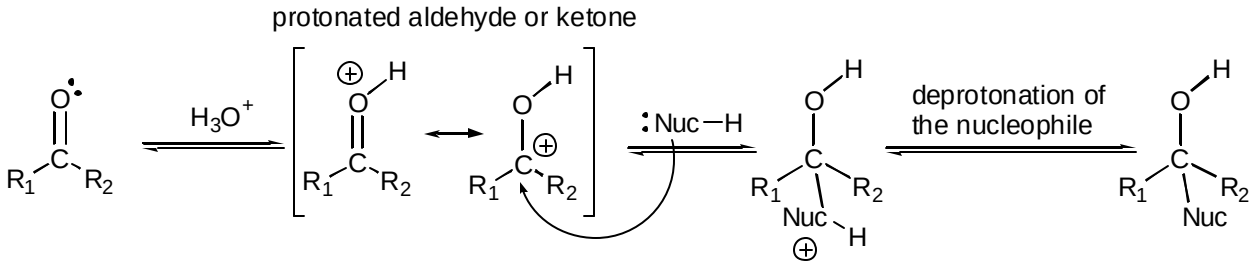
NUCLEOPHILIC ADDITION REACTIONS TO ALDEHYDES AND KETONES

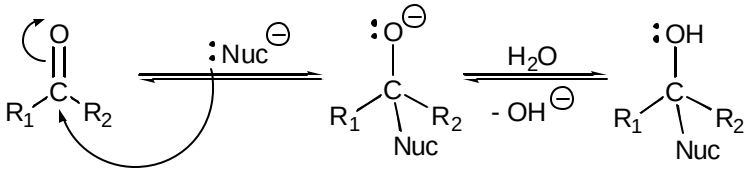
1. There are two general mechanisms for the reactions of aldehydes and ketones with nucleophiles:

   A. Simple addition mechanism – as seen from the scheme below, it can be acid- or base-catalyzed. In either case, the final product is a molecule in which the former carbonyl carbon is now a tetrahedral center (i.e. sp^3 hybridized). Almost all reactions are reversible!!!

Acid-Catalyzed Addition:



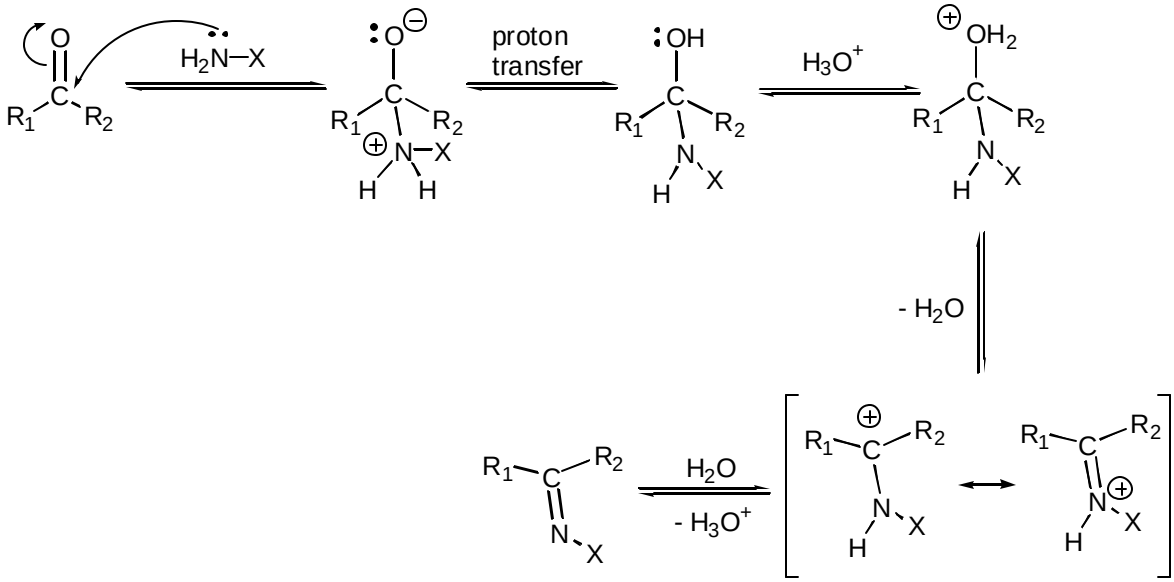
Base-Catalyzed Addition:



NOTE: The reaction of aldehyde or ketone with alcohol follows the above mechanisms ONLY up to the formation of *hemiacetal*!!!

   B. Addition – Elimination Mechanism – the addition of nucleophile leads to the generation of tetrahedral intermediate, which looses (eliminates) water or another simple molecule to give an end product with a multiple bond (usually C = N or C = C). Again, reactions are reversible!

The generalized addition of molecules X-NH_2 (where X = H, R, Ar, OH, NH_2, NHR, NR_2, $NHCONH_2$):



2. Nucleophiles:

A. Negatively charged: **$^{-}$OH** (base-catalyzed addition of water and formation of hydrates)

$^{-}$H (reduction by complex hydrides)

$^{-}CR_3$ (addition of Grignard and organolithium reagents)

$^{-}$OR (base-catalyzed formation of hemiacetals)

$^{-}$CN (formation of cyanohydrins)

B. Neutral: **HOH** (acid-catalyzed formation of hydrates)

ROH (acid-catalyzed formation of hemiacetals)

X-NH_2 (formation of imines, oximes, hydrazones, semicarbazones)