# 19.5: NUCLEOPHILIC ADDITION REACTIONS OF KETONES AND ALDEHYDES

CARBONYLS ARE ELECTROPHILES

Before we consider in detail the reactivity of aldehydes and ketones, we need to look back and remind ourselves of what the bonding picture looks like in a carbonyl. Carbonyl carbons are sp^2 hybridized, with the three sp^2 orbitals forming soverlaps with orbitals on the oxygen and on the two carbon or hydrogen atoms. These three bonds adopt trigonal planar geometry. The remaining unhybridized 2p orbital on the central carbonyl carbon is perpendicular to this plane, and forms a 'side-by-side' pbond with a 2p orbital on the oxygen.
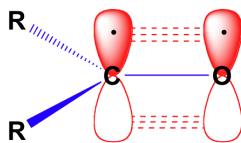

The carbon-oxygen double bond is polar: oxygen is more electronegative than carbon, so electron density is higher on the oxygen side of the bond and lower on the carbon side. Recall that bond polarity can be depicted with a dipole arrow, or by showing the oxygen as holding a partial negative charge and the carbonyl carbon a partial positive charge.
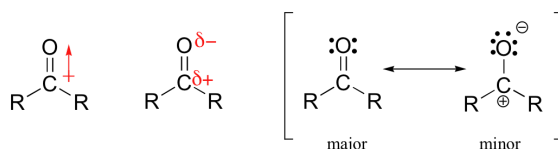
A third way to illustrate the carbon-oxygen dipole is to consider the two main resonance contributors of a carbonyl group: the major form, which is what you typically see drawn in Lewis structures, and a minor but very important contributor in which both electrons in the pbond are localized on the oxygen, giving it a full negative charge. The latter depiction shows the carbon with an empty 2p orbital and a full positive charge.

The result of carbonyl bond polarization, however it is depicted, is straightforward to predict. The carbon, because it is electron-poor, is an electrophile: it is a great target for attack by an electron-rich nucleophilic group. Because the oxygen end of the carbonyl double bond bears a partial negative charge, anything that can help to stabilize this charge by accepting some of the electron density will increase the bond's polarity and make the carbon more electrophilic. Very often a general acid group serves this purpose, donating a proton to the carbonyl oxygen.


carbon becomes more electrophilic
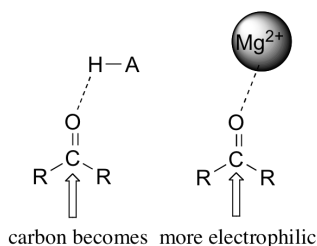
The same effect can also be achieved if a Lewis acid, such as a magnesium ion, is located near the carbonyl oxygen.
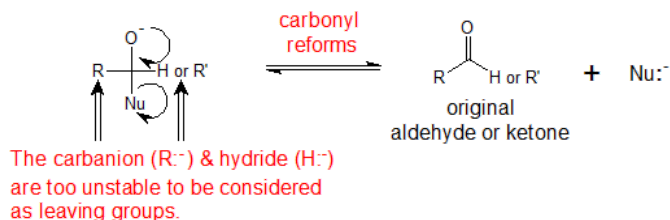
NUCELOPHILIC ADDITION TO A CARBONYL

When a nucleophile reacts with the carbonyl carbon of an aldehyde or ketone, there is no leaving group – the incoming nucleophile simply 'pushes' the electrons in the pi bond up to the oxygen. After the carbonyl has reacted with the nucleophile, the negatively charged oxygen has the capacity to act as a nucleophile. The nucleophile can be charged or neutral. However, most commonly the oxygen acts as a base, abstracting a proton from a nearby acid group in the solvent or enzyme active site. The nucelophiiles studied in this chapter are water (H_2O), cyanide (CN^-), Grignard reagent (RMgX), amines (and ammonia), hydrazine (N_2H_4), alcohols (ROH), and phosphorus ylides ($R_3P=CRH$).

The generic mechanism for a strong nucleophile generally occurs under basic conditions as shown below.
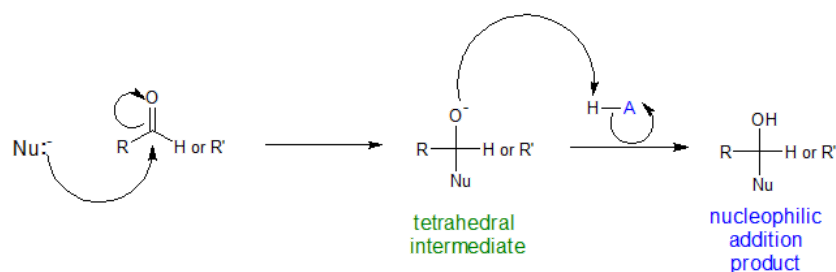
A closer look at the tetrahedral intermediate shows us that if the carbonyl reforms, then the original aldehyde or ketone is reformed.

It is possible for the nucleophile to repeatedly add and leave the carbonyl group. Protonation of the tetrahedral intermediate to form the nucleophilic additon product is favored by the low activation energy of proton transfer reactions.

For reaction with weak nucleophiles generally occurs under acidic conditions to increase the electrophilicity of the carbonyl group as resonance form below illustrates.
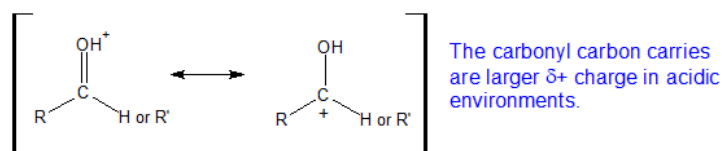
While the net result of the reaction is similar, the mechanism is slightly different due to the order of the proton transfer reactions.
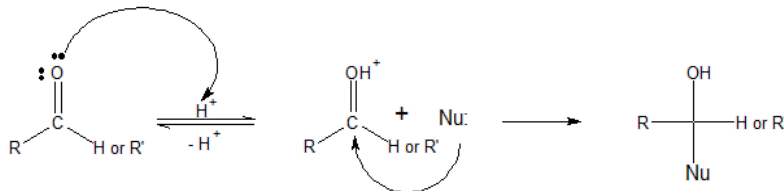
## RELATIVE REACTIVITY OF CARBONYL COMPOUNDS TO NUCLEOPHILIC ADDITION

In general aldehydes are more reactive than ketones because of the lack of stabilizing alkly groups. The primary carbocation formed in the in the polarizing resonance structure of an aldehyde (discussed above) is less stable and therefore more reactive than the secondary carbocation formed by a ketone.
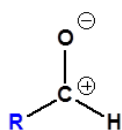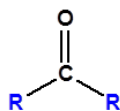
1° Carbocation
(Less Stable, More Reactive)
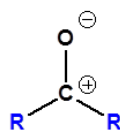
2° Carbocation
(MoreStable, Less Reactive)
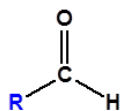
Aldehyde
Less Stabilization
More Reactive

Ketone
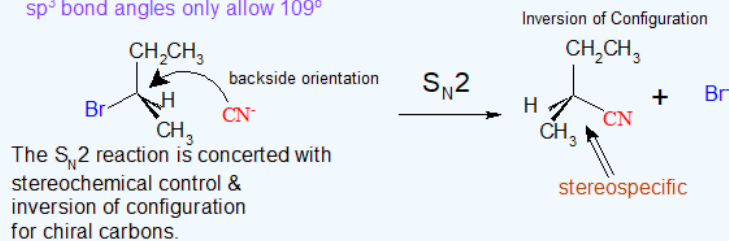**Less Stabilization**
More Reactive

Exercise

4. Compare the mechanisms of

an S_N2 reaction between 2-bromobutane and cyanide

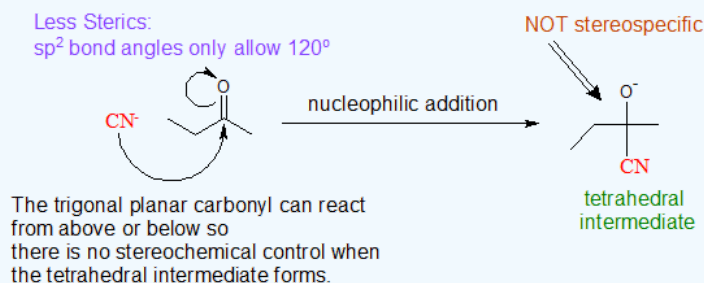tetrahedral complex formation between 2-butanone and cyanide.

Answer

4.

Greater Sterics:
sp^3 bond angles only allow 109°

backside orientation

S_N2

Inversion of Configuration

CH_2CH_3

$+$ Br⁻

stereospecific

The S_N2 reaction is concerted with stereochemical control & inversion of configuration for chiral carbons.

Less Sterics:
sp^2 bond angles only allow 120°

NOT stereospecific

nucleophilic addition

tetrahedral intermediate

The trigonal planar carbonyl can react from above or below so there is no stereochemical control when the tetrahedral intermediate forms.

CONTRIBUTORS AND ATTRIBUTIONS

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