

## Chapter 11 Carbonyl Compounds

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Carbon atoms form double and triple bonds. Similarly, oxygen atoms can form double bonds. There are several functional groups such as aldehyde groups, keto groups, and carboxy groups in which oxygen atoms are involved in double bonds. In this chapter, aldehydes and ketones, or comprehensively named carbonyl compounds, will be treated.

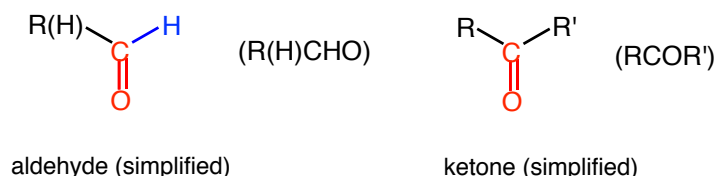
Aldehydes and ketones as such, or as raw substances of various compounds, are very important. Some of aldehydes and ketones are naturally occurring, and many others can be synthesized *via* functional group conversion methods. The simplest one is the oxidation of alcohols. A variety of organic compounds are synthesized *via* aldehydes and ketones because of their high reactivity.

The chemistry of carbonyl compounds may be regarded as the key of organic chemistry in respect to structures, reactions, and syntheses.

## 11.1 Types and nomenclature of carbonyl compounds

### (a) Types of carbonyl compounds

Functional groups composed of carbon-oxygen double bonds are the carbonyl group, and compounds containing carbonyl groups are named carbonyl compounds. If carbonyl groups are bonded with one hydrogen atom, aldehydes are formed. If carbonyl groups are bonded with two hydrocarbon moieties, ketones are formed.



Except formaldehyde, which is bonded with two hydrogen atoms, all have at least one hydrocarbon moiety. Depending on the nature of the hydrocarbon moiety, aldehydes are roughly classified into two groups, aliphatic aldehydes and aromatic aldehydes. In Table 11.1 some examples of aldehydes are given.

**Table 11.1** Representative aldehydes

common name	systematic name	simplified structure	melting point (°C)	boiling point (°C)
formaldehyde	methanal	HCHO	-118.3--117.8	19.3
acetaldehyde	ethanal	CH <sub>3</sub> CHO	-13.5	20.2
propionaldehyde	propanal	CH <sub>3</sub> CH <sub>2</sub> CHO	-80.05	47.83
acrolein	2-propenal	CH <sub>2</sub> =CHCHO	-86.95	52.69
butyraldehyde	butanal	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CHO	-99	74.7--74.9
benzaldehyde	benzenecarbaldehyde	C <sub>6</sub> H <sub>5</sub> CHO	-56.5	178

In ketones two hydrocarbon moieties are bonded to a carbonyl group. When one of the hydrocarbon moieties are aliphatic, these are classified as aliphatic ketones. When at least one hydrocarbon moiety is aromatic, these are classified as aromatic ketones. In Table 11.2, some ketones are given.

**Table 11.2** Representative ketones

common name	systematic name	simplified structure	melting point (°C)	boiling point (°C)
acetone	2-propanone	CH <sub>3</sub> COCH <sub>3</sub>	-94.82	56.3
ethyl methyl ketone	2-butanone	CH <sub>3</sub> COCH <sub>2</sub> CH <sub>3</sub>	-87.35	79.53
methyl vinyl ketone	3-butene-2-one	CH <sub>3</sub> COCH=CH <sub>2</sub>	—	81.4
acetophenone	acetophenone	C <sub>6</sub> H <sub>5</sub> COCH <sub>3</sub>	19.65	202
benzophenone	benzophenone	C <sub>6</sub> H <sub>5</sub> COC <sub>6</sub> H <sub>5</sub>	48.4--48.5	305.9

### (b) Nomenclature of carbonyl compounds

#### (1) Nomenclature of aldehydes

Generally aldehydes are named by the substitutive nomenclature, but some have common names. There are two ways in the substitutive nomenclature.

(1) The end of the name (alkane) is changed to suffix (-al).

[Example]  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CHO}$ ; butanal (substitutive nomenclature)

(2) The suffix “-carbaldehyde” is added to the name of hydrocarbons.

[Example]  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CHO}$ ; propane-1-carbaldehyde (substitutive nomenclature)

Method (1) is more popular, but for alicyclic aldehydes method (2) is sometimes used.

Common names are often made from the common names of corresponding carboxylic acids.

[Example]  $\text{CH}_3\text{CHO}$ ; acetaldehyde (derived from  $\text{CH}_3\text{COOH}$  acetic acid)

## (2) Nomenclature of ketones

Ketones are named by substitutive and radicofunctional nomenclatures. When substitutive methods are used, the end of hydrocarbons are changed into suffix “-one “ with the locant indicating the position of the carbonyl group. When no complication is involved, locants may be omitted (Ch. 5.1).

When radicofunctional nomenclature is used, two names of hydrocarbon radicals are arranged in alphabetical order followed by the functional group name “ketone”.

[Example]  $\text{CH}_3\text{CH}_2\text{COCH}_3$

2-butanone (substitutive name)

ethyl methyl ketone (radicofunctional name)

Several familiar ketones have common names:-

[Example]  $\text{CH}_3\text{COCH}_3$

acetone (common name)

2-propanone (substitutive name)

Several aromatic ketones have suffixes “phenone”

[Example]  $\text{C}_6\text{H}_5\text{COCH}_3$

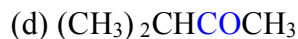
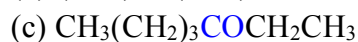
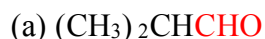
acetophenone (common name and systematic name)

methyl phenyl ketone (this radicofunctional name are seldom used. )

**Exercise 11.1** Naming of carbonyl compounds

(1)

Give the names to the following aldehydes and ketones.



(2)

Draw the structures of the following compounds

(e) propanal

(f) 4-chlorobutanal

(g) 2-hexanone

(h) ethyl phenyl ketone

**Answer**

(1)

(a) 2-methylpropanal (trivial name; isobutyraldehyde)

(b) 5,5-dimethylhexanal

(c) 3-heptanone (substitutive name); butyl ethyl ketone (radicofunctional name)

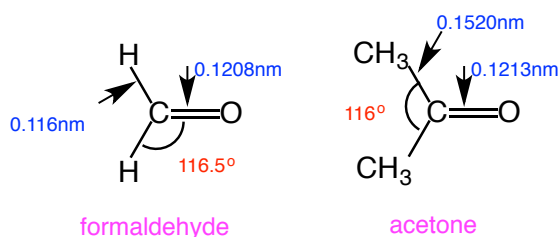
(d) 3-methyl-2-butanone; isopropyl methyl ketone (radicofunctional name)

(2)

**11.2 Structure of carbonyl compounds****(a)  $\text{sp}^2$  hybridized oxygen atom**

In the case of oxygen atom, three equivalent  $\text{sp}^2$  hybridized orbitals are formed from three  $2s$ ,  $2p_x$ , and  $2p_y$  atomic orbitals. These three orbitals lay in one plane, and the angle defined by two orbitals is  $120^\circ$ , and  $2p_z$  orbital is perpendicular to this plane.

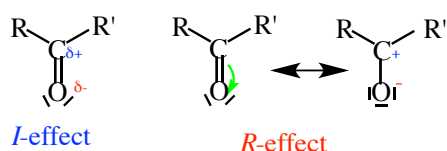
The  $\text{C}=\text{O}$  double bond is formed from the  $\sigma$  bond made by two  $\text{sp}^2$  hybridized orbitals from carbon atom and oxygen atom vertically joined, and the  $\pi$  bond made by two  $\text{sp}^2$  hybridized orbitals horizontally joined. The remaining two  $\text{sp}^2$  hybridized orbitals belonging to the carbon atom are overlapped with  $1s$  orbitals of hydrogen atoms. For this reason, four atoms of formaldehyde lie in one plane. Similarly the oxygen atom and three carbon atoms of acetone lie in one plane.



The bond length of C=O double bond is almost identical regardless of the kind of substituents. In formaldehyde, the H-C-O angle  $116.5^\circ$  and the deviation from the theoretical value,  $120^\circ$ , is small.

### (b) Polarization of the carbonyl group

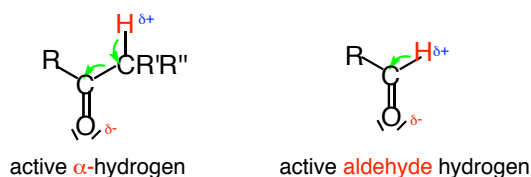
The high reactivity of carbonyl compounds depends on the specific reactivity of the functional group, "carbonyl group". The electron is withdrawn from the carbonyl carbon to carbonyl oxygen by the high electronegativity of oxygen atom so that partial positive charge is induced in the carbon atom (*I* effect). The situation is much the same with halides and alcohols. Furthermore,  $\pi$  electron of double bond moves to oxygen, to induce resonance formula in which carbon and oxygen bears positive and negative charge (*R* effect). For this reason, the polarization of C=O double bonds of carbonyl compounds is considerably larger than that of C-O of alcohols.



Because of this extreme polarization, when a hydrogen atom is bonded to the carbon atom ( $C_\alpha$ ) next to the carbonyl group, this  $\alpha$ -hydrogen of aldehyde group also bears partial positive charge.

However, because of the nomenclature rule, in the case of halides, the one bearing the partial positive charge is named the hydrogen atom ( $H_\alpha$ ) bonded to  $C_\alpha$  atom.

In the case of aldehydes, the hydrogen atom of the aldehyde group bears also a partial positive charge to enhance its reactivity. Because of this, many reactions of aldehydes involve hydrogen atoms.

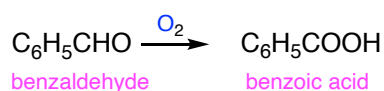


In the above structures, the polarization structures of  $H_\alpha$  and aldehyde hydrogen atom is incorporated in the structures indicating *I* effect. Much the same polarization structures are possible in the structures indicating *R* effect.

## 11.3 Oxidation and reduction

### (a) Oxidation

In the previous chapter, we have already learned that oxidation of alcohols gives carboxylic acids *via* aldehydes. Aldehydes are readily oxidized. For instance, benzaldehyde (a liquid) is gradually oxidized by the oxygen in the air, to form crystals of benzoic acid.



To the contrary, ketones are difficult to oxidize.

To take advantage of this property, many reactions of detecting aldehydes are devised. Particularly well-known are silver- mirror test and Fehling's reagent.



In silver-mirror test, a dilute ammoniacal aqueous solution in which silver ion ( $\text{Ag}(\text{NH}_3)_2^+$  is dissolved) is employed. Aldehydes are oxidized to carboxylic acids, and silver ion is reduced to silver. If the reaction condition is appropriately arranged, silver precipitates form a thin membrane of silver (silver mirror) on the wall of the container.

Fehling's solution is a weak oxidizing reagent containing  $\text{Cu}^{2+}$  ion. When it oxidizes aldehydes,  $\text{Cu}^{2+}$  ion is reduced and the resultant  $\text{Cu}^+$  forms red precipitates of  $\text{Cu}_2\text{O}$ . Thus, aldehydes are conveniently detected.

In both reactions oxidizing reagents oxidize aldehydes to change themselves into conspicuous substances. Under the same reaction condition, ketones do not react. Hence aldehydes and ketones are readily distinguished.

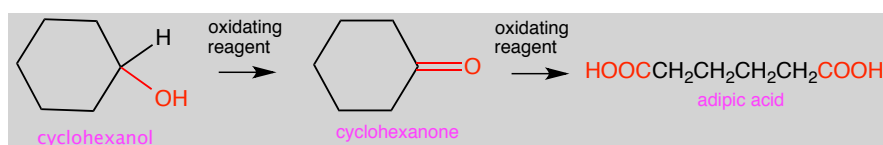
If attempts are made to oxidize ketones under a strong condition, the bond between the carbonyl carbon atom and the adjacent carbon atom is cleaved to give carboxylic acids. When acetone, for instance, is oxidized with a strong oxidizing agent such as potassium dichromate acidified with sulfuric acid, acetic acid and carbon dioxide are formed.

### Exercise 11.2 Oxidation of ketones

When cyclohexanol is strongly oxidized, a ring opening takes place to give a dicarboxylic acid. Guess its structure.

#### Answer

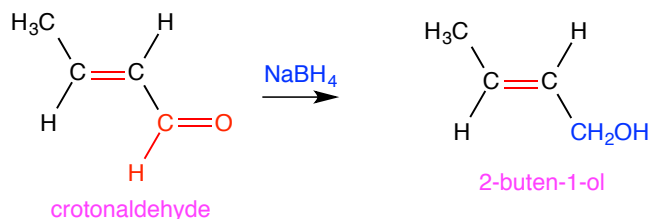
First, it is oxidized to cyclohexanone, and one of the carbon (O)-carbon bonds is cleaved, and then both terminals change into carboxy groups.



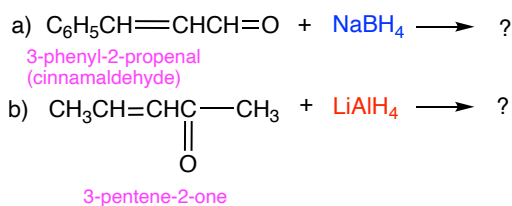
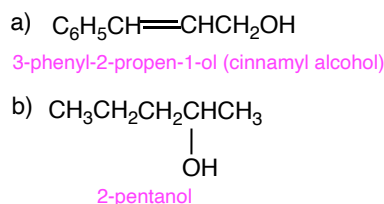
### (b) Reduction

The double bonds of alkenes are reduced by adding hydrogen in the presence of metal catalyst



**Exercise 11.3** Reduction

Predict the compound to be obtained by the following reaction.

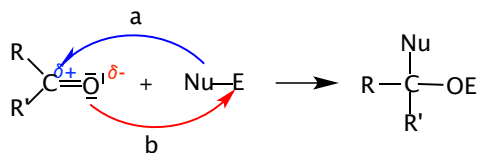
**Answer****11.4 Nucleophilic addition****(a) Driving force of nucleophilic additions**

Addition reactions to carbon-oxygen double bonds take place as is the case with carbon-carbon double bonds. In the case of the addition of carbon-carbon double bonds, the major role is the  $\pi$  electron of the double bond, and the driving force of the reaction is the approach of the electron-deficient reagent, that is, the electrophilic reagent, to the  $\pi$  electron.

In the case of the carbonyl group, the situation is different since the  $\text{C}=\text{O}$  double bond is polarized, and the driving force of the reaction is the attack of nucleophilic reagent on the electron-deficient carbonyl carbon atom. The situation will be explained with the help of Figure 11.2. Suppose the nucleophilic reagent will be divided into two parts, Nu-E where Nu is the nucleophilic part of the nucleophilic reagent and E is the rest of the reagent, electrophilic part.

The first stage (a) of addition is approach of the nucleophilic part Nu to the electron-deficient carbon. The following second stage (b) is the approach of the electrophilic part E to electron-rich oxygen. Since this reaction starts from the nucleophilic attack (not electrophilic attack) of reagent, this type of reactions is named **nucleophilic addition**.

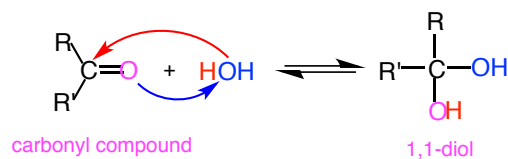




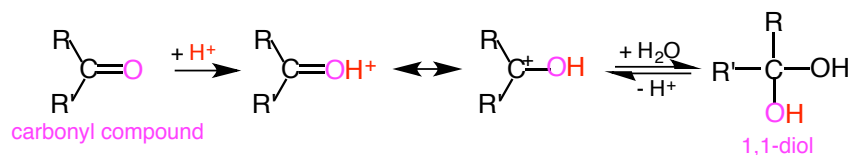
**Figure 11.2** The mechanism of nucleophilic addition to carbonyl group

### (b) Addition of water

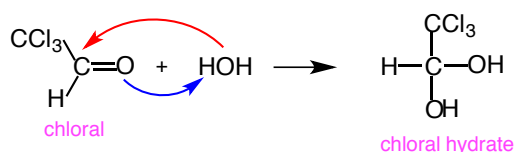
The simplest reagent to add to the carbonyl group is water  $\text{H}_2\text{O}$ . The nucleophilic part Nu is  $\text{OH}^-$  while the electrophilic part E is  $\text{H}^+$ . If water is added to a carbonyl group, 1,1-diol is formed. The reaction is in fact an equilibrium between a carbonyl compound and water



The position of equilibrium depends on the nature of the carbonyl group. Generally speaking, the equilibrium involving an aldehyde is shifted to 1,1-diol while the one involving a ketone is shifted to ketone side. This reaction is catalyzed by an acid, and the mechanism is given below.

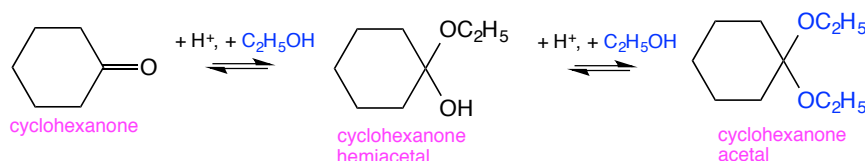


Sometimes an 1,1-diol of an aldehyde can be isolated. Such a stable 1,1-diol as chloral (trichloroacetaldehyde) can form a hydrate.



### (c) Addition of alcohol

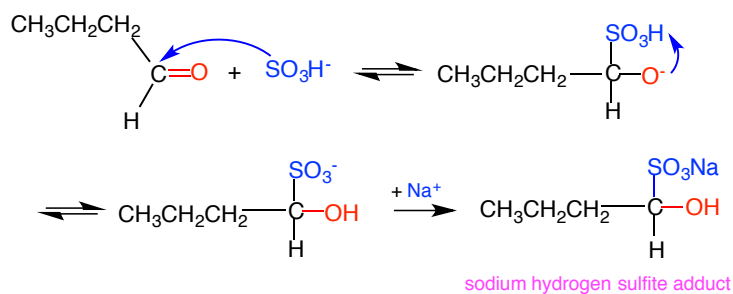
Under an acid-catalyzed condition, alcohols also add to the carbonyl groups. The product is a kind of ethers. Such types of ethers from carbonyl compounds are called **hemiacetal**, or **acetal**.



### (d) Addition of sodium hydrogen sulfite

Like oxygen atoms, sulfur atoms possess lone pairs to form nucleophilic reagents which can attack carbonyl groups. Sodium hydrogen sulfite is one of such sulfur nucleophilic reagents

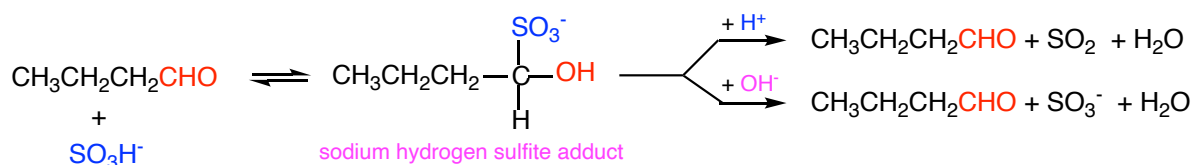
(Figure 11.3). Sodium hydrogen sulfite thus obtained is a kind of a salt, and relatively soluble in water.



**Figure 11.3** Addition of sodium hydrogen sulfite

When organic impurities are mixed with aldehydes or ketones, or conversely, aldehydes or ketones are mixed as impurities with other organic compounds, it will be possible to separate two components by changing aldehydes or ketones into derivatives soluble in water. This method has long been used in laboratories.

Similar to many addition reactions to carbonyl compounds, this is also a reversible reaction. If an acid or a base is added to the sodium hydrogen sulfite adduct in an equilibrium state, the adduct is broken and carbonyl compounds are regenerated (Figure 11.4).



**Figure 11.4** Decomposition of sodium hydrogen sulfite adduct

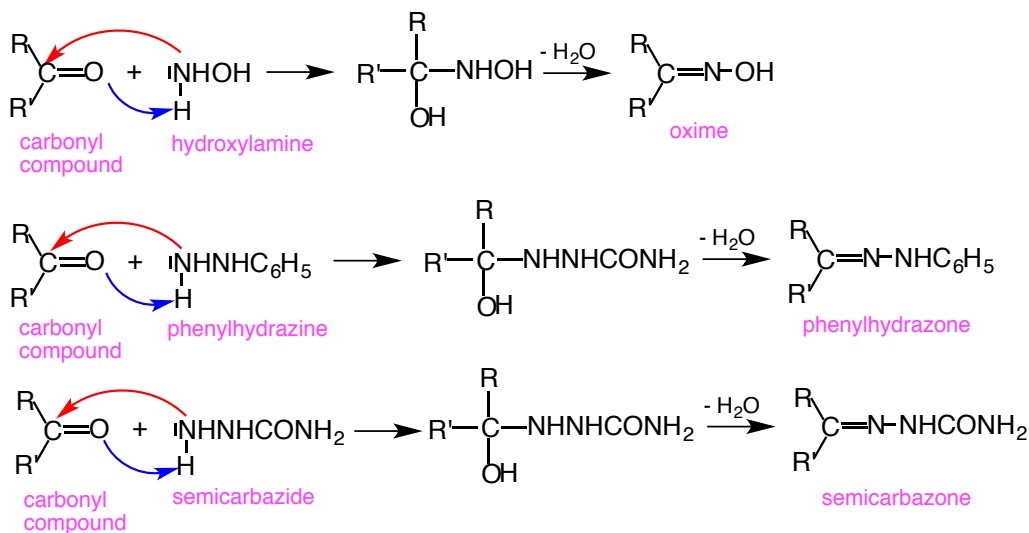
### (e) Addition of nitrogen compounds

Since nitrogen atoms also have lone pairs, compounds containing nitrogen also behave as nucleophilic reagents to form adducts by adding to carbonyl groups (Figure 11.5). Nitrogen compounds derived by substituting hydrogen atoms of ammonia by hydrocarbon moieties and others may be formally regarded as derivatives of ammonia.

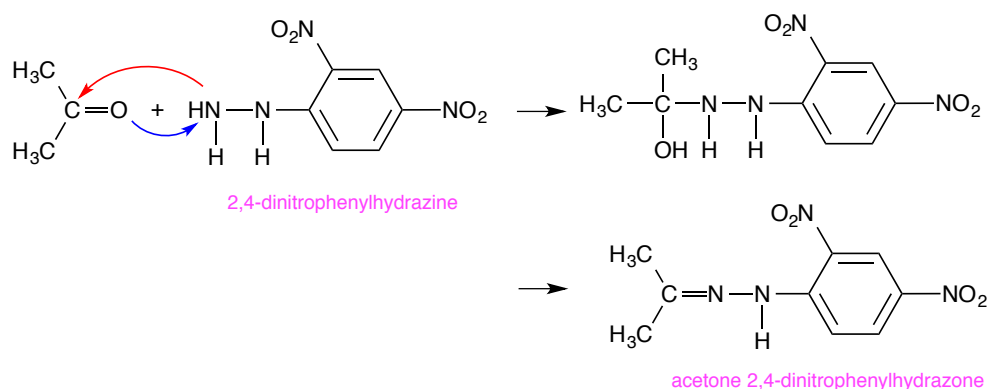
In many cases one molecule of water is eliminated from the adducts to give unsaturated derivatives. Such unsaturated species are readily crystallized as compared with the original carbonyl compounds. This property has long been used to identify carbonyl compounds that are difficult to handle or identify because they tend to be liquid at room temperature.

Nowadays the same information can more easily be obtained by spectroscopic methods, and for this reason use of such reagents is less frequent. Nevertheless, the method is very important to understand the reactivity of carbonyl compounds. In Figure 11.5 important nitrogen nucleophilic reagents and the corresponding products (adducts) are listed.

2,4-Dinitrophenylhydrazine produces particularly readily crystallizable derivatives and is an excellent nucleophilic reagent (Figure 11.6).



**Figure 11.5** Formation of carbonyl derivatives:  
the left side bar of nitrogen atoms indicates a lone pair.



**Figure 11.6** Formation of acetone 2,4-dinitrophenylhydrazone

#### Exercise 11.4 Carbonyl derivatives

Complete the following reaction formulas.

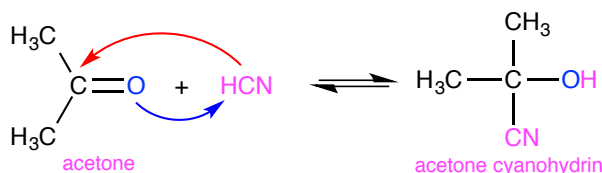
- $(\text{CH}_3)_2\text{C}=\text{O} + \text{H}_2\text{NOH} \rightarrow ?$
- $\text{CH}_3\text{CHO} + \text{C}_6\text{H}_5\text{NHNH}_2 \rightarrow ?$

#### Answer

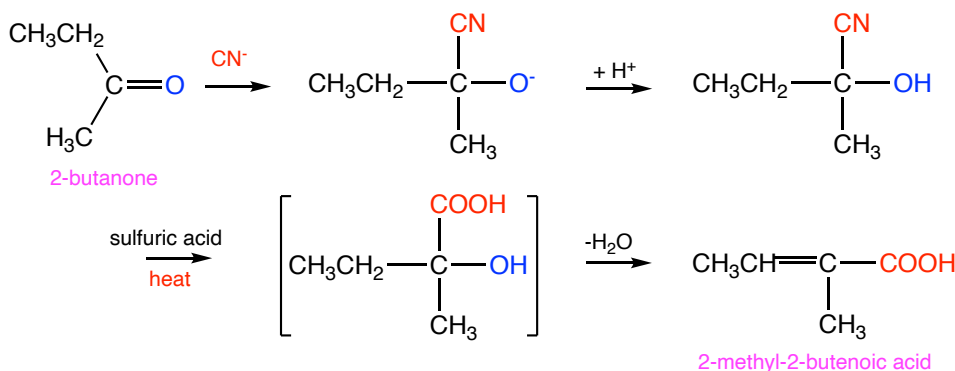
- $(\text{CH}_3)_2\text{C}=\text{O} + \text{H}_2\text{NOH} \rightarrow (\text{CH}_3)_2\text{C}=\text{N}-\text{OH} + \text{H}_2\text{O}$
- $\text{CH}_3\text{CHO} + \text{C}_6\text{H}_5\text{NHNH}_2 \rightarrow \text{C}_6\text{H}_5\text{CH}=\text{NNHC}_6\text{H}_5 + \text{H}_2\text{O}$

#### (f) Addition of cyanide ion

Cyanide ions are good nucleophilic reagents, and by attacking alkyl halides, cyanides (nitriles) are obtained *via* nucleophilic substitution (Ch. 9.3(a)). Cyanide ions, like other nucleophilic reagents, react with carbonyl compounds through nucleophilic addition to give compounds named cyanohydrins. The following example is the reaction between acetone and hydrogen cyanide.



This reaction is nothing other than the formation of a new carbon-carbon bond. By hydrolysis, a cyano group turns into a carboxy group (Figure 11.7). Depending on the reaction condition or the structure of reactants, dehydration may take place, and an unsaturated carboxylic acid is obtained.



**Figure 11.7** Formation of a carboxylic acid with one additional carbon atom prepared from 2-butanone

### (g) Addition of metal hydrides

Among the nucleophiles to the carbonyl group, notable ones are metal hydrides of alkali metals, alkaline earth metals, and metals belonging to the 3<sup>rd</sup> group. Some examples are given below.

sodium hydride NaH ( $\text{Na}^+ \dots \text{H}^-$ )

magnesium hydride  $\text{MgH}_2$  ( $\text{Mg}^{2+} \dots 2\text{H}^-$ )

aluminum hydride  $\text{AlH}_3$  ( $\text{Al}^{3+} \dots 3\text{H}^-$ )

Metal hydrides are ionic species and hydride ions  $\text{H}^-$  are the negative ions. These metal hydrides are decomposed when contacted with water, but these are stable in well-dried organic solvents, maintaining the reactivity of hydrides.

Lithium aluminum hydride  $\text{LiAlH}_4$  and sodium borohydride  $\text{NaBH}_4$ , which have been discussed in relation to reduction, are also metal hydrides. The details of their reaction are also described in relation to reduction.

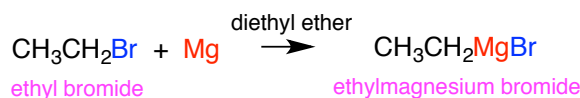
## 11.5 Grignard reaction

The Grignard reaction is one of the most useful reactions in the field of organic synthesis, and is briefly described in Ch. 9. Grignard reaction can be regarded to have the widest range of application among few reactions employed to increase the number of carbon atoms in the molecule

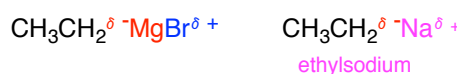
The mechanism of the reaction is very similar to the addition of metal hydrides. Reactions usually proceed in two steps.

**(a) Preparation of Grignard reagent**

When a halide such as ethyl bromide and small piece (powder or flakes) of magnesium metal are mixed in anhydrous diethyl ether (inhomogeneous reaction), an exothermic reaction takes place and magnesium gradually disappears to give a brown solution indicating the formation of Grignard reagent (ethylmagnesium bromide).

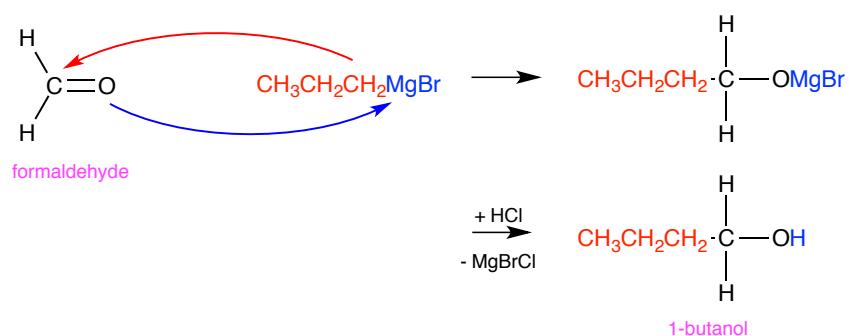


Formally a MgBr unit is equivalent to a monovalent cation. Then the polarization of ethylmagnesium bromide is the same with that of ethylsodium.

**(b) Grignard reaction**

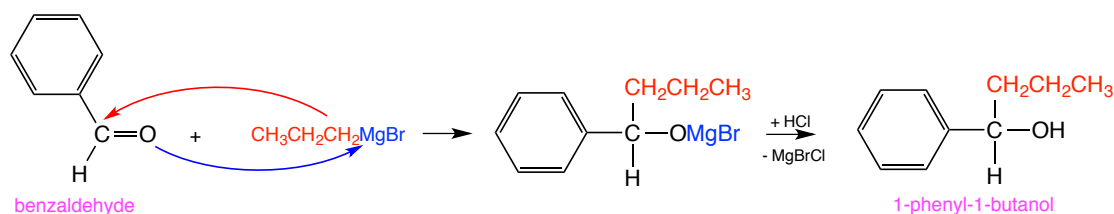
If freshly prepared Grignard reagent is added to an ether solution of a carbonyl compound, a reaction takes place. Since the ethyl group of ethylmagnesium bromide is a kind of carboanion, it acts as a good nucleophilic reagent. The process of the reaction is close to that of metal hydrides and carbonyl compounds. In this case, alcohols are obtained by hydrolysis of initially formed alkoxides. In the case of the Grignard reaction, however, the obtained alcohols have an increased number of carbon atoms.

By the reaction between formaldehyde and a Grignard reagent, a primary alcohol is obtained regardless of the type of the latter (Figure 11.8).



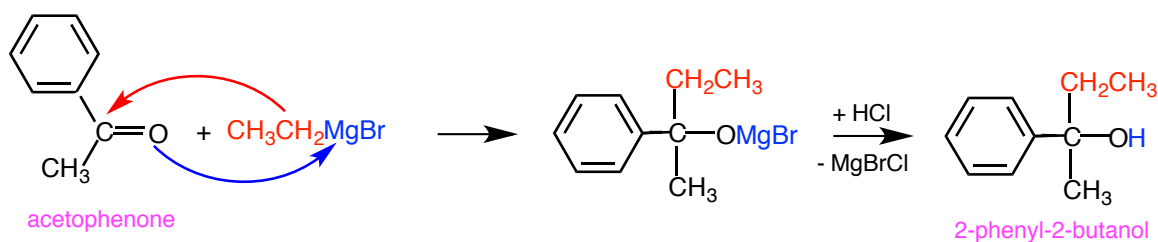
**Figure 11.8** Grignard reaction of formaldehyde

In the case of Grignard reactions between aldehydes other than formaldehyde and Grignard reagents, secondary alcohols are always obtained (Figure 11.9).



**Figure 11.9** Grignard reaction of benzaldehyde

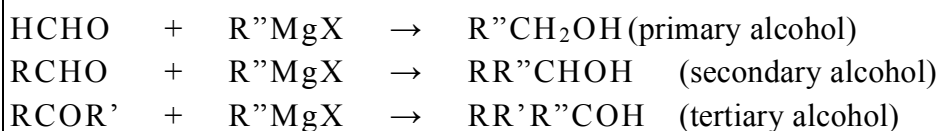
The reaction between ketones and Grignard reagents always give tertiary alcohols (Figure 11.10).



**Figure 11.10** Grignard reaction of acetophenone

Grignard reactions can be summarized as below.

**Point:** Grignard reaction

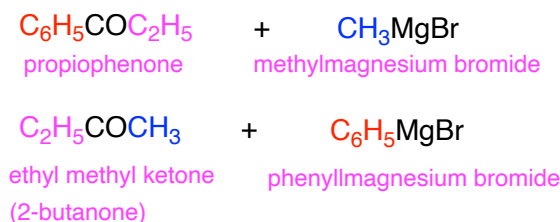


**Exercise 11.5** Grignard reaction

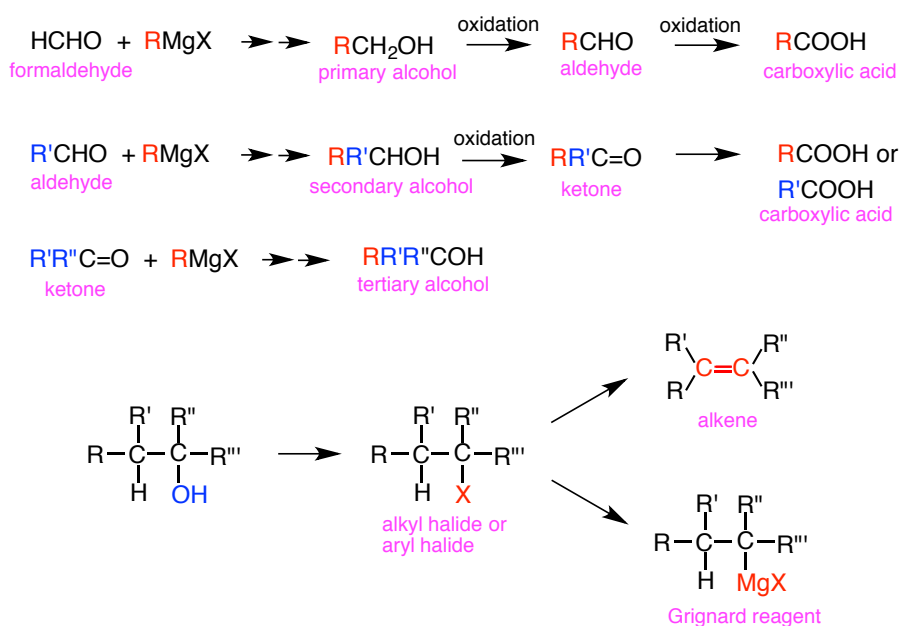
Suppose 2-phenyl-2-butanol is to be synthesized by Grignard reaction. There may be some combinations of carbonyl compounds and Grignard reagents other than the one indicated in Figure 11.10. What combinations may be possible?

**Answer**

The point is to assign two out of three hydrocarbon groups -CH<sub>3</sub>, -C<sub>2</sub>H<sub>5</sub>-, and -C<sub>6</sub>H<sub>5</sub> to the ketone. Besides the examples in Figure 11.10, two other combinations are possible.



By using Grignard reactions, primary, secondary, and tertiary alcohols with a variety of skeleton can be synthesized (Figure 11.11).



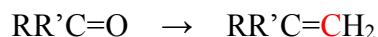
**Figure 11.11** Key role of Grignard reaction in organic synthesis

Oxidation of primary and secondary alcohols affords aldehydes and ketones, respectively. If these products are further reacted with Grignard reagents, primary, secondary, and tertiary alcohols with any skeletons you would like to have.

It is possible to prepare a variety of alcohols using Grignard reaction which plays the key role. By oxidation, these alcohols can be converted to aldehydes or ketones depending on their structures. Carbonyl compounds thus obtained have increased number of carbon atoms in their structure. Alcohols are readily converted to halides, which can be converted to alkenes by dehydrohalogenation, and form Grignard reagents by the reaction with magnesium. A series of reactions given in Figure 11.11 is the fundamentals of organic synthesis.

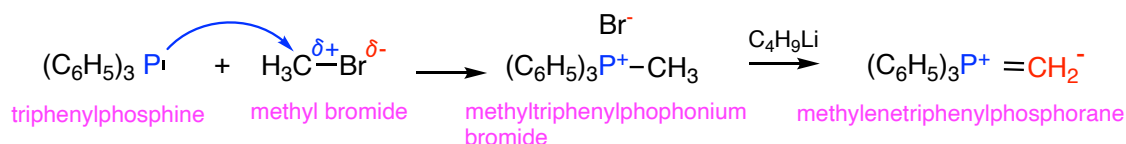
### 11.6 Wittig reaction

By Wittig reaction, proposed by a German chemist Georg Friedrich Karl Wittig (1894-1987), the oxygen atom of carbonyl group is substituted by a hydrocarbon group. Thus, Wittig reaction causes an increase of the number of carbon atoms. This reaction also proceeds in two steps.



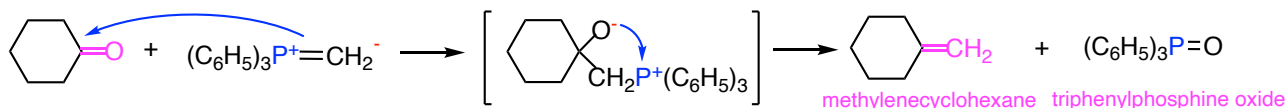
#### (a) Preparation of Wittig reagent

The Wittig reagent, the major role of Wittig reaction, is a kind of **ylide**, in which positive and negative charges adjoin. The typical Wittig reagent can be prepared by the reaction between triphenylphosphine and alkyl halide. The first step of the reaction is the nucleophilic attack of phosphorous to the carbon atom with partial positive charge as a nucleophilic reagent. In the next step, withdrawal of HBr by butyllithium  $\text{C}_4\text{H}_9\text{Li}$  takes place to give the ylide.



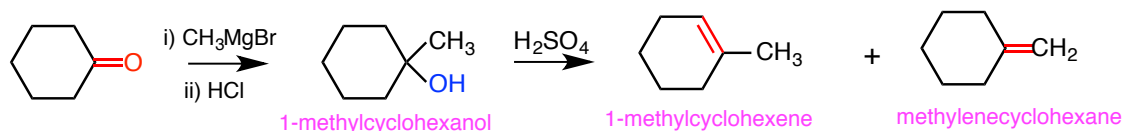
**(b) Reaction between carbonyl compounds and Wittig reagents**

The carbon atom bonded to phosphorous of Wittig reagent is a negatively charged nucleophilic reagent and attacks to carbonyl carbon atom. The role of positively charged phosphorous is to withdraw oxygen.



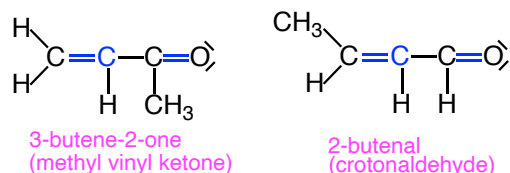
As compared with widely used methods of preparation of alkenes, that is, dehydration of alcohols or dehydrohalogenation of alkyl halides, Wittig reaction has an advantage that the product is only one kind and possibility of by-product formation is not high.

For instance, methylenecyclohexane can be prepared from cyclohexanone by Grignard reaction followed by dehydration. The orientation problem is involved, however, and 1-methylcyclohexene is necessarily formed. In this regard, Wittig reaction is highly selective in that only one product with exocyclic double bond is formed.

**11.7 Conjugate addition****(a)  $\alpha$ ,  $\beta$ -Unsaturated carbonyl compounds**

1,3-butadiene, a conjugate diene, in which two double bonds are connected with one single bond, exhibits reactivity different from standard alkenes. In the addition reaction of bromine, 1,3-butadiene gives not only the product in which only one double bond is involved in the reaction (1,2-addition), but also both double bonds are involved (1,4-addition) (see Ch. 6.3) .

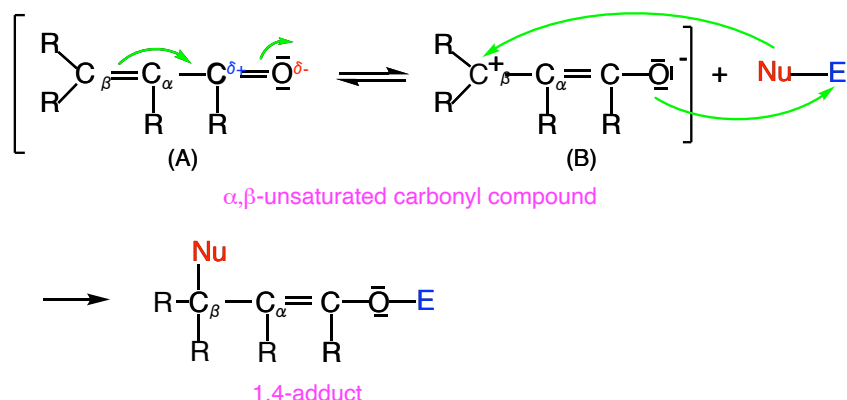
A compound in which a carbonyl group and a double bond (or a triple bond) is connected with a single bond is a kind of conjugate system, and such a compound is called  $\alpha,\beta$ -unsaturated carbonyl compound. If such a carbonyl compound is an aldehyde, it is  $\alpha,\beta$ -unsaturated aldehyde, and if the carbonyl compound is ketone, it is  $\alpha,\beta$ -unsaturated ketone (enone). Well-known examples are given below.

**(b) Mechanism of conjugate addition**

As compared with dienes, the carbonyl group of  $\alpha,\beta$ -unsaturated carbonyl compound is a system in which electrons move relatively easily. In Figure 11.12, the contribution of resonance structure (B) will be larger. For this reason, the nucleophilic part Nu of the reagent Nu-E attacks



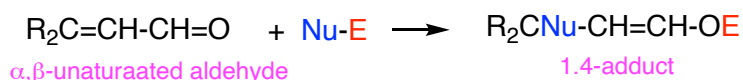
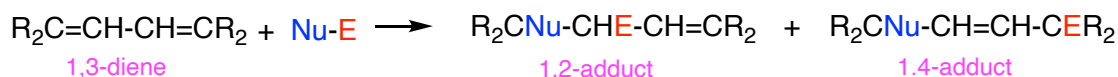
not only the carbonyl carbon atom bearing partial positive charge of resonance structure (A), but also positively charged  $\beta$  carbon atom of resonance structure (B).



**Figure 11.12** Mechanism of conjugate addition

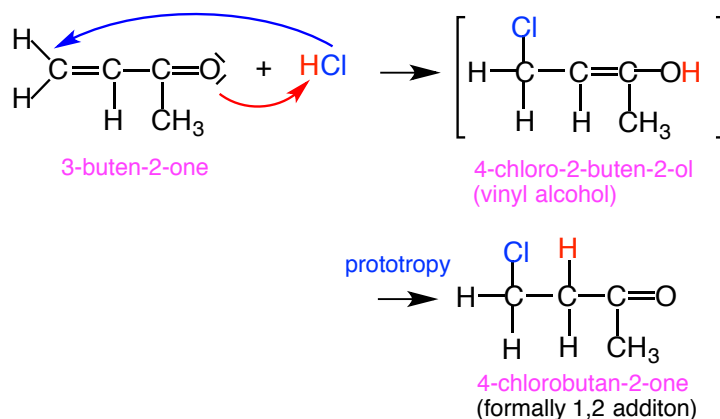
If the reaction proceeds in the latter manner, a reaction similar to the conjugate addition of 1,3-butadiene will take place to  $C_\beta$  atom, and the electrophilic part E is bonded to negatively charged oxygen atom. The result is 1,4-addition.

**Point:** Conjugate addition



**(c) Addition of hydrogen chloride**

The situation is not so simple. When the electrophilic part E is proton  $H^+$  as is the case with the addition of hydrogen chloride to  $\alpha,\beta$ -unsaturated ketone, the product is 1,2-adduct, but not 1,4-adduct. For instance, the product is 3-buten-2-one (methyl vinyl ketone) (Figure 11.13).

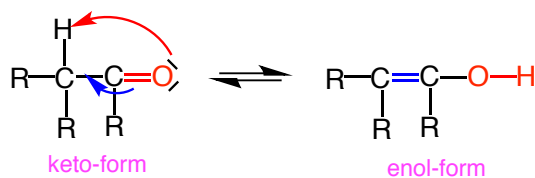


**Figure 11.13** Conjugate addition followed by prototropy

In fact the reaction proceeds *via* 1,4-addition to give firstly 4-chloro-2-buten-2-ol. This compound is so-called a vinyl alcohol, and is unstable to transform a more stable ketone. In this case, the proton of hydroxy group moves to the adjacent carbon atom, *i.e.*, **prototropy**.

Formally the product is 1,2-adduct, but this compound is formed by rearrangement. The initial product is in fact 1,4-adduct.

The transformation of vinyl alcohol to ketone is the most popular one of **keto-enol tautomerism** (Ch. 6.5(3)). The position of equilibrium depends on the structure of the molecule. In this case keto-form is more stable than enol-form to induce prototropy.



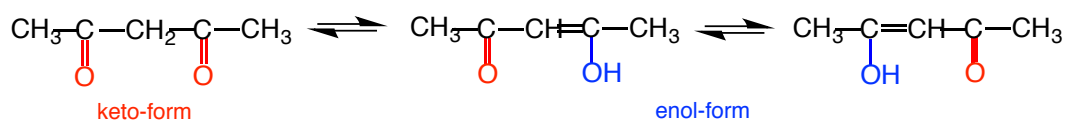
### Exercise 11.6 Tautomerism

Explain keto-enol tautomerism of pentane-2,4-dione (acetylacetone) by chemical formula.

#### Answer

Such compounds as acetylacetone in which two carbonyl groups are separated by one carbon atom is called  $\beta$ -dicarbonyl compounds. Acetylacetone is a representative  $\beta$ -diketone.

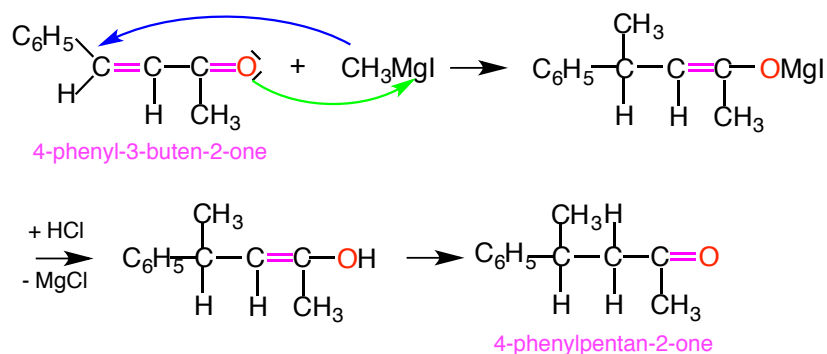
$\beta$ -dicarbonyl compounds with movable proton(s) will exhibit keto-enol tautomerism. Since they have two carbonyl groups, there are two species of enol form.



#### (d) Michael addition

The conjugate addition of carboanions to  $\alpha,\beta$ -unsaturated ketones or  $\alpha,\beta$ -unsaturated carboxylic acids are named **Michael addition**, proposed by an American chemist Arthur Michael (1853-1942). This reaction is important in organic synthesis. As an example the reaction between 4-phenyl-3-butene-2-one, an  $\alpha,\beta$ -unsaturated ketone, and a Grignard reagent, ethylmagnesium iodide is shown (Figure 11.14). As a conjugate addition, the nucleophilic part  $\text{CH}_3^-$  is combined to  $\text{C}_\beta$  and then  $\text{MgI}^+$ , the electrophilic part, is combined to oxygen to form 1,4-adduct. The product is hydrolyzed by hydrochloric acid, and  $\text{MgI}^+$  is replaced by proton to form enol, which is changed into 4-phenylpentane-2-one, formally 1,2-adduct, by tautomerism.

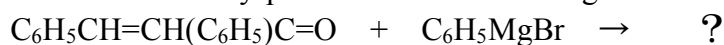
Michael addition is important in organic synthesis as one of the reactions to form a new carbon-carbon bond. Details of the related reactions will be discussed in Ch. 12.



**Figure 11.14** Reaction between  $\alpha,\beta$ -unsaturated ketone and a Grignard reagent

### Exercise 11.7 Michael addition

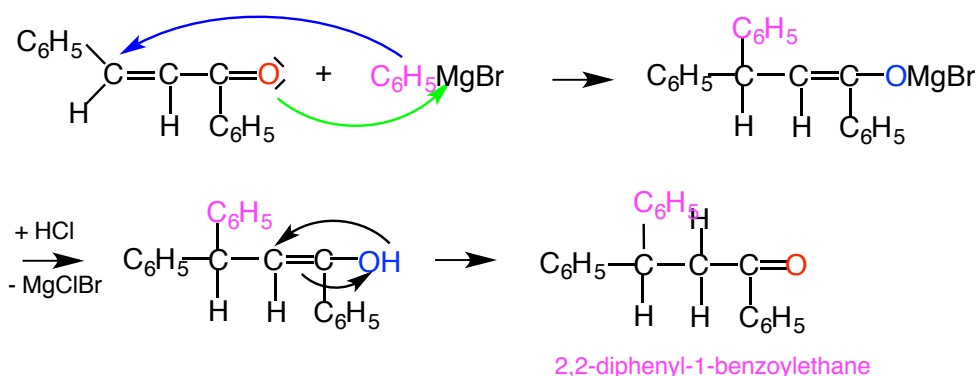
Predict the main- and by-products of the following reaction.



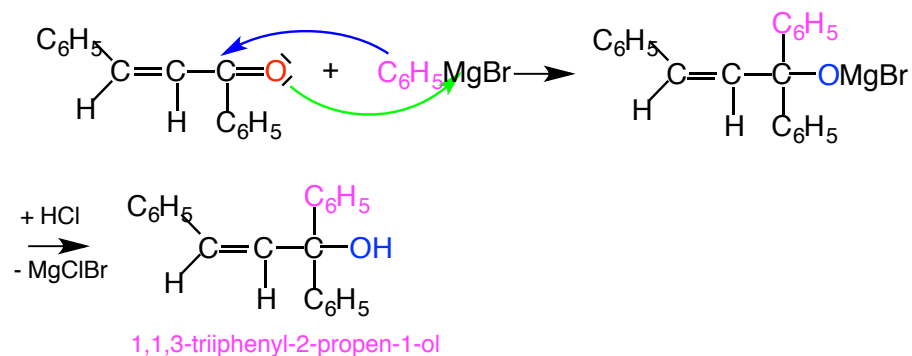
### Answer

The 1,4-adduct turns into a ketone, the main product (94%), by keto-enol tautomerism. The by-product (small amount) is the 1,2-adduct.

main product



by-product



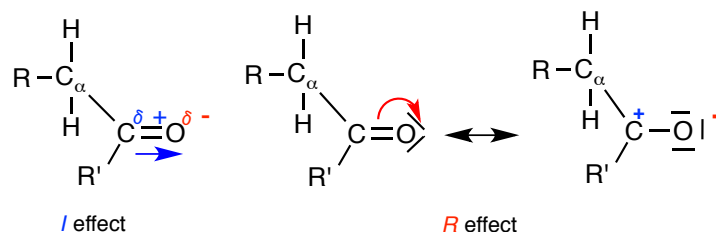
## 11.8 Aldol condensation

### (a) Reactivity of $\alpha$ -carbon atom of carbonyl group

In all reactions so far investigated, the carbonyl carbon atom is the center of the reaction. On the  $\alpha$ -carbon atom  $\text{C}_\alpha$  which forms a conjugate system with the carbonyl group, reactions can take place.

Positive charge is generated on the carbonyl carbon atom because of the polarization of C=O bond due to both *I*- and *R*-effects (Figure 11.15). Electrons around neighboring carbon atom  $C_{\alpha}$  are withdrawn by carbonyl carbon atom, and consequently  $C_{\alpha}$  will bear positive charge, and as a result, H which is bonded to  $C_{\alpha}$  will also bear positive charge.

The fact that  $H_{\alpha}$  bears positive charge means that  $H_{\alpha}$  will relatively easily electronically dissociates. In other word,  $H_{\alpha}$  will become somewhat acidic.

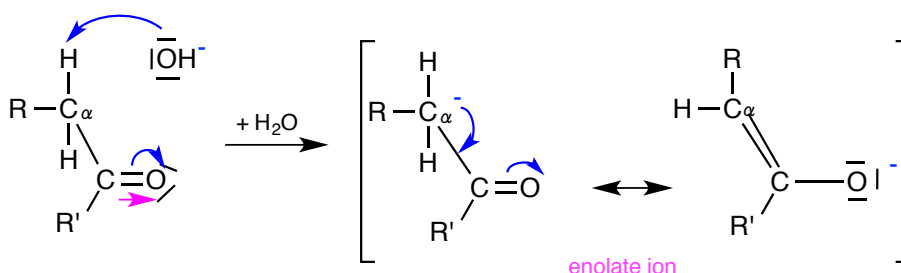


**Figure 11.15** *I*-effect and *R*-effect of carbonyl group

### (b) Enolate ion

The reason why a hydrogen atom bonded to the carbon atom is withdrawn is the special stability of resultant carboanion even though the hydrogen atom becomes a little more easily electronically dissociates. If electron transfer takes place after the dissociation of proton, the resonance structure in which oxygen atom, rather than carbon atom, is negatively charged (Figure 11.16).

This structure is enolate anion formed by elimination of proton from enol. Carboanions derived from carbonyl compounds which can be stabilized by resonance with enolate ion is far more stable than standard carboanions, and more readily formed. A good example to show this effect is aldol condensation.



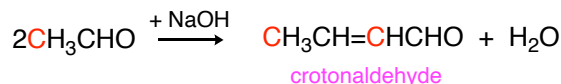
**Figure 11.16** Enolate ion

### (c) Aldol condensation

**Aldol condensation** is a base-catalyzed self condensation (dimerization) of an aldehyde or a ketone having  $H_{\alpha}$  (hydrogen atom bonded to  $C_{\alpha}$ ). With carbonyl compounds which are devoid of  $H_{\alpha}$  (such as formaldehyde HCHO or benzaldehyde  $C_6H_5CHO$ ), aldol condensation does not take place.

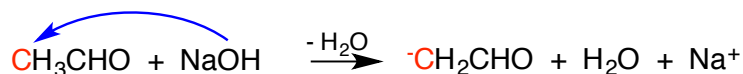
In relation to aldol condensation, aldehydes are more reactive than ketones, and most examples are chosen from the reactions of aldehydes. Among the reactions of ketones, however, there are some important examples.

By adding strong bases as sodium hydroxide or sodium ethoxide to acetaldehyde, crotonaldehyde is formed.



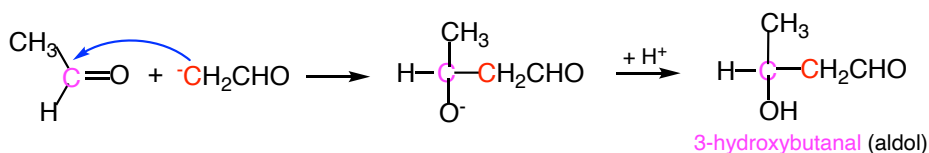
This reaction will proceed in three steps.

[1] Formation of carbanion: Hydroxy ion withdraws  $\text{H}_\alpha$  of aldehyde to leave carbanion.



[2] Formation of aldol

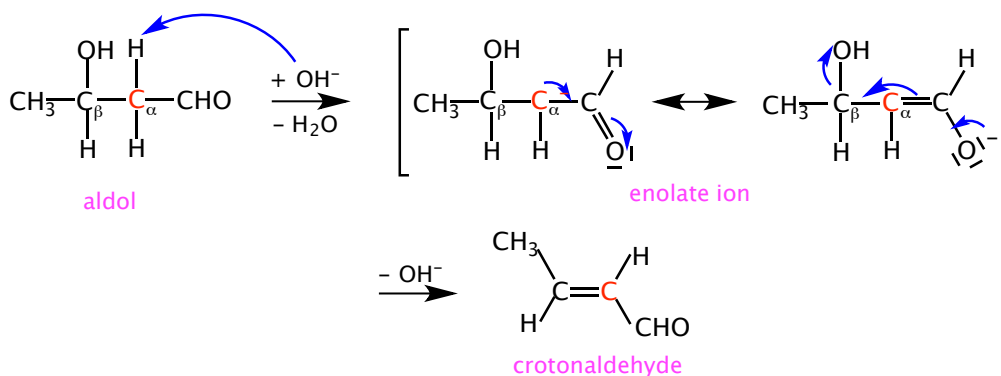
The carboanion formed attacks the carbonyl carbon of the second acetaldehyde (which is not converted to carbanion), and in addition, proton, the counterion, is bonded to oxygen. This is nucleophilic addition common to all carbonyl compounds, and the adduct formed is called **aldol**.



[3] Formation of crotonaldehyde

Dehydration of alcohol requires relatively severe condition such as heating with conc. sulfuric acid. In aldol where the hydroxy group is bonded to  $\text{C}_\beta$ , dehydration occurs rather easily.

Withdrawal of  $\text{H}_\alpha$  by hydroxy group proceeds smoothly because of stabilization by enolate ion. Subsequently hydroxy group is removed to yield crotonaldehyde (Figure 11.17)



**Figure 11.17** Formation of crotonaldehyde

Any aldehyde exhibits the same reaction as long as it has  $\text{H}_\alpha$ . The reaction of propanal is given in Figure 11.18 as an example.

If the general formula of aldehydes having  $\text{H}_\alpha$  is represented as  $\text{RCH}_2\text{CHO}$ , the general formula of carbanion derived from it is always  $\text{RC}^-\text{HCHO}$ . Notice that aldehyde carbon is always attacked by this carboanion.

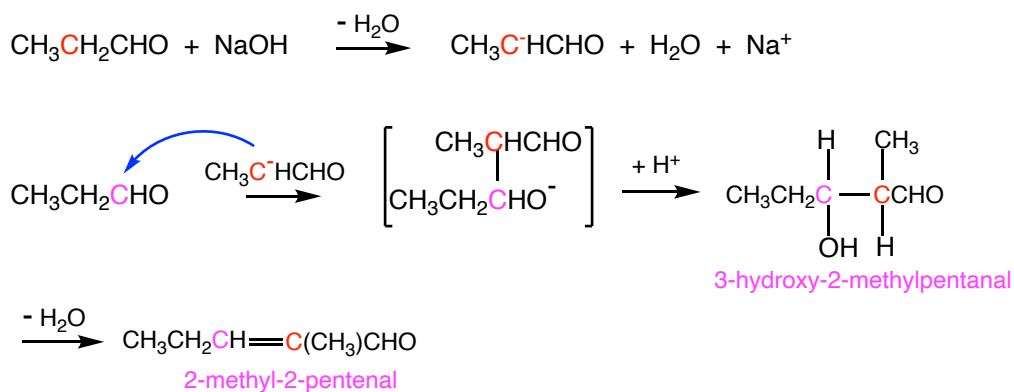


Figure 11.18 Aldol condensation of propanal

**Exercise 11.8** Enolate ion

Draw the structure of the enolate ion derived from aldol condensation of propanal.

**Answer**

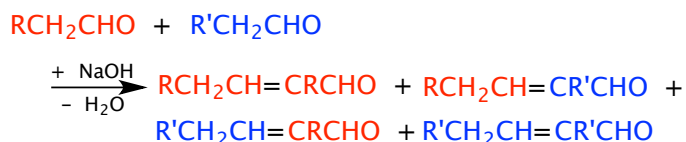
A proton is withdrawn from  $\text{CH}_2$  moiety rather than from  $\text{CH}_3$  moiety. It is important to show the resonance with enol form.



It is clear from these examples that aldol condensation is one of the most important reaction in the field of organic synthesis. Aldol condensation has already been known from the middle of 19<sup>th</sup> century. The reaction is continuously improved, and even now the importance of aldol condensation is increasing.

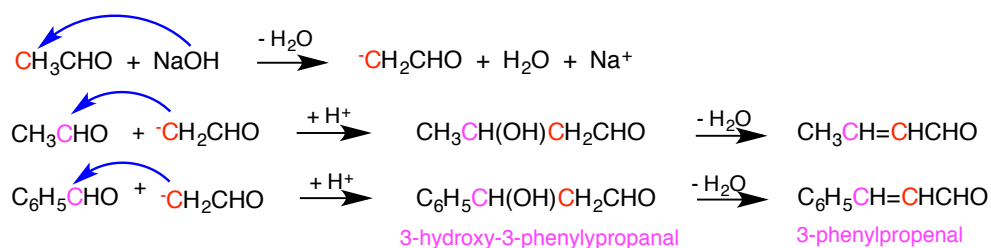
**(d) Mixed aldol condensation**

When two carbonyl compounds with  $\text{H}_\alpha$ , respectively, are mixed and aldol condensation is caused, a mixture of four kinds of products are obtained depending on which one will take the role of the nucleophilic reagent or the role of the carbonyl compounds. Thus, generally speaking, mixed aldol condensations are not appropriate for synthetic purposes since these reactions tend to give several products.



For such carbonyl compounds as formaldehyde or benzaldehyde, which do not have  $\text{H}_\alpha$ , aldol condensation does not take place. When these carbonyl compounds and other carbonyl compounds possessing  $\text{H}_\alpha$ , are placed under the condition of aldol condensation, the former basically acts as a carbonyl compounds rather than a nucleophilic reagent. Thus, the products are only two kinds. For instance, the number of products of aldol condensation between benzaldehyde

and acetaldehyde is limited to two.



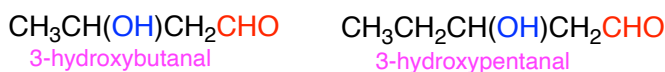
### Exercise 11.9 Mixed aldol condensation

When a strong base is added to the mixture of acetaldehyde and propanal (propionaldehyde), a mixture of aldols is obtained. Guess the structures of these aldols and those of unsaturated aldehydes obtained by dehydration of these aldols.

#### Answer

Two kinds of carbanion are generated from two kinds of aldehydes.

aldols obtained from  $\text{C}^-\text{H}_2\text{CHO}$



unsaturated aldehydes obtained from  $\text{C}^-\text{H}_2\text{CHO}$



aldols obtained from  $\text{CH}_3\text{C}^-\text{HCHO}$



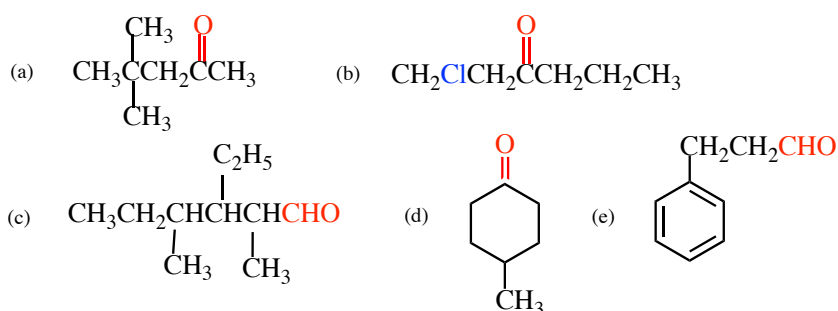
unsaturated aldehyde obtained from  $\text{CH}_3\text{C}^-\text{HCHO}$



It is not wise to use the mixture of acetaldehyde and propanal to synthesize 2-methyl-2-propanal.

**Problems****11.1**

Name the following compounds.

**11.2**

Draw the structures of the following compounds.

- 4,4-dimethylpentanal
- 4-methylheptane-2,6-dione
- 5-chlorohexanal
- 3-cyclohexene-1-one
- benzyl phenyl ketone

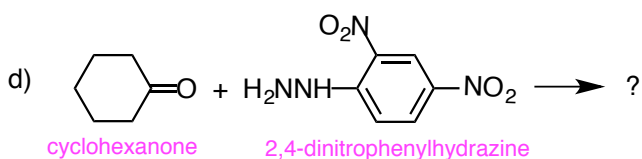
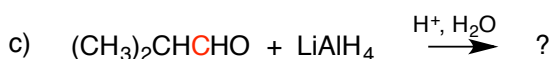
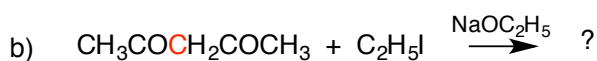
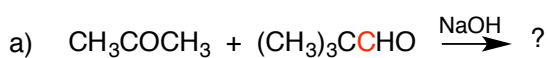
**11.3**

Concerning each of the following Grignard reactions, draw the structures and give names of the products after hydrolysis.

- Reaction between butanal and methylmagnesium bromide
- Reaction between benzophenone and phenylmagnesium bromide
- Reaction between 4-methyl-2-pentanone and ethylmagnesium bromide

**11.4**

Draw the structures and give names of the final products of the following reactions.

**11.5**

Suppose 3-methyl-3-hexanol is to be prepared using Grignard reaction. Show all possible combinations of carbonyl compounds and alkyl halides.



### 11.6

Answer the following questions on Wittig reaction.

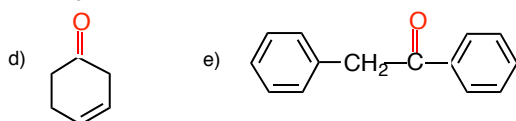
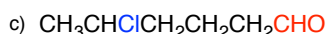
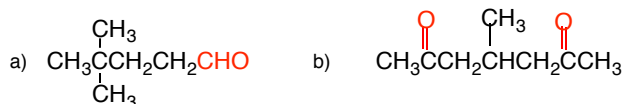
(1) Draw the structure and give the name of the product of the following reaction.



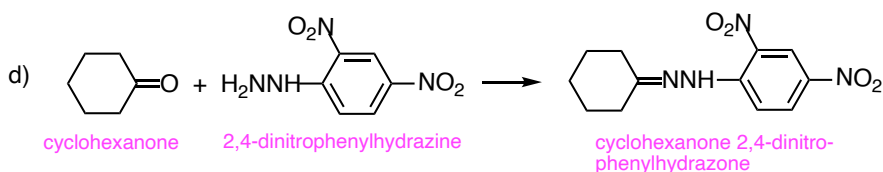
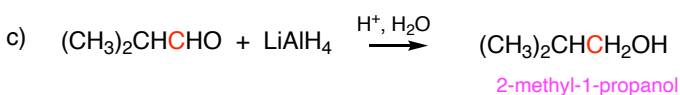
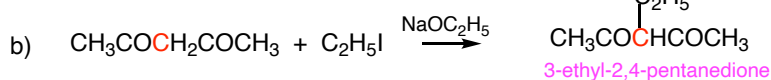
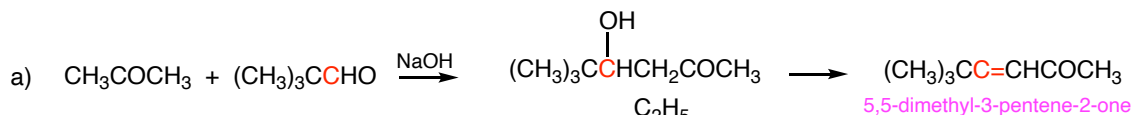
(2) Indicate the carbonyl compound and alkyl halide to be used to synthesize 2-methyl-2-hexene *via* Wittig reaction.

**Answers****11.1**

- (a) 4,4-dimethyl-2-pentanone  
 (b) 1-chloro-3-hexanone  
 (c) 3-ethyl-2,4-dimethylhexanal  
 (d) 4-methylcyclohexanone  
 (e) 3-phenylpropanal

**11.2****11.3**

- (a)  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}(\text{OH})\text{CH}_3$  (2-pentanol)  
 (b)  $(\text{C}_6\text{H}_5)_3\text{COH}$  (triphenylmethanol)  
 (c)  $(\text{CH}_3)_2\text{CHCH}_2\text{C}(\text{OH})(\text{CH}_3)\text{CH}_2\text{CH}_3$  (3,5-dimethyl-3-hexanol)

**11.4****11.5**

3-Methyl-3-hexanol, a tertiary alcohol, has methyl-, ethyl-, and propyl groups. A ketone must be used for the carbonyl side. Possible combinations are given below.

- (i)  $\text{CH}_3\text{COC}_2\text{H}_5$  (2-butanone) +  $\text{CH}_3\text{CH}_2\text{CH}_2\text{Br}$  (propyl bromide)  
 (ii)  $\text{CH}_3\text{COC}_3\text{H}_7$  (2-pentanone) +  $\text{CH}_3\text{CH}_2\text{Br}$  (ethyl bromide)  
 (iii)  $\text{C}_2\text{H}_5\text{COC}_3\text{H}_7$  (3-hexanone) +  $\text{CH}_3\text{Br}$  (methyl bromide)

11.6

