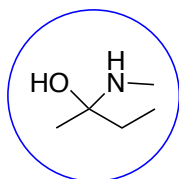


Formation of Cyanohydrins, Imines, Enamines

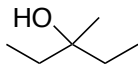
from chapter(s) _____ in the recommended text

A. Introduction

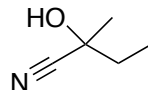
B. Tetrahedral Intermediates And Beyond



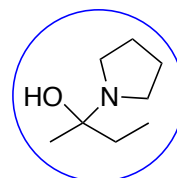
methylamine



EtMgX



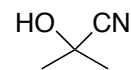
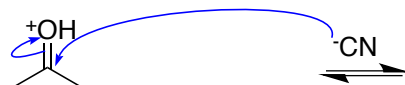
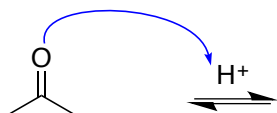
HCN



pyrrolidine

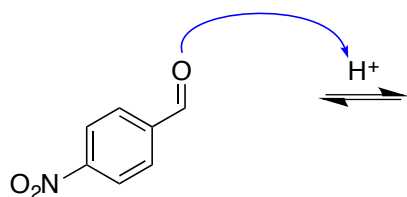
C. With HCN

weak

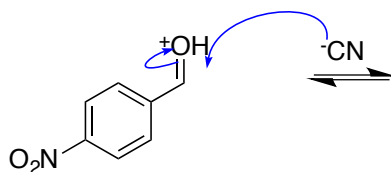


protonated carbonyl

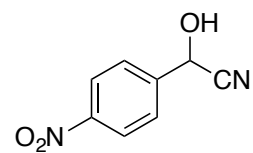
cyanohydrin adduct



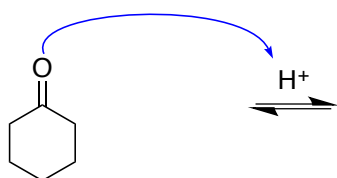
4-nitrobenzaldehyde



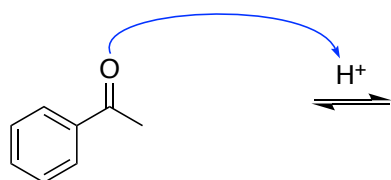
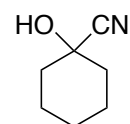
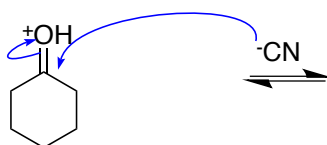
protonated carbonyl



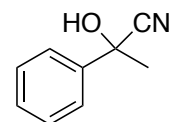
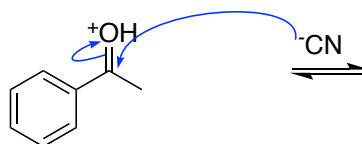
cyanohydrin adduct



cyclohexanone



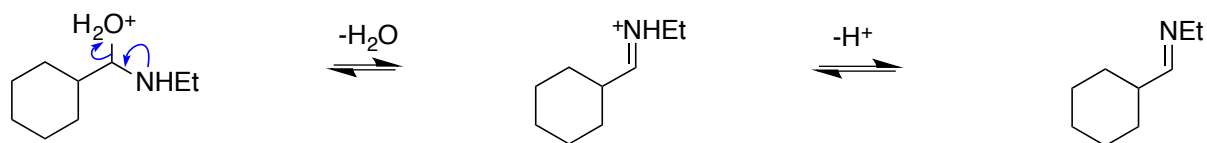
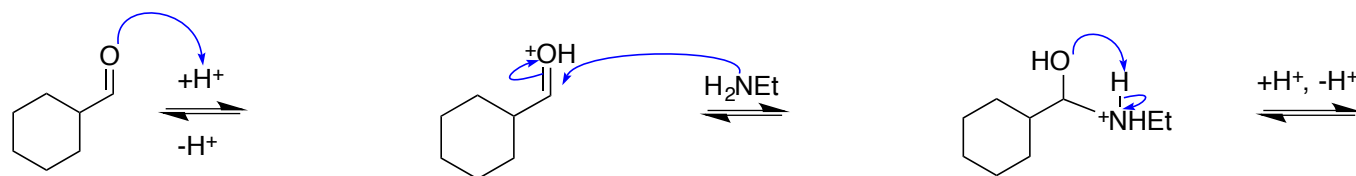
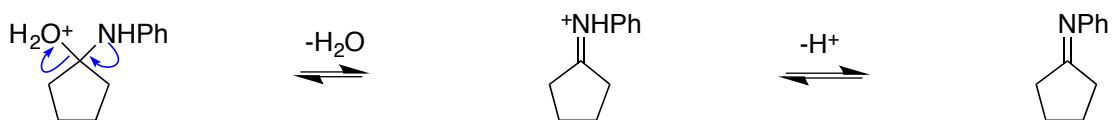
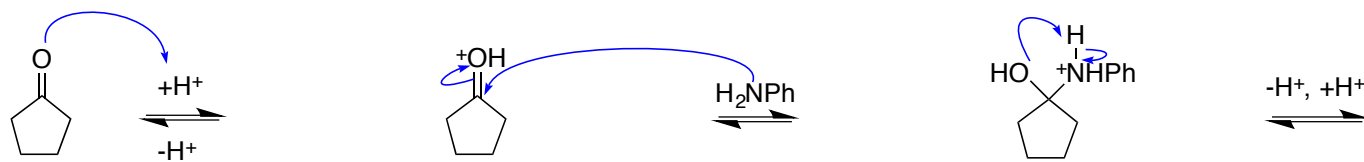
phenylethanone



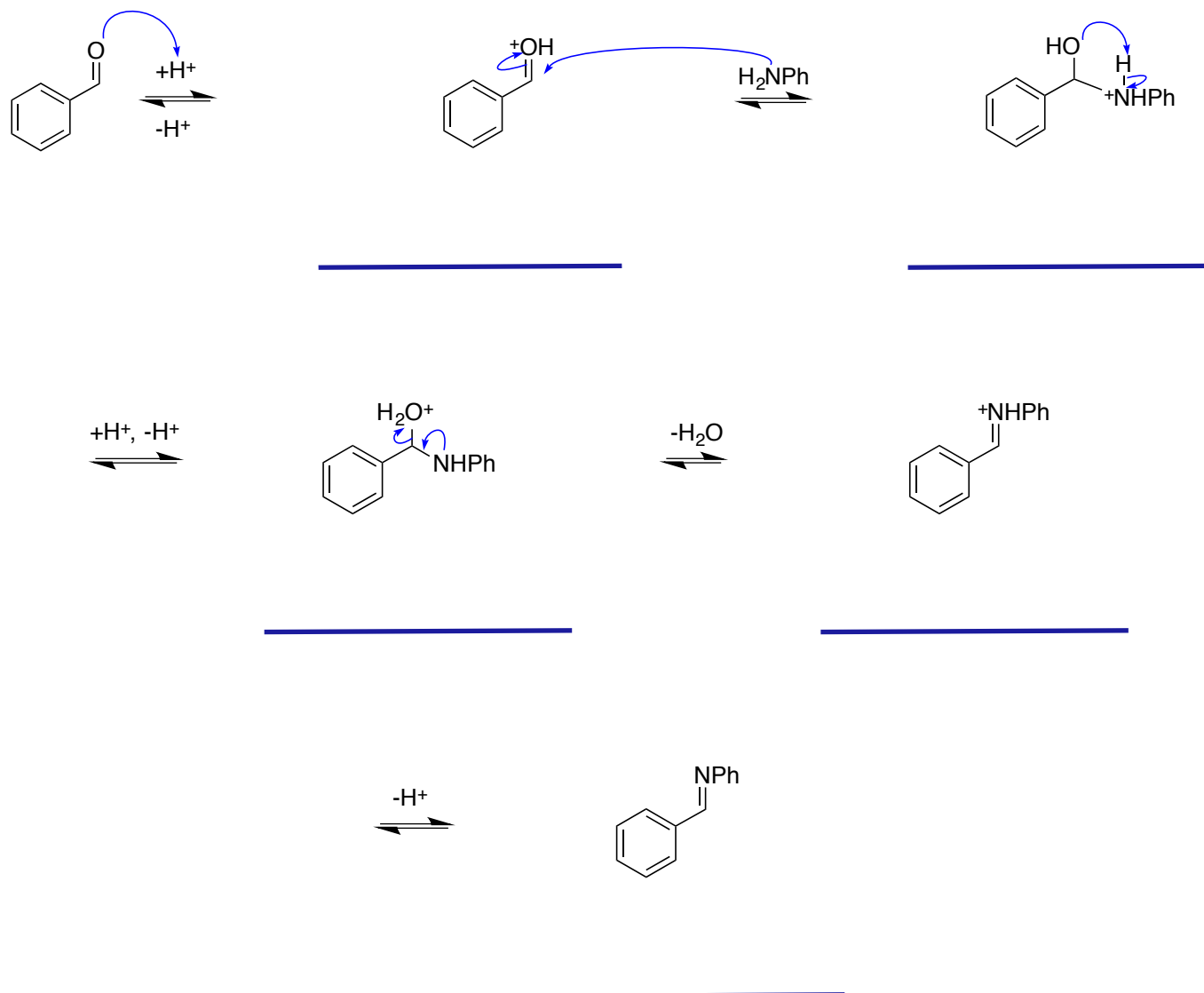
D. Condensations Of Aldehydes Or Ketones With $\text{H}_2\text{N-R}$ Or $\text{H}_2\text{N-X}$

Primary Amines Form Imines

(*loose* water)



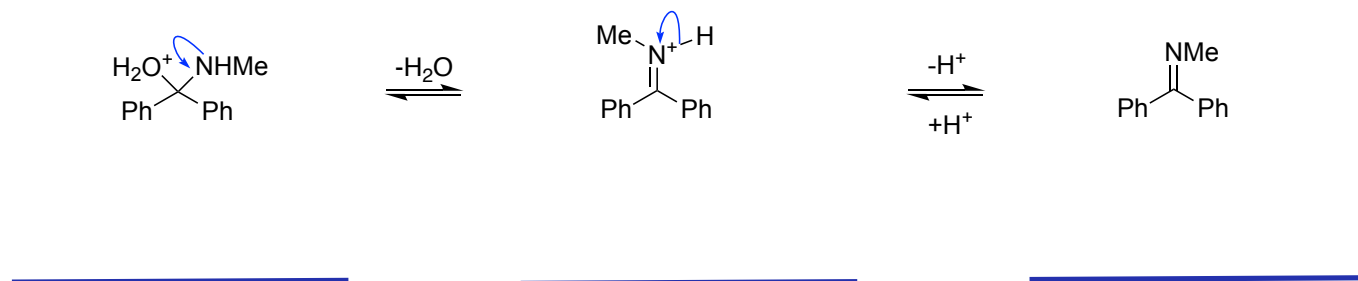
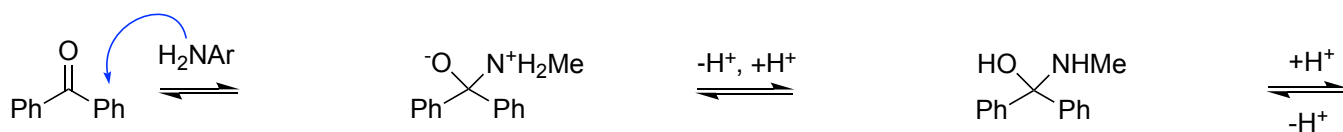
because: at this pH, the carbonyl will be protonated leading to activation of carbonyl group, facilitating the nucleophilic addition of amines. If the pH is lower than 4.5, most of the amine will be protonated making it non-nucleophilic, slowing the rate of reaction.



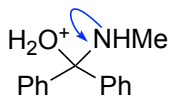
THE FOLLOWING IS A NEW SECTION, ADDED FOR THE SECOND EDITION OF THE BOOK

An Alternative Mechanism For Imine Formation

Draw a mechanism for imine formation that involves nucleophilic attack of an amine *without* protonation of the carbonyl first.



Identify the first intermediate that is common to both mechanisms, *ie* the one involving protonation of the carbonyl first, and the one above (it is the one that precedes loss of water).

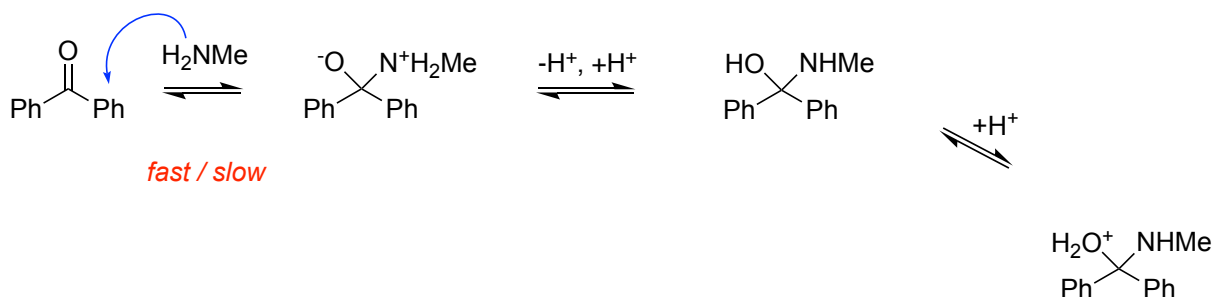


amino-oxonium intermediate

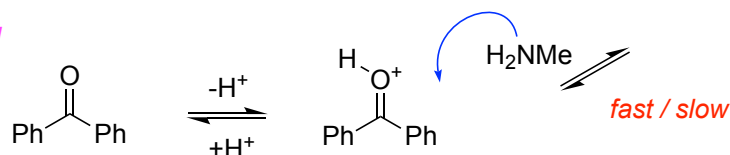
Condensation of amines with aldehydes and ketones proceeds most quickly at around pH 4. Under those conditions amines are *more / less* protonated than the carbonyl compounds they are mixed with. The mechanism used mostly in this chapter shows protonation of the carbonyl before attack of the amine, and under these conditions, pH 4, the amine is *mostly protonated / mostly present in the unprotonated form*.

An alternative mechanism that invokes shows nucleophilic attack on the carbonyl *without* protonation also involves attack of the free amine at pH 4, but on a neutral carbonyl, and this is likely to be *slower / faster* than attack of an amine on the same carbonyl, but when it is protonated. Indicate the relative rates of the two steps on the diagram below.

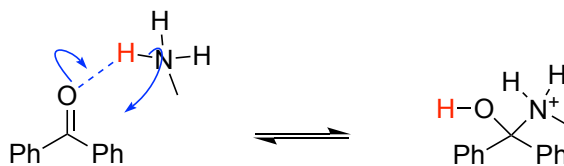
without protonation of the carbonyl



with protonation of the carbonyl



Draw yet another mechanism that involves formation of the amine-oxonium intermediate above in a single step which involves hydrogen bonding of the carbonyl with an ammonium salt formed from protonation of the amine at pH 4.



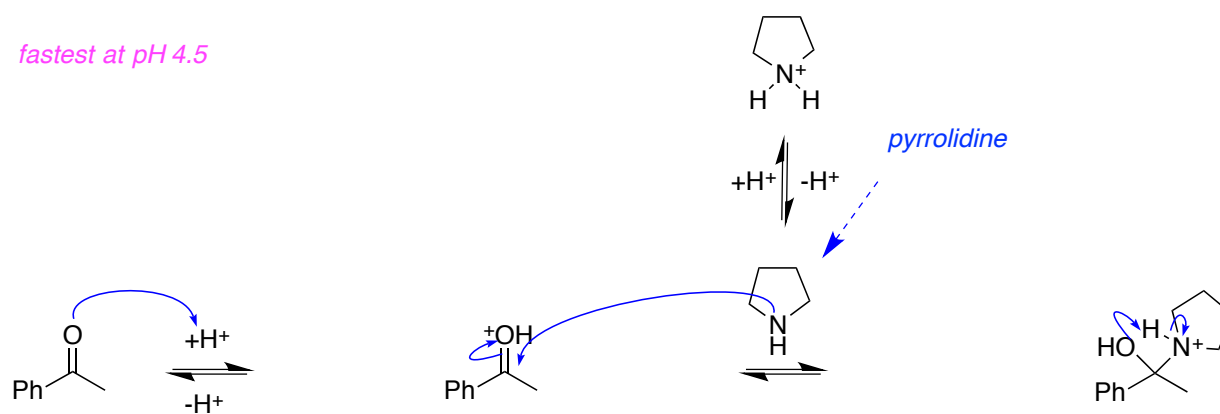
show H-bond and curly arrows

Secondary Amines Form Iminium Ions Then Enamines

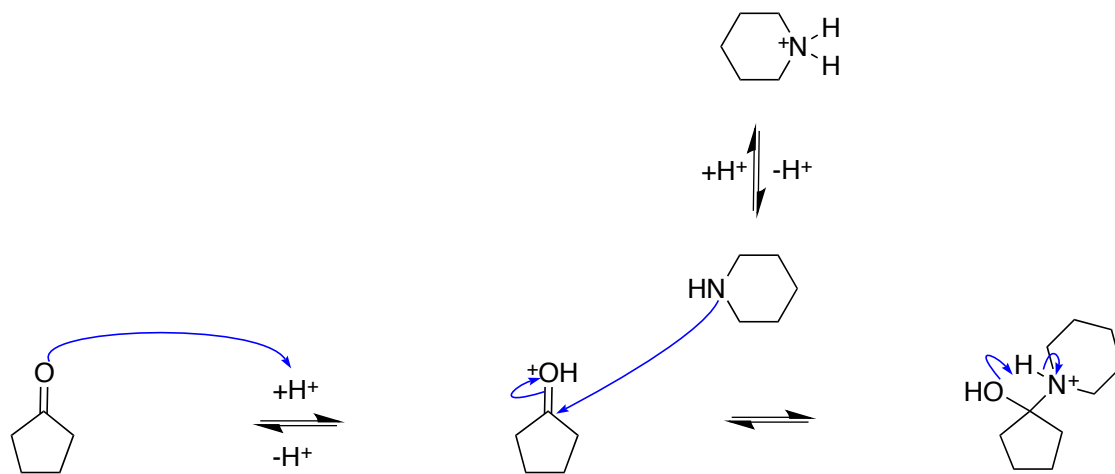
α carbon.

are reversible.

fastest at pH 4.5



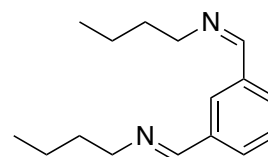
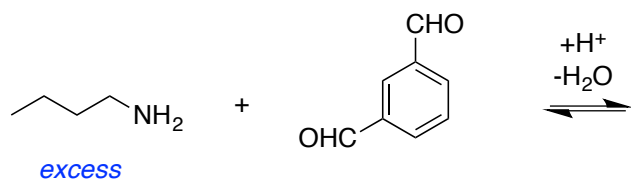
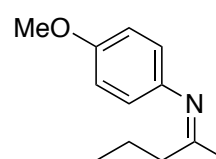
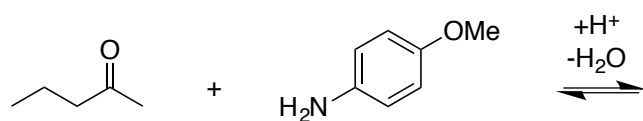
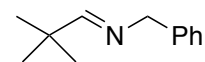
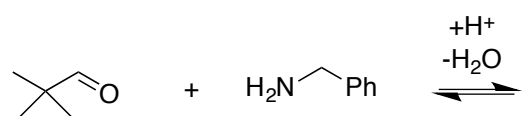
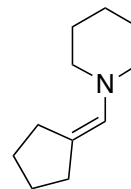
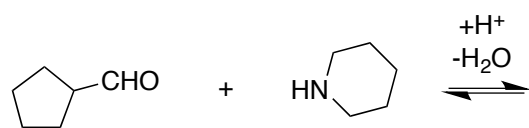
piperidine

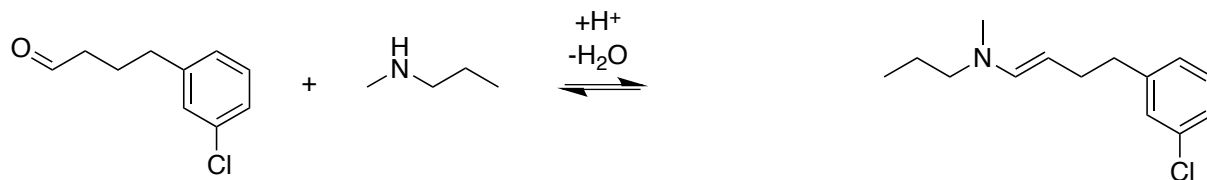


cyclopentanone



do hydrolyze

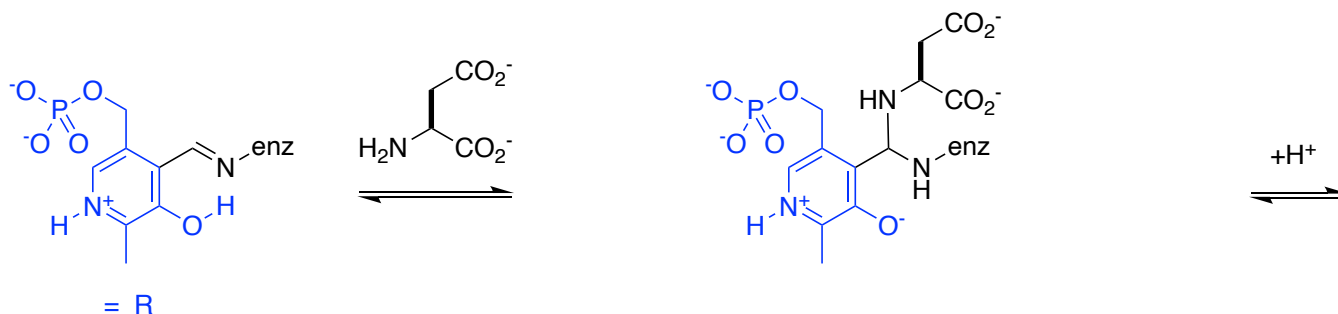




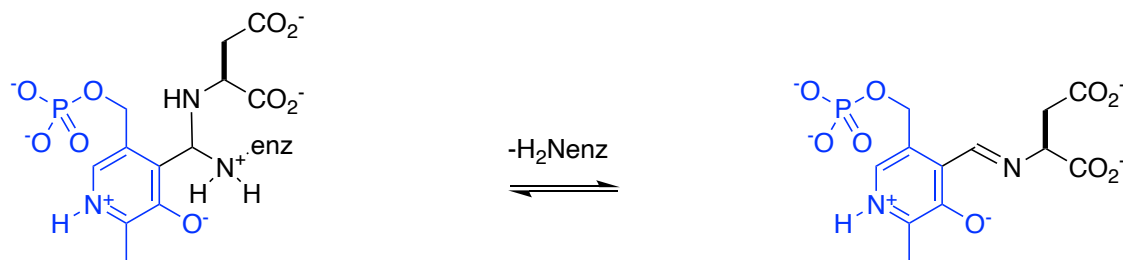
is:

Primary amines have two protons; one can be transferred to OH group then loss of water and another is removed to neutralize iminium to form imines. On the other hand, secondary amines have only one proton involved in dehydration step but no proton left to neutralize iminium ion. So the mechanism must involve losing a proton from the α -carbon to neutralize iminium ion thus forming enamines.

E. Transamination

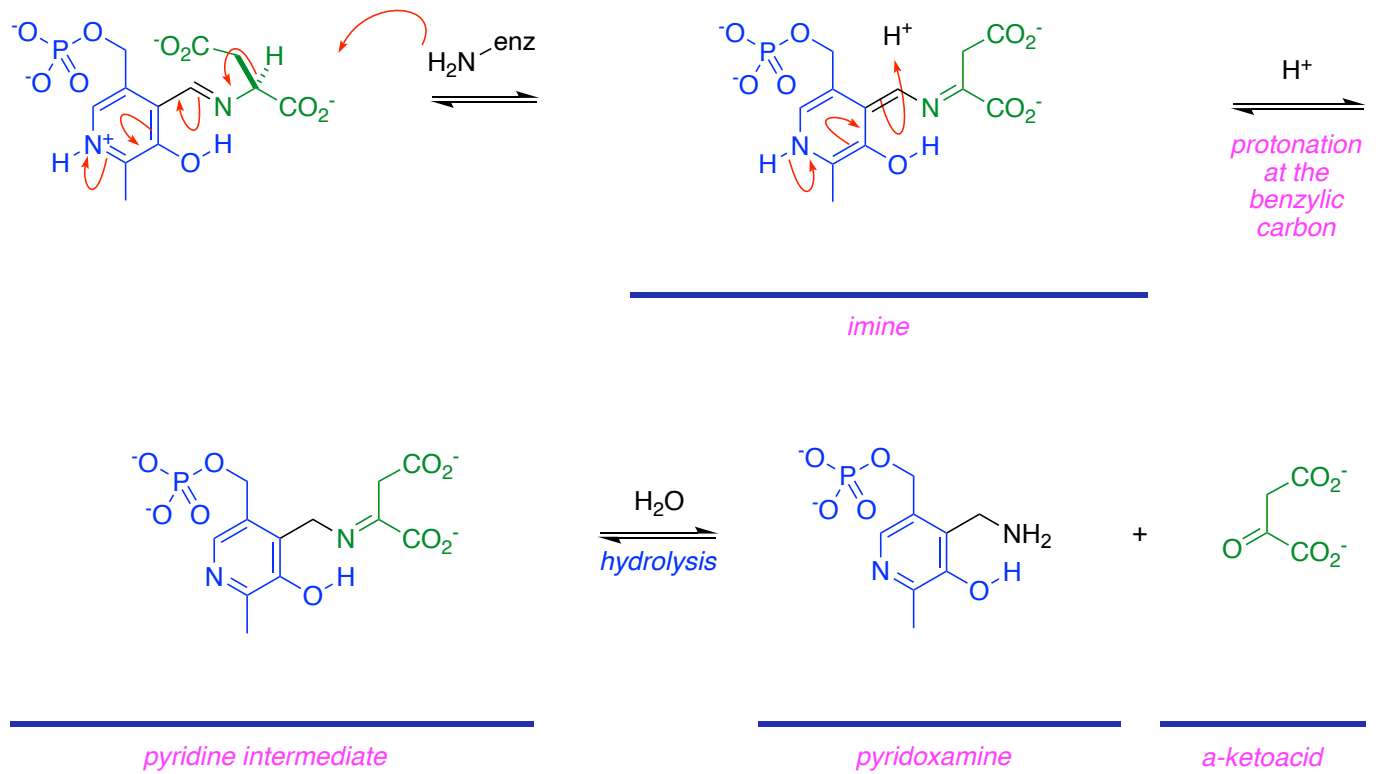


tetrahedral intermediate



tetrahedral intermediate

imine



oxidation of

amine

degrade one and form another.