

20.13

## Preparation of Amides

## *Preparation of Amides*

Amides are prepared from amines by acylation with:

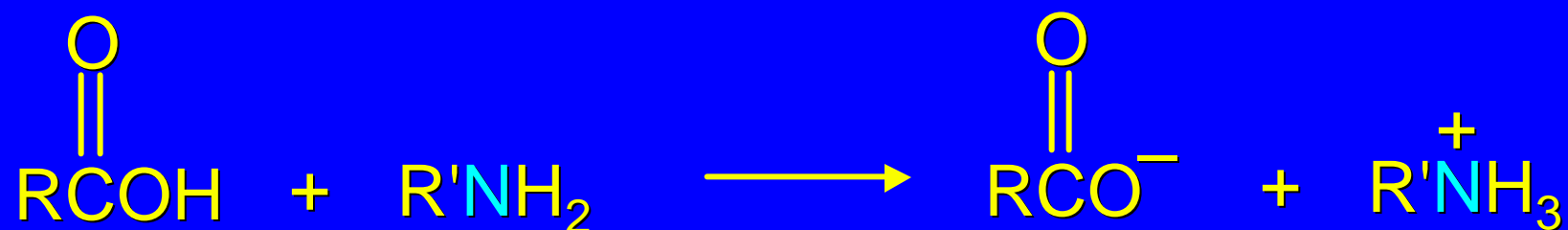
acyl chlorides (Table 20.2)

anhydrides (Table 20.3)

esters (Table 20.6)

## *Preparation of Amides*

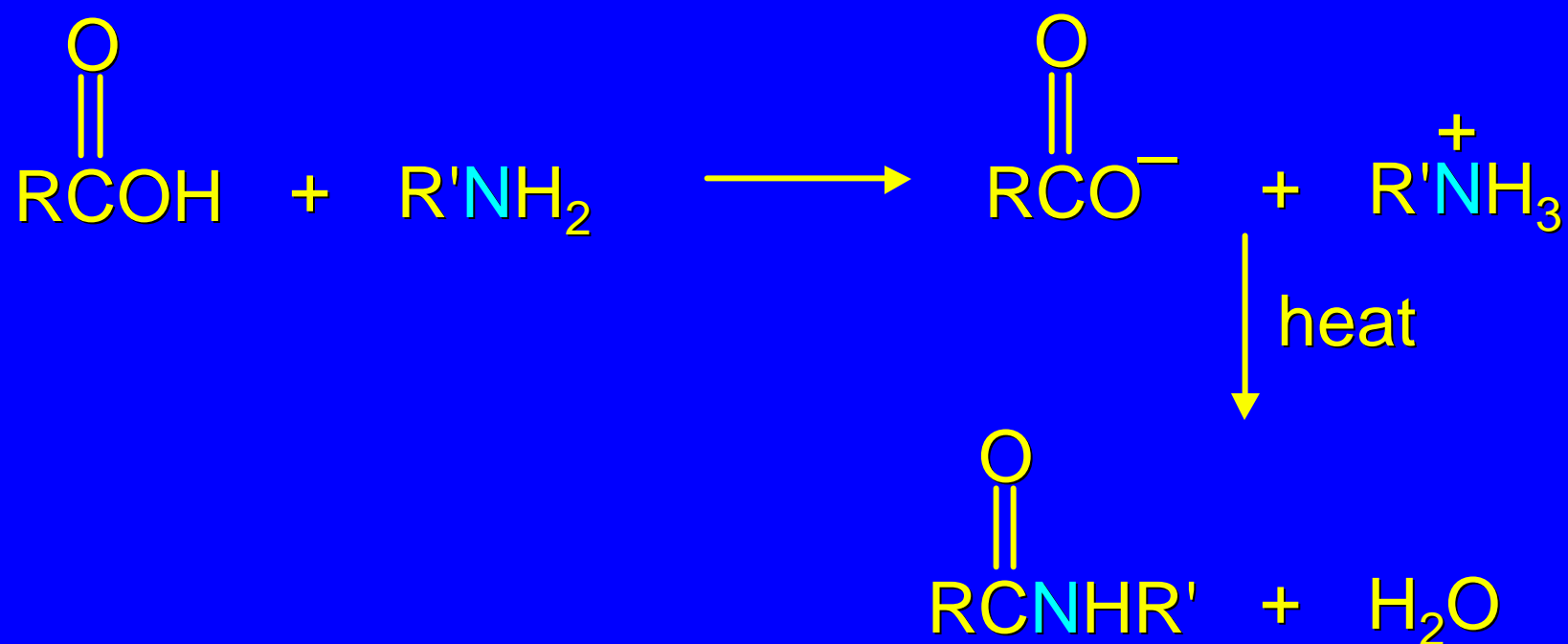
Amines do not react with carboxylic acids to give amides. The reaction that occurs is proton-transfer (acid-base).



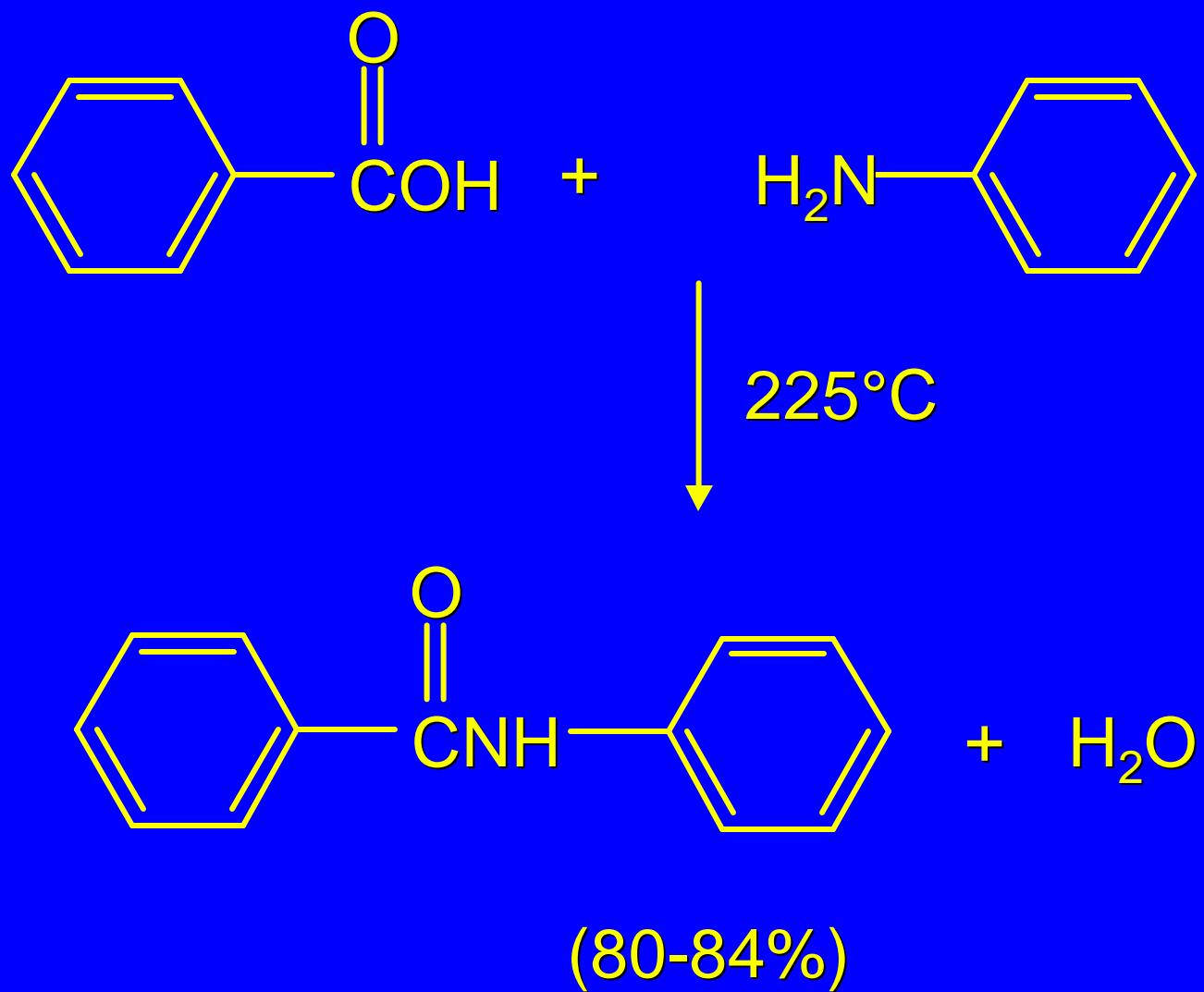
If no heat-sensitive groups are present, the resulting ammonium carboxylate salts can be converted to amides by heating.

## Preparation of Amides

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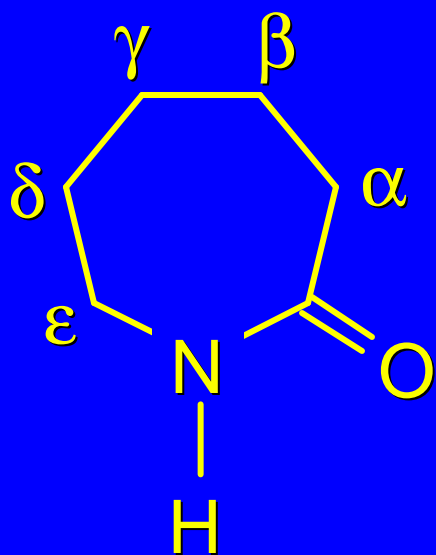
*Example*



20.14  
Lactams

## Lactams

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

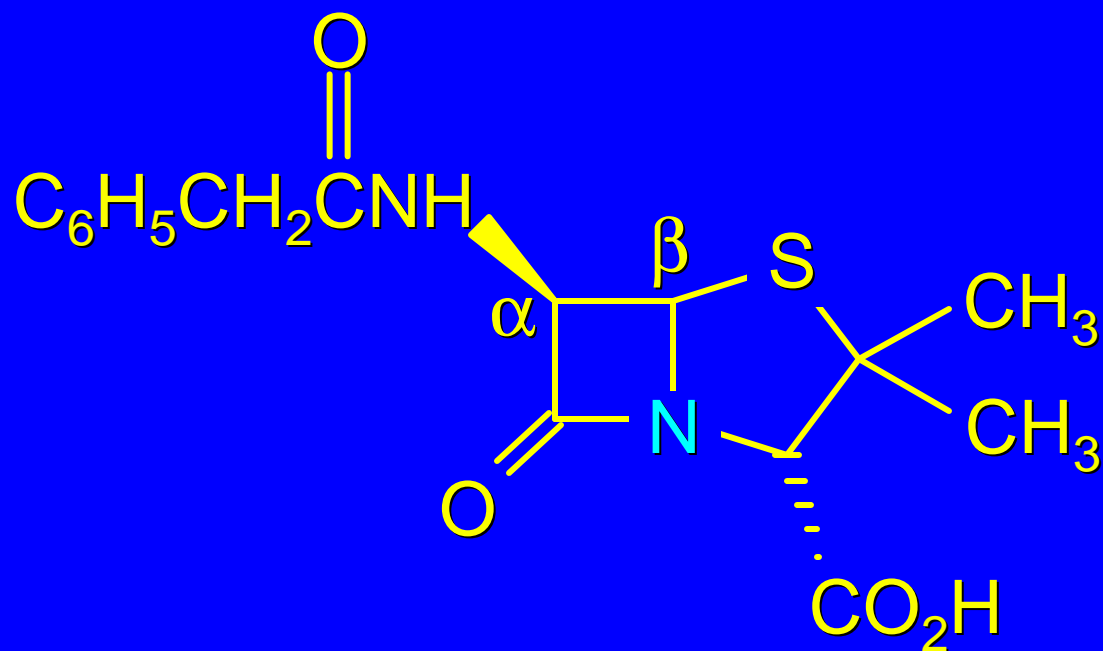


$\epsilon$ -Caprolactam\*: used to prepare a type of nylon

\*Caproic acid is the common name for hexanoic acid.

## Lactams

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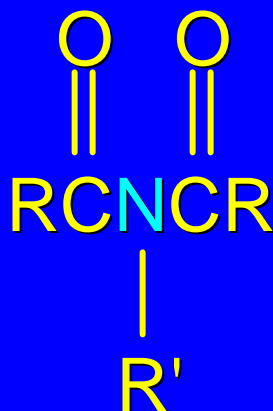


Penicillin G: a  $\beta$ -lactam antibiotic

20.15  
Imides

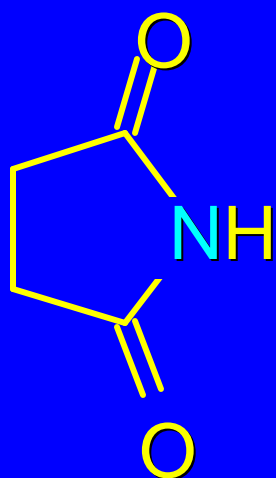
## *Imides*

Imides have 2 acyl groups attached to the nitrogen.



## *Imides*

The most common examples are cyclic imides.



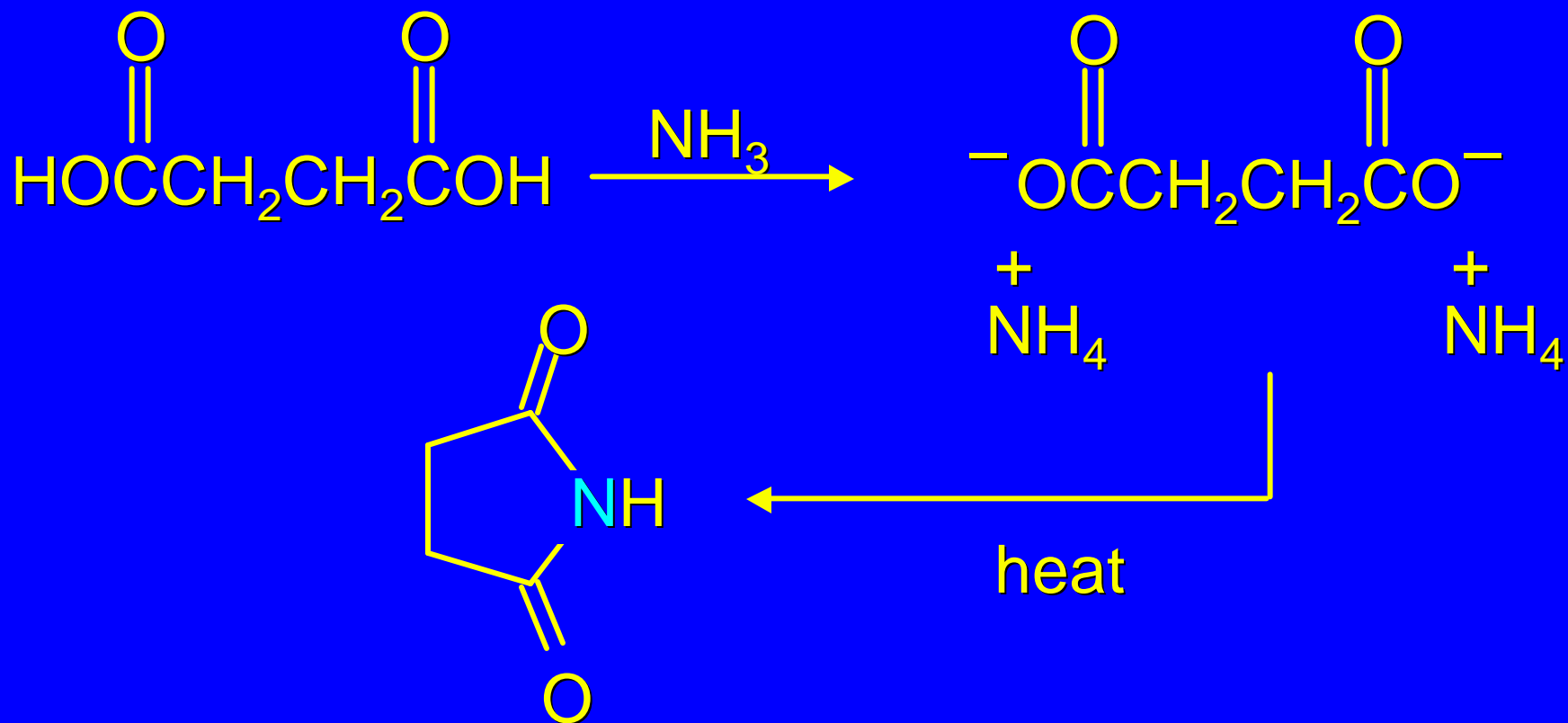
Succinimide



Phthalimide

## Preparation of Imides

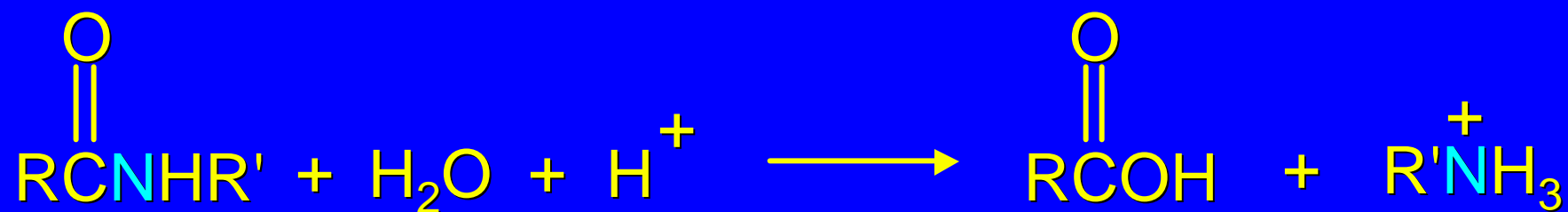
Cyclic imides are prepared by heating the ammonium salts of dicarboxylic acids.



20.16  
Hydrolysis of Amides

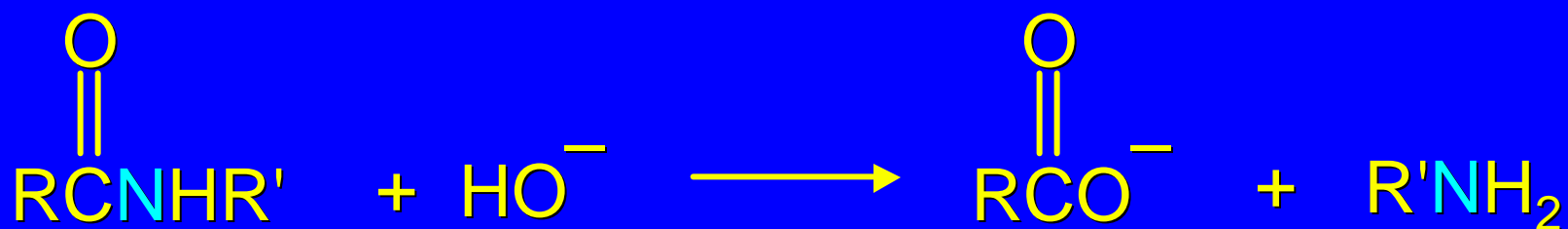
## *Hydrolysis of Amides*

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

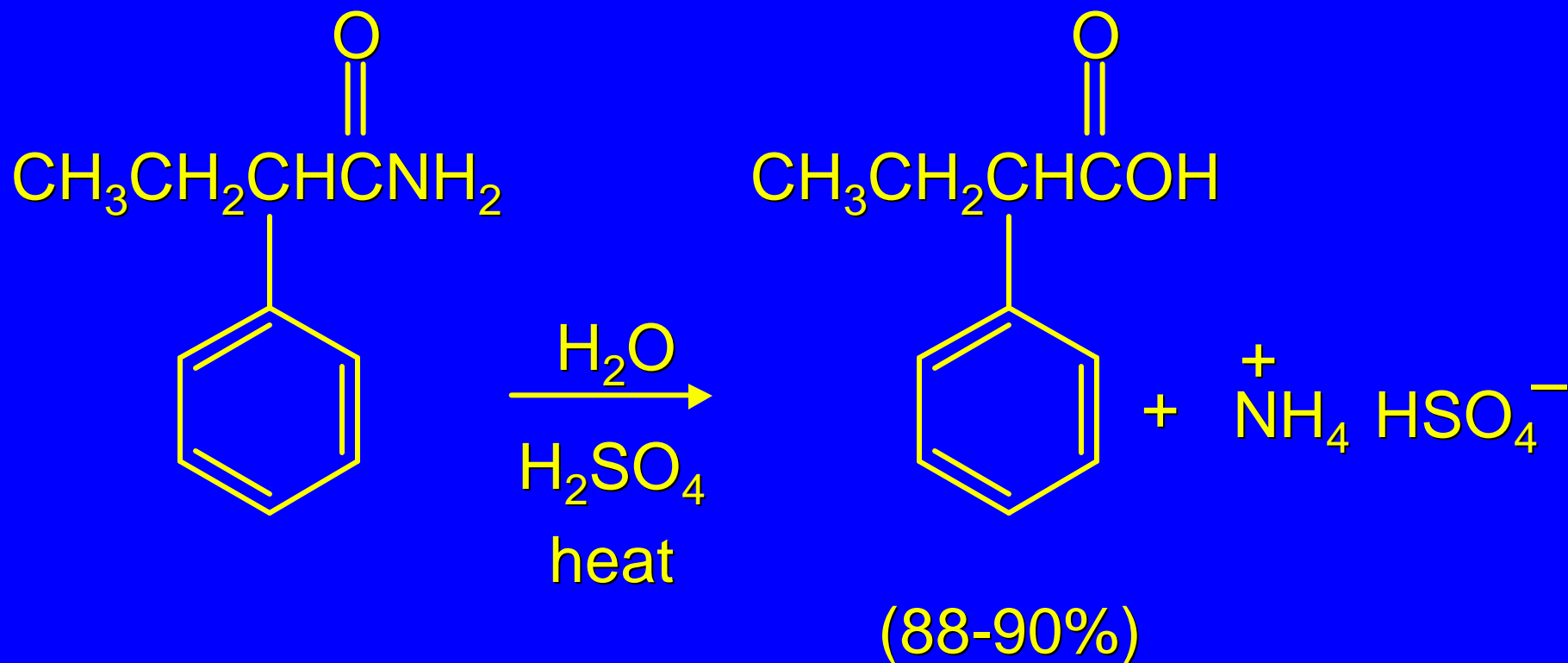


## *Hydrolysis of Amides*

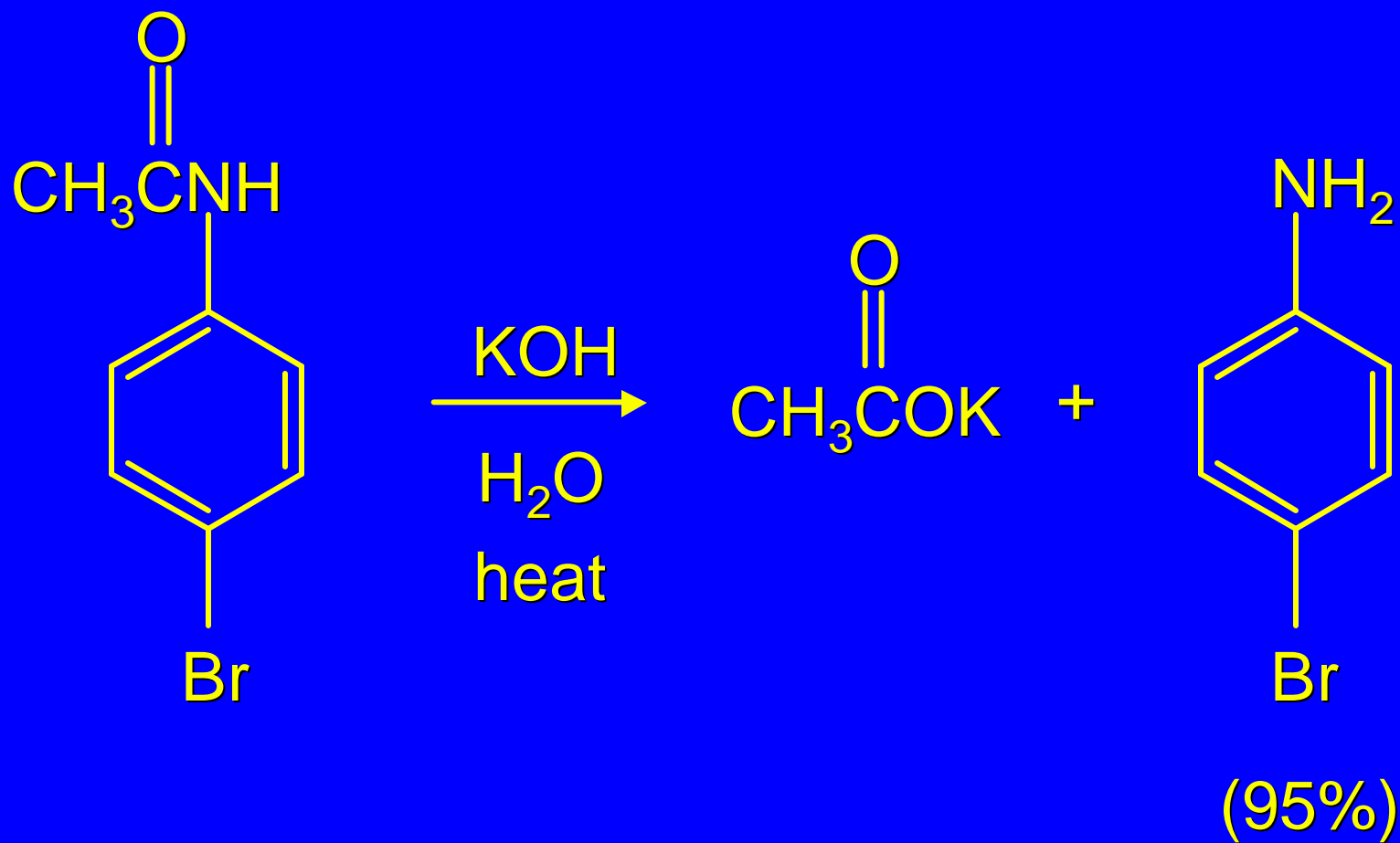
In basic solution the carboxylic acid product is deprotonated to give a carboxylate ion.



*Example: Acid Hydrolysis*



## Example: Basic Hydrolysis

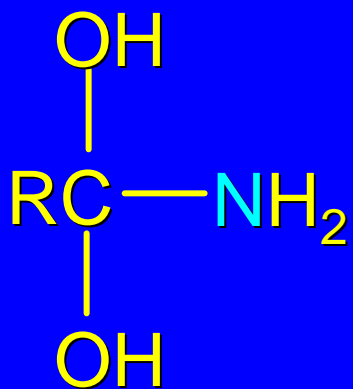
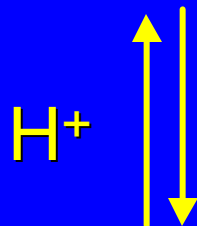
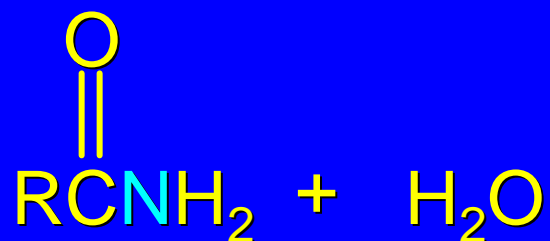


## *Mechanism of Acid-Catalyzed Amide Hydrolysis*

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

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

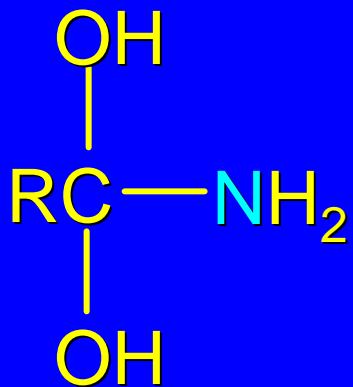
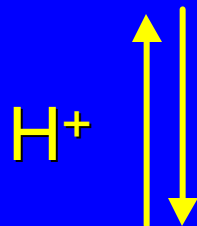
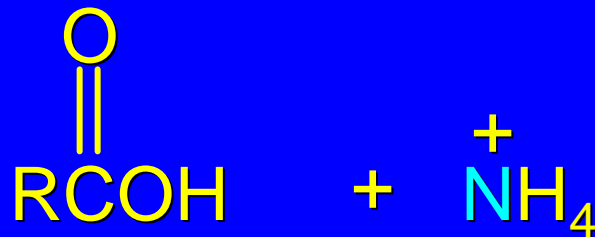
## *First stage: formation of tetrahedral intermediate*



water adds to the carbonyl group of the amide

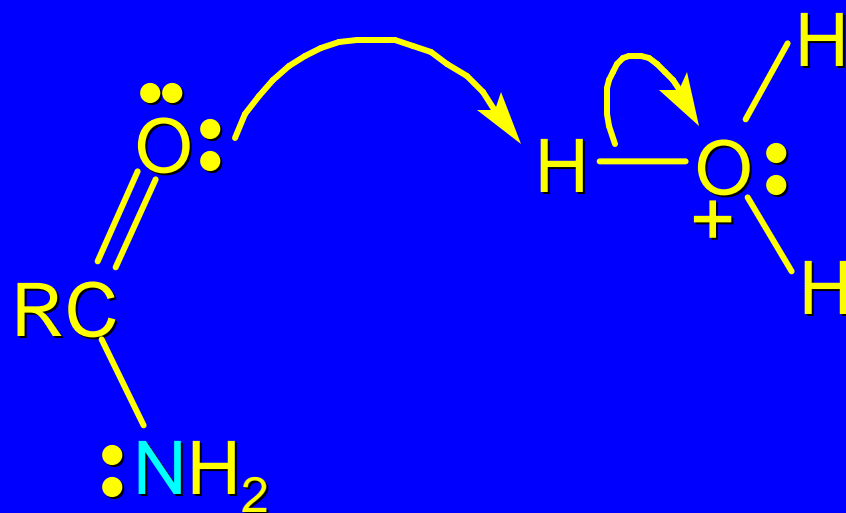
this stage is analogous to the acid-catalyzed addition of water to a ketone

*Second stage: cleavage of tetrahedral intermediate*

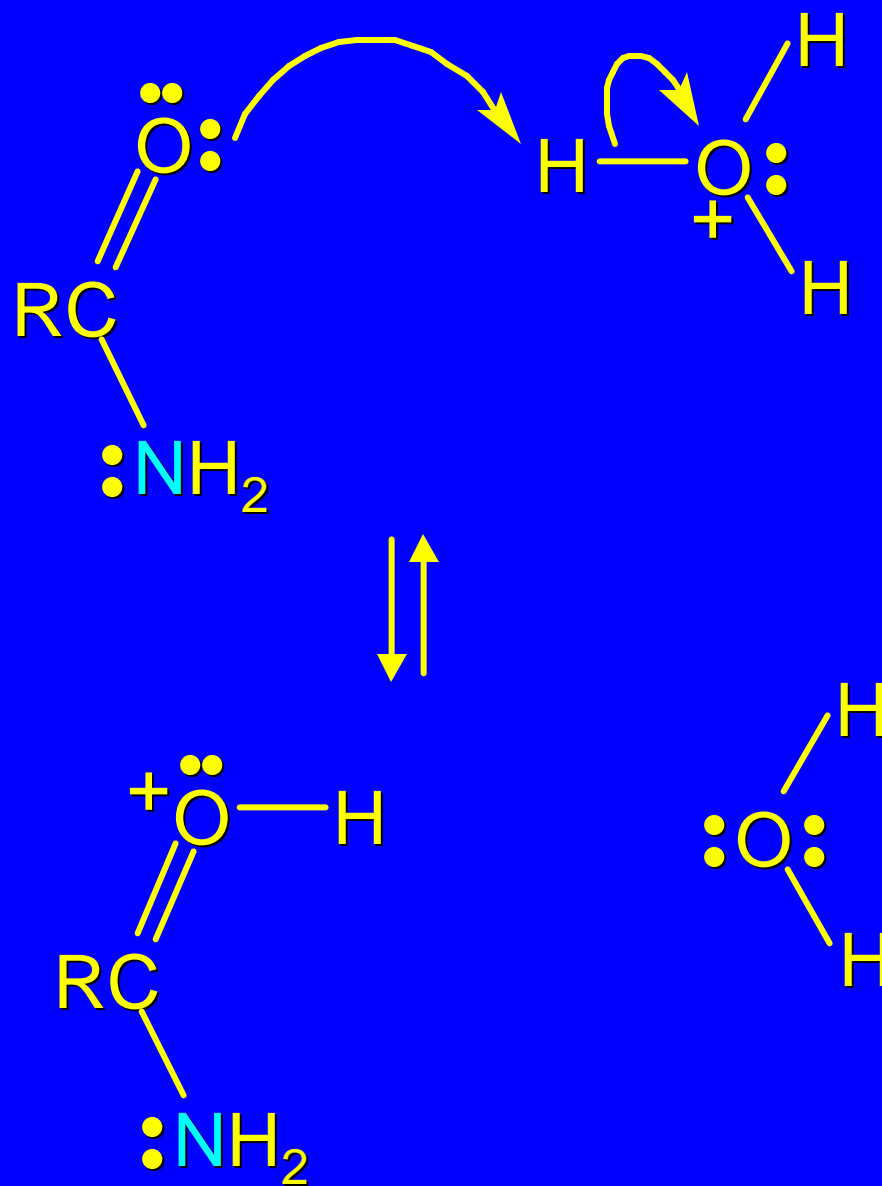


*Mechanism of formation  
of  
tetrahedral intermediate*

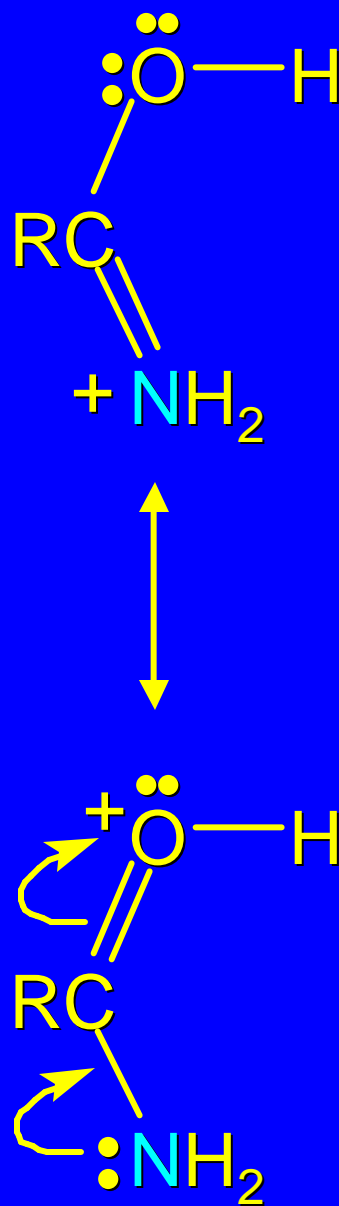
*Step 1*



Step 1

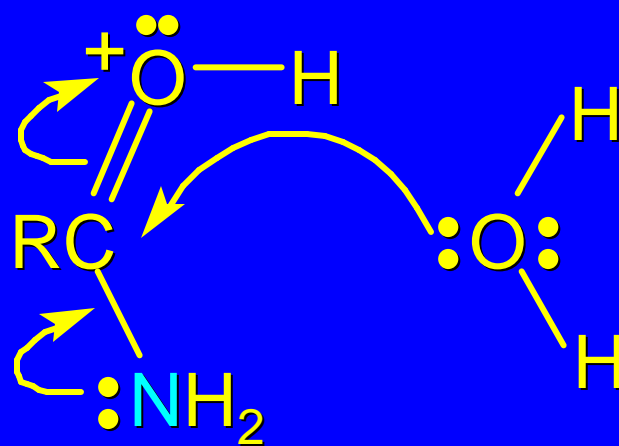


Step 1

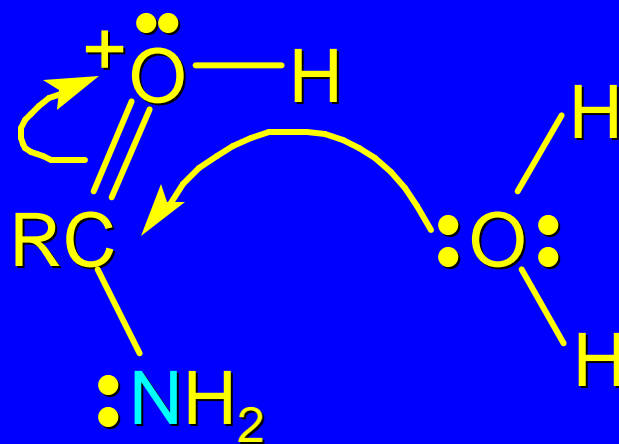
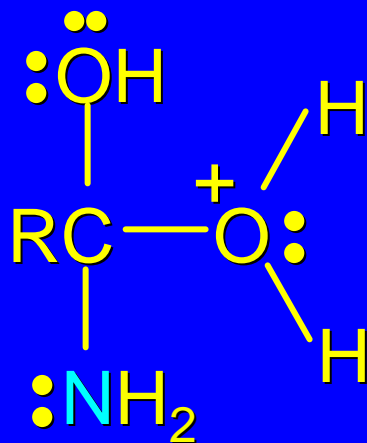


carbonyl oxygen is protonated because cation produced is stabilized by electron delocalization (resonance)

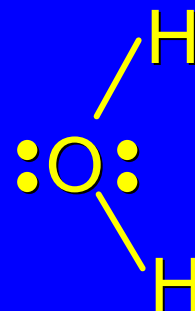
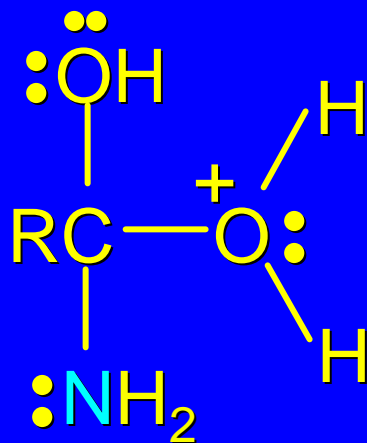
Step 2



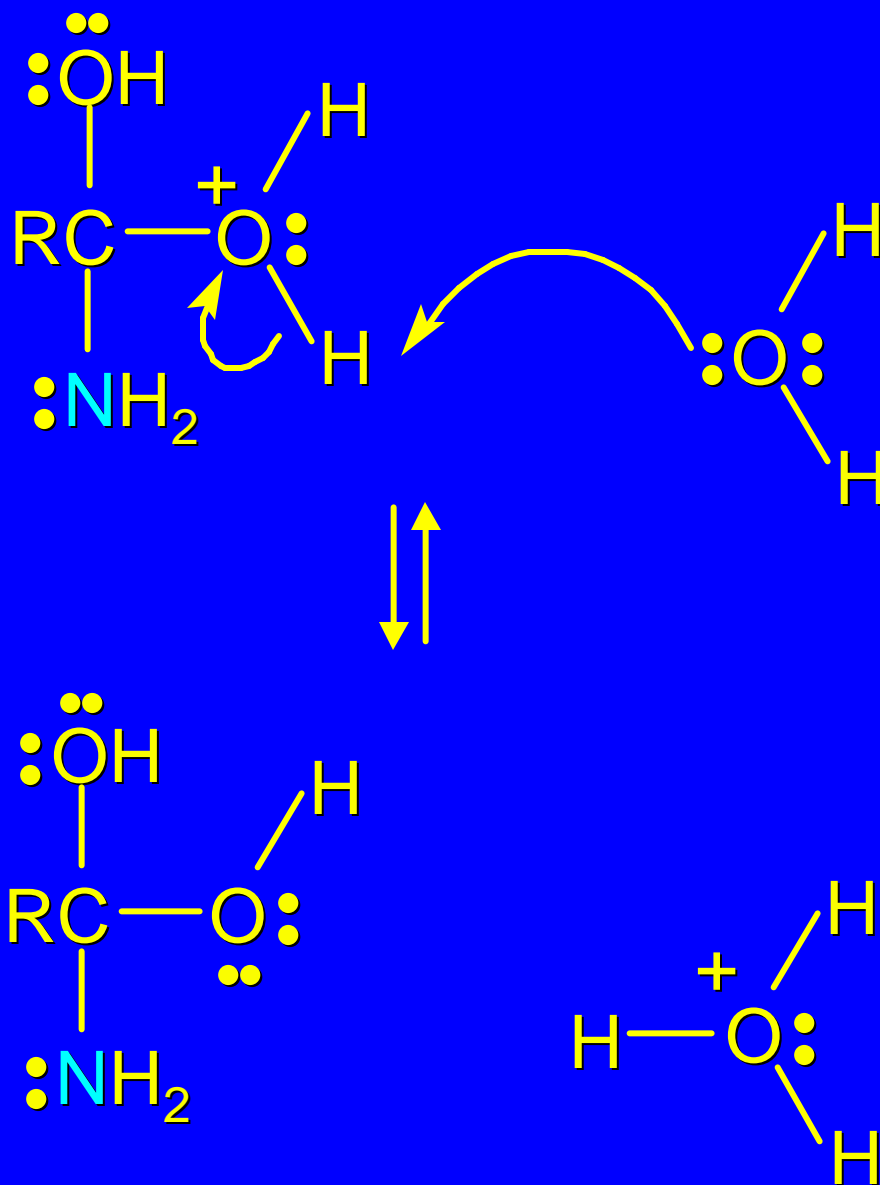
Step 2



Step 3

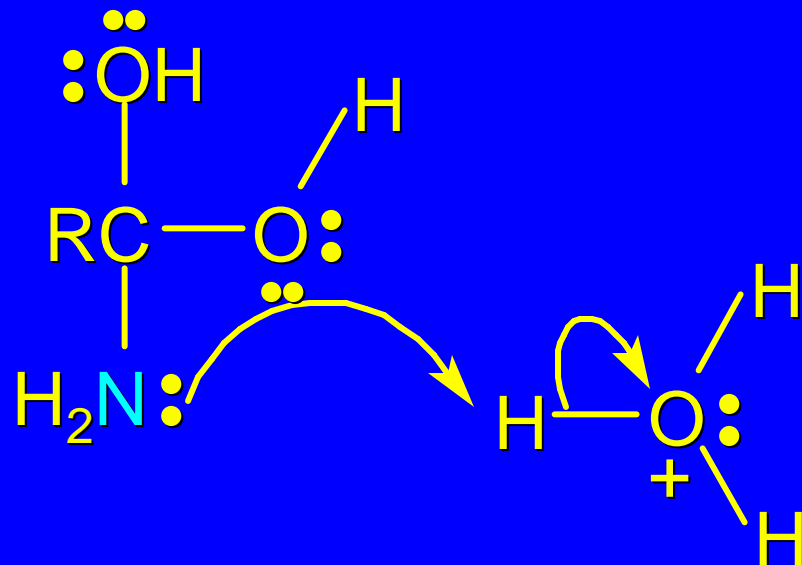


### Step 3

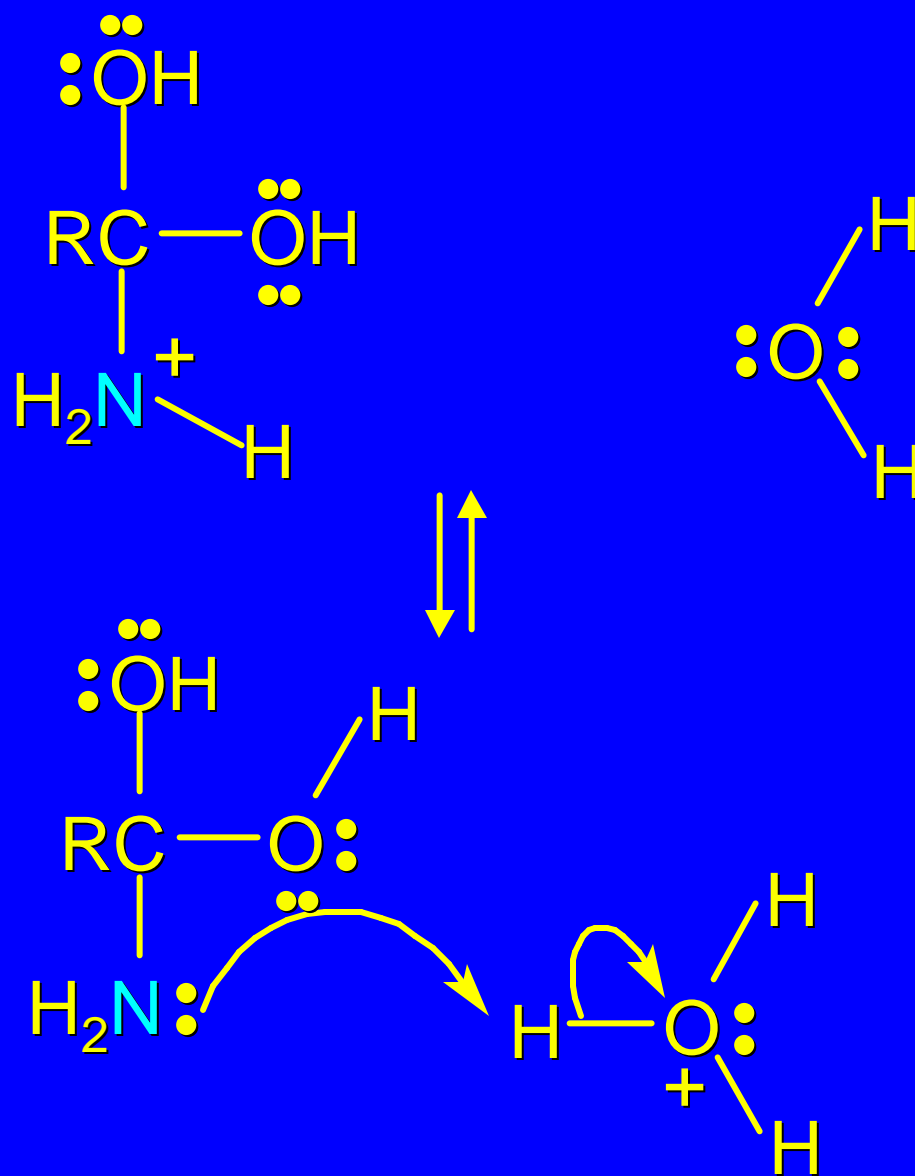


*Cleavage of tetrahedral  
intermediate*

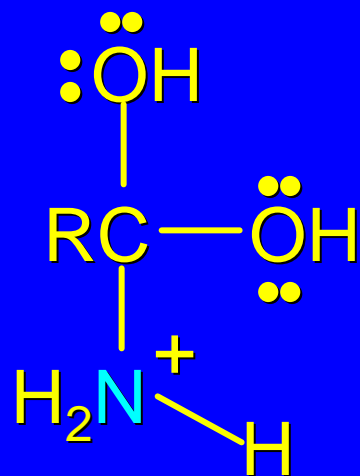
Step 4



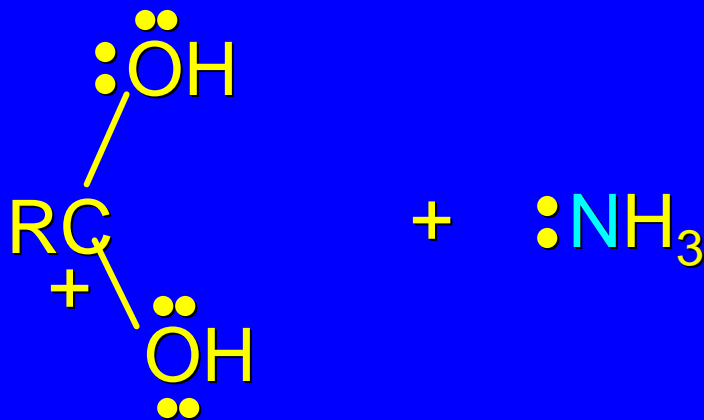
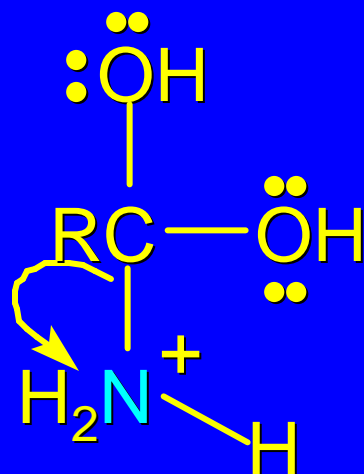
Step 4



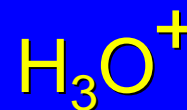
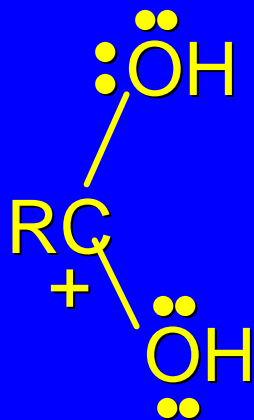
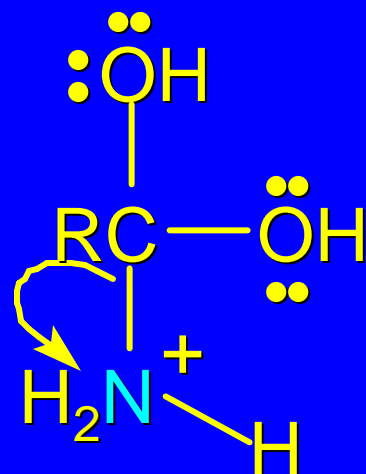
Step 5



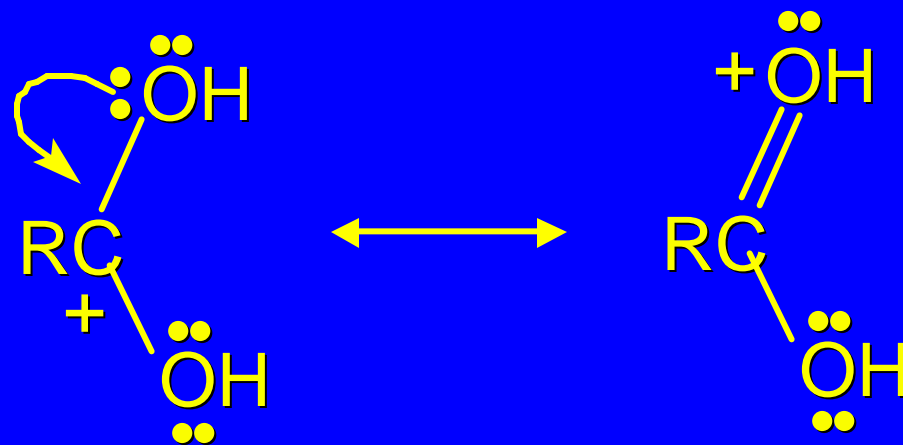
Step 5



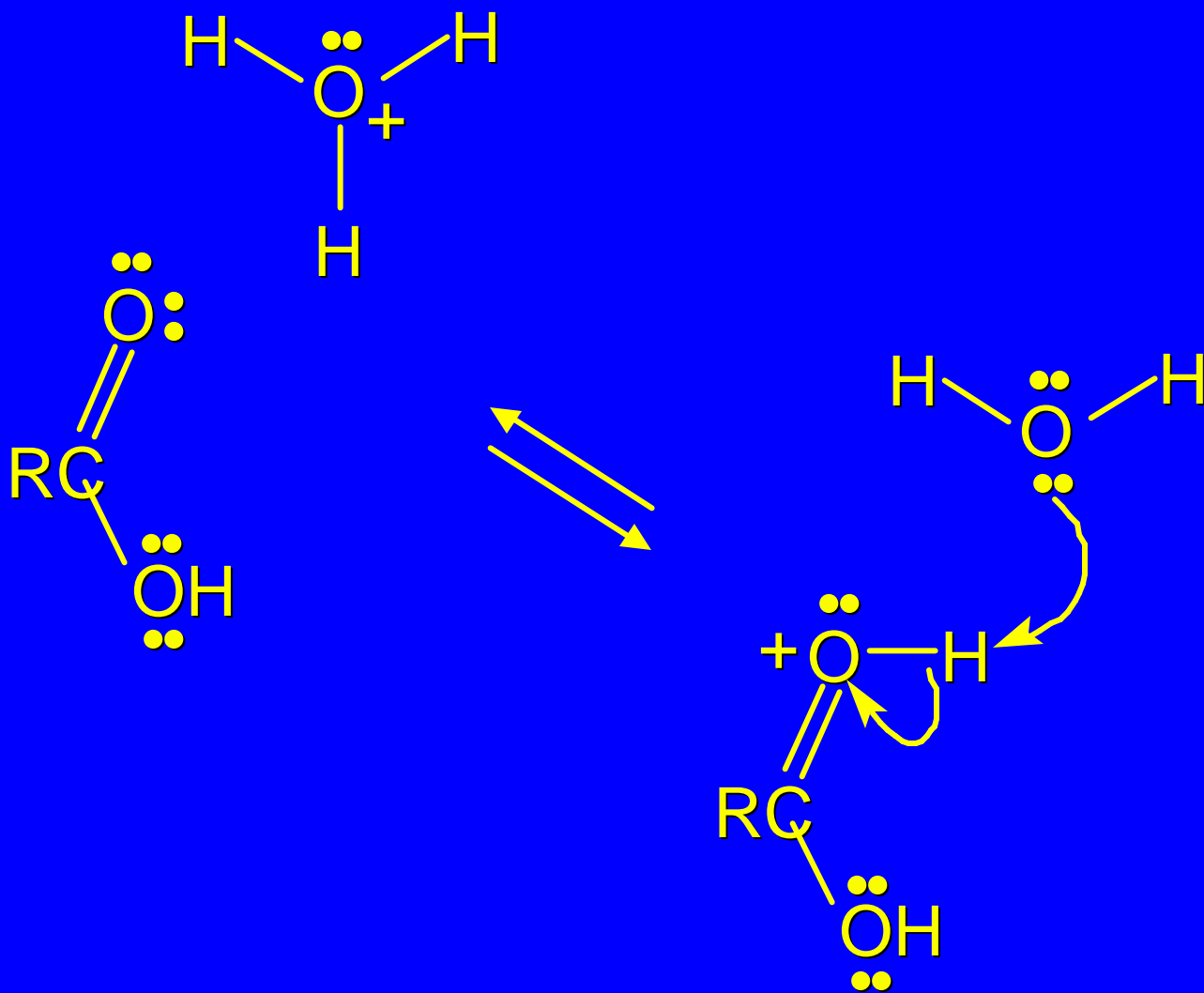
Step 6



Step 6



Step 6

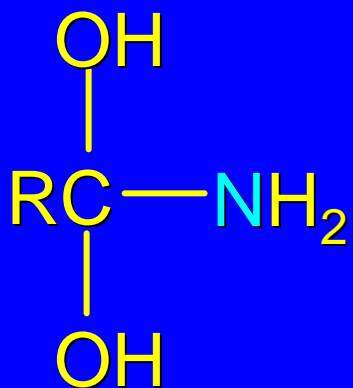
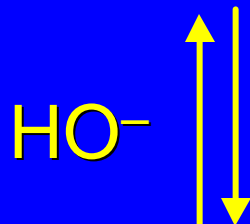
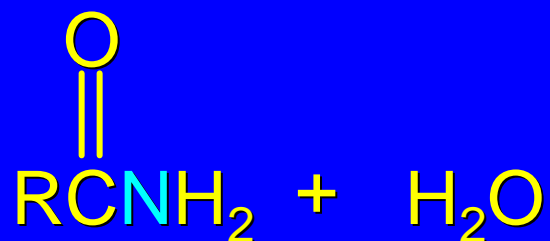


## *Mechanism of Amide Hydrolysis in Base*

Involves two stages:

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

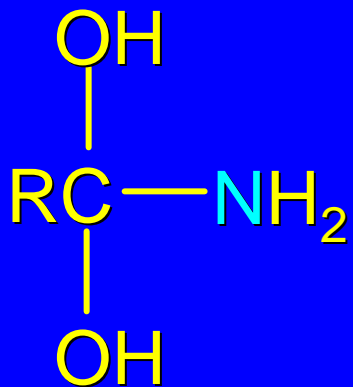
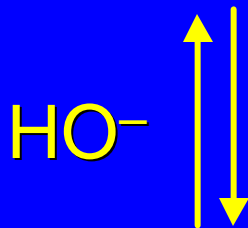
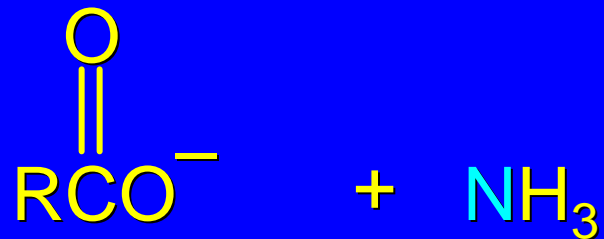
## *First stage: formation of tetrahedral intermediate*



water adds to the carbonyl group of the amide

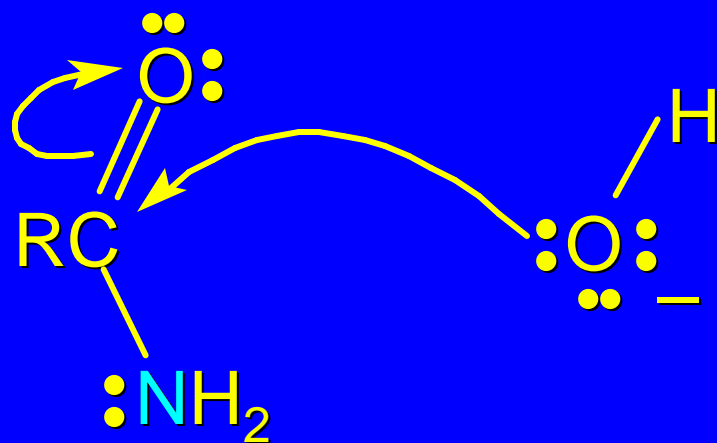
this stage is analogous to the base-catalyzed addition of water to a ketone

*Second stage: cleavage of tetrahedral intermediate*

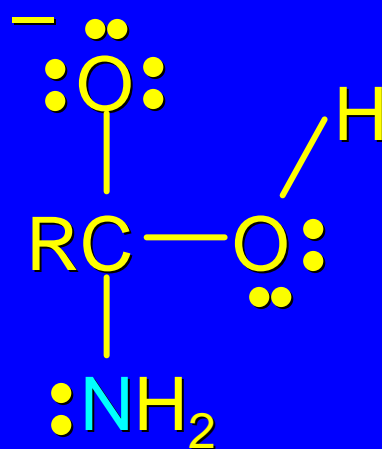
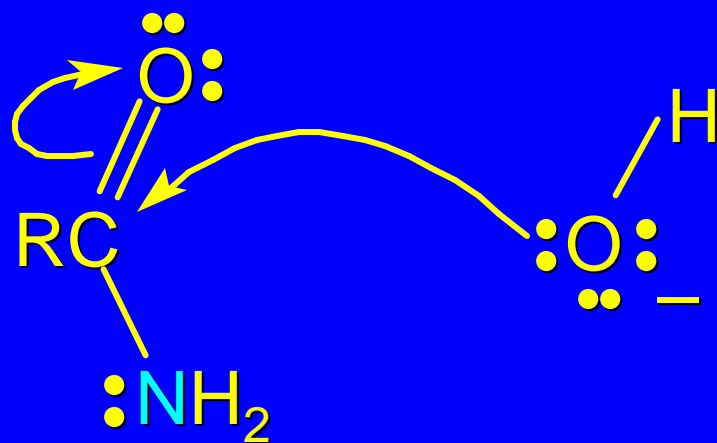


*Mechanism of formation  
of  
tetrahedral intermediate*

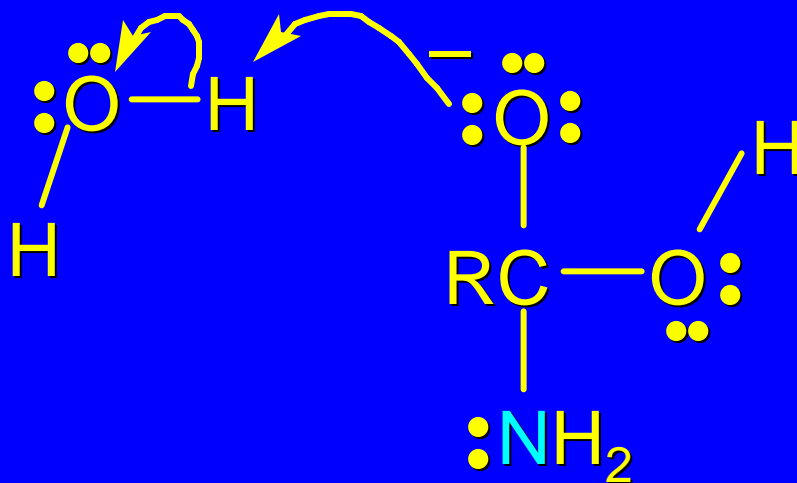
Step 1



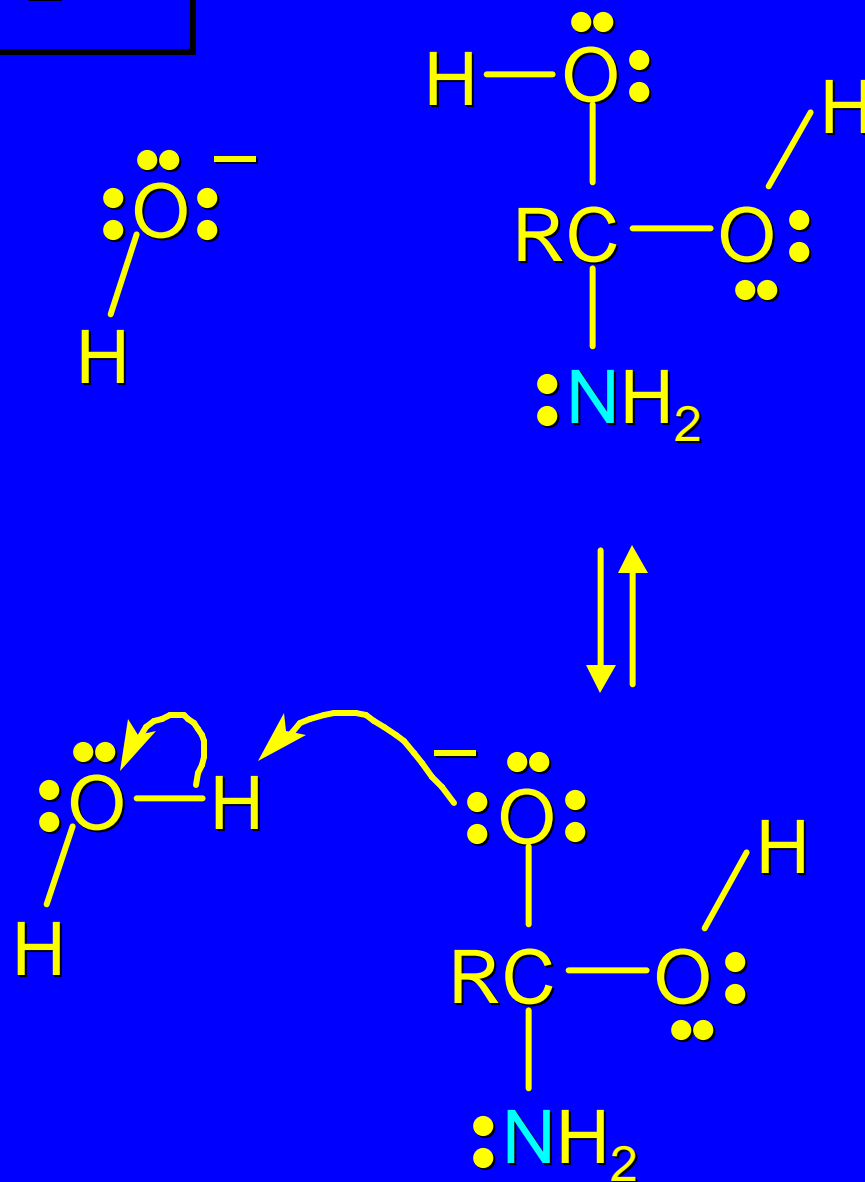
Step 1



Step 2

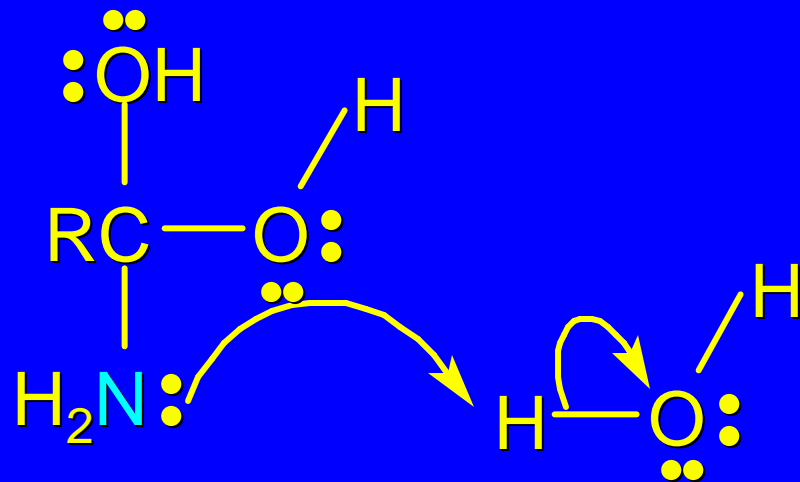


Step 2

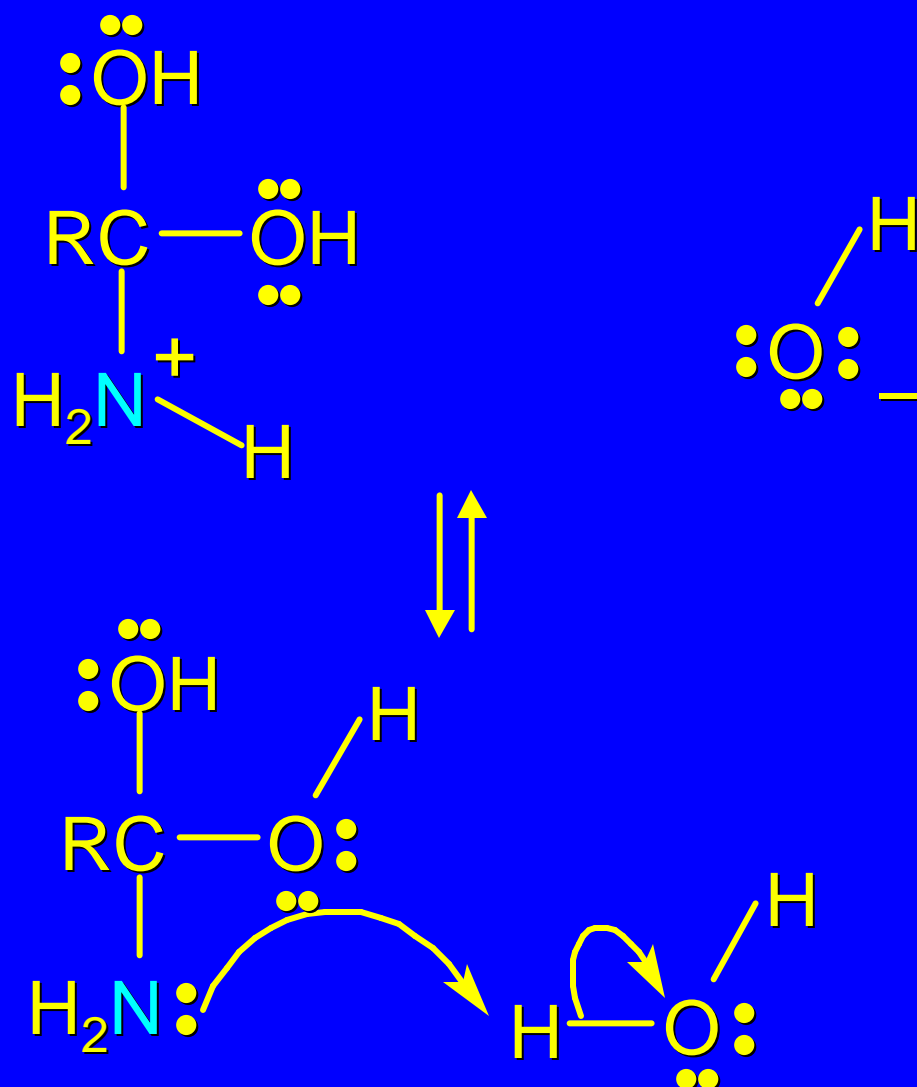


*Dissociation of  
tetrahedral intermediate*

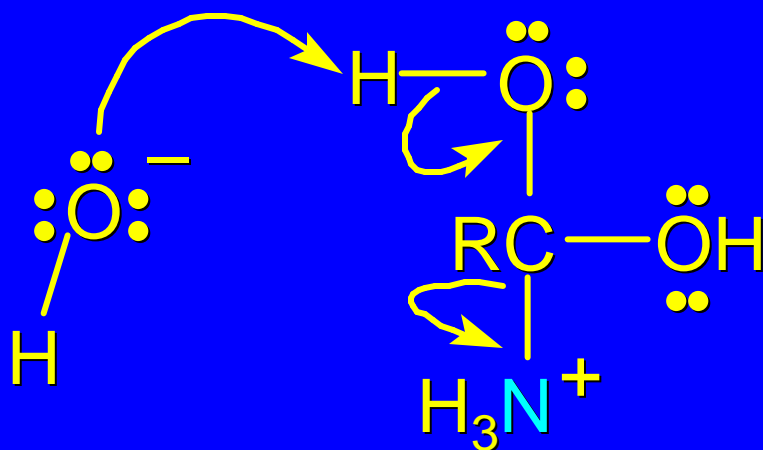
Step 3



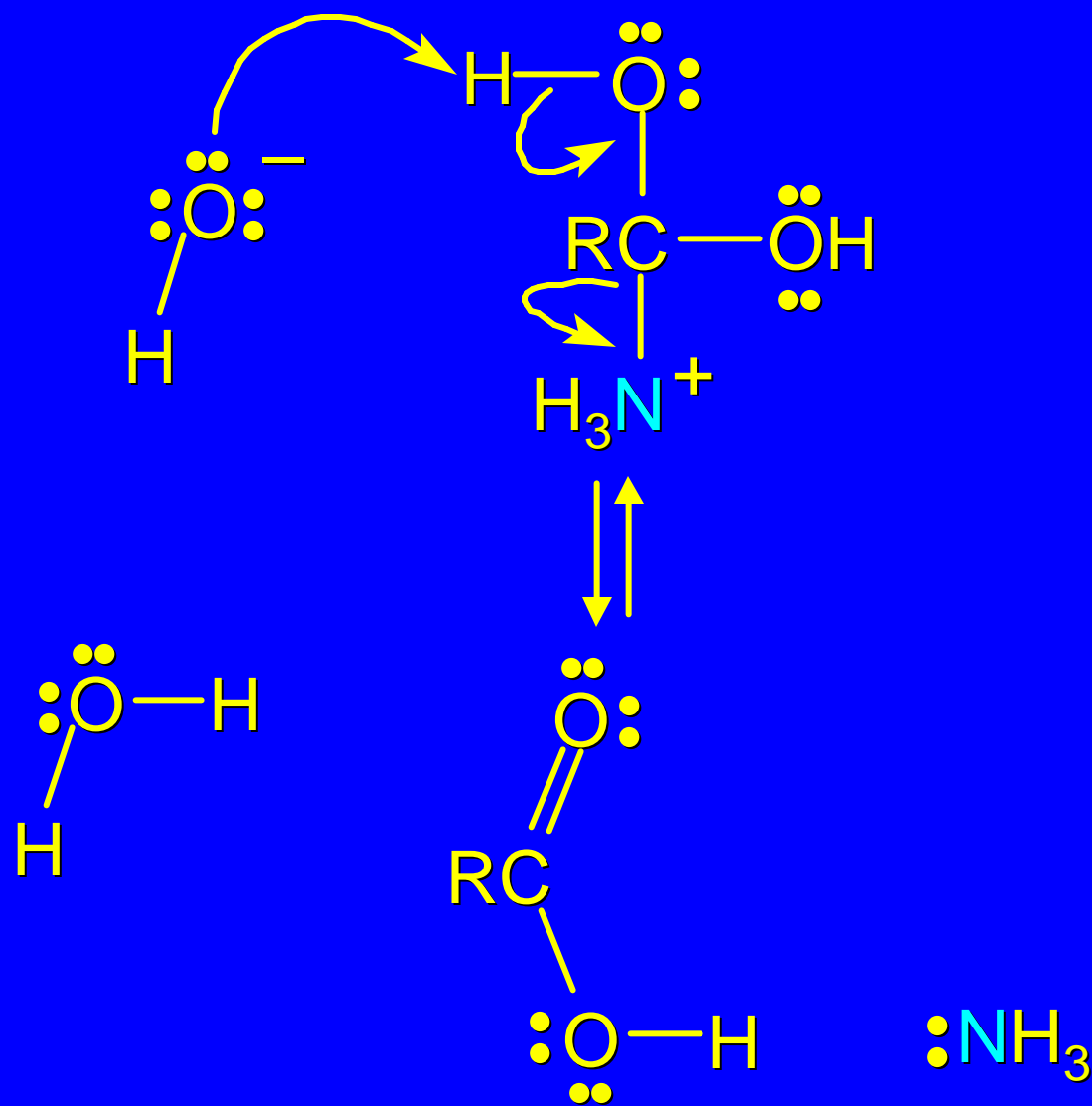
Step 3



Step 4



Step 4



Step 5

