

Course Chem 345Lecturer GellmanDay FridayDate 3/20/2015Notes Taken By Keslie RankTotal # of Pages 4

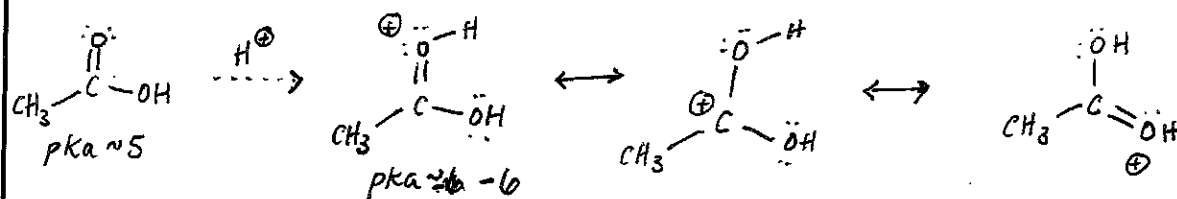
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Recall: Carboxylic acid Derivatives

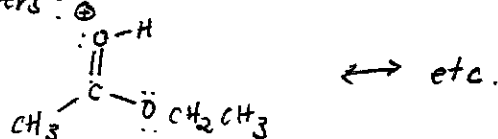
Ester
 Acid chlorides
 Anhydride
 amide
 Nitrile

} Hydrolyzed to carboxylic acid

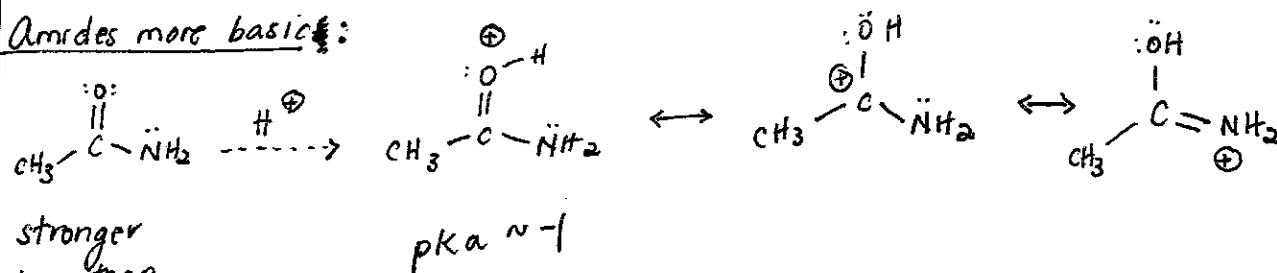
Acid-base behavior:



Similar for esters:



Amides more basic:

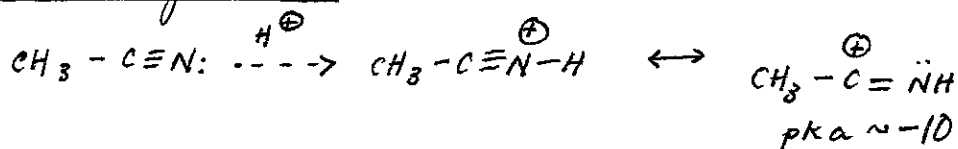


stronger
 base than
 carboxylic acid
 or ester

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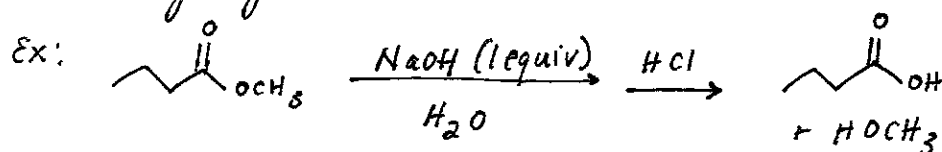
Nitriles = very weak bases



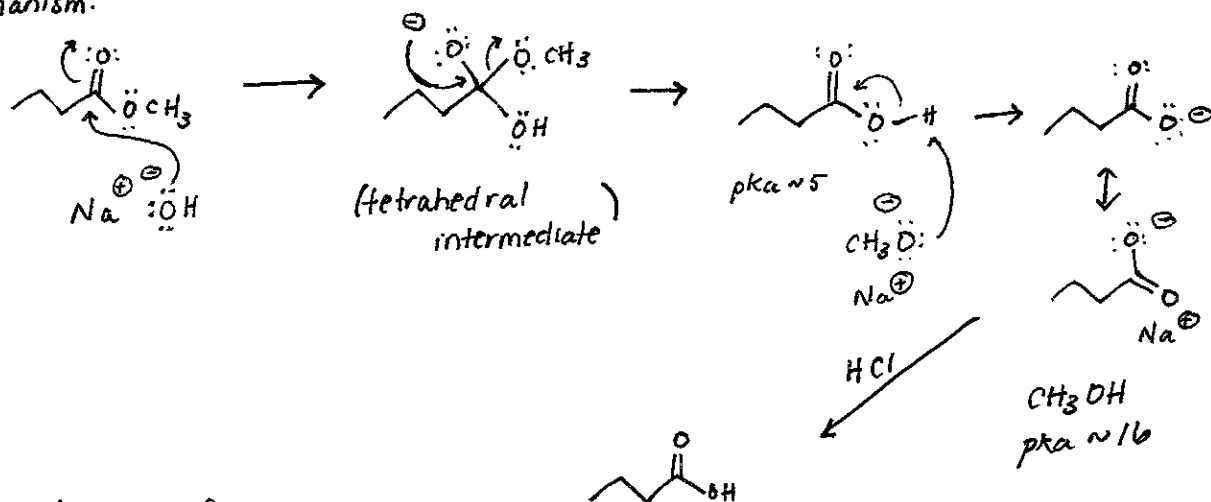
Rxns of carboxylic acid derivatives

→ Hydrolysis rxns

Alkaline hydrolysis of esters:



Mechanism:



* Note: 1 equiv of NaOH is consumed!

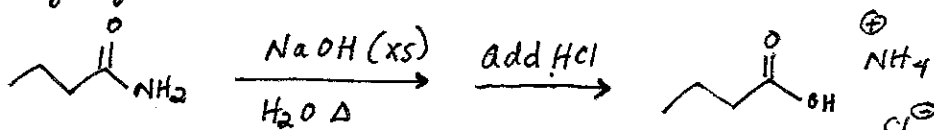
* Complementary acid-catalyzed ester hydrolysis - see text (reverse of acid-catalyzed ester formation)

* Distinction: Acid-cat. hydrolysis reversible, but alkaline hydrolysis is not because of carboxylate formation.

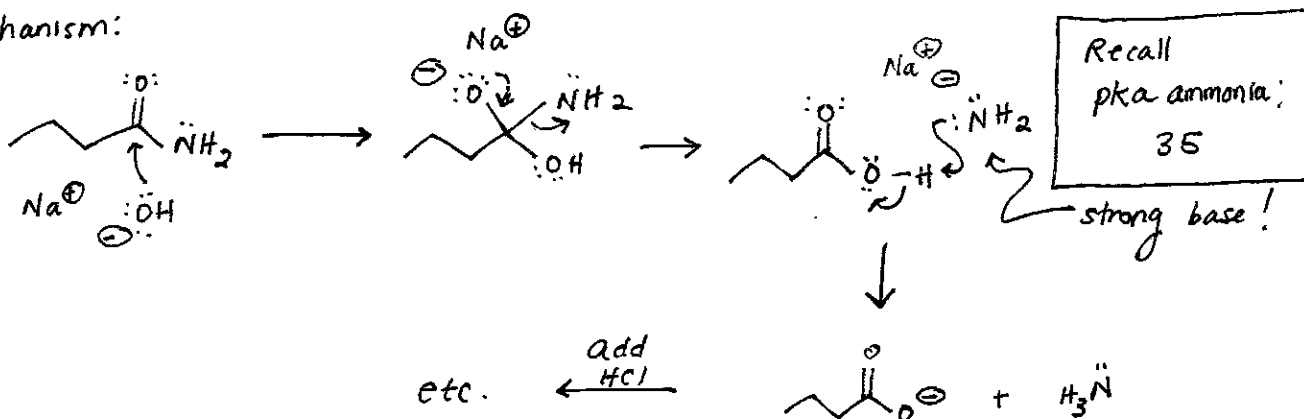
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Amide hydrolysis - acidic and basic (alkaline) versions require harsher conditions relative to ester hydrolysis.

Amide hydrolysis, alkaline conditions:



Mechanism:

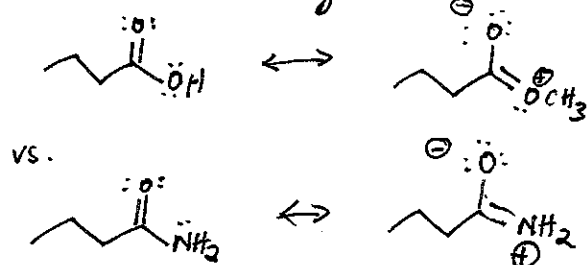


Why is amide hydrolysis "harder" than ester hydrolysis?

2 considerations:

1) amide + ester are stabilized by resonance, lost upon OH^- attack.

More resonance stabilization for amide than ester



Thus, amide loses more stabilization than ester upon tetrahedral intermediate formation

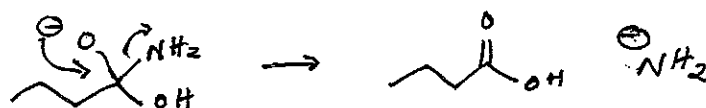
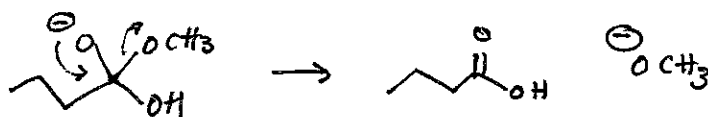
(N less electronegative than O)

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Why is amide hydrolysis "harder" than ester hydrolysis?

2) Breakdown of T.I. (tetrahedral intermediate)



NH₂⁻ much stronger base than O⁻CH₃

O⁻NH₂ much worse leaving group