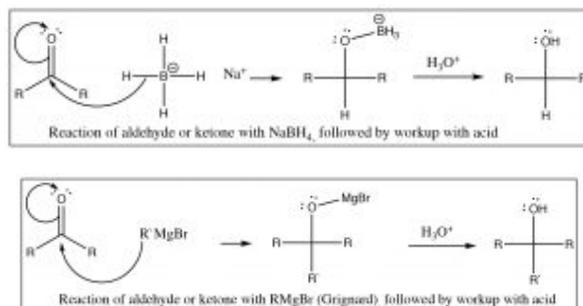


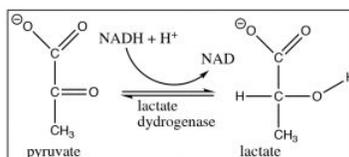
7.7: Nucleophilic Attack by Hydride or Carbanions

As we discussed in Chapter 6, aldehydes and ketones react with reagents that are able to deliver hydride (for example from sodium borohydride) or a carbanion (in the form of a Grignard reagent) to the carbonyl group.

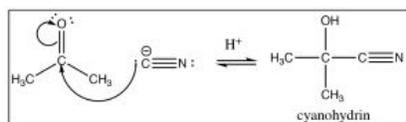


In addition to Grignard reagents, carbanions can also be generated by treating alkyl halides with lithium under dry conditions. These alkyl lithium reagents (RLi) behave in a very similar way to Grignard reagents, although they are somewhat more reactive.

These two reactions: addition of hydride (reduction) or a carbanion (resulting in carbon-carbon bond formation) to a carbonyl are analogous. They also have something else in common in that, under normal laboratory conditions, they are not reversible because reversing the reaction would require that the hydride ion or carbanion be expelled from the central carbon. These species are very unstable, very strong bases. The reagents that produced them (NaBH_4 , RMgX , RLi) are specialized reagents that do not contain “naked” hydride ions or carbanions. If we wanted to reverse them, we would have to use completely different reaction conditions that avoided the expulsion of the high-energy hydride or carbanion. For example, to accomplish the reverse of the reduction reaction, we would have to use an oxidizing agent (such as Cr(VI)) under completely different conditions. The reduction of a ketone group is central to the reactions of glycolysis, in which pyruvate (the conjugate base of pyruvic acid^[3]) is reduced to lactate (the conjugate base of lactic acid) by NADH (see Chapter 6). This reaction can be also reversed under different conditions (in this case, the presence of the enzyme lactate dehydrogenase). Glycolysis will be discussed in more detail in Chapter 9.



Reaction with other carbanions:



There are a number of other ways to generate carbanions: for example, terminal alkynes are quite acidic ($\text{pK}_a 22$) and can be deprotonated by sodium amide (Chapter 5). The resulting carbanion adds to the carbonyl just as we might expect. Similarly, cyanide ion (CN^-) is another source of a negatively charged carbon. It is a good nucleophile, and just as one might expect, it adds to carbonyl groups, and after reaction with a dilute acid, the resulting cyanohydrin is formed. There are two items to note here:

1. Sodium cyanide NaCN (the usual form of cyanide ion) is highly toxic, so don't try this at home.
2. The oxidation state of the carbon in the cyano group is the same as a carboxylic acid. As we will see later, this reaction will come in very useful. All of these reactions are the result of a **nucleophilic addition** to the carbonyl group, during the course of which the carbonyl carbon rehybridizes from sp^2 to sp^3 .

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