

20.13

Preparation of Amides

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Amides are prepared from amines by acylation with:

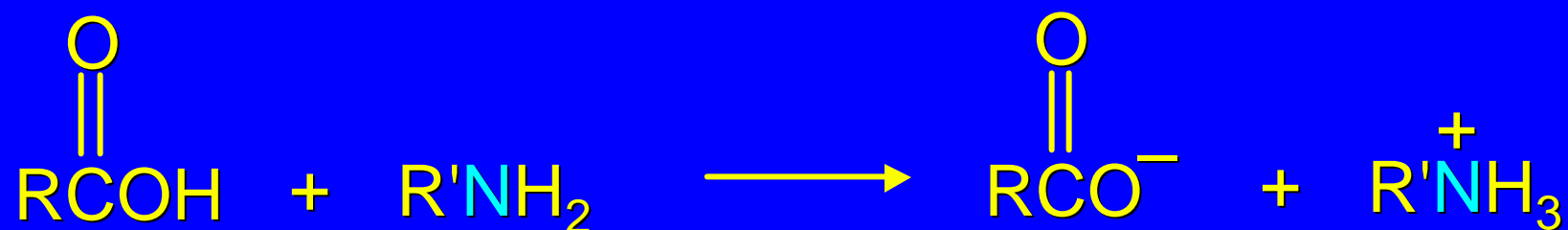
acyl chlorides (Table 20.2)

anhydrides (Table 20.3)

esters (Table 20.6)

Preparation of Amides

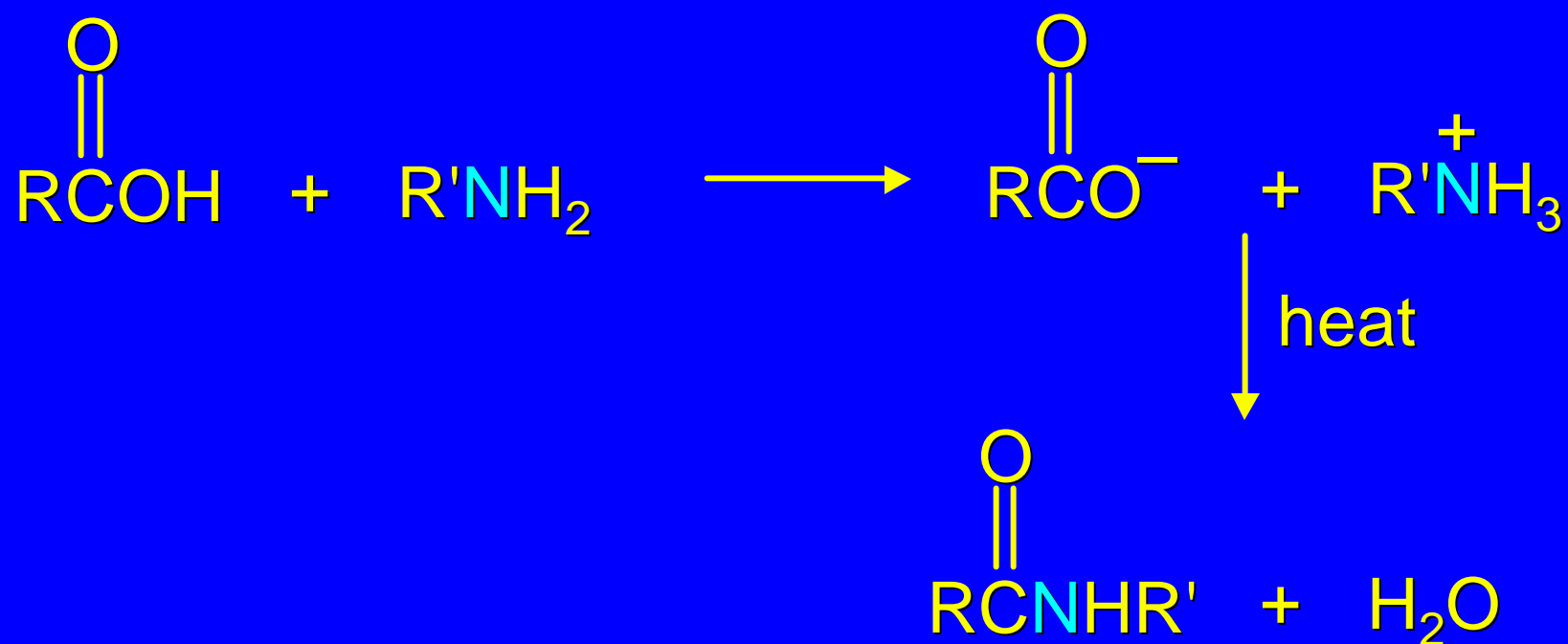
Amines do not react with carboxylic acids to give amides. The reaction that occurs is proton-transfer (acid-base).



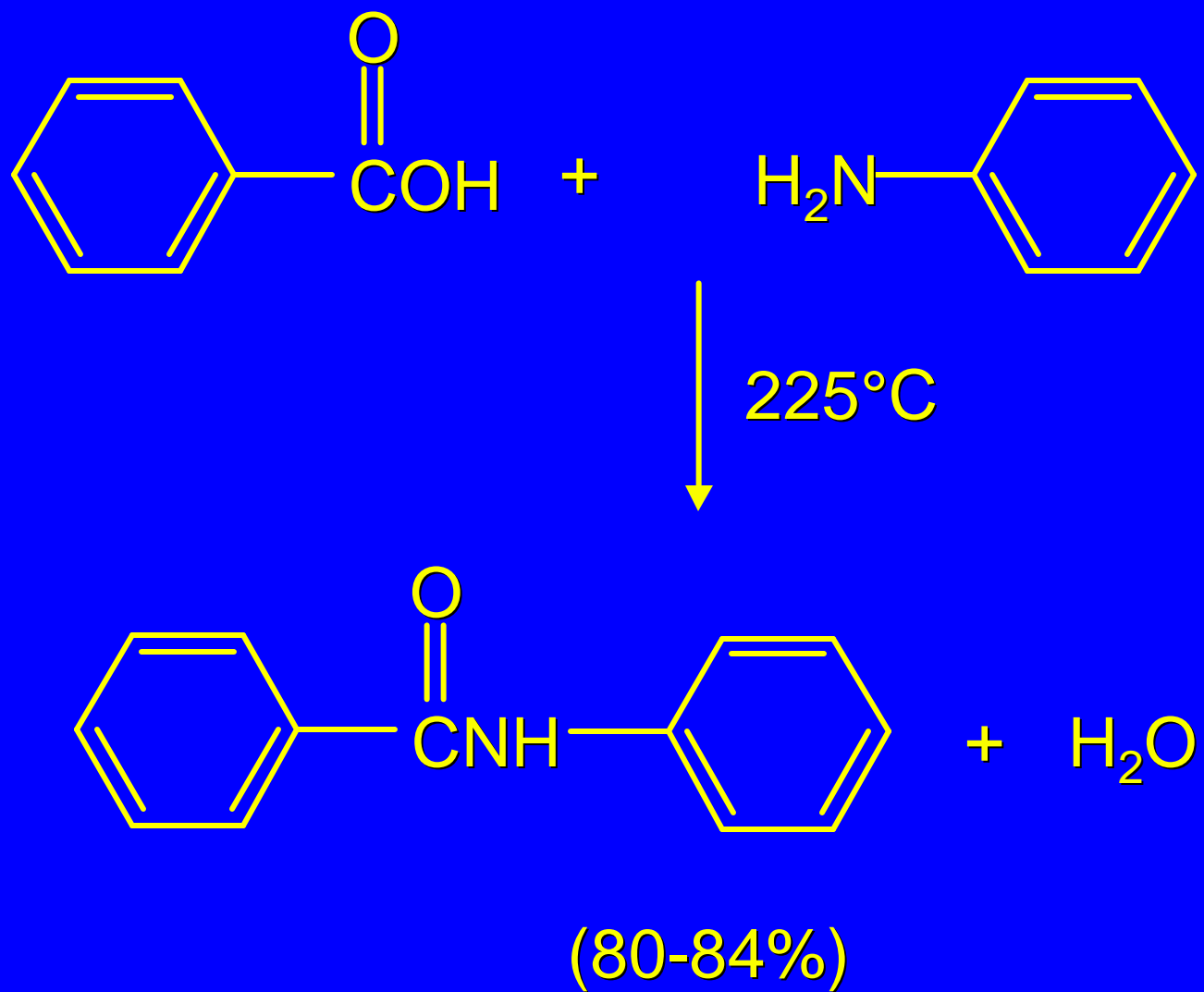
If no heat-sensitive groups are present, the resulting ammonium carboxylate salts can be converted to amides by heating.

Preparation of Amides

Amines do **not** react with carboxylic acids to give amides. The reaction that occurs is proton-transfer (acid-base).



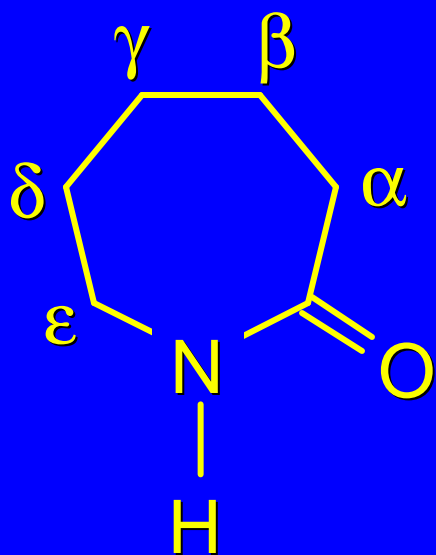
Example



20.14
Lactams

Lactams

Lactams are cyclic amides. Some are industrial chemicals, others occur naturally.

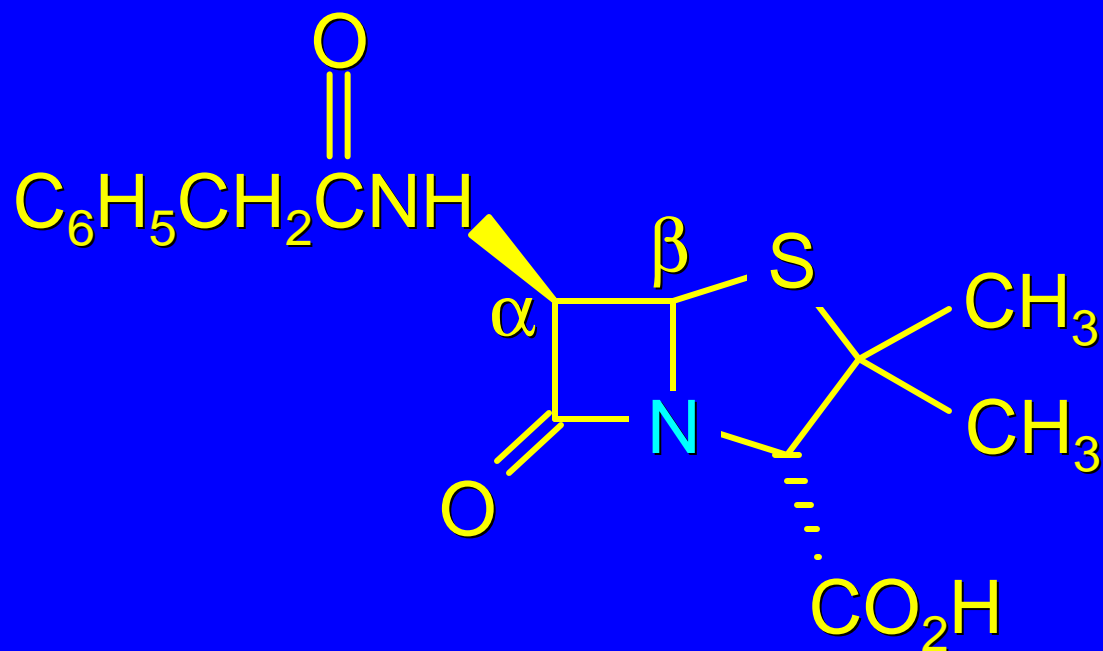


ϵ -Caprolactam*: used to prepare a type of nylon

*Caproic acid is the common name for hexanoic acid.

Lactams

Lactams are cyclic amides. Some are industrial chemicals, others occur naturally.

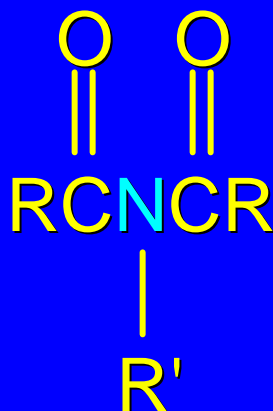


Penicillin G: a β -lactam antibiotic

20.15
Imides

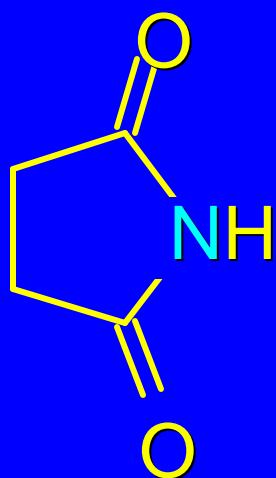
Imides

Imides have 2 acyl groups attached to the nitrogen.



Imides

The most common examples are cyclic imides.



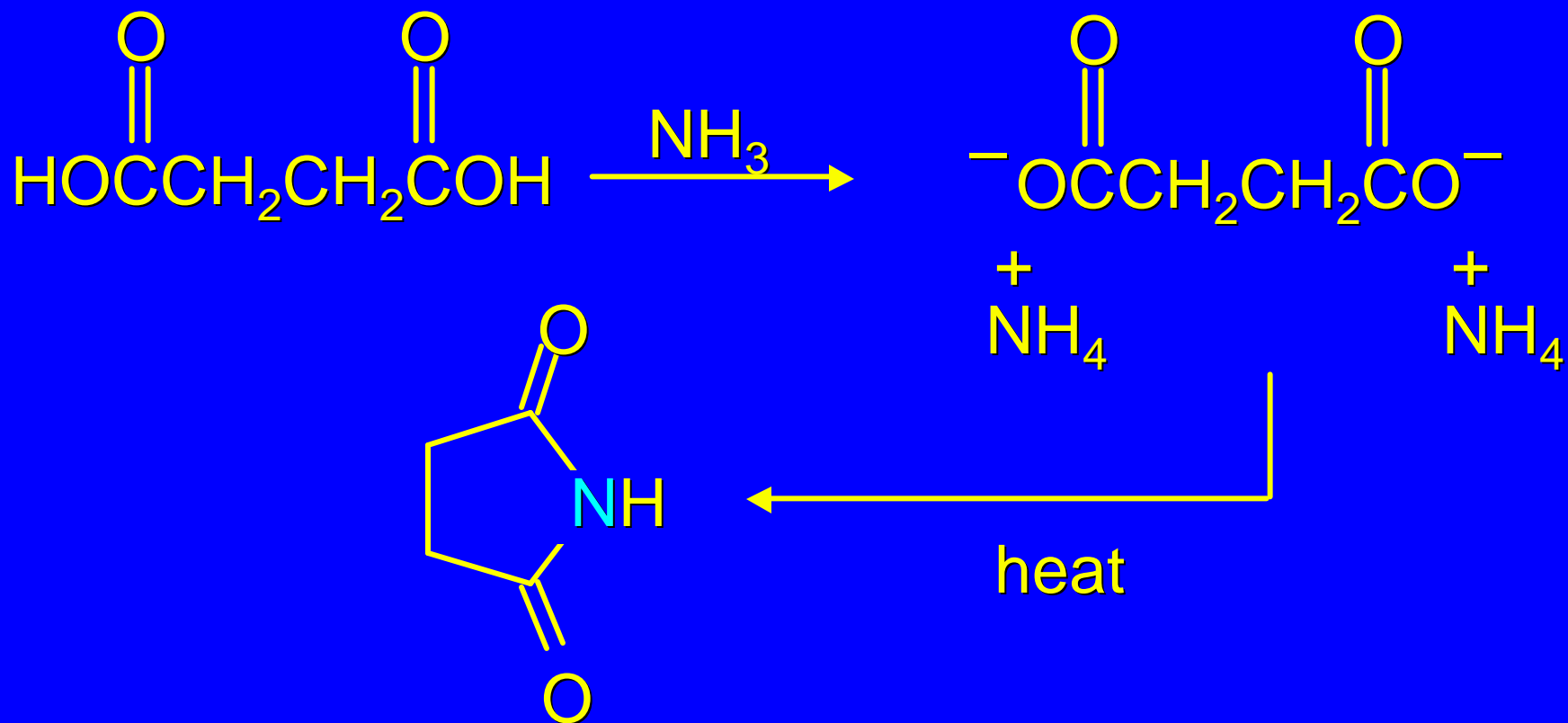
Succinimide



Phthalimide

Preparation of Imides

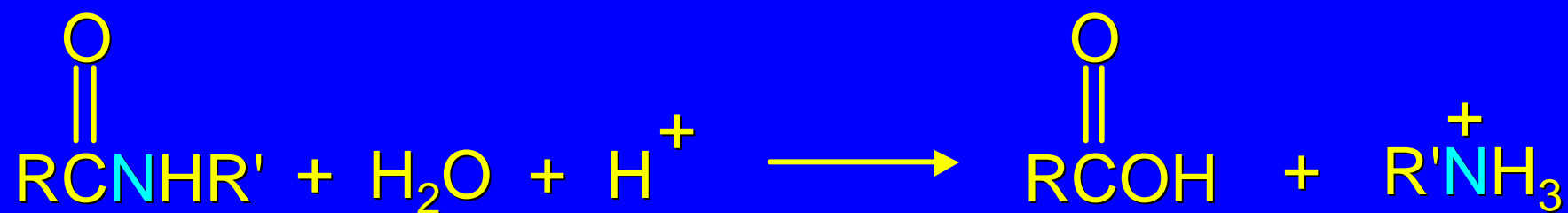
Cyclic imides are prepared by heating the ammonium salts of dicarboxylic acids.



20.16
Hydrolysis of Amides

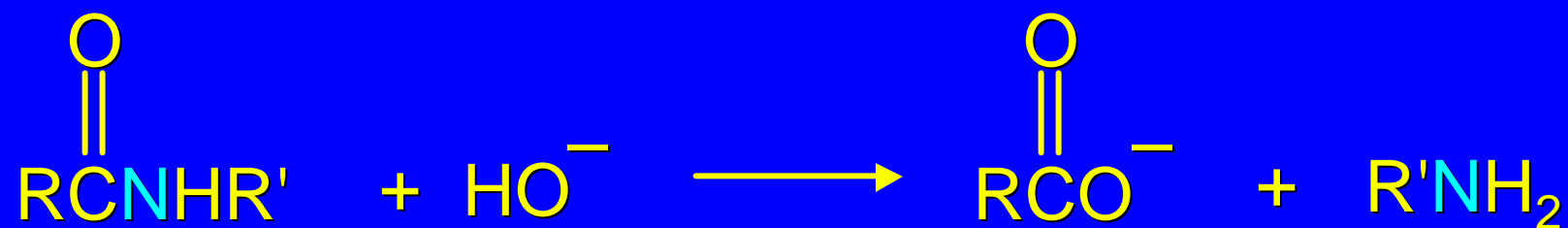
Hydrolysis of Amides

Hydrolysis of amides is irreversible. In acid solution the amine product is protonated to give an ammonium salt.

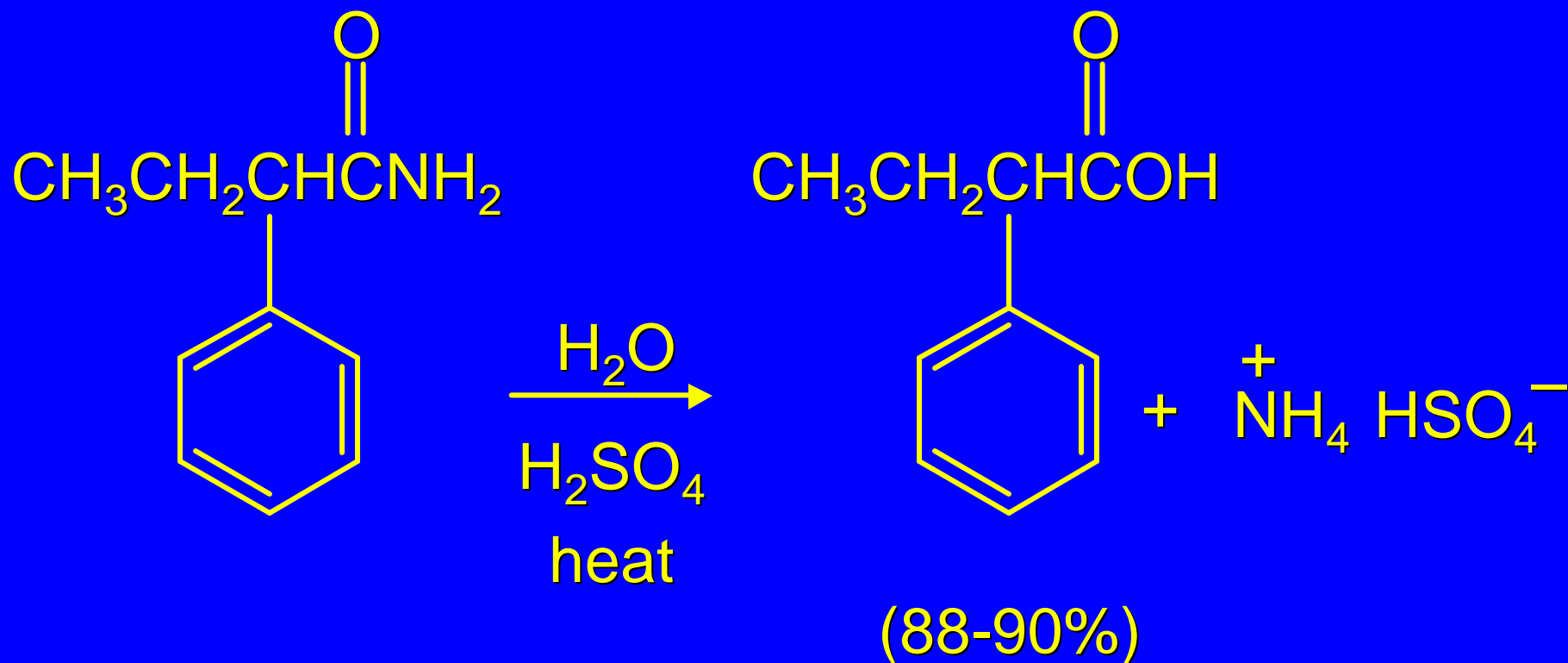


Hydrolysis of Amides

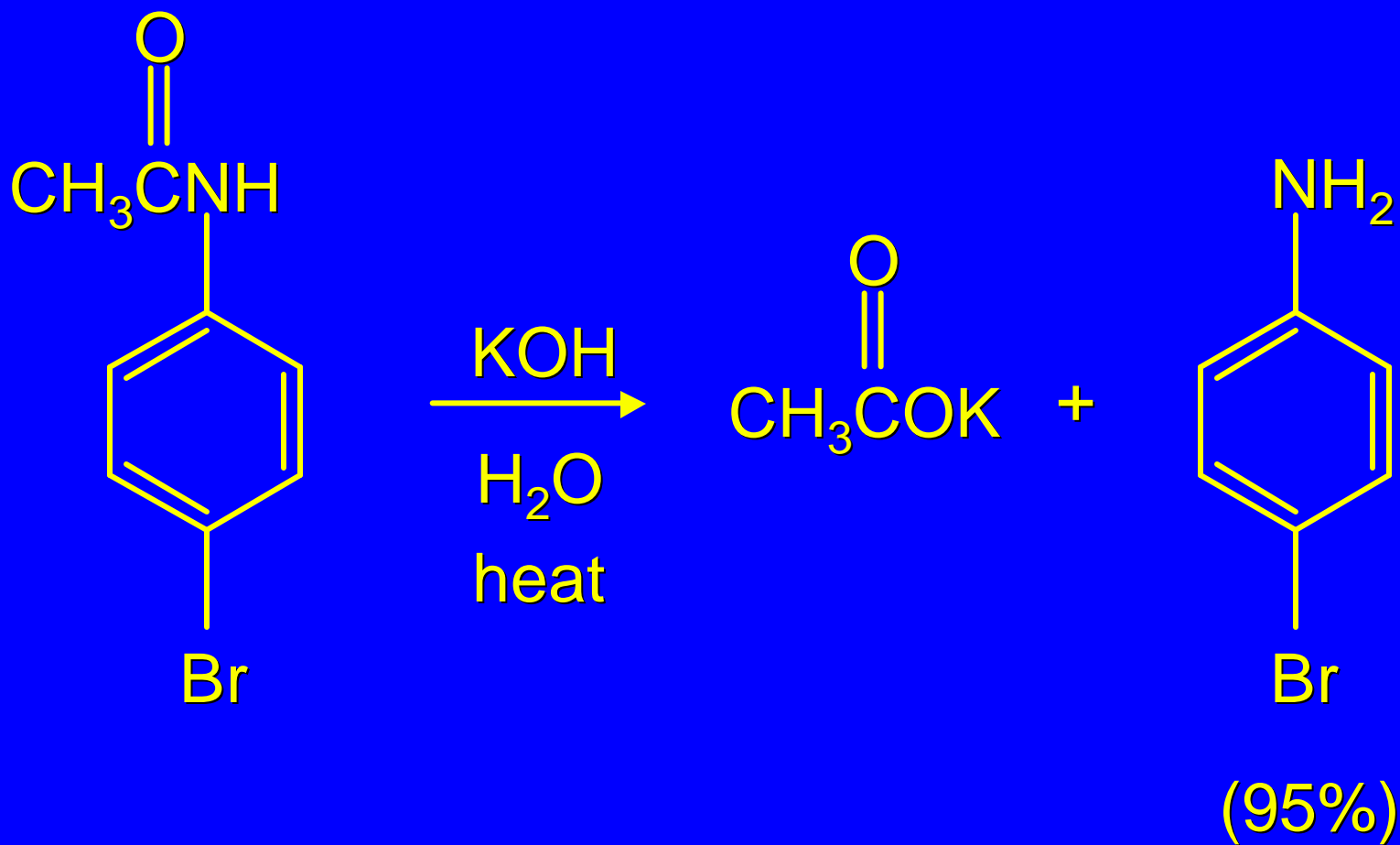
In basic solution the carboxylic acid product is deprotonated to give a carboxylate ion.



Example: Acid Hydrolysis



Example: Basic Hydrolysis

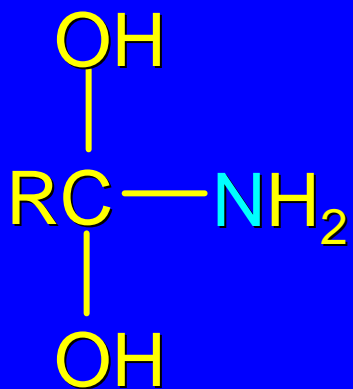
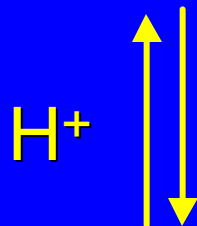
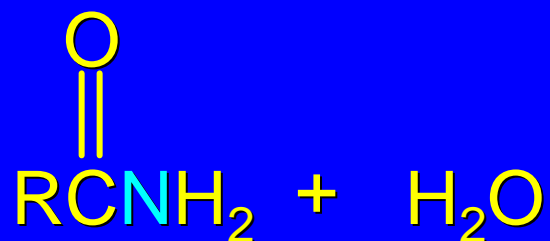


Mechanism of Acid-Catalyzed Amide Hydrolysis

Acid-catalyzed amide hydrolysis proceeds via the customary two stages:

- 1) formation of tetrahedral intermediate
- 2) dissociation of tetrahedral intermediate

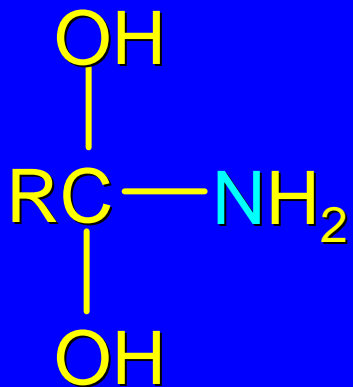
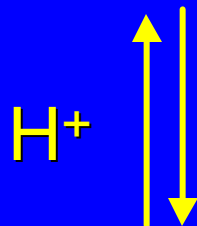
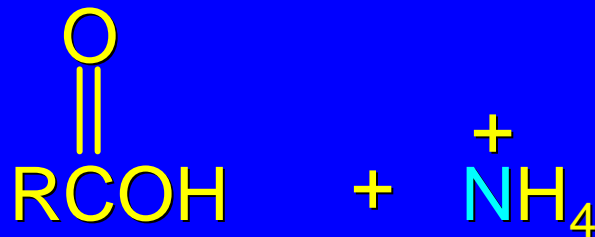
First stage: formation of tetrahedral intermediate



water adds to the carbonyl group of the amide

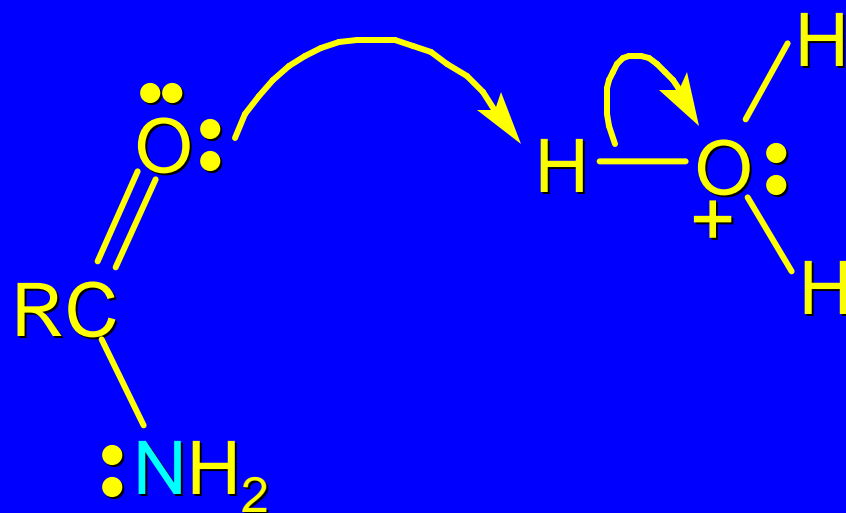
this stage is analogous to the acid-catalyzed addition of water to a ketone

Second stage: cleavage of tetrahedral intermediate

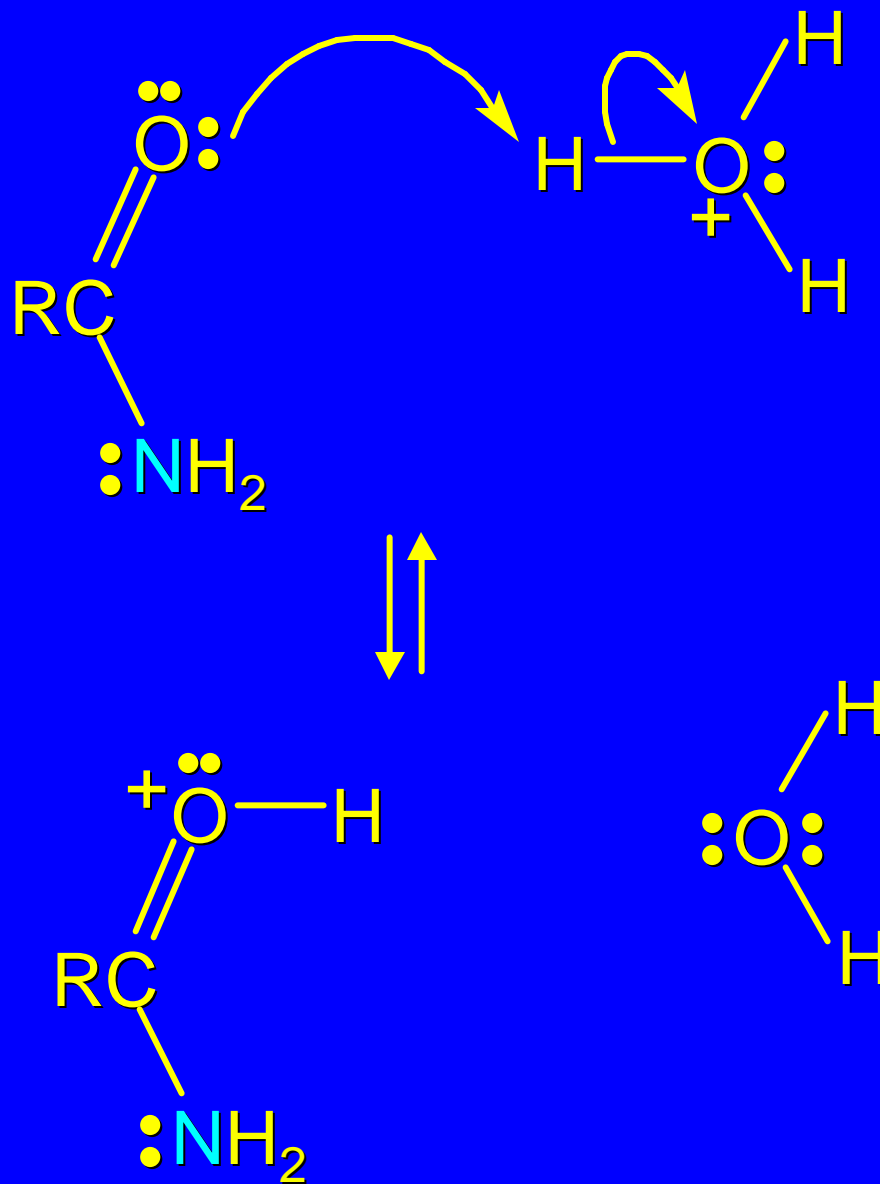


*Mechanism of formation
of
tetrahedral intermediate*

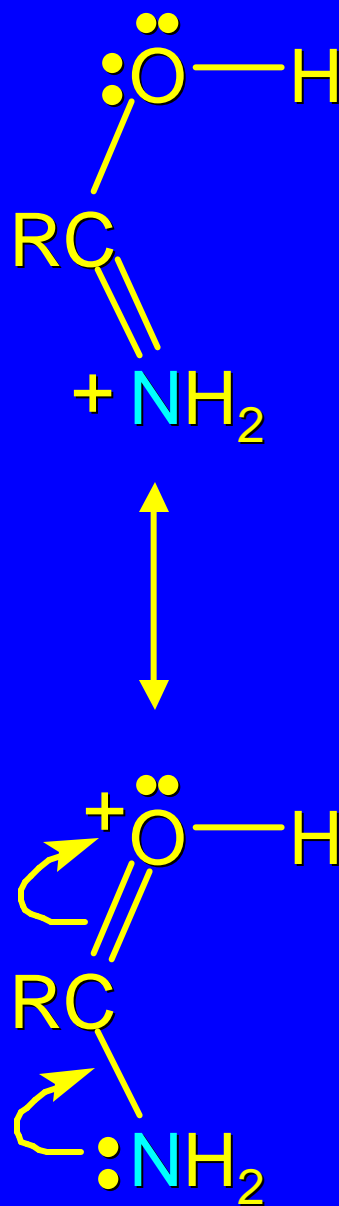
Step 1



Step 1

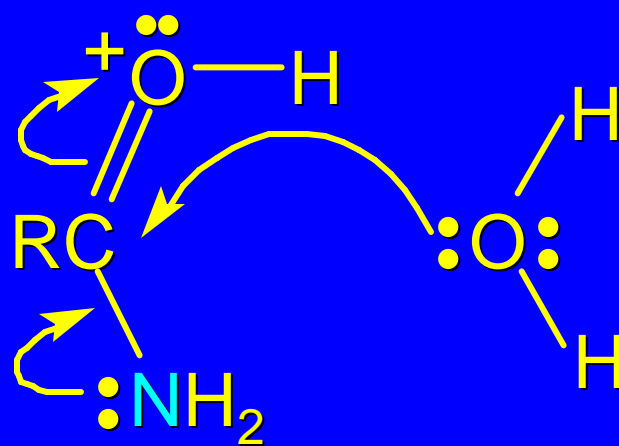


Step 1

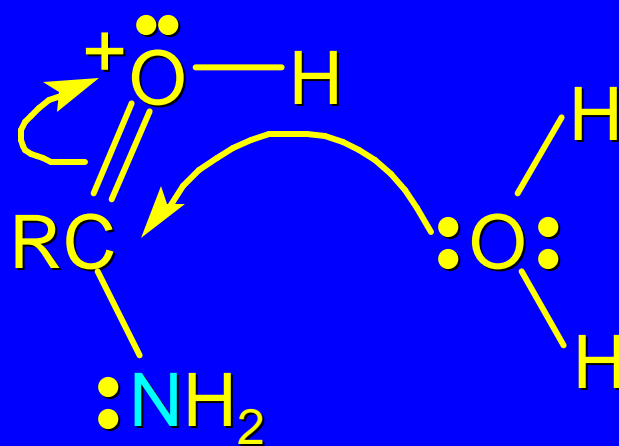
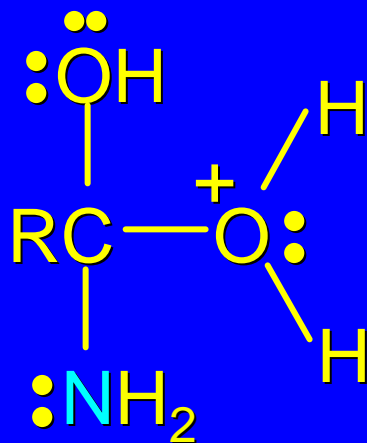


carbonyl oxygen is protonated because cation produced is stabilized by electron delocalization (resonance)

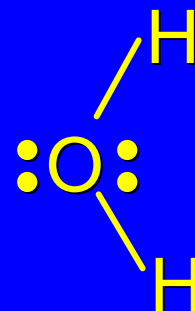
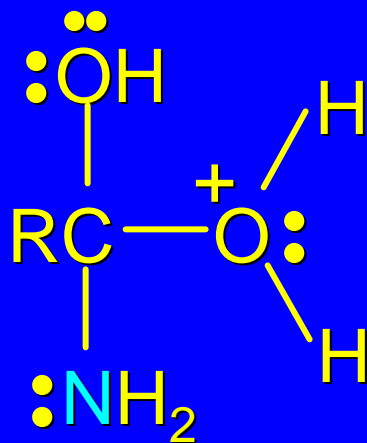
Step 2



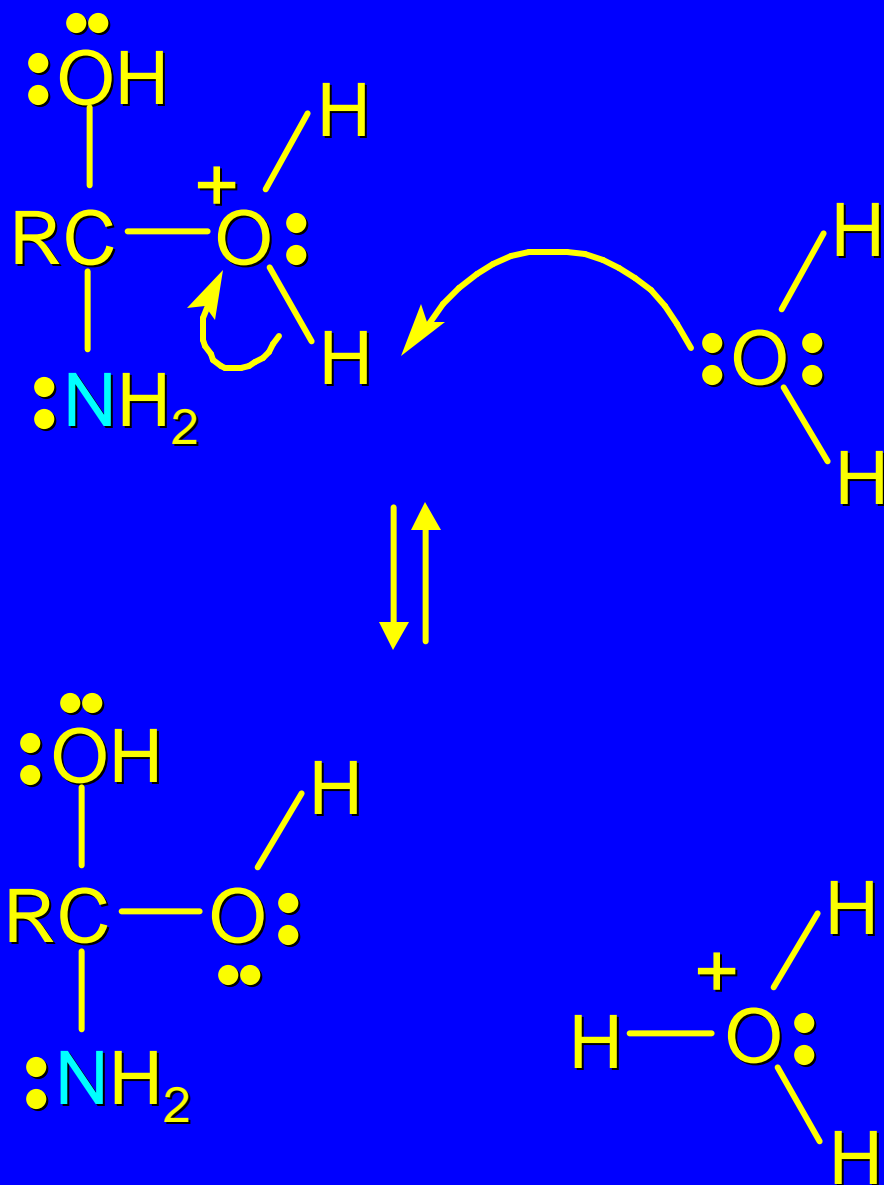
Step 2



Step 3

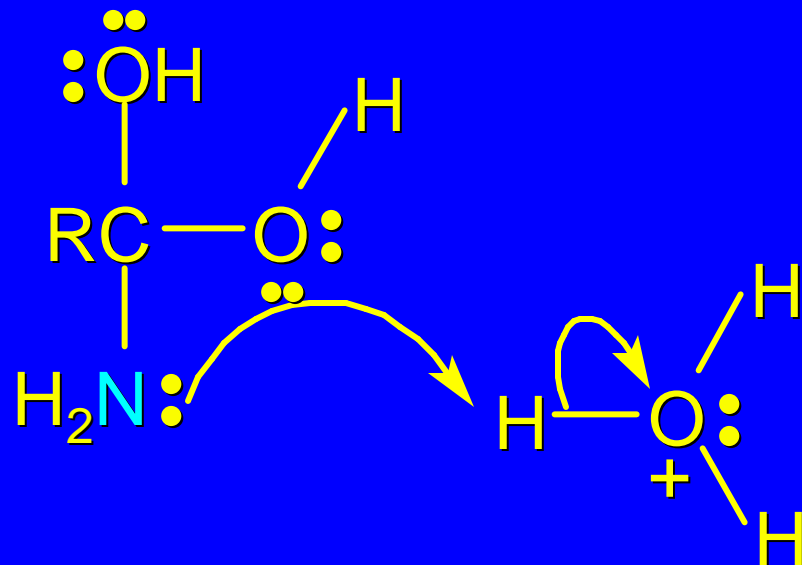


Step 3

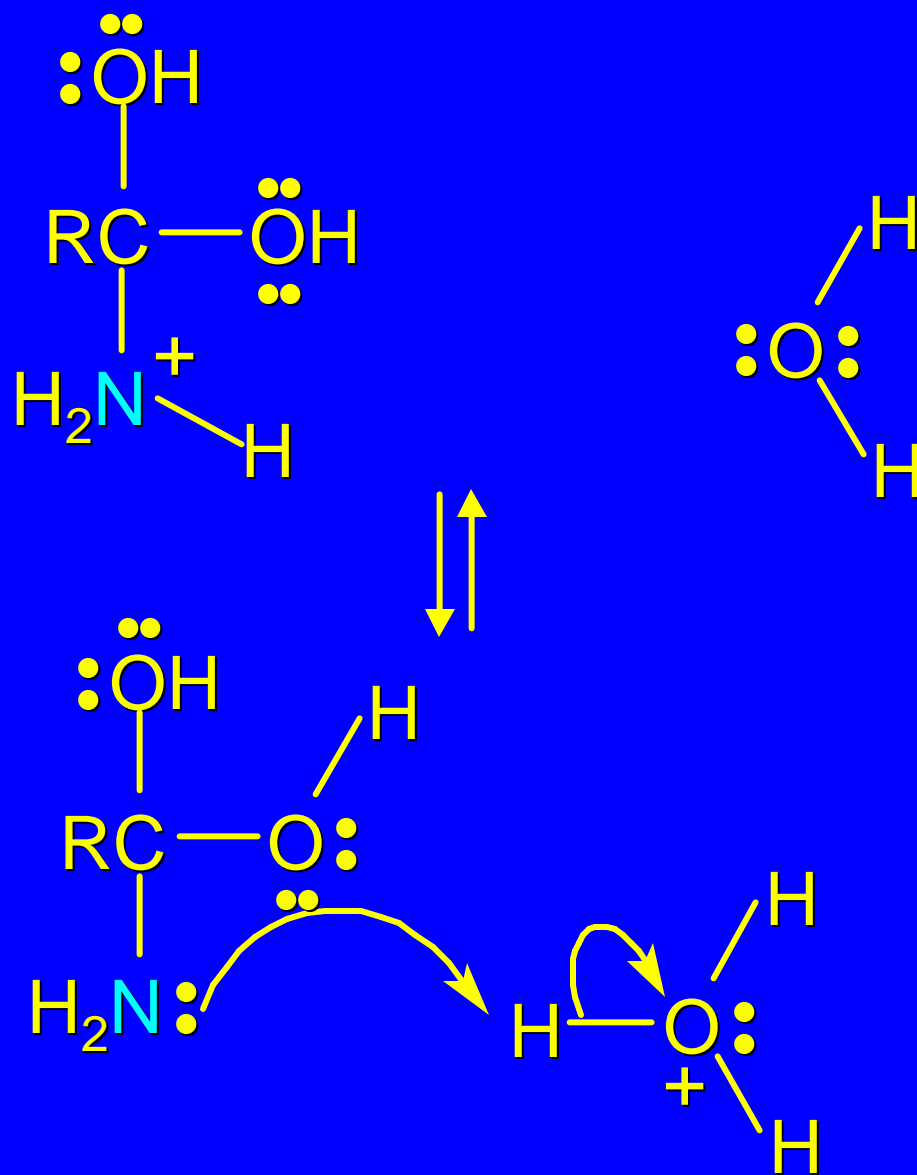


*Cleavage of tetrahedral
intermediate*

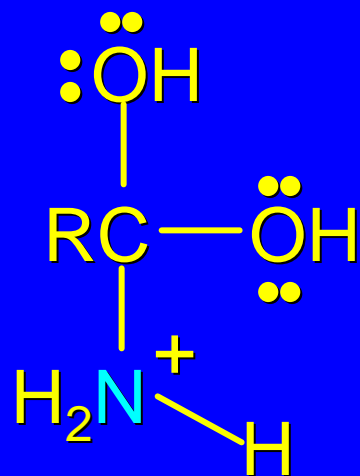
Step 4



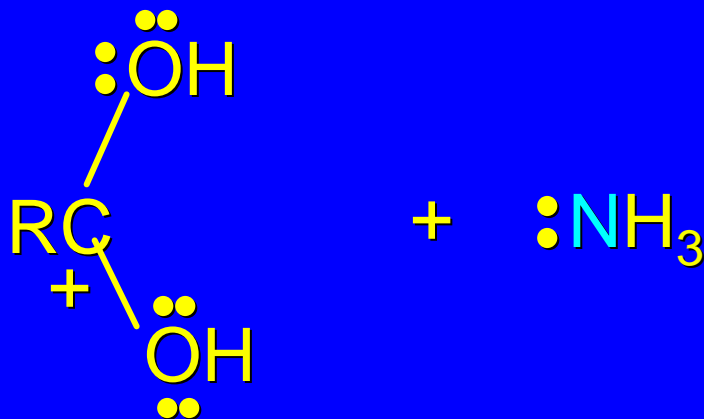
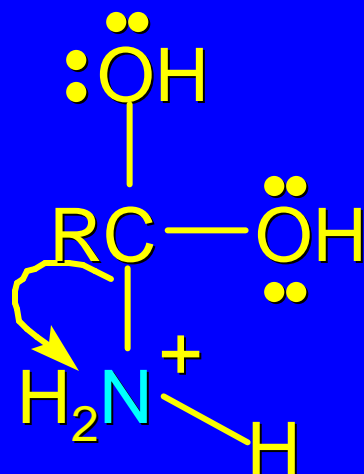
Step 4



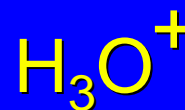
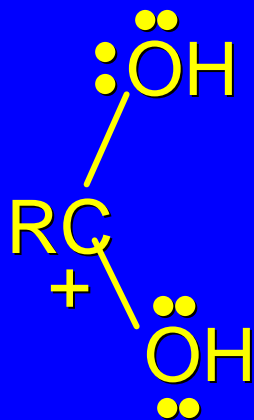
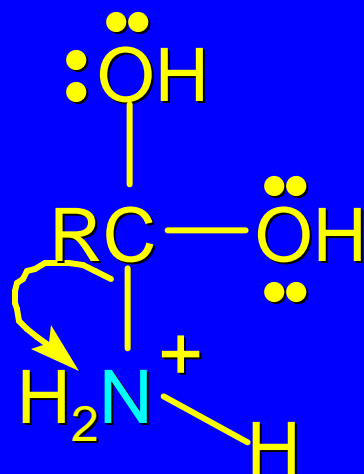
Step 5



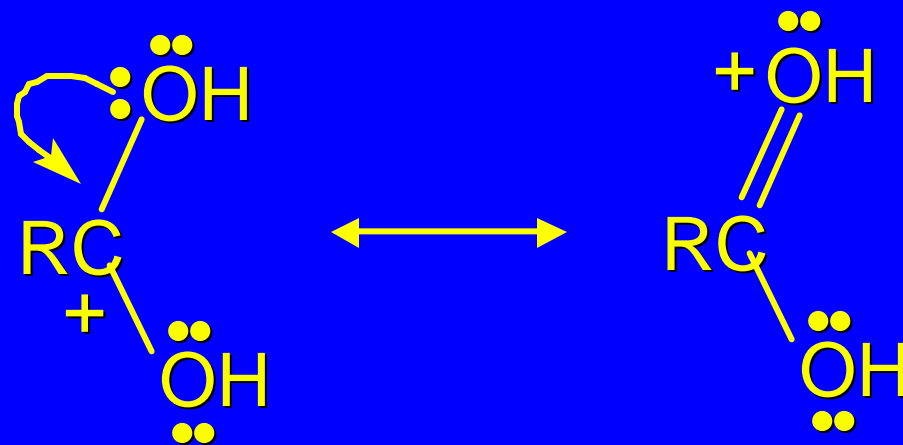
Step 5



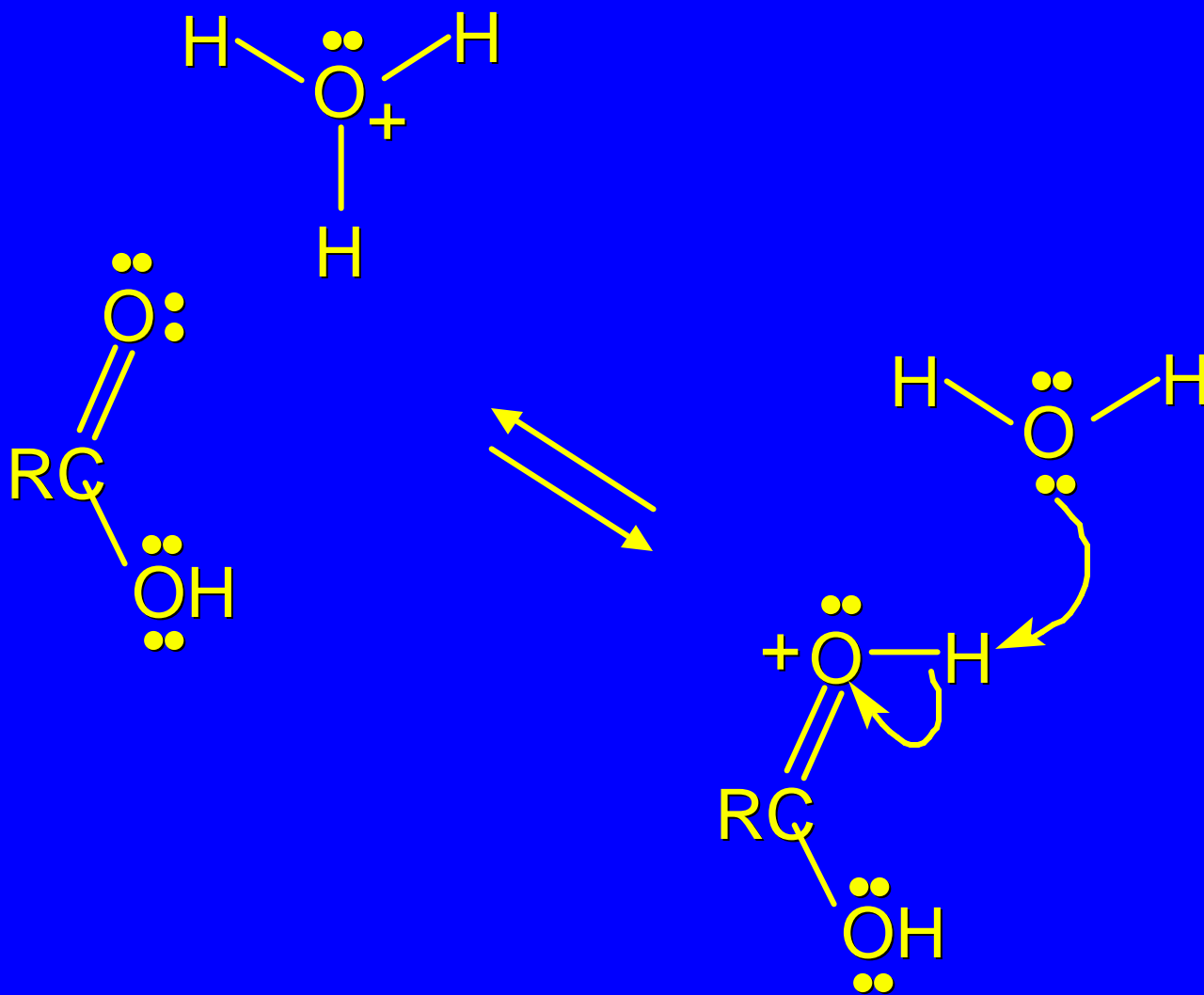
Step 6



Step 6



Step 6

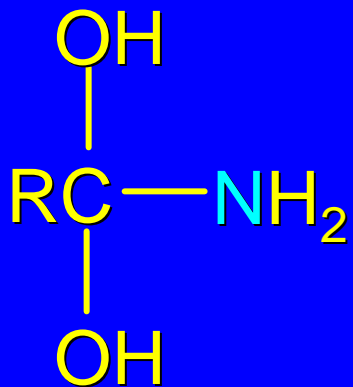
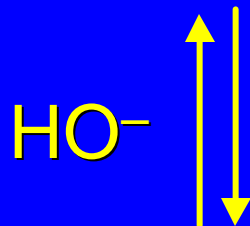
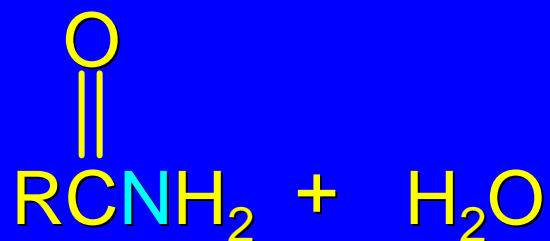


Mechanism of Amide Hydrolysis in Base

Involves two stages:

- 1) formation of tetrahedral intermediate
- 2) dissociation of tetrahedral intermediate

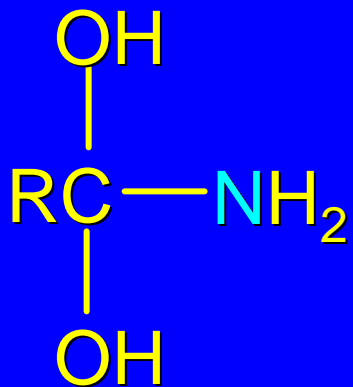
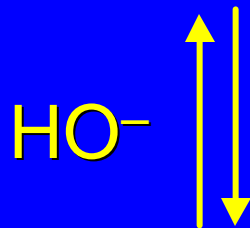
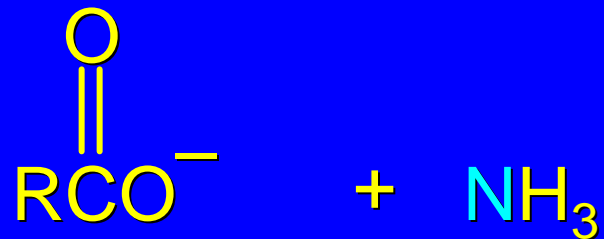
First stage: formation of tetrahedral intermediate



water adds to the carbonyl group of the amide

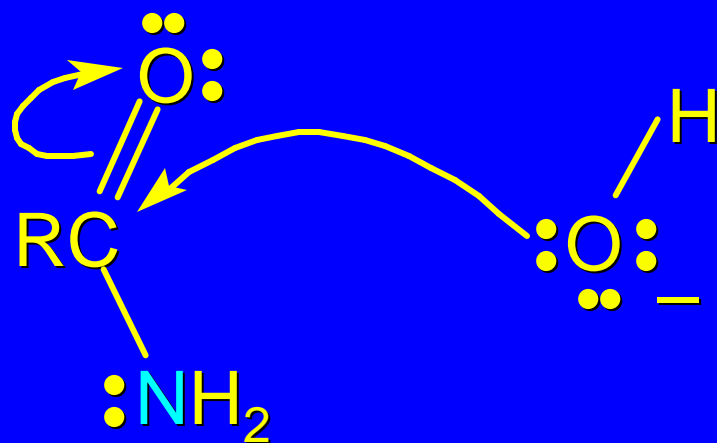
this stage is analogous to the base-catalyzed addition of water to a ketone

Second stage: cleavage of tetrahedral intermediate

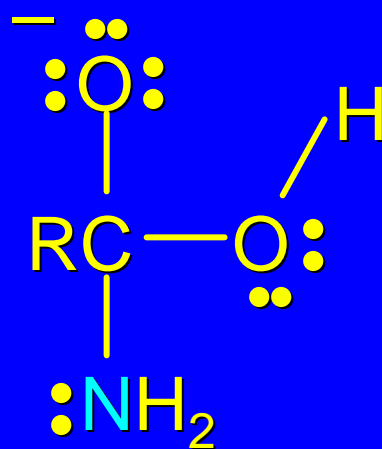
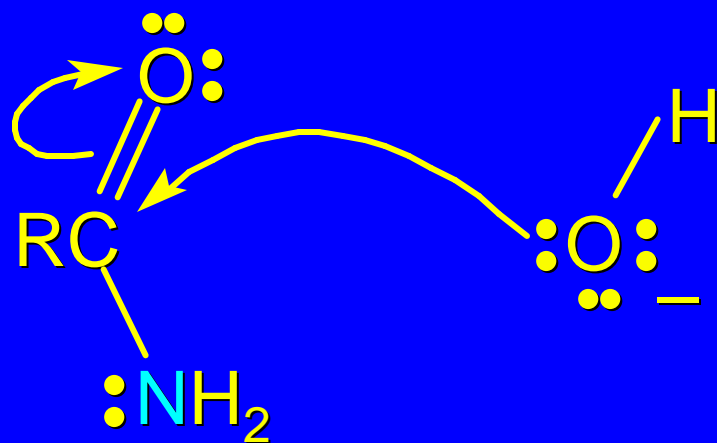


*Mechanism of formation
of
tetrahedral intermediate*

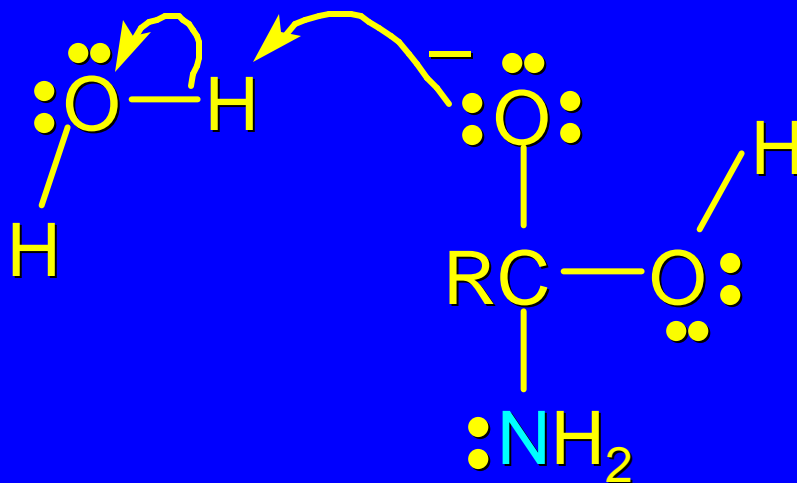
Step 1



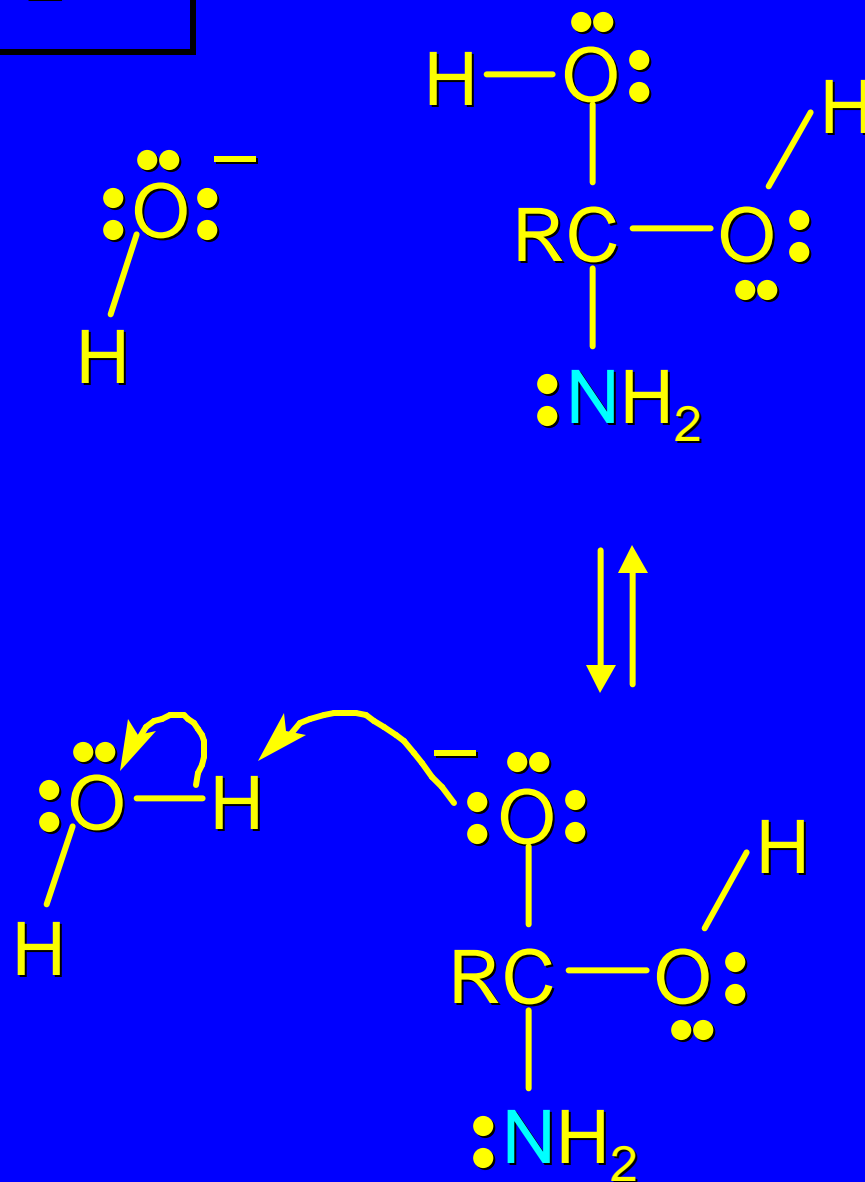
Step 1



Step 2

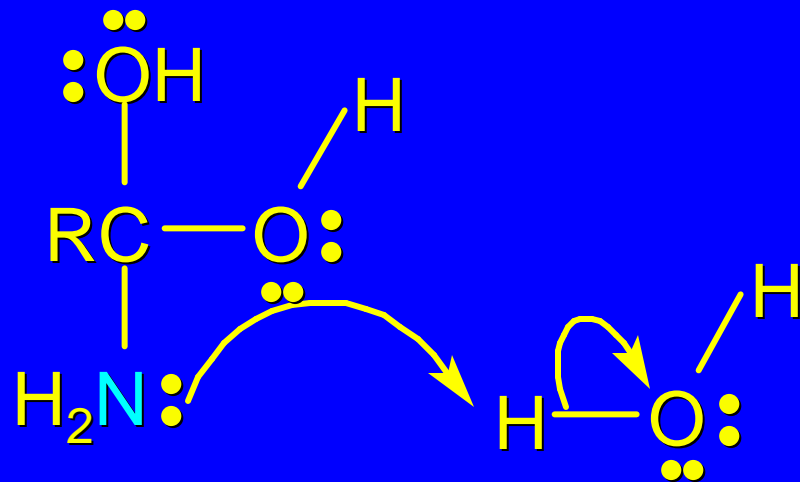


Step 2

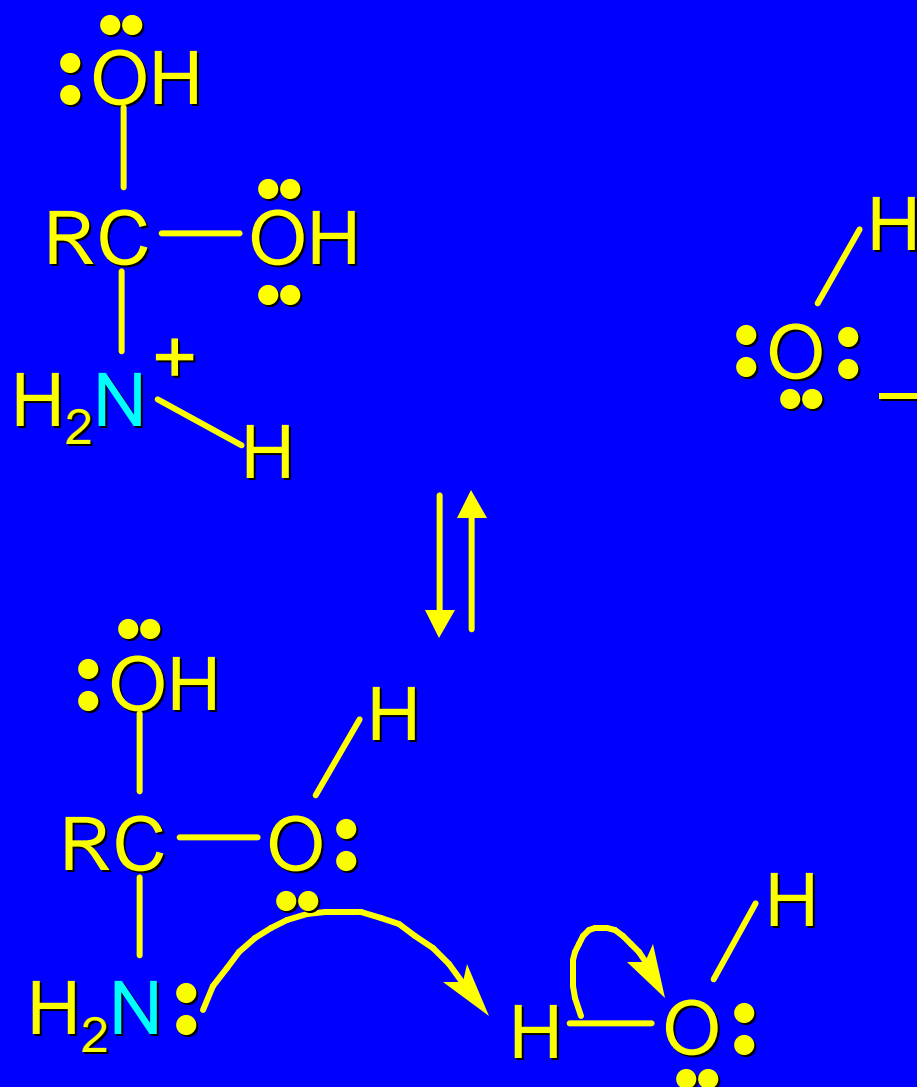


*Dissociation of
tetrahedral intermediate*

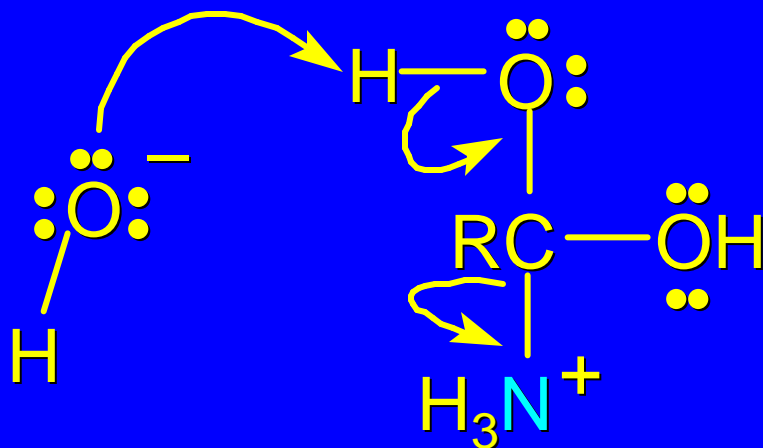
Step 3



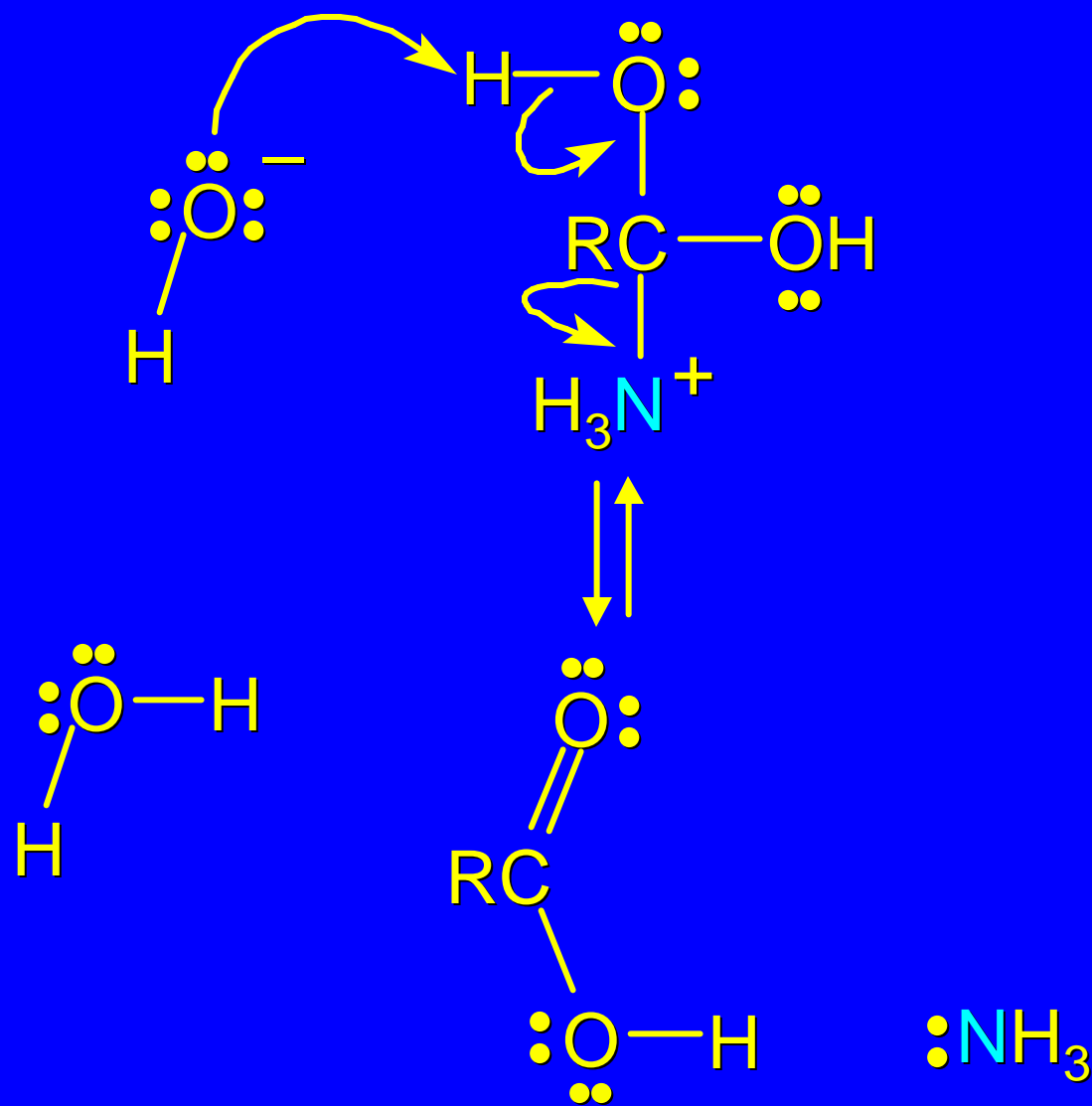
Step 3



Step 4



Step 4



Step 5

