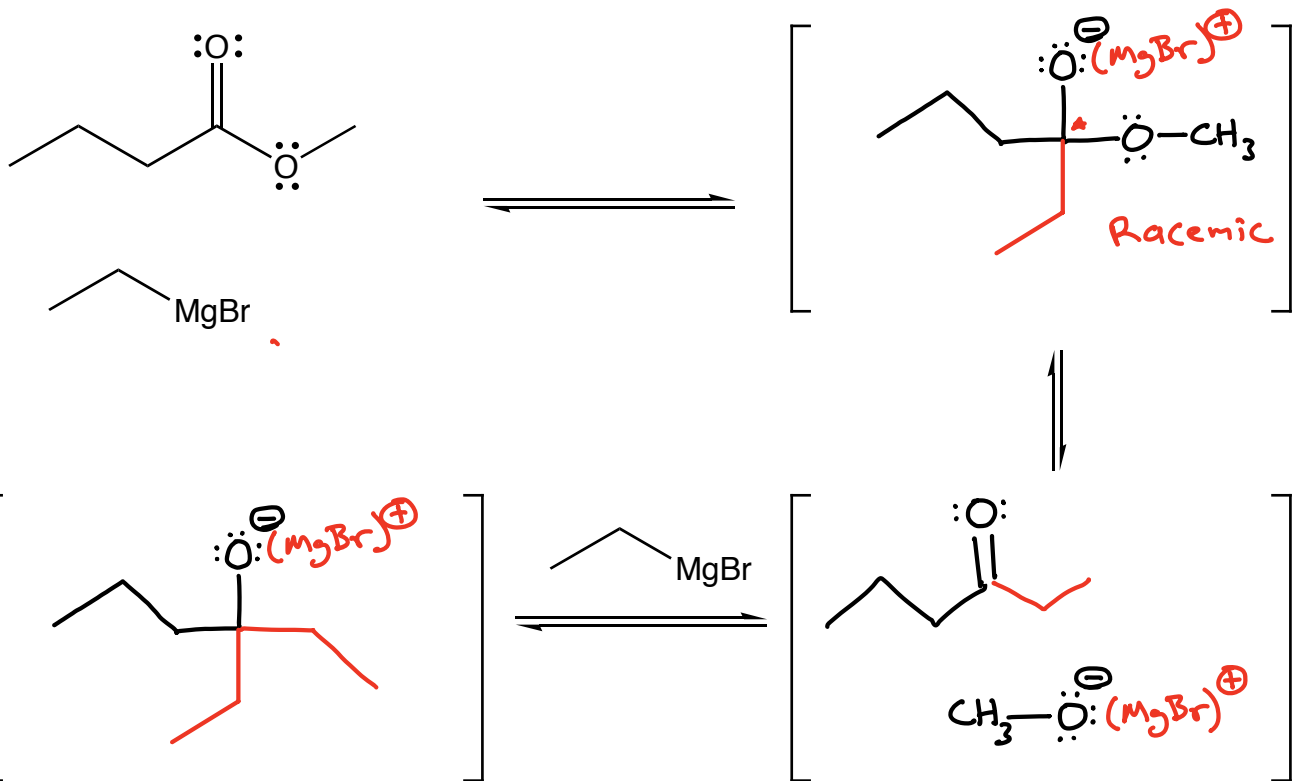
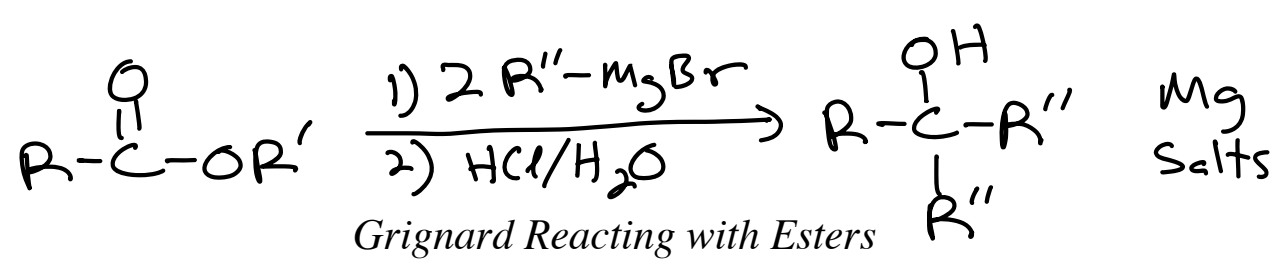


Chemist Opens Flask

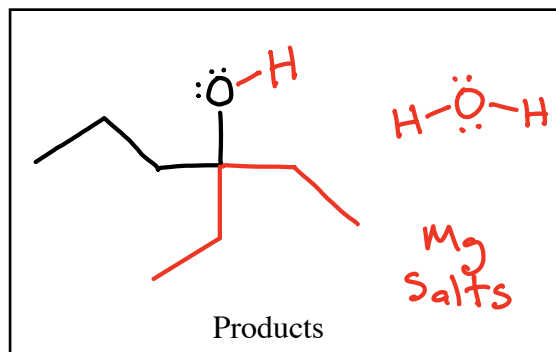
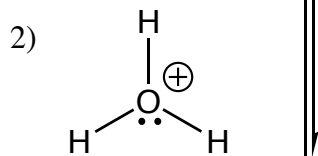
2)



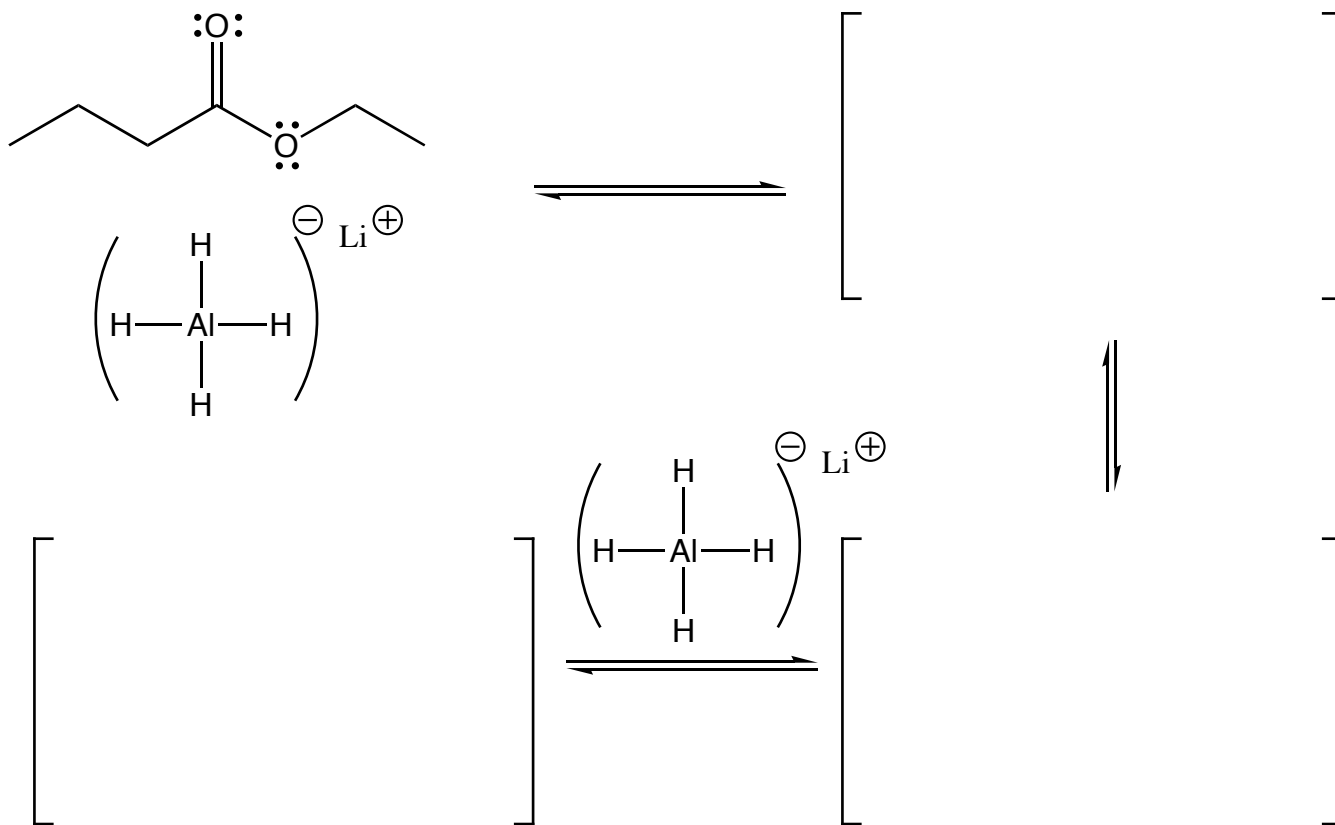
Products



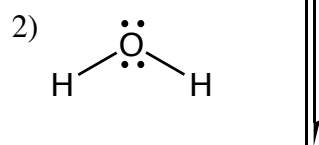
Chemist Opens Flask



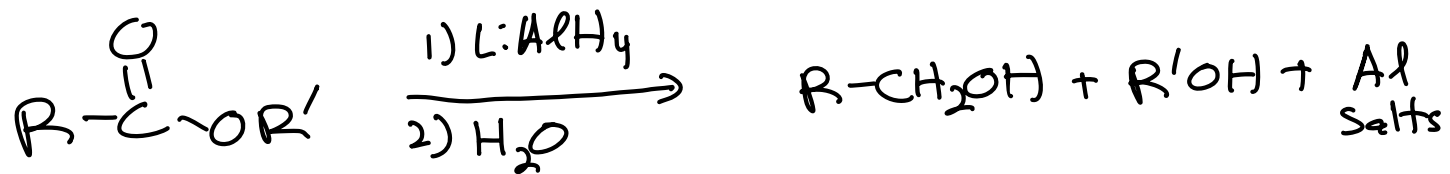
Reduction of Esters with LiAlH_4



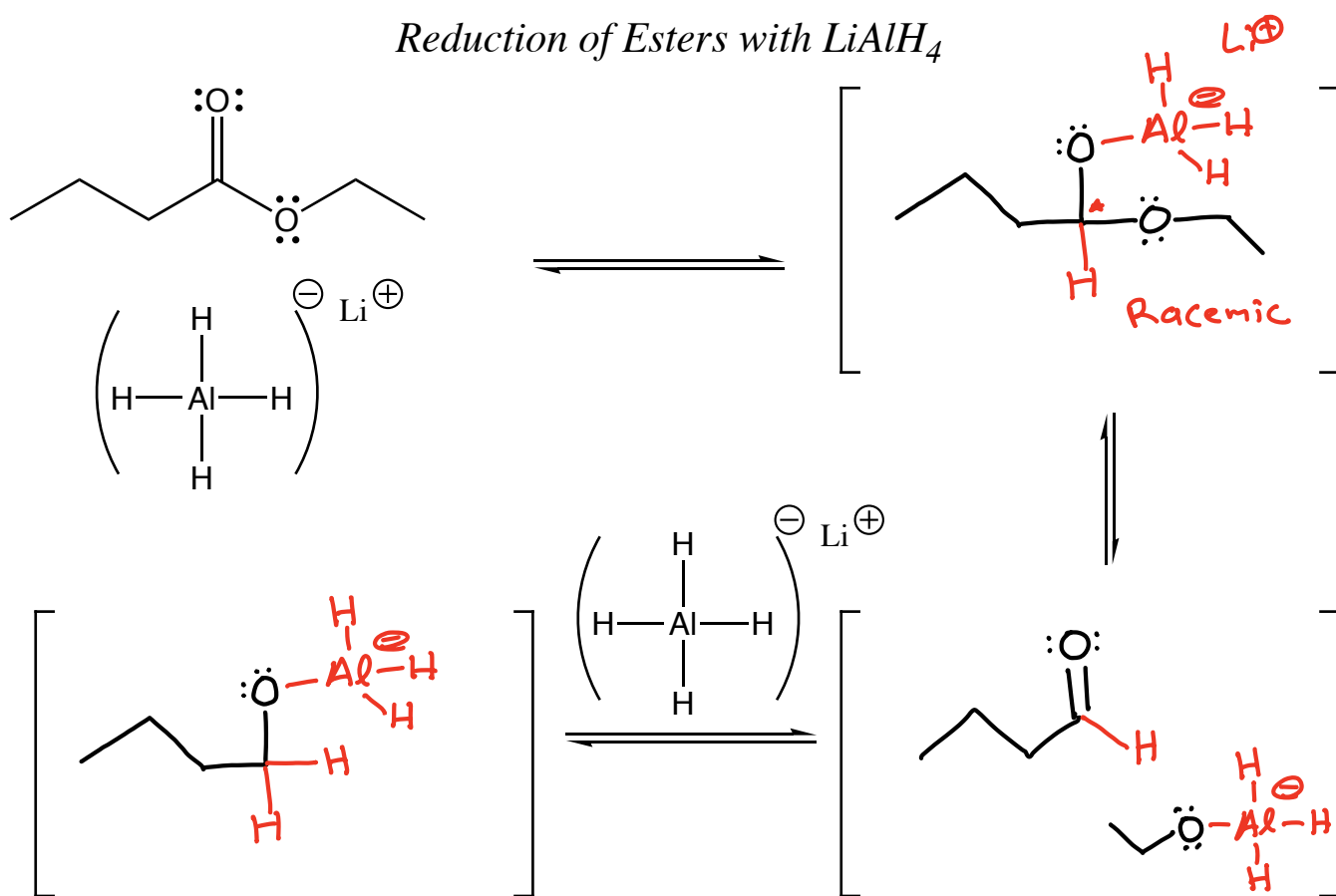
Chemist Opens Flask



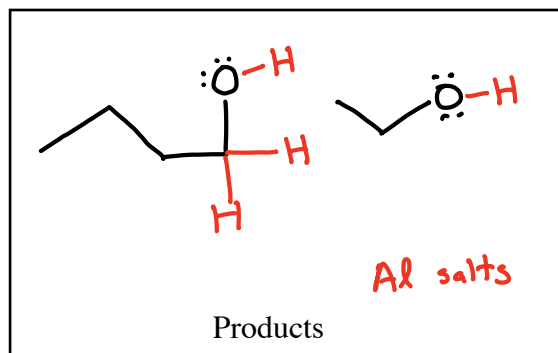
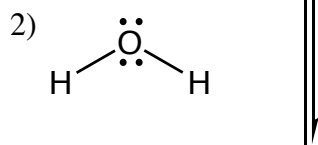
Products



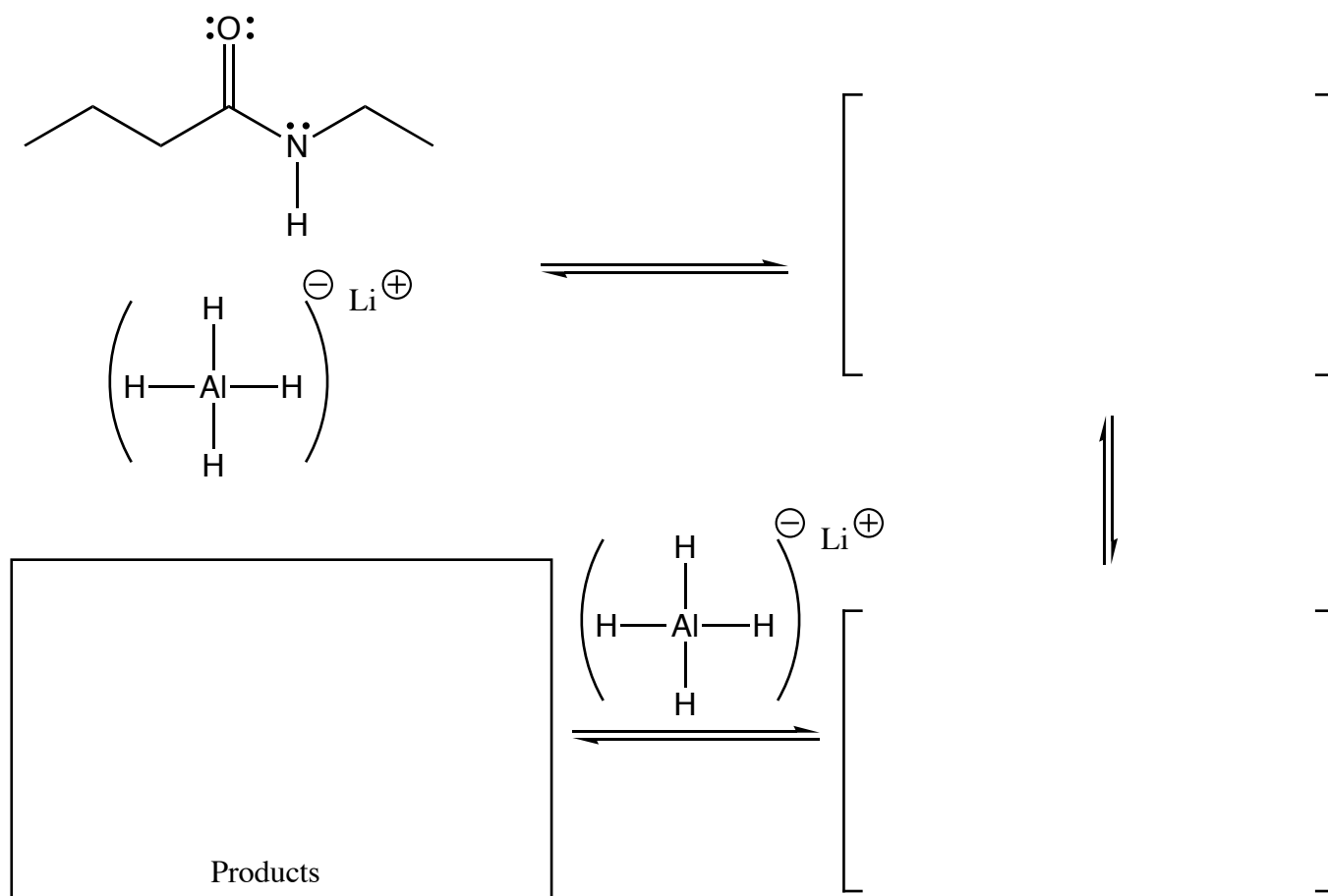
Reduction of Esters with $LiAlH_4$



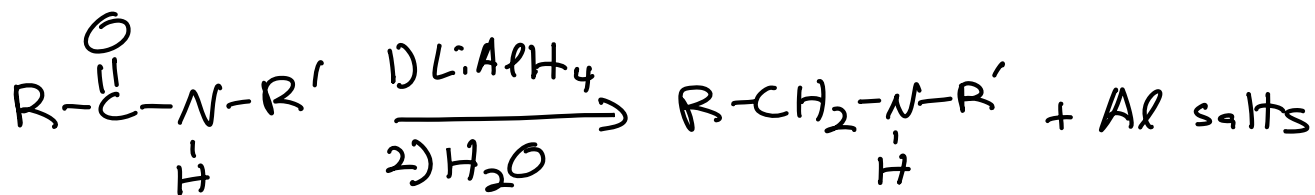
Chemist Opens Flask



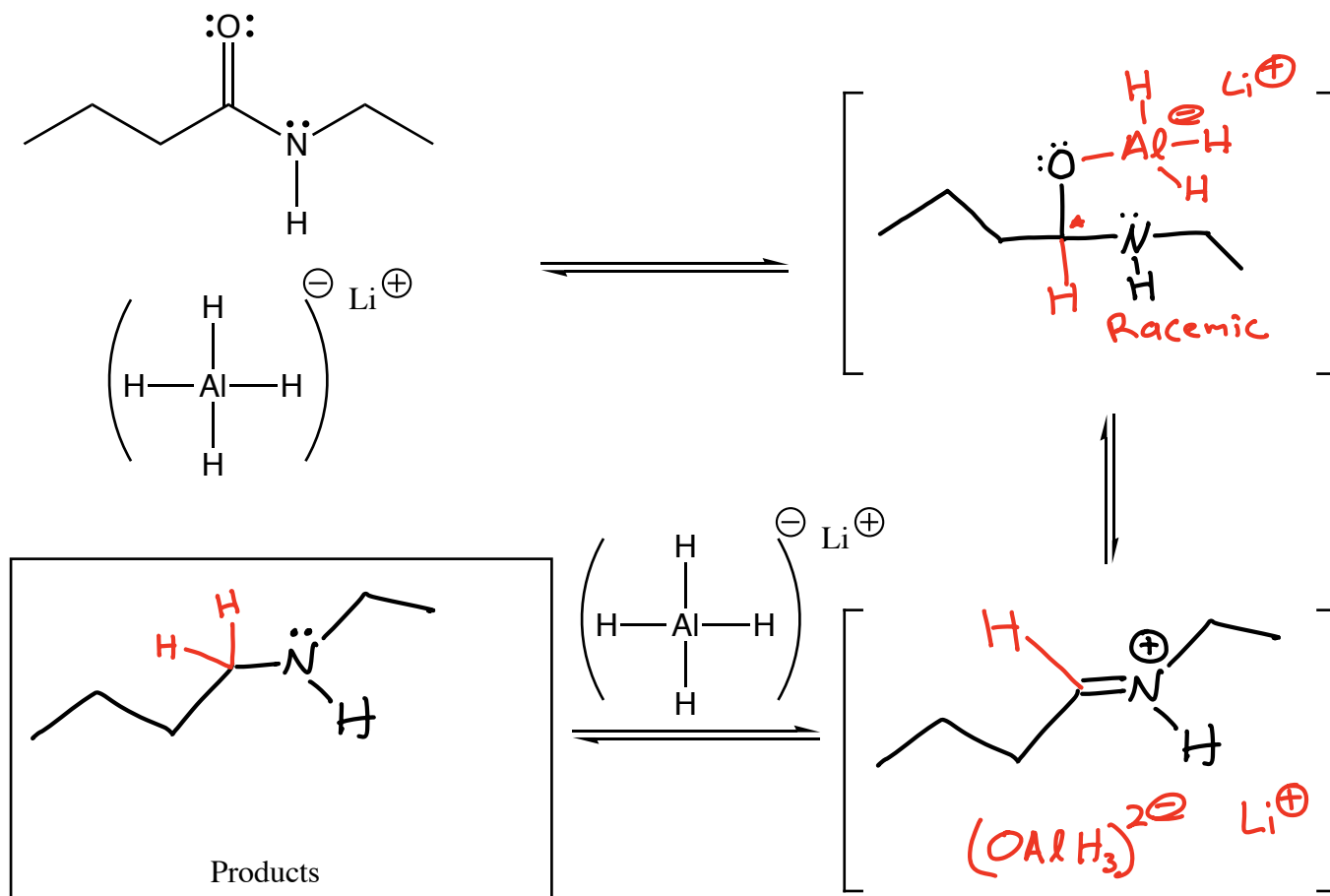
Reduction of Amides with LiAlH_4



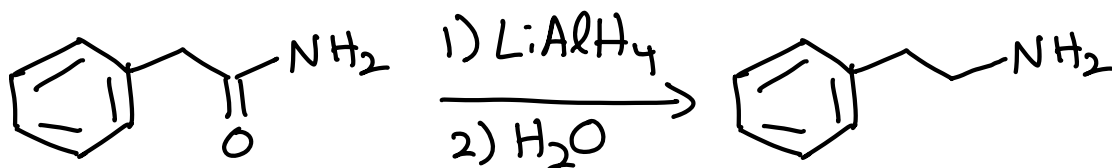
Note: In this reaction the chemist opens the flask and adds water in a second step that quenches any excess LiAlH_4 . Therefore, you need a second step to add water when using this reaction in synthesis even though it is not shown in the mechanism above.



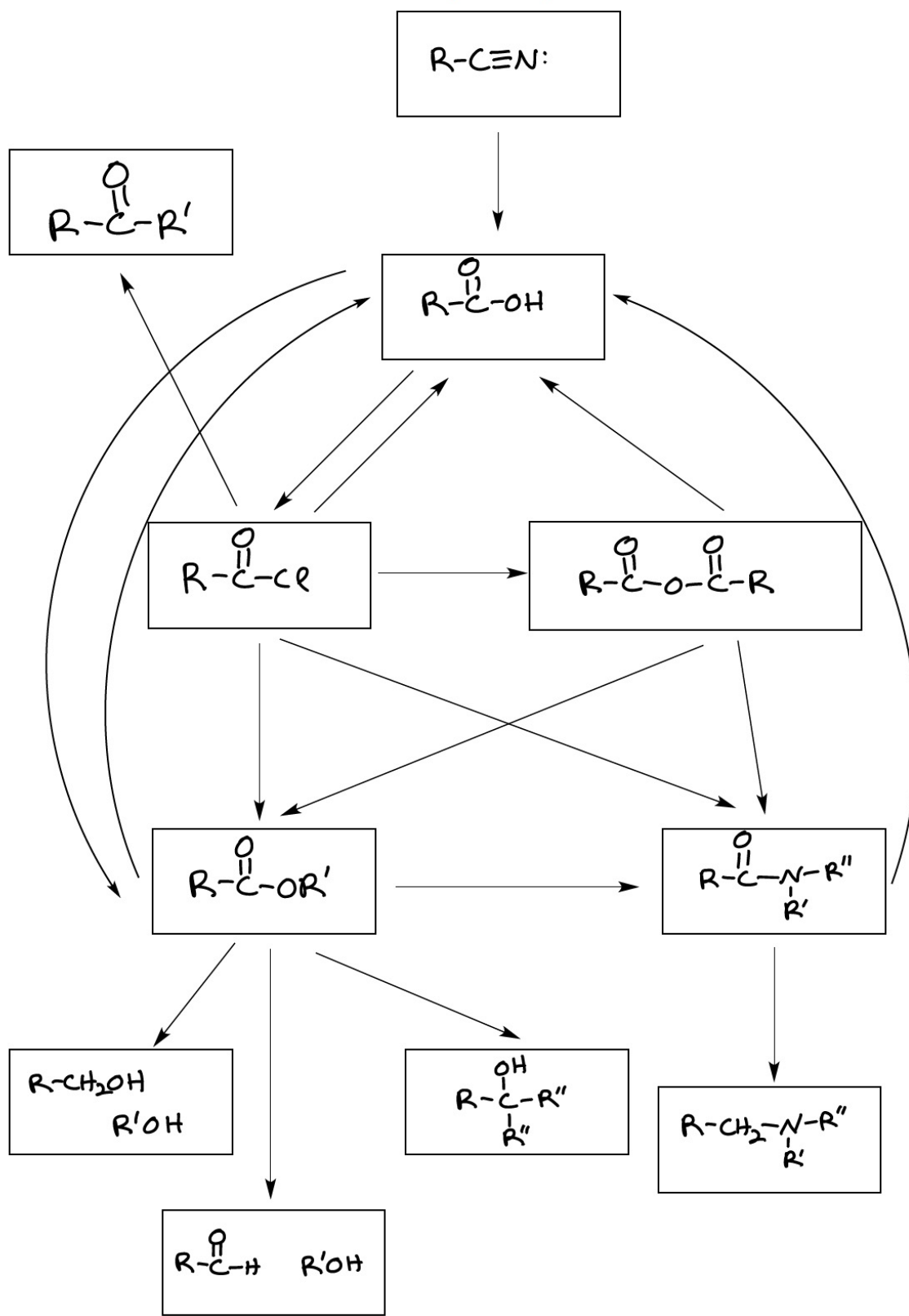
Reduction of Amides with LiAlH₄

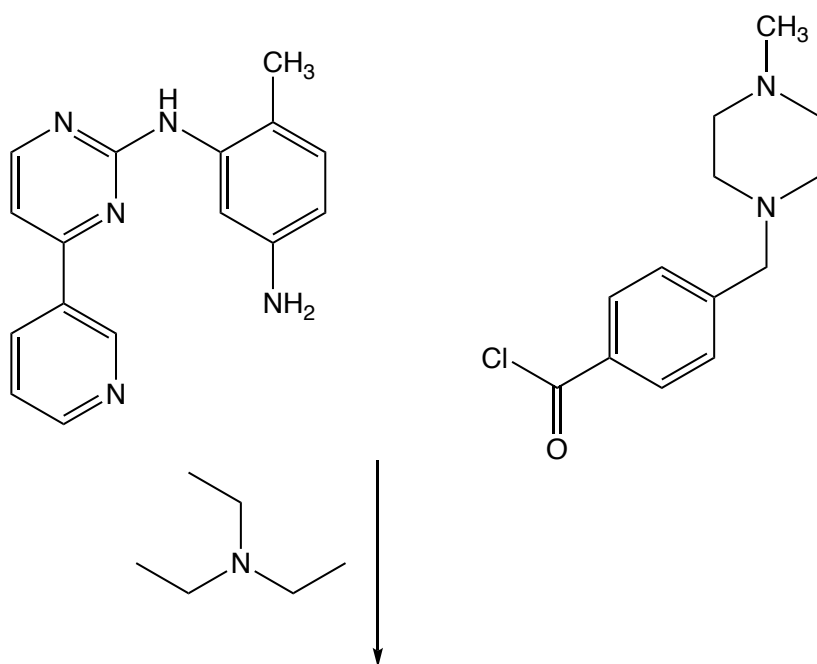


Note: In this reaction the chemist opens the flask and adds water in a second step that quenches any excess LiAlH₄. Therefore, you need a second step to add water when using this reaction in synthesis even though it is not shown in the mechanism above.




Interconversion of Carboxylic Acid Derivatives





Gleevec – Novartis (\$4.65 Billion in sales in 2015). A kinase inhibitor that is a first of its kind pill capable of treating certain blood cancers with only limited side effects. It was designed to combat leukemias with the relatively common “Philadelphia chromosome” (BCR-ABL kinase gene fusion)

Weaker bases are favored at equilibrium

Compound		pK _a	
	H-Cl	-7	Strongest Acid (Weakest conjugate base)
Carboxylic acids*	R-CO-H	3-5	
β-Dicarbonyls*	$\text{RC(=O)-CH}_2\text{-C(=O)R'}$	10	
β-Ketoesters*	$\text{RC(=O)-CH}_2\text{-C(=O)OR'}$	11	
β-Diesters*	$\text{ROC(=O)-CH}_2\text{-C(=O)OR'}$	13	
Water	HOH	15.7	
Alcohols	RCH_2OH	15-19	
Acid chlorides*	$\text{RCH}_2\text{-COCl}$	16	
Aldehydes*	$\text{RCH}_2\text{-CHO}$	18-20	
Ketones*	$\text{RCH}_2\text{-C(=O)R'}$	18-20	
Esters*	$\text{RCH}_2\text{-C(=O)OR'}$	23-25	
Terminal alkynes	$\text{RC}\equiv\text{C-H}$	25	
LDA	$\text{H-N}(i\text{-C}_3\text{H}_7)_2$	40	
Terminal alkenes	$\text{R}_2\text{C=CH}_2$	44	
Alkanes	$\text{CH}_3\text{CH}_2\text{-H}$	51	Weakest Acid (Strongest conjugate base)

A) Reactions are favored (i.e. have a motive) if they lead to formation of a weaker acid and/or weaker base.

B) Checking pK_a values can predict if a reaction has a motive even if there are other steps besides a proton transfer.

C) Recall that the conjugate base of a stronger acid (lower pK_a) is a weaker base.

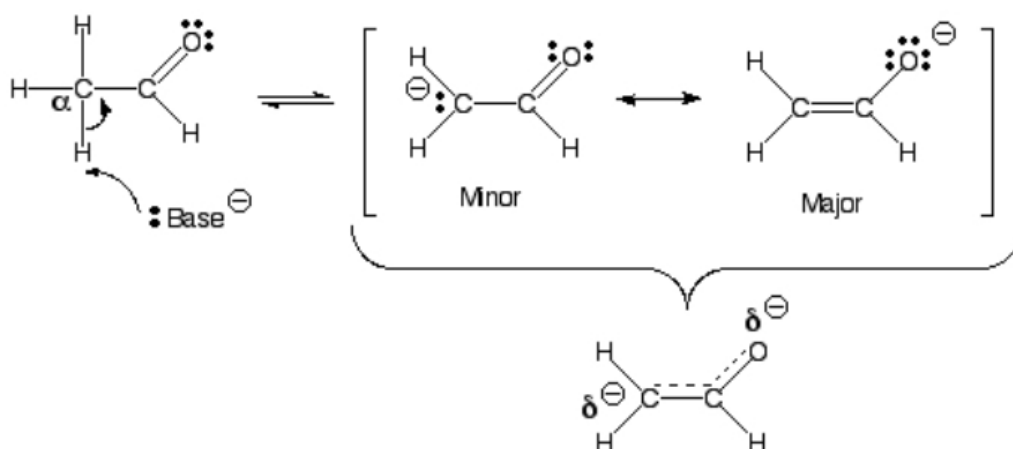
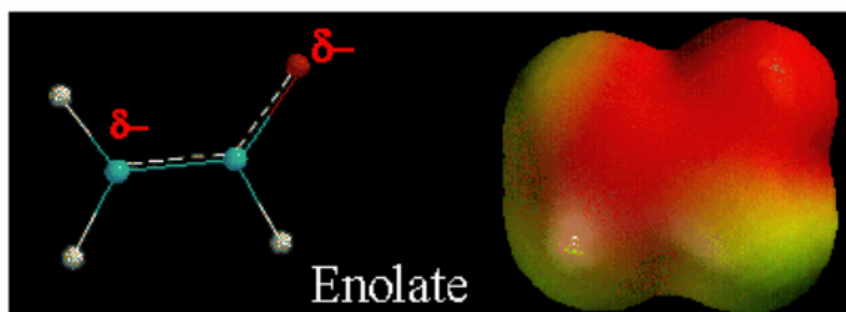
D) Check the pK's of the conjugate acid of the bases on either side of the equation. Lower pK_a value corresponds to stronger acid of the conjugate acid, and thus weaker conjugate base. The base with a stronger conjugate acid (lower pK_a value) will be the weaker base and will be favored at equilibrium.

E) Another way to look at it is that the base that is favored at equilibrium is the one that has the more stabilized anion, i.e. the one with the charge spread around more (electronegative) atoms.

F) Above is a pK_a table that we will refer to often.

*These have resonance stabilized anions

Enolates as nucleophiles



- A) Enolates are resonance stabilized, with a partial negative charge on carbon and oxygen.
- B) Enolates are nucleophiles, so they could react at either the carbon atom or oxygen atom. The partial negative charges give them the **opportunity** to react at either the carbon or oxygen.
- C) Reaction at the carbon atom gives the final product a C=O bond, while reaction at the oxygen atom gives the final product a C=C bond. However, C=O bonds are stronger than C=C bonds, **so the motive is to react at the carbon atom with most electrophiles.**

Aldol Reaction

