Comparison of Carbonyl Reaction Types

I. Nucleophilic addition and nucleophilic acyl substitution involve the same first step—nucleophilic attack on the electrophilic carbonyl carbon to form a tetrahedral intermediate.

II. The difference between the two reactions is what then happens to the intermediate.

III. Aldehydes and ketones cannot undergo substitution because they do not have a good leaving group bonded to the newly formed sp^3 hybridized carbon.

c) Ester/Carboxylic acid

R' = H = Carboxylic acid

R' = Alkyl/aryl = Ester

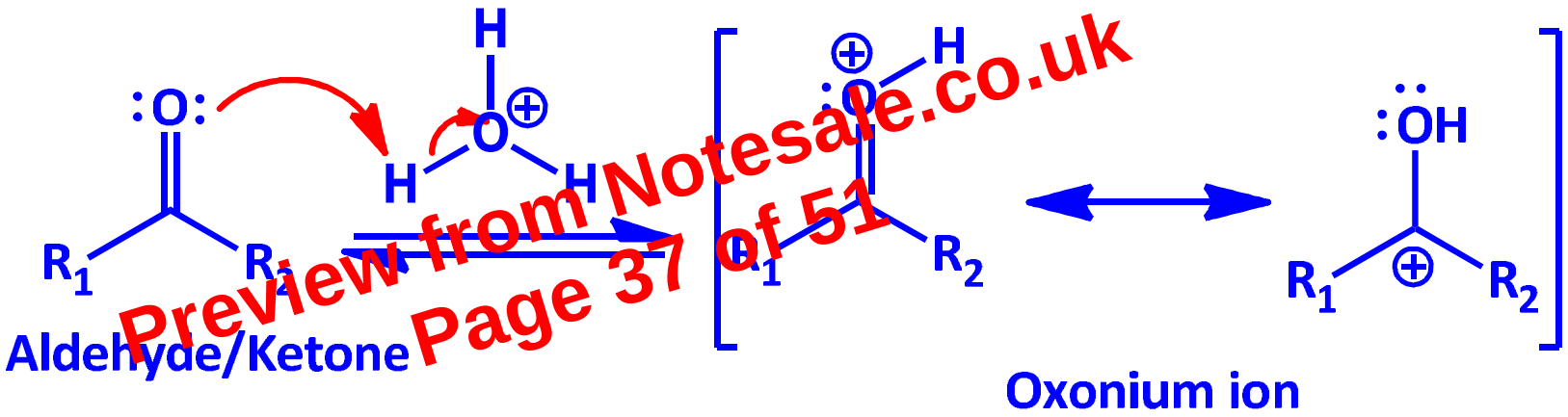
The oxygen atoms lone pair conjugates with the carbonyl group, causing a significant reduction of the positive change at the carbonyl carbon.

Carbonyl compounds will react with nucleophiles without the use of the catalysts only when the carbonyl carbon is very electrophilic or the nucleophile is strong.

Otherwise catalysts must be used that will increase either the electrophilicity of the carbonyl carbon or the nucleophilicity of the nucleophile. This can be achieved by using acid and base catalysts.

Acid Catalyzed Nucleophilic Addition Reaction

Step I: Protonation of the carbonyl oxygen

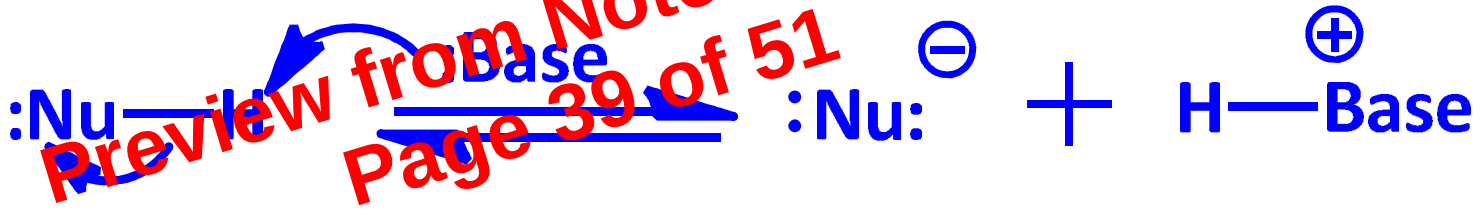


In the acid catalyzed mechanism the first step is the protonation of the carbonyl oxygen to give an oxonium.

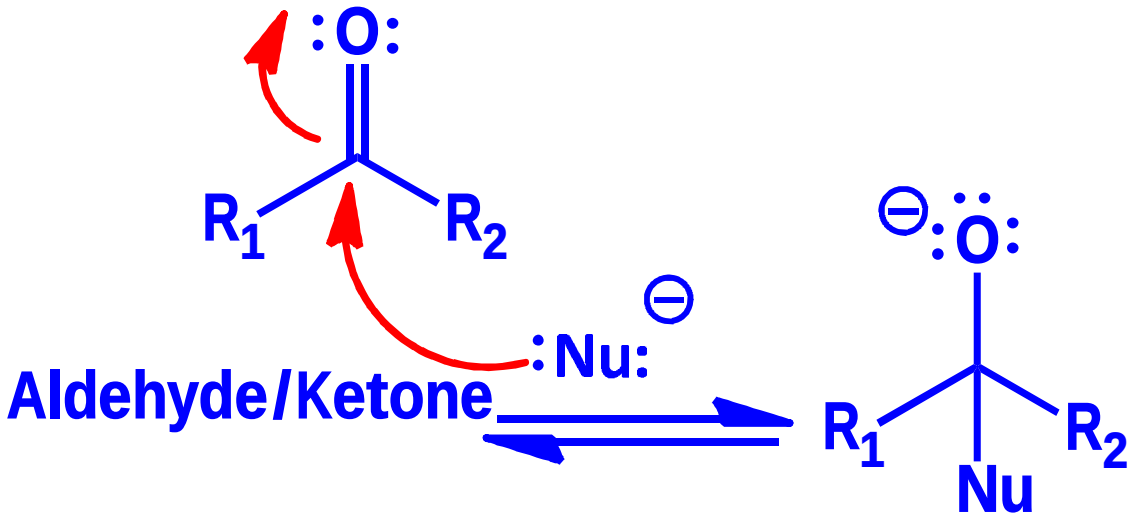
A contributing resonance structure puts the positive charge on the carbonyl carbon. The net effect of protonation is to make the carbonyl carbon even more electron deficient than it was.

Base Catalyzed Nucleophilic Addition Reaction

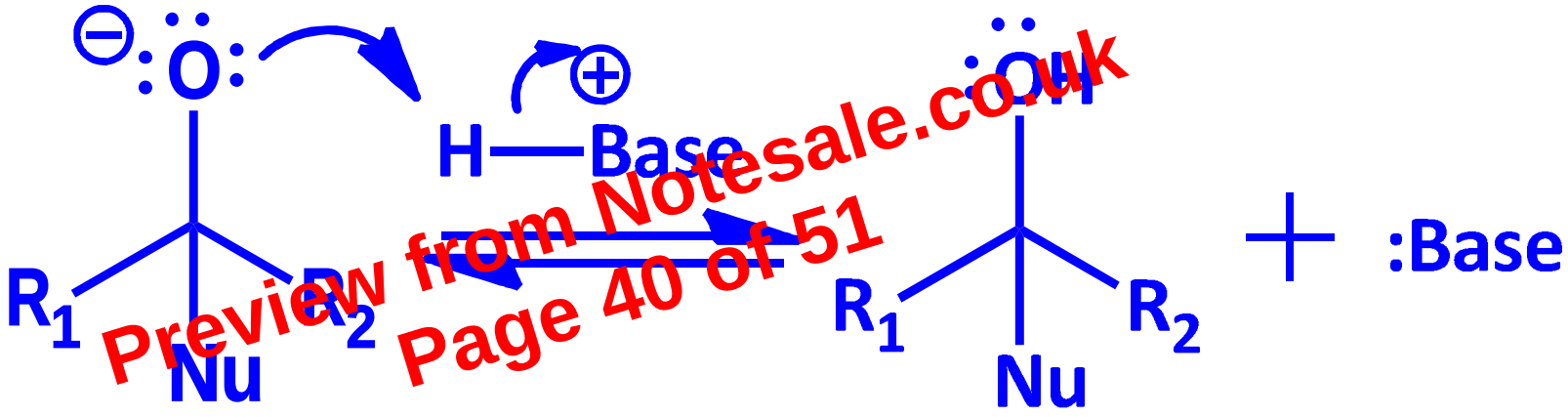
A base removes a hydrogen from the nucleophile (H-Nu:) and generates a strong nucleophile (:Nu:$^-$).



Step I: Nucleophilic attack

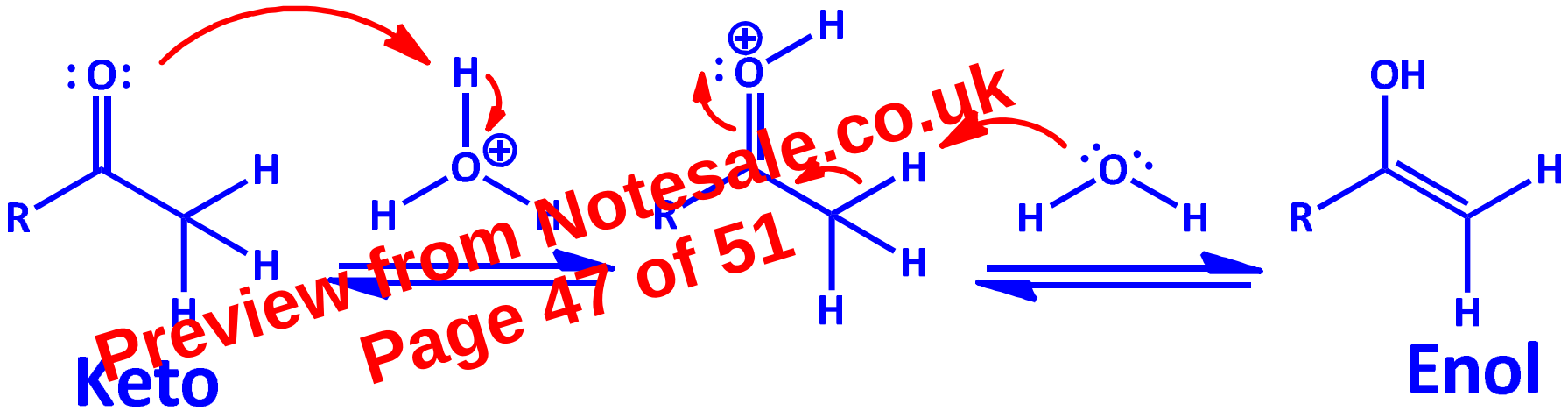


Step II: Protonation of the oxygen



The same argument also applies for nucleophilic acyl substitution reaction.

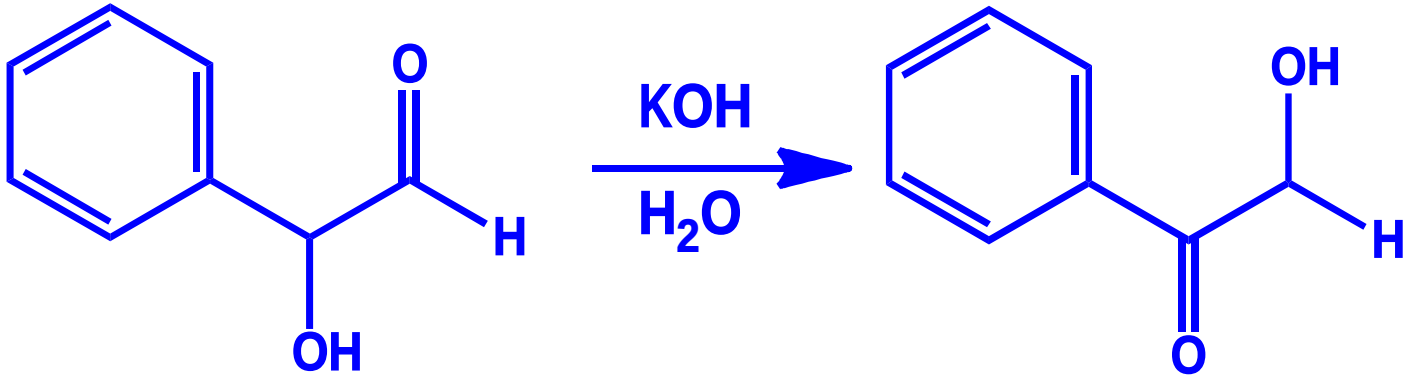
Tautomerization under acidic condition.



Tautomerization, the process of converting one tautomer into another, is catalyzed by both acid and base. Tautomerization always requires two steps (protonation and deprotonation), but the order of these steps depends on whether the reaction takes place in acid or base.

Assignment 2

I. For a long time attempts to prepare compound A were thwarted by its ready isomerization to compound B. The isomerization is efficiently catalyzed by traces of base. Write a reasonable mechanism for this isomerization.



A B