June 9th 2014

IV. Reactions with Water: Hydrolysis

A. Acid Chlorides and Acid Anhydrides

1. Low-weight acid chlorides and acid anhydrides will react with water to form carboxylic acids.

a. Acid chloride → 1 CA.

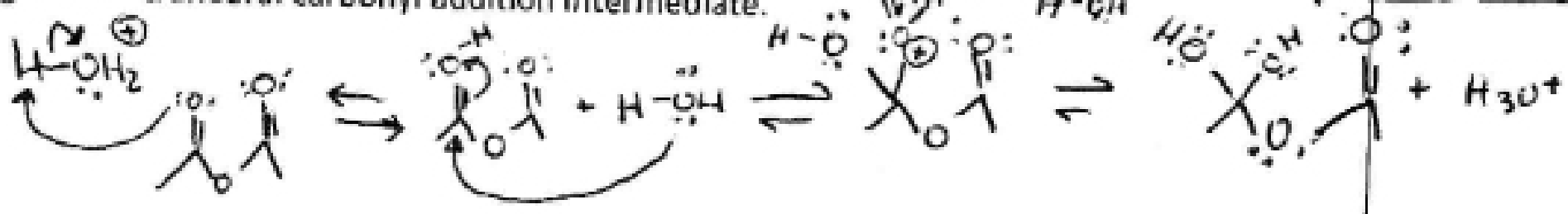
b. Acid hydride → 2 C.A.

c. The mechanism is the same for both.

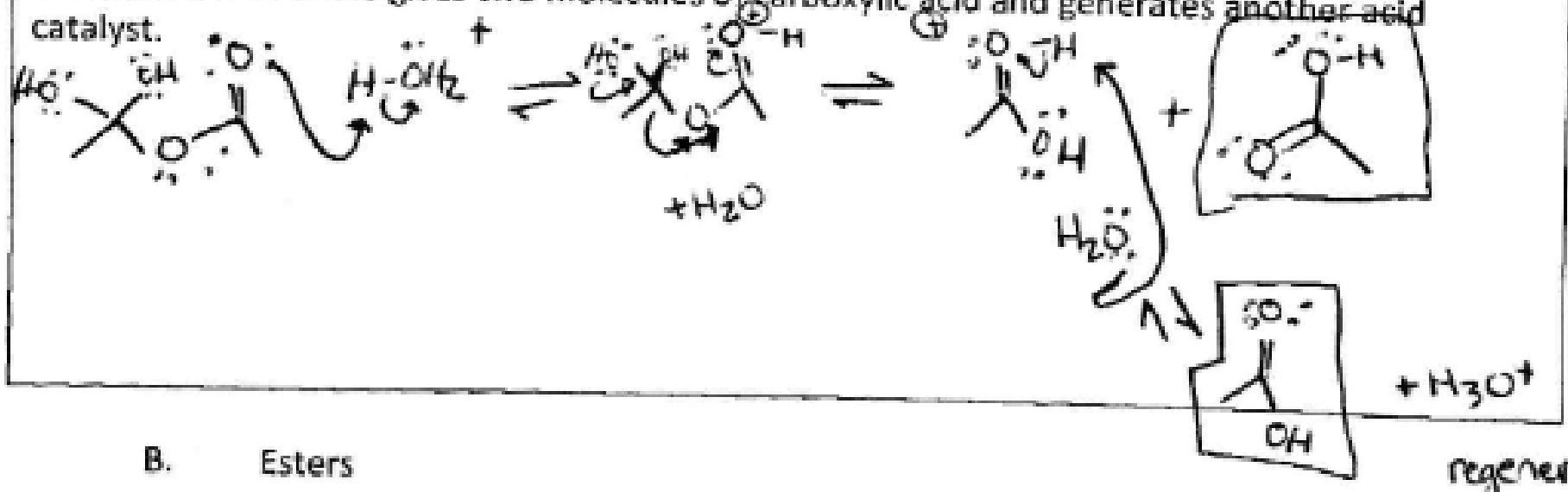
Mechanism #1: Hydrolysis of an Acid Anhydride

two on 1 is hydroxyls carbon unstable

*Step 1:* Protonation of a carbonyl oxygen followed by addition of $H_2O$ to one of the carbonyl groups gives a tetrahedral carbonyl addition intermediate.



*Step 2:* Protonation of the leaving group followed by collapse of the tetrahedral carbonyl addition intermediate gives two molecules of carboxylic acid and generates another acid catalyst.




regenerated catalyst!

B. Esters

1. Esters hydrolyze very slowly, but the process moves faster if an ester is refluxed with aqueous acid or base.

2. This is essentially the Fischer esterification reaction in reverse – remember that that mechanism occurs *in equilibrium*!

a. How do we use the acid catalyst?

3. What happens with we use a base catalyst?

a. - Saponification : hydrolysis of an ester with a base (-OH)

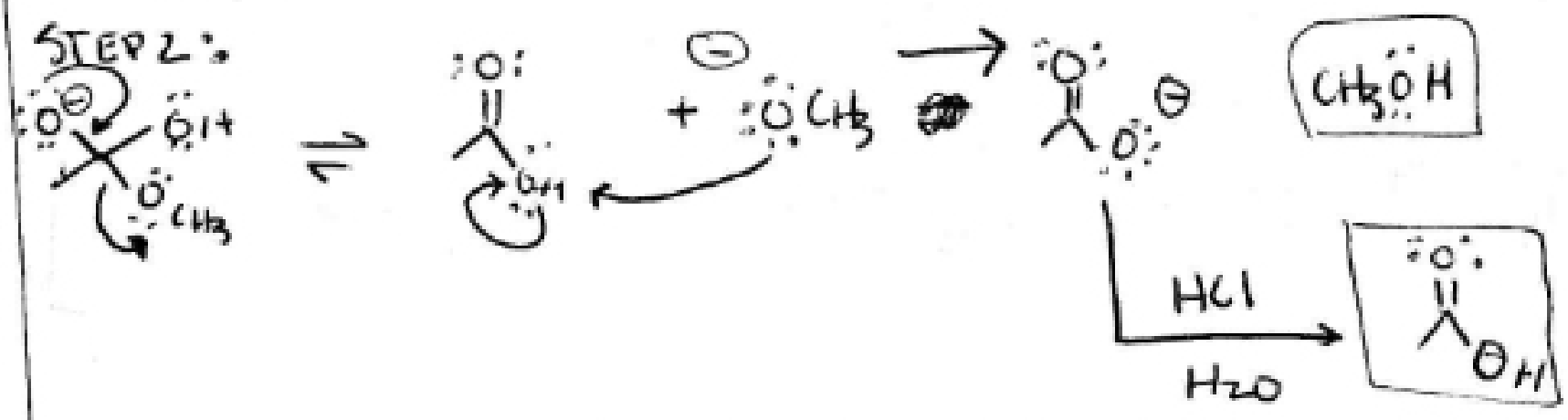
1. Hydroxide ion is a good nucleophile and can attack at the carbonyl carbon.

Mechanism #2: Hydrolysis of an Ester in Aqueous Base (Saponification)

*Step 1*: Addtion of hydroxide ion to the carbonyl carbon of the ester gives a tetrahedral carbonyl addition intermediate.

*Step 2*: Collapse of this intermediate gives a carboxylic acid and an alkoxide ion.

*Step 3*: Proton transfer between the carboxyl group and the alkoxide ion gives the carboxylate anion. This strongly exothermic acid-base reaction drives the whole reaction to completion.




4. One last point about using acids and bases for hydrolysis:

a. If you use acid, you only can use "catalytic amounts" of acid to get the reaction b/c its a true catalyst

b. If you use base, you only can use "stoichiometric amounts" of base to get the reaction going b/c its a true reactant.

c. Acid-catalyzed reaction is reversible, but the base-catalyzed reaction is irreversible (carboxylate anion is not attacked by an alcohol molecule (a weak nucleophile).

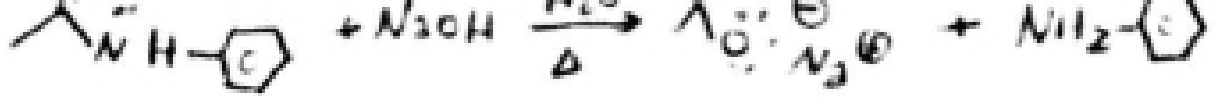
D. Amides

1. Amide can react w/ acids and bases, but it must require a refluxing period for the reaction to take place

* stoichiometric amount of HCl

2. Acid catalyzed hydrolysis reactions will lead to the formation of a carboxylic acid and an ammonium ion.

3. Base-catalyzed reactions form a carboxylate salt and ammonia if 1° or amine if 2° or 3°

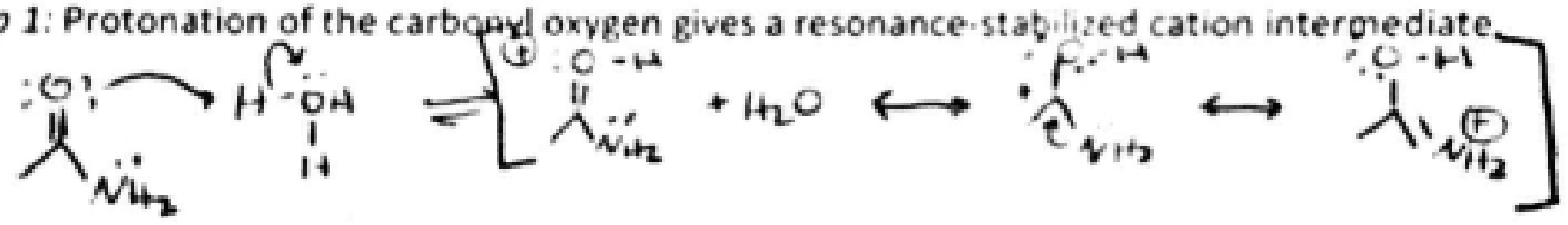


3. One mole of either acid or base is required for each reaction.

4. These reactions are similar to the hydrolysis of esters mechanisms.

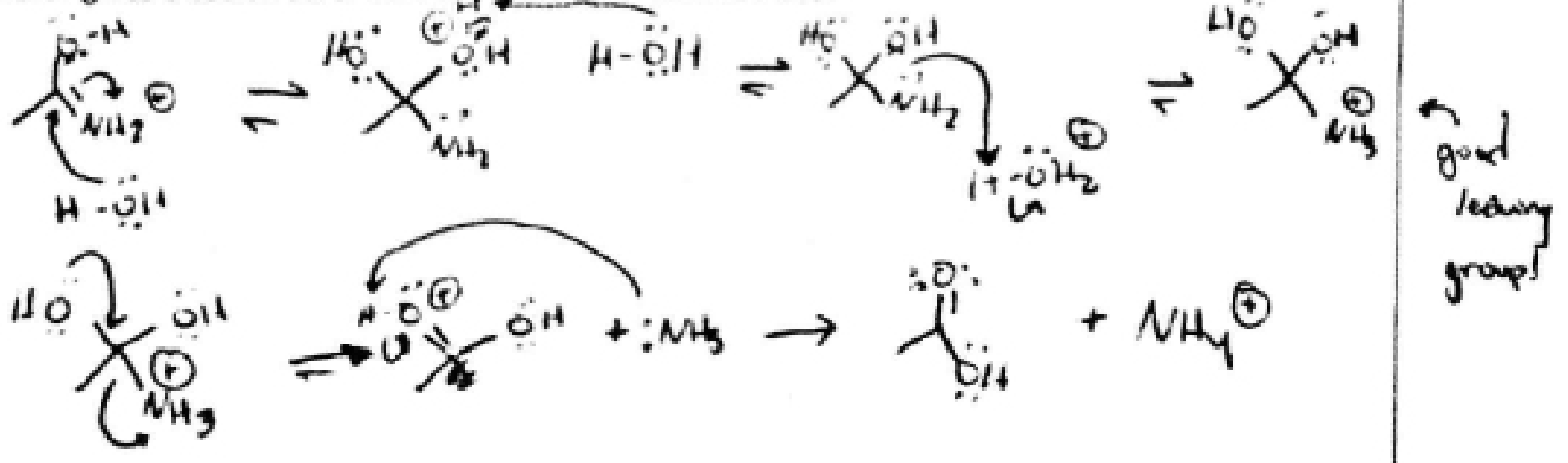
Mechanism #3: Hydrolysis of an Amide in Aqueous Acid

*Step 1*: Protonation of the carbonyl oxygen gives a resonance-stabilized cation intermediate.



*Step 2*: Addition of water to the carbonyl carbon of the cation intermediate followed by proton transfer gives a tetrahedral carbonyl addition intermediate.

can use any of the resonance structures.



good leaving group!