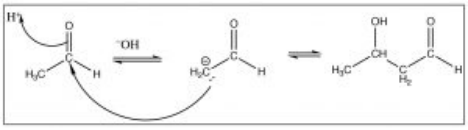
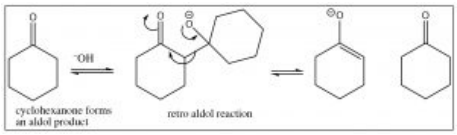
9.2: The Aldol Reaction

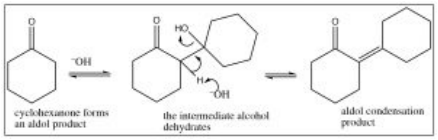
As we have previously discussed, the carbonyl group has a kind of split personality. The carbonyl group is susceptible to nucleophilic attack at the carbonyl carbon and carbonyl compounds can be nucleophiles at the alpha carbon. Therefore, we should not be too surprised to learn that carbonyl compounds can (and do) react with themselves. For example, when acetaldehyde, the simplest carbonyl compound that is capable of forming an enol, is treated with a reversible base such as NaOH, it will form a small amount of the enolate anion, which can then react with the carbonyl of another molecule as shown. This reaction is known as the aldol reaction. As the enolate is used up in the reaction, more is formed and more aldol reaction occurs. The product is a beta-hydroxy aldehyde.

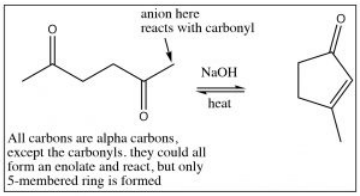


Typically, aldehydes undergo this reaction readily and the aldol product is formed in good yield. The reaction is reversible, however, and ketones often do not give good yields of the aldol product. The reverse reaction is called a “retro aldol” and occurs via deprotonation of the alcohol and loss of the enolate anion as shown.



In fact, the aldol reaction rarely ends at the simple addition of one carbonyl and its corresponding enolate. Usually, the reaction is heated and, under these conditions, the alcohol that is formed undergoes an elimination to form the alpha, beta unsaturated carbonyl. When this happens, the reaction is called an aldol condensation (the term “condensation” is usually used for reactions in which water is lost).





Aldol condensation is often used to synthesize rings via an intramolecular aldol condensation. In these cases, although there may be the potential to form different ring sizes, typically only the most stable rings are produced: that is, five- or six-membered rings.