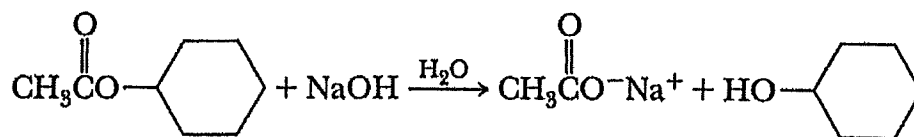
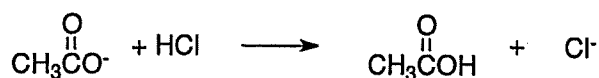


**5. Hydrolysis of an Ester (Section 18.4C)** Esters are hydrolyzed only in the presence of acid or base. Acid is a catalyst. Base is required in an equimolar amount. In acid, the mechanism involves protonation of the acyl oxygen, attack by water to create the tetrahedral addition intermediate, transfer of a proton to the oxygen of the —OR group, and departure of the leaving alcohol.

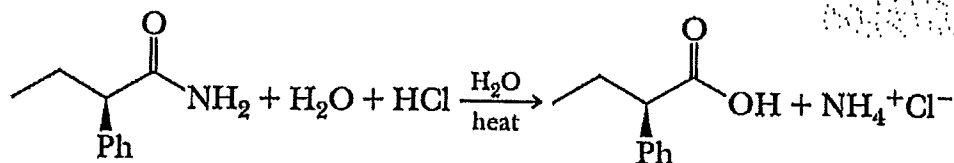


In base, the mechanism involves direct addition of the strong nucleophile  $\text{HO}^-$  to give the tetrahedral addition intermediate, followed by collapse to give a carboxylic acid and an alkoxide, which transfers a proton from the relatively acidic carboxylic acid to the relatively basic alkoxide to give the carboxylate ion and alcohol as final products.

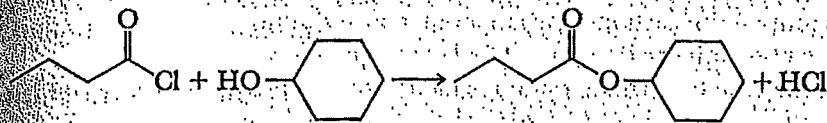
The hydrolysis of an ester under basic conditions (also called saponification) yields a salt of a carboxylic acid. This salt is usually treated with a mineral acid (HCl or  $\text{H}_2\text{SO}_4$ ) to obtain the free carboxylic acid.



**6. Hydrolysis of an Amide (Section 18.4D)** acid is required in an amount equivalent to that of the amide. In acid, the mechanism is similar to that for esters, except the departing amine is basic and reacts with a proton to give an ammonium ion product. This last step consumes a proton, explaining why the process is not catalytic in acid.

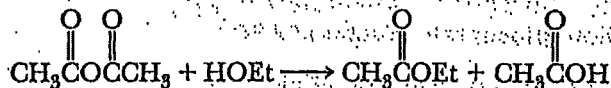


8) **Reaction of an Acid Chloride with an Alcohol (Section 18.5A)** Treating an acid chloride with an alcohol gives an ester plus HCl.

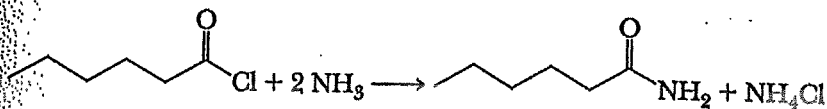


Preparation of an acid-sensitive ester is carried out using an equimolar amount of triethylamine or pyridine to neutralize the HCl.

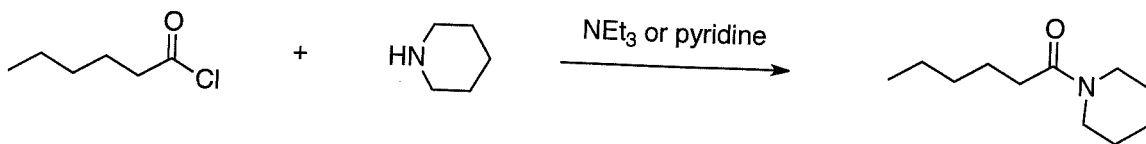
9) **Reaction of an Acid Anhydride with an Alcohol (Section 18.5B)** Treating an acid anhydride with an alcohol gives one mole of ester and one mole of carboxylic acid.



10) **Reaction of an Acid Chloride with Ammonia or an Amine (Section 18.6A)** Reaction requires two moles of ammonia or amine, one to form the amide and one to neutralize the HCl byproduct. The mechanism involves nucleophilic addition of ammonia or the amine to the carbonyl carbon, followed by a proton transfer to give a tetrahedral addition intermediate that can directly eliminate chloride and lose a proton to give products.

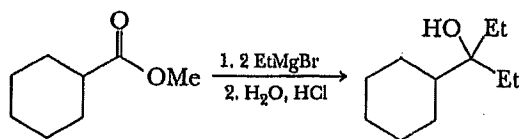


Ammonia is very cheap and an excess can be used to soak up the HCl that is formed during the reaction. However in case of a more expensive amine a tertiary amine such as triethylamine or even pyridine is added. For example:

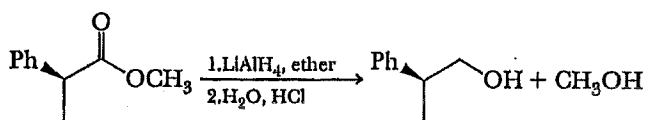


Please remember tertiary amines do not form amides.

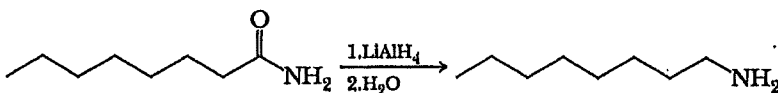
- 15. Reaction of an Ester with a Grignard Reagent (Section 18.9A)** Treating a formic ester with a Grignard reagent followed by hydrolysis gives a secondary alcohol. Treating any other ester with a Grignard reagent gives a tertiary alcohol. The mechanism involves nucleophilic attack of the Grignard reagent on the carbonyl carbon atom to give a tetrahedral addition intermediate, which collapses with the departure of alkoxide ion to give a ketone intermediate (an aldehyde in the case of formate esters), which reacts with a second mole of Grignard reagent.



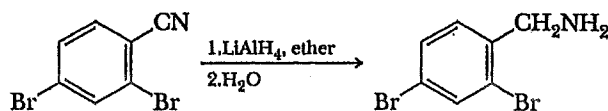
- 17. Reduction of an Ester (Section 18.10A)** Reduction of an ester by lithium aluminum hydride gives two alcohols. The mechanism involves initial nucleophilic attack by a hydride ion onto the carbonyl carbon to give a tetrahedral addition intermediate, which collapses through the loss of alkoxide to give an aldehyde, which reacts with a second hydride to give the product alcohol.



- 18. Reduction of an Amide (Section 18.10B)** Reduction of an amide by lithium aluminum hydride gives an amine. The mechanism involves initial nucleophilic reaction of a hydride equivalent with the carbonyl carbon to give a tetrahedral addition intermediate, followed by a Lewis acid-base reaction to give an oxygen-aluminum bond that rearranges electron pairs to eject an Al-O species to give an electrophilic iminium ion, which reacts with another equivalent of hydride to give the amine product.

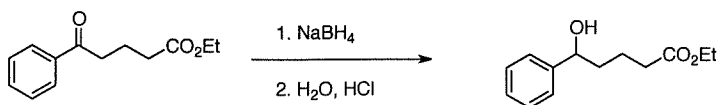


- 19. Reduction of a Nitrile (Section 18.10C)** Reduction of a cyano group by lithium aluminum hydride gives a primary amino group.



Carboxylic acids, and carboxylic acid derivatives including esters, amides and nitriles are ONLY reduced by LiAlH<sub>4</sub>. No reduction occurs with NaBH<sub>4</sub>

Therefore:



However,

