الكلية	**العلوم**
القسم	**علوم الكيمياء**
المادة باللغة الانجليزية	Organic chemistry
المادة باللغة العربية	**الكيمياء العضوية**
المرحلة الدراسية	**الثانية**
اسم التدريسي	**وهج رائد عباس**
عنوان المحاضرة باللغة الانجليزية	Functional groups
عنوان المحاضرة باللغة العربية	**المجاميع الوظيفية**
رقم المحاضرة	**1**
المصادر والمراجع	Fundamental of organic chemistry, T. W. Craham Solomon
	Organic chemistry, 10th Ed, T. W. Craham Solomon & Craig B. fryhle
	Organic chemistry, 8th Ed, L. G. WADE JR

متن المحاضرة بعد الجدول

FUNCTION GROUP AND THEIR DERIVATIVES

By: Wahaj Raed Abbas

Introduction

A functional group is an atom or a group of atoms with characteristic chemical and physical properties. It is the reactive part of the molecule. The importance of a functional group cannot be overstated. Molecules containing these functional groups may be simple or very complex. A functional group determines all the following properties of a molecule:

- Bonding and shape
- Type and strength of intermolecular forces
- Physical properties
- Nomenclature
- Chemical reactivity

Type of function group

- Hydrocarbons
- Compounds containing a C – Z bond (where Z= an electronegative element)
- Compounds containing a C = O (or C=Z) group.

Hydrocarbons: are compounds made up of only the elements carbon and hydrogen. They may be aliphatic or aromatic.

Aliphatic hydrocarbons:

Aliphatic hydrocarbons can be divided into three subgroups.

•Alkanes have only C–C σ bonds and no functional group. Ethane, CH_3 -CH_3, is a simple alkane.

•Alkenes have a C – C double bond as a functional group. Ethylene, CH_2=CH_2, is a simple alkene.

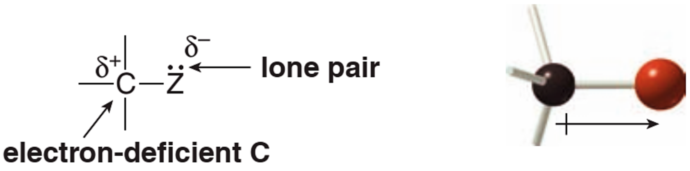
•Alkynes have a C – C triple bond as a functional group. Acetylene, C_2H_2, is a simple alkyne.

Aromatic hydrocarbons.

This class of hydrocarbons was so named because many of the earliest known aromatic compounds had strong, characteristic odors. The simplest aromatic hydrocarbon is benzene. The six-membered ring and three π bonds of benzene comprise a single functional group.

Compounds Containing C–Z σ Bonds:

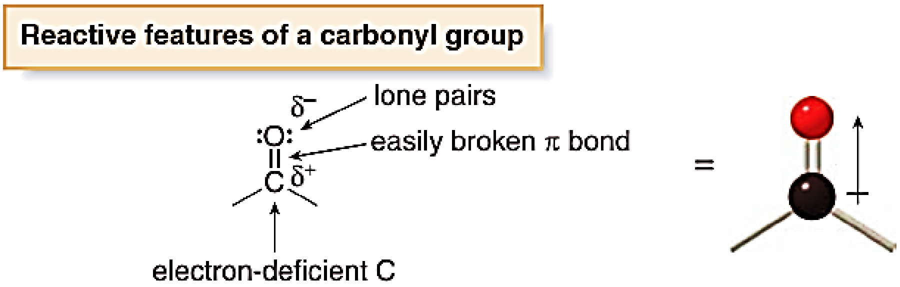
Several types of functional groups that contain C – Z σ bonds. The electronegative heteroatom Z creates a polar bond, making carbon electron deficient. The lone pairs on Z are available for reaction with protons and other electrophiles, especially when Z = N or O. This type of compounds include alkyl halide, alcohol, ether, amine, thiol, and sulfide



Several simple compounds in this category are widely used. As an example, chloro-ethane (CH_3CH_2Cl, commonly called ethyl chloride) is an alkyl halide used as a local anesthetic.

Compounds Containing a C=O Group

Many different types of functional groups possess a C – O double bond (a carbonyl group),. The polar C – O bond makes the carbonyl carbon an electrophile, while the lone pairs on O allow it to react as a nucleophile and base. The carbonyl group also contains a π bond that is more easily broken than a C – O σ bond. This type of compounds include aldehyde, ketone, carboxylic acid, acid chloride ester, amide,



Alkanes

Alkanes are aliphatic hydrocarbons having only C – C and C – H bonds. Because their carbon atoms can be joined together in chains or rings, they can be categorized
as acyclic or cyclic. Alkanes are often described as saturated hydrocarbons: hydrocarbons because they contain only carbon and hydrogen; saturated because they
have only C-C and C- H single bonds and thus contain the maximum possible number of hydrogens per carbon.

Acyclic alkanes: have the molecular formula C_nH_{2n+2} (where n = an integer) and contain only linear and branched chains of carbon atoms. They are also called saturated hydrocarbons because they have the maximum number of hydrogen atoms per carbon.

Cycloalkanes contain carbons joined in one or more rings. Because their general formula is C_nH_{2n}, they have two fewer H atoms than an acyclic alkane with the same number of carbons. The primary sources of alkanes are natural gas and petroleum. These fossil fuels account for approximately 85% of the total energy consumed in the United States. Nuclear electric power, hydroelectric power, and renewable energy sources such as solar and wind power, make up most of the remaining 15%. In addition, these fossil fuels provide the bulk of the raw materials for the organic chemicals used worldwide.

CH_4

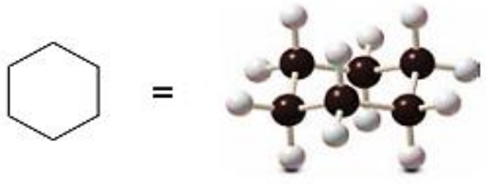
Methane, CH_4

CH_3CH_3

Ethane, C_2H_6

$CH_3CH_2CH_3$

Propane, C_3H_8



cyclohexane
C_6H_{12}

Reaction of alkanes

Oxidation and Reduction Reactions:

Oxidation and reduction are opposite processes. As in acid–base reactions, there are always two components in these reactions. One component is oxidized and one is reduced. To determine if an organic compound undergoes oxidation or reduction, we concentrate on the carbon atoms of the starting material and product, and compare the relative number of C – H and C – Z bonds, where Z = an element more electronegative than carbon (usually O, N, or X). Oxidation and reduction are then defined in two complementary ways.

Oxidation results in an increase in the number of C – Z bonds, or in a decrease in the number of C – H bonds.

Reduction results in a decrease in the number of C – Z bonds, or in an increase in the number of C – H bond.

The oxidation of alkanes by O_2 to give carbon dioxide and water is by far their most economically important reaction. Oxidation of saturated hydrocarbons is the basis for their use as energy sources for heat (natural gas, liquefied petroleum gas (LPG), and fuel oil) and power (gasoline, diesel fuel, and aviation fuel). Following are balanced equations for the complete oxidation of methane (the major component of natural gas) and propane (the major component of LPG).

$$CH_4 + 2O_2 \longrightarrow CO_2 + 2H_2O \qquad \Delta H^\circ = -890.4\ \text{kJ}\ (-212.8\ \text{kcal})/\text{mol}$$

Methane

$$CH_3CH_2CH_3 + 5O_2 \longrightarrow 3CO_2 + 4H_2O \qquad \Delta H^\circ = -2220\ \text{kJ}\ (-530.6\ \text{kcal})/\text{mol}$$

Propane

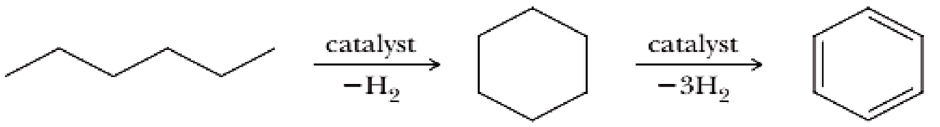
Cracking:

is a process whereby a saturated hydrocarbon is converted into an unsaturated hydrocarbon plus H_2. Ethane is cracked by heating it in a furnace at 800 - 900°C for a fraction of a second.

$$CH_3CH_3 \xrightarrow{800\text{–}900^\circ C} CH_2{=}CH_2 + H_2$$

Ethane **Ethene (Ethylene)**

The two most common reforming processes are cracking, as illustrated by the thermal conversion of ethane to ethylene, and catalytic reforming. Catalytic reforming is illustrated by the conversion of hexane first to cyclohexane and then to benzene.



Hexane **Cyclohexane** **Benzene**

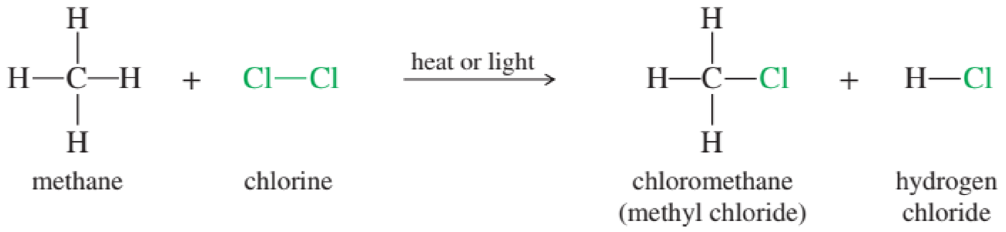
Synthesis gas is prepared by passing steam over hot coal; it is also prepared by partial oxidation of methane with oxygen.

$$CH_4 + \frac{1}{2}O_2 \xrightarrow{\text{catalyst}} CO + 2H_2$$

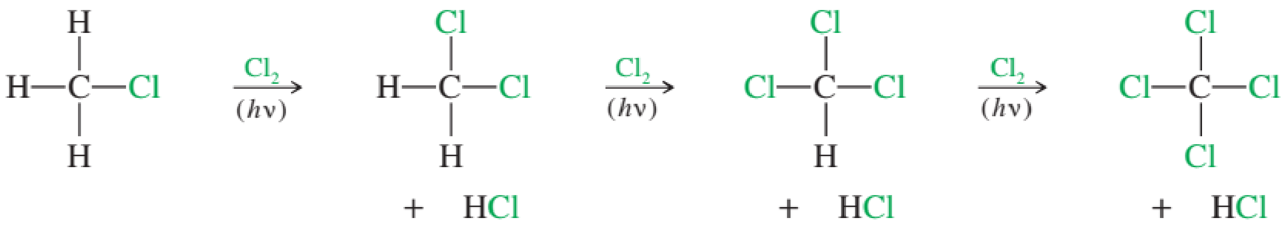
Methane

Halogenation of alkanes:

The chlorination of methane is an important industrial reaction, with a relatively simple mechanism that illustrates many of the important principles of a reaction. The reaction of methane with chlorine produces a mixture of chlorinated products, whose composition depends on the amount of chlorine added and also on the reaction conditions. Either light or heat is needed for the reaction to take place at a useful rate. When chlorine is added to methane, the first reaction is



$$H-\overset{H}{\underset{H}{C}}-H + Cl-Cl \xrightarrow{\text{heat or light}} H-\overset{H}{\underset{H}{C}}-Cl + H-Cl$$

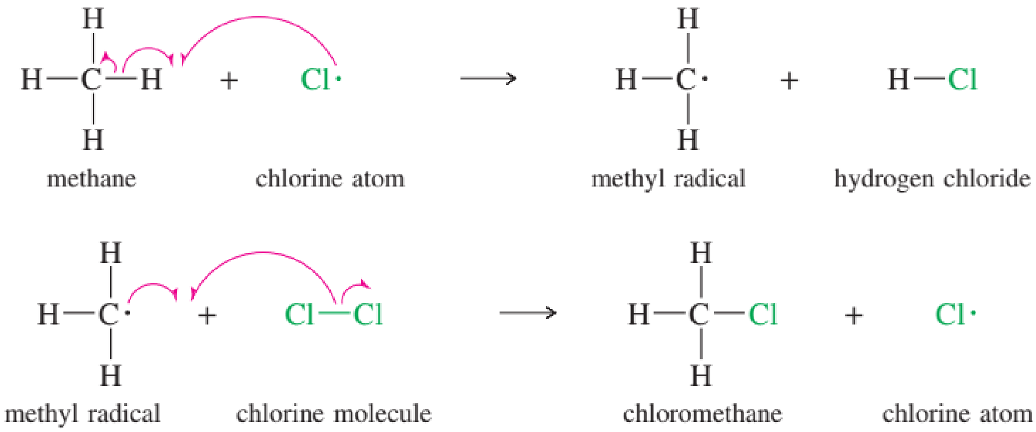


$$H-\overset{H}{\underset{H}{C}}-Cl \xrightarrow[(h\nu)]{Cl_2} H-\overset{Cl}{\underset{H}{C}}-Cl + HCl \xrightarrow[(h\nu)]{Cl_2} Cl-\overset{Cl}{\underset{H}{C}}-Cl + HCl \xrightarrow[(h\nu)]{Cl_2} Cl-\overset{Cl}{\underset{Cl}{C}}-Cl + HCl$$

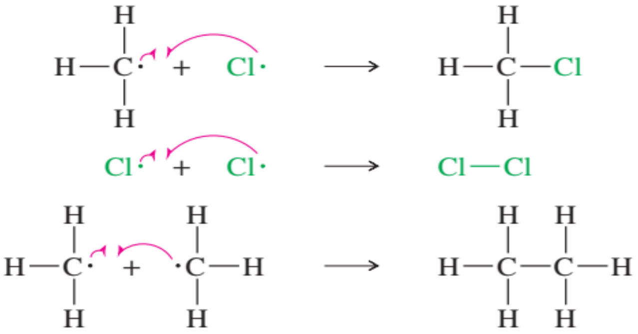
A chain reaction mechanism has been proposed to explain the chlorination of methane. A chain reaction consists of three kinds of steps:

1. The initiation step, which generates a reactive intermediate.

2 .Propagation steps, in which the reactive intermediate reacts with a stable molecule to form a product and another reactive intermediate, allowing the chain to continue until the supply of reactants is exhausted or the reactive intermediate is destroyed.



3 .Termination steps, side reactions that destroy reactive intermediates and tend to slow or stop the reaction.



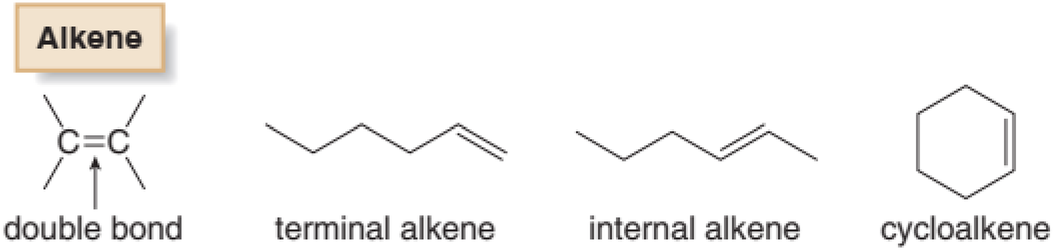
Spectroscopy Of Alkane:

IR: C-H bond stretching at frequency 3000-2850 cm^{-1}, $-CH_3$ bend at 1450 & 1375 cm^{-1} , and $-CH_2$ bend at 1465cm^{-1}

^{1}H-NMR: methyl group (CH3) will produce a signal near 0.9 ppm, a methylene group (CH2) will produce a signal near 1.2 ppm, and a methine group (CH) will produce a signal near 1.7 ppm.

Alkene

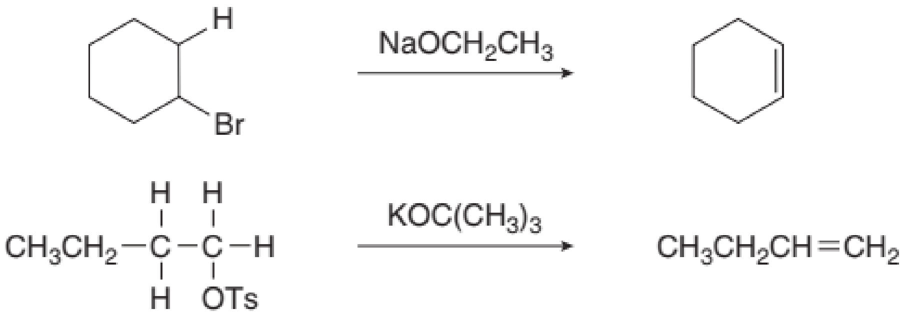
Alkenes are hydrocarbons with carbon–carbon double bonds. Alkenes are sometimes called olefins. Terminal alkenes have the double bond at the end of the carbon chain, whereas internal alkenes have at least one carbon atom bonded to each end of the double bond. Cycloalkenes contain a double bond in a ring. The double bond of an alkene consists of one σ bond and one π bond. Each carbon is sp2 hybridized and trigonal planar, and all bond angles are approximately 120°.



The π bond is much weaker than the σ bond of a C – C double bond, making it much more easily broken. As a result, alkenes undergo many reactions that alkanes do not, Because a carbon–carbon double bond is relatively reactive, it is considered to be
a functional group, and alkenes are characterized by the reactions of their double bonds.

Preparation Of Alkenes

Alkenes can be prepared from alkyl halides and alcohols via elimination reactions. For example, dehydrohalogenation of alkyl halides with strong base yields alkenes via an E2 mechanism.



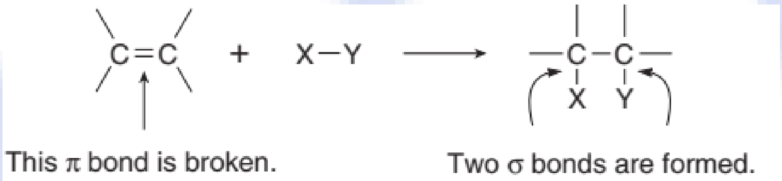
Typical bases include –OH and –OR [especially –OC(CH3)3], and nonnucleophilic bases such as DBU and DBN. Alkyl tosylates can also be used as starting materials under similar reaction conditions. The acid-catalyzed dehydration of alcohols with H_2SO_4 or TsOH yields alkenes, too.

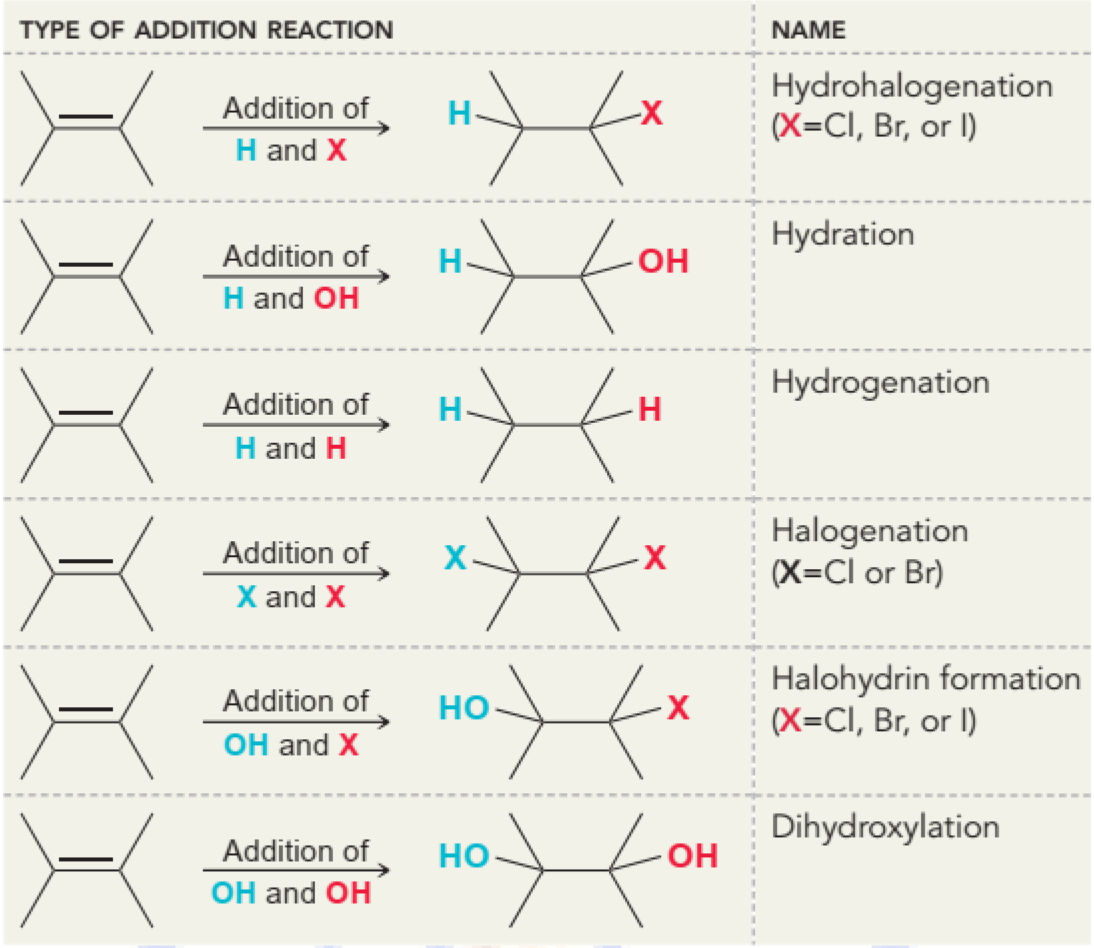
The reaction occurs via an E1 mechanism for 2° and 3° alcohols, and an E2 mechanism for 1° alcohols. E1 reactions involve carbocation intermediates, so rearrangements are possible. Dehydration can also be carried out with $POCl_3$ and pyridine by an E2 mechanism. Also, alkenes can preparation from cracking of alkanes.

Alkene Reaction

Addition Reactions

Because the C – C π bond of an alkene is much weaker than a C – C σ bond, the characteristic reaction of alkenes is addition: the o bond is broken and two new r bonds are formed. Every reaction of alkenes involves addition: the o bond is always broken. Because alkenes are electron rich, simple alkenes do not react with nucleophiles or bases, reagents that are themselves electron rich. Alkenes react with electrophiles.

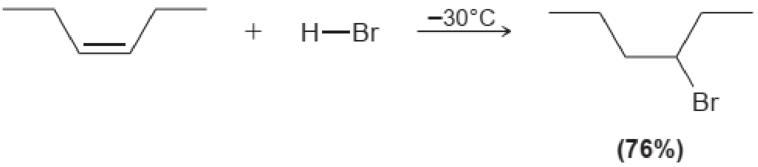




TYPE OF ADDITION REACTION	NAME
Addition of H and X	Hydrohalogenation (X=Cl, Br, or I)
Addition of H and OH	Hydration
Addition of H and H	Hydrogenation
Addition of X and X	Halogenation (X=Cl or Br)
Addition of OH and X	Halohydrin formation (X=Cl, Br, or I)
Addition of OH and OH	Dihydroxylation

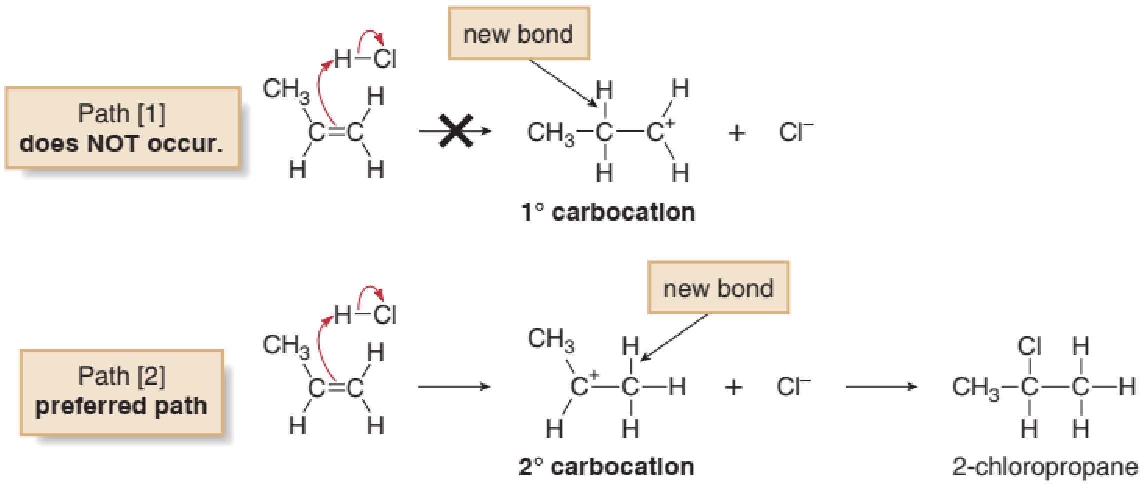
Hydrohalogenation

The treatment of alkenes with HX (where X = Cl, Br, or I) results in an addition reaction called hydrohalogenation, in which H and X are added across the π bond:

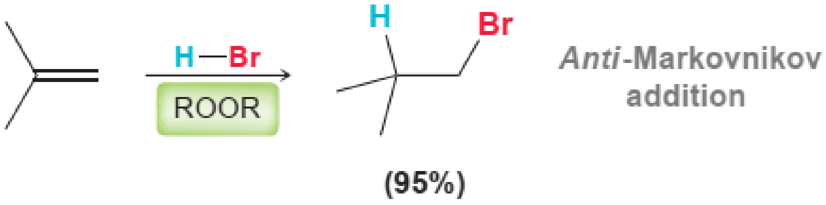


In cases where the alkene is unsymmetrical, the ultimate placement of H and X must be considered. In the following example، there are two possible vinylic positions where X can be placed.

Markovnikov rule: In the addition of HX to an unsymmetrical alkene, the H atom bonds to the less substituted carbon atom—that is, the carbon that has more H atoms to begin with. The regioselectivity of electrophilic addition depend on this rule.

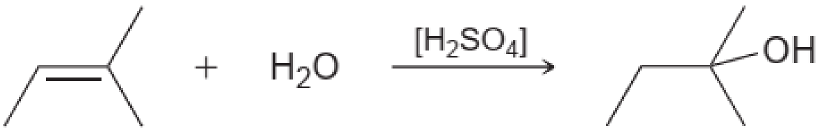


The addition in the above reaction depends on the stability of carbocation that formed as intermediate compound in the reaction mechanism. The more stable, more substituted carbocation is formed by addition of the electrophile to the less substituted carbon. Specifically, Markovnikov addition was observed whenever purified reagents were used, while the use of impure reagents sometimes led to anti-Markovnikov addition. Further investigation revealed the identity of the impurity that most greatly affected the regioselectivity of the reaction. It was found that peroxides (ROOR), even in trace amounts, would cause HBr to add across an alkene in an anti-Markovnikov fashion.

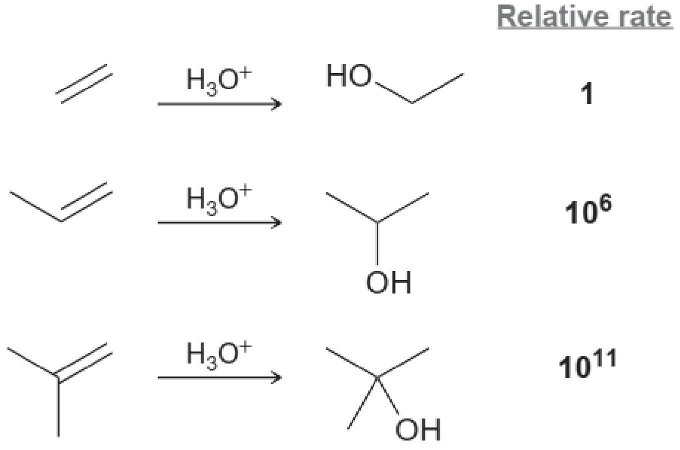


Hydration

Adding water (H and OH) across a double bond to yield alcohols, a process called hydration. The reaction takes place on treatment of the alkene with water and a strong acid catalyst, such as H_2SO_4. protonation of an alkene double bond yields a carbocation intermediate, which reacts with water to yield a protonated alcohol product, ROH_2+. Loss of H+ from this protonated alcohol gives the neutral alcohol and regenerates the acid catalyst.

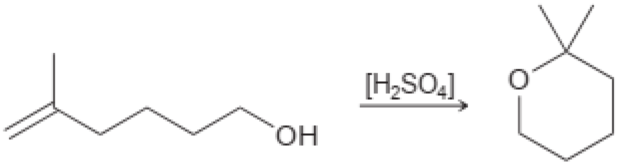


The rate of an acid-catalyzed hydration is very much dependent on the structure of the starting alkene. Compare the relative rates of the following three reactions, and analyze the effects of an alkyl substituent on the relative rate of each reaction. With each additional alkyl group, the reaction rate increases by many orders of magnitude.

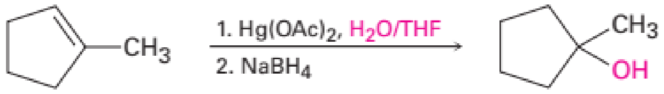


If an alkene is protonated and the solvent is an alcohol rather than water, a reaction takes place that is very similar to acid-catalyzed hydration, but in the second step of the mechanism the alcohol functions as a nucleophile instead of water. Draw a plausible mechanism for the following process:

Using the reaction in the previous problem as a reference, propose a plausible mechanism for the following intramolecular reaction:



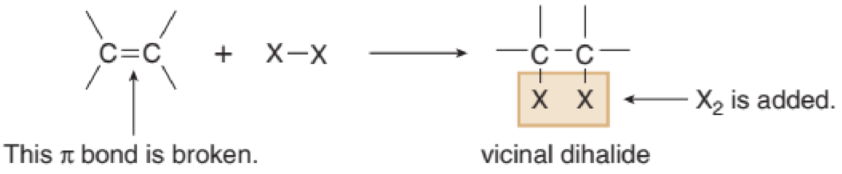
alkenes are often hydrated by the oxymercuration–demercuration procedure. Oxymercuration involves electrophilic addition of Hg^{2+} to the alkene on reaction with mercury(II) acetate [$(CH_3CO_2)_2Hg$, often abbreviated Hg(OAc)2] in aqueous tetrahydrofuran (THF) solvent. When the intermediate organomercury compound is then treated with sodium borohydride, $NaBH_4$, demercuration occurs to produce an alcohol. For example:

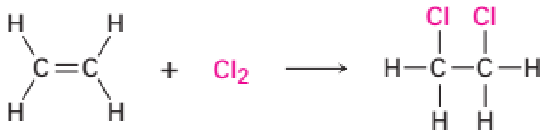


1-Methylcyclopentene **1-Methylcyclopentanol (92%)**

Halogenation of Alkenes: Addition of X_2

Bromine and chlorine add rapidly to alkenes to yield 1,2-dihalides, a process called halogenation. For example, more than 18 million tons 1,2-dichloroethane (ethylene dichloride) is synthesized worldwide each year, much of it by addition of Cl_2 to ethylene. The product is used both as a solvent and as starting material for the manufacture of poly(vinyl chloride), PVC. Fluorine is too reactive and difficult to control for most laboratory applications, and iodine does not react with most alkenes.



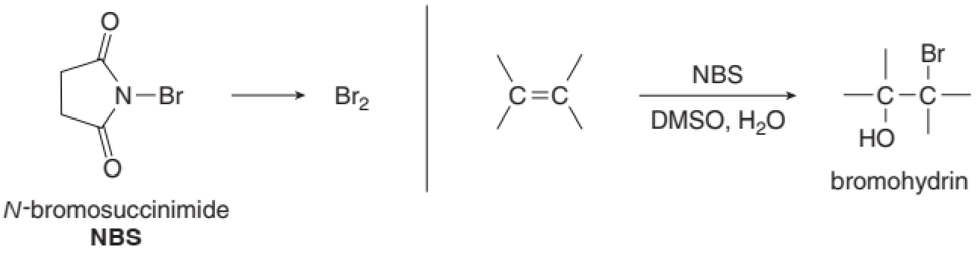


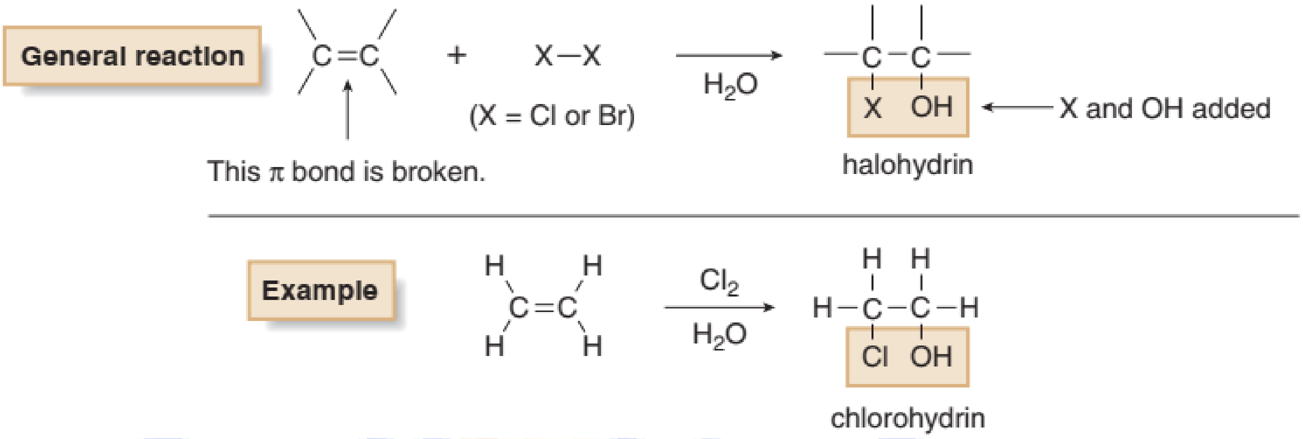
Ethylene **1,2-Dichloroethane (ethylene dichloride)**

The electron-rich double bond induces a dipole in an approaching halogen molecule, making one halogen atom electron deficient and the other electron rich ($X^{\delta+} – X^{\delta-}$). The electrophilic halogen atom is then attracted to the nucleophilic double bond, making addition possible. Is these reaction of alkenes, no rearrangements occur, and second, only anti addition of X_2 is observed.

Halohydrin Formation

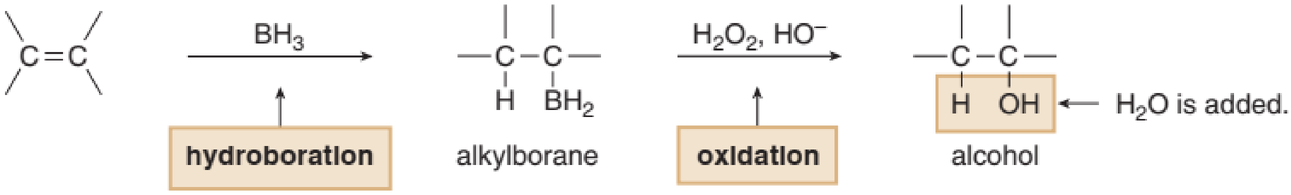
Treatment of an alkene with a halogen X_2 and H_2O forms a halohydrin by addition of the elements of X and OH to the double bond. Although the combination of Br2 and H_2O effectively forms bromohydrins from alkenes, other reagents can also be used. Bromohydrins are also formed with N-bromosuccinimide (abbreviated as NBS) in aqueous DMSO [$(CH_3)_2S = O$]. NBS serves as a source of Br_2, which then goes
on to form a bromohydrin.





Hydroboration–Oxidation

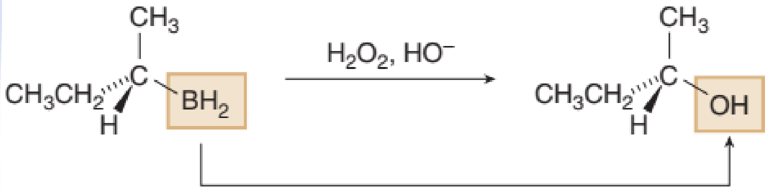
Hydroboration–oxidation is a two-step reaction sequence that converts an alkene to an alcohol.



Hydroboration is the addition of borane (BH_3) to an alkene, forming an alkylborane Oxidation converts the C – B bond of the alkylborane to a C – O bond. The term organoborane is used for any compound with a carbon–boron bond.

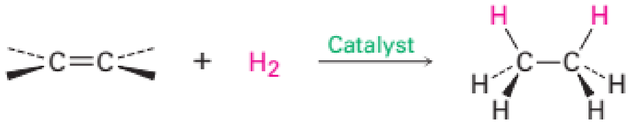
Oxidation of the Alkylborane

Because alkylboranes react rapidly with water and spontaneously burn when exposed to the air, they are oxidized, without isolation, with basic hydrogen peroxide (H_2O_2, HO–). Oxidation replaces the C – B bond with a C – O bond, forming a new OH group with retention of configuration; that is, the OH group replaces the BH2 group in the same position relative to the other three groups on carbon.

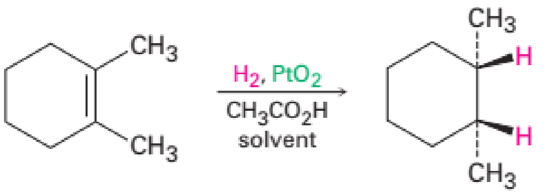


Hydrogenation

Alkenes react with H_2 in the presence of a metal catalyst such as palladium or platinum to yield the corresponding saturated alkane addition products. We describe the result by saying that the double bond has been hydrogenated, or reduced. Platinum and palladium are the most common laboratory catalysts for alkene hydrogenations. Palladium is normally used as a very fine powder “supported” on an inert material such as charcoal (Pd/C) to maximize surface area. Platinum is normally used as PtO_2, a reagent known as Adams’ catalyst after its discoverer, Roger Adams.

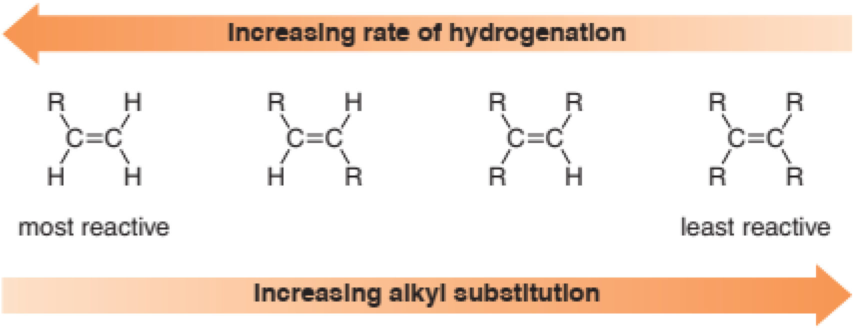


An alkene **An alkane**



1,2-Dimethyl-cyclohexene ***cis*-1,2-Dimethyl-cyclohexane (82%)**

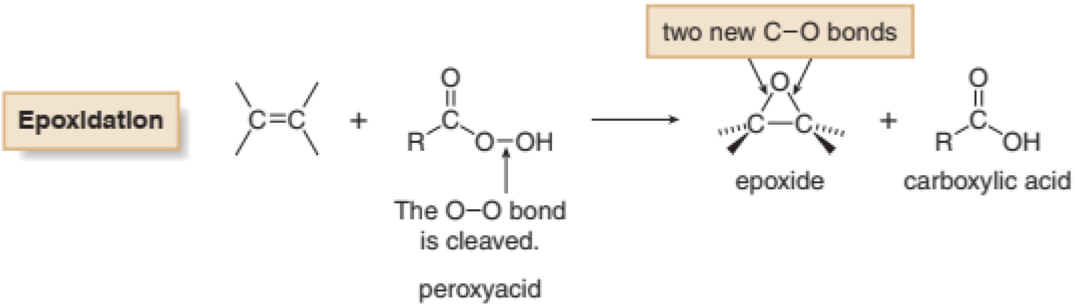
Rapid, sequential addition of H2 occurs from the side of the alkene complexed to the metal surface, resulting in syn addition. Less crowded double bonds complex more readily to the catalyst surface, resulting in faster reaction.



Oxidation of alkenes

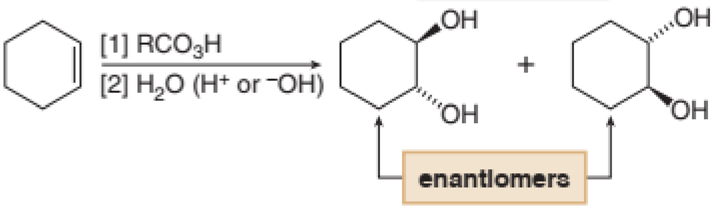
Epoxidation:

Epoxidation is the addition of a single oxygen atom to an alkene to form an epoxide. The weak π bond of the alkene is broken and two new C – O σ bonds are formed. Epoxidation is typically carried out with a peroxyacid, resulting in cleavage of the weak O – O bond of the reagent.



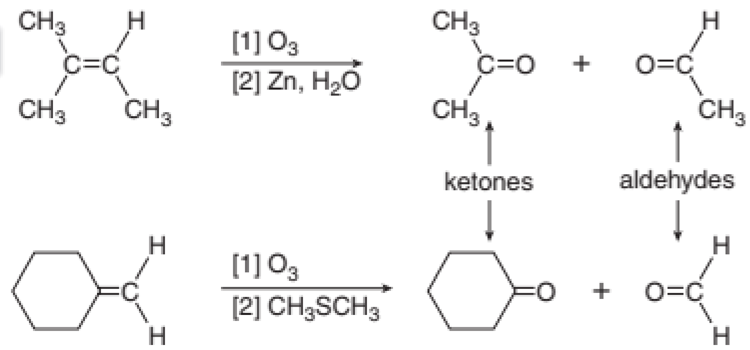
Dihydroxylation

Dihydroxylation is the addition of two hydroxy groups to a double bond, forming a 1,2-diol or glycol. Depending on the reagent, the two new OH groups can be added to the opposite sides (anti addition) or the same side (syn addition) of the double bond.



Oxidative Cleavage of Alkenes

Oxidative cleavage of an alkene breaks both the r and o bonds of the double bond to form two carbonyl groups. Depending on the number of R groups bonded to the double bond, oxidative cleavage yields either ketones or aldehydes.



Spectroscopy Of Alkenes:

IR: =C-H Stretch for sp2 C-H occurs at values greater than 3000 cm^{-1} (3095–3010 cm−1). =C-H Out-of-plane (oop) bending occurs in the range 1000–650 cm^{-1}.These bands can be used to determine the degree of substitution on the double bond. C=C Stretch occurs at 1660–1600 cm^{-1};

Alkynes

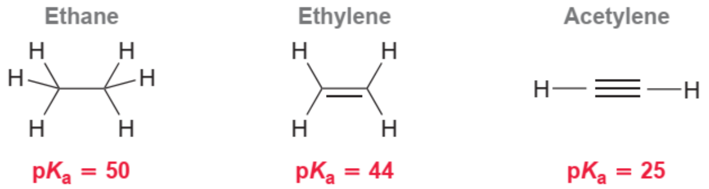
Alkynes are hydrocarbons that contain carbon–carbon triple bonds. Alkynes are also called acetylenes because they are derivatives of acetylene, the simplest alkyne. was once widely used in industry as the starting material for the preparation of acetaldehyde, acetic acid, vinyl chloride, and other high-volume chemicals, but more efficient routes to these substances using ethylene as starting material are now available. Acetylene is still used in the preparation of acrylic polymers, but is probably best known as the gas burned in high-temperature oxy–acetylene welding torches.

$H-C\equiv C-H$	$CH_3CH_2-C\equiv C-H$	$CH_3-C\equiv C-CH_3$
acetylene	ethylacetylene	dimethylacetylene
ethyne	but-1-yne	but-2-yne

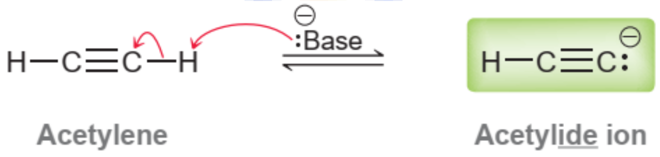
The chemistry of the carbon–carbon triple bond is similar to that of the double bond. Alkynes undergo most of the same reactions as alkenes, especially the additions and the oxidations.

Acidity of Acetylene and Terminal Alkynes

Terminal alkynes are much more acidic than other hydrocarbons. Removal of an acetylenic proton forms an acetylide ion, which plays a central role in alkyne chemistry. The acidity of an acetylenic hydrogen stems from the nature of the sp hybrid. The acidity of a bond varies with its hybridization, increasing with the increasing s character of the orbitals.



Recall that a lower pKa corresponds to a greater acidity. Therefore, acetylene (pKa = 25) is significantly more acidic than ethane or ethylene. To be precise, acetylene is 19 orders of magnitude (10^9 times) more acidic than ethylene. The relative acidity of acetylene can be explained by exploring the stability of its conjugate base, called an acetylide ion (the suffix “ide” indicates the presence of a negative charge):



Preparation of alkynes

Manufacture preparation of Acetylene

Acetylene, one of the cheapest organic chemicals, is made from coal or from natural gas. The synthesis from coal involves heating lime and coke (roasted coal) in an electric furnace to produce calcium carbide. Addition of water to calcium carbide produces acetylene and hydrated lime.

$$\underset{\text{coke}}{3\,C} + \underset{\text{lime}}{CaO} \xrightarrow{\text{electric furnace, 2500 °C}} \underset{\text{calcium carbide}}{CaC_2} + CO$$

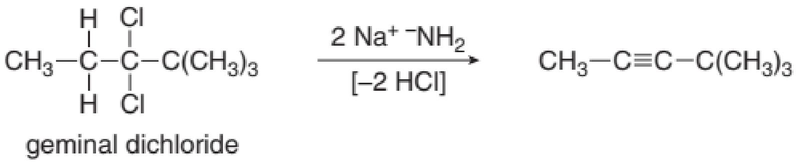
$$CaC_2 + 2\,H_2O \longrightarrow \underset{\text{acetylene}}{H{-}C{\equiv}C{-}H} + \underset{\text{hydrated lime}}{Ca(OH)_2}$$

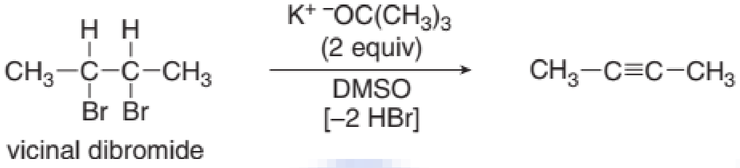
The synthesis of acetylene from natural gas is a simple process. Natural gas consists mostly of methane, which forms acetylene when it is heated for a very short period of time.

$$2\ CH_4 \xrightarrow[0.01\ sec]{1500\ ^\circ C} H-C\equiv C-H\ +\ 3\ H_2$$

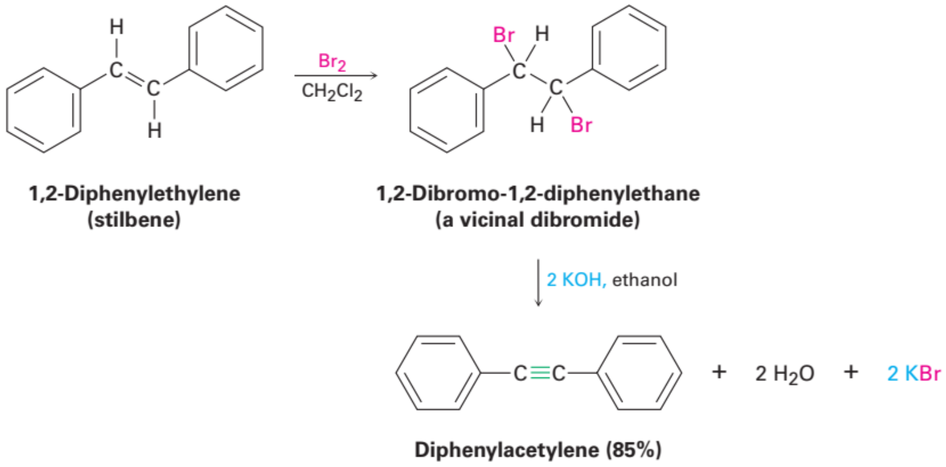
Elimination reaction

Alkynes can be prepared from alkyl dihalides. An alkyl dihalide has two leaving groups. A strong base removes two equivalents of HX from a vicinal or geminal dihalide to yield an alkyne by two successive E2 eliminations.



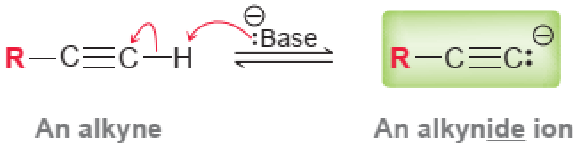


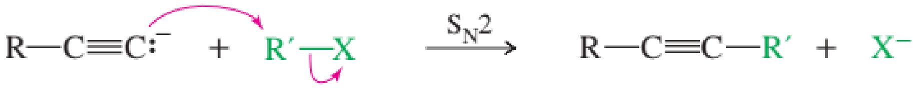
The starting vicinal dihalides are themselves readily available by addition of Br_2 or Cl_2 to alkenes. Thus, the overall halogenation/dehydrohalogenation sequence makes it possible to go from an alkene to an alkyne.



Alkylation of Acetylide Ions

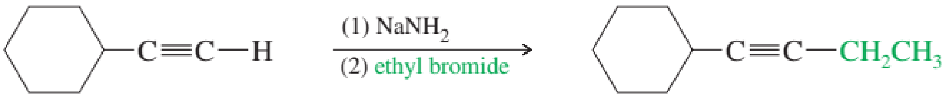
An acetylide ion is a strong base and a powerful nucleophile. It can displace a halide
ion from a suitable substrate, giving a substituted acetylene.





(R′—X must be a primary alkyl halide)

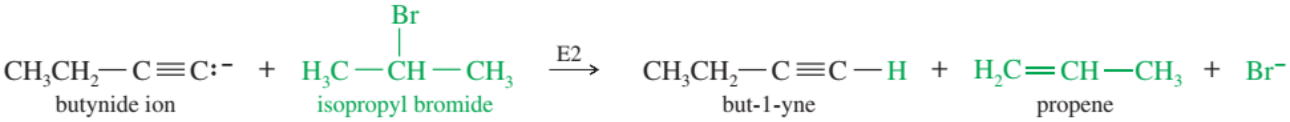
If this reaction is to produce a good yield, the alkyl halide must be an excellent substrate: It must be methyl or primary, with no bulky substituents or branches close to the reaction center. In the following examples, acetylide ions displace primary halides to form elongated alkynes.



ethynylcyclohexane
(cyclohexylacetylene)

1-cyclohexylbut-1-yne
(ethylcyclohexylacetylene)
(70%)

If the back-side approach is hindered, the acetylide ion may abstract a proton, giving elimination by the E2 mechanism.

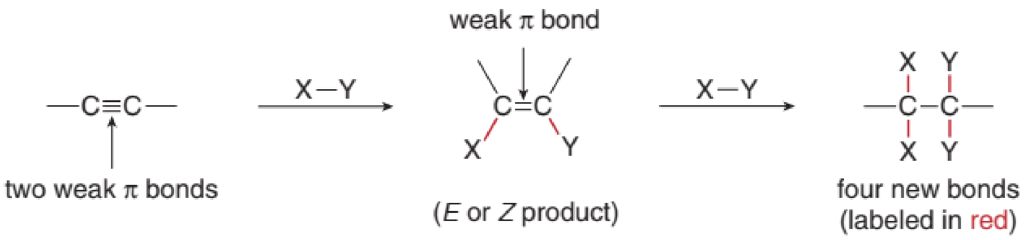


$$CH_3CH_2-C\equiv C:^- + H_3C-\overset{\overset{Br}{|}}{C}H-CH_3 \xrightarrow{E2} CH_3CH_2-C\equiv C-H + H_2C=CH-CH_3 + Br^-$$

butynide ion; isopropyl bromide; but-1-yne; propene

Reaction of alkynes

Like alkenes, alkynes undergo addition reactions because they contain weak π bonds. Two sequential reactions take place: addition of one equivalent of reagent forms an alkene, which then adds a second equivalent of reagent to yield a product having four new bonds.

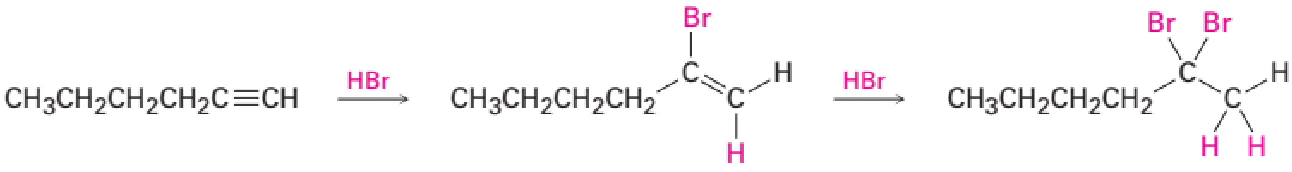


Alkynes are electron rich, The two π bonds form a cylinder of electron density between the two sp hybridized carbon atoms, and this exposed electron density makes a triple bond nucleophilic. As a result, alkynes react with electrophiles.

Addition of HX

Alkynes undergo hydrohalogenation, the addition of hydrogen halides, HX (X = Cl, Br, I). Two equivalents of HX are usually used: addition of one mole forms a vinyl halide, which then reacts with a second mole of HX to form a geminal dihalide. Addition of HX to an alkyne is example of electrophilic addition, because the electrophilic (H) end of the reagent is attracted to the electron-rich triple bond. The

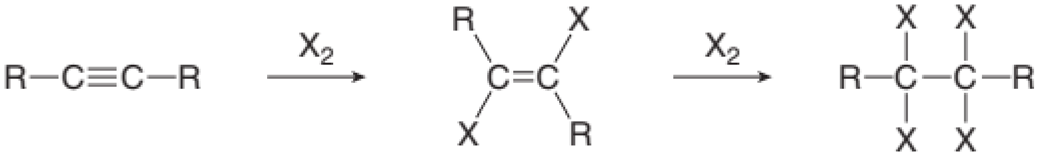
reaction often can be stopped after addition of 1 equivalent of HX, but reaction with an excess of HX leads to a dihalide product. the regiochemistry of addition follows Markovnikov’s rule, with halogen adding to the more highly substituted side of the alkyne bond and hydrogen adding to the less highly substituted side.



1-Hexyne **2-Bromo-1-hexene** **2,2-Dibromohexane**

Addition of X_2

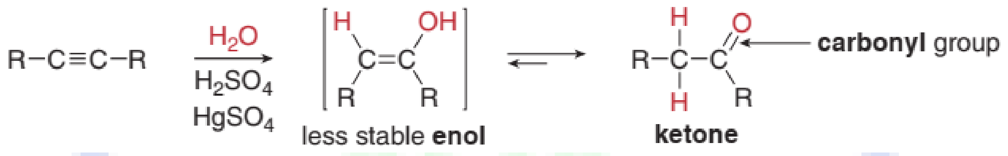
Halogens, X_2 (X = Cl or Br), add to alkynes in much the same way they add to alkenes. Addition of one mole of X_2 forms a trans dihalide, which can then react with a second mole of X_2 to yield a tetrahalide.



trans dihalide tetrahalide

Addition of Water

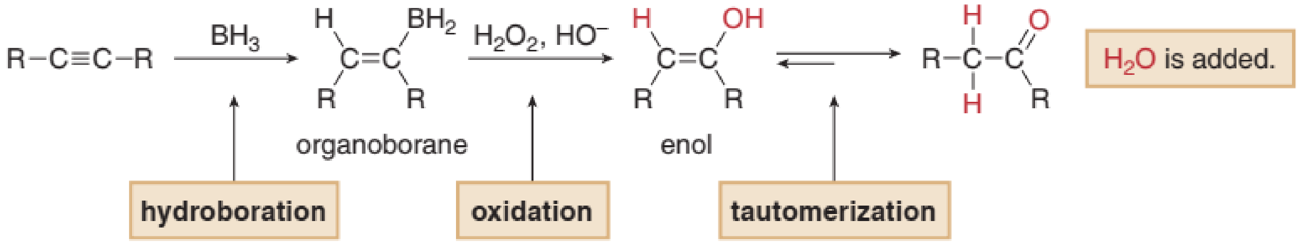
Although the addition of H_2O to an alkyne resembles the acid-catalyzed addition of H_2O to an alkene in some ways, an important difference exists. In the presence of strong acid or Hg^{2+} catalyst, the elements of H_2O add to the triple bond, but the initial addition product, an enol, is unstable and rearranges to a product containing a carbonyl group—that is, a C = O. A carbonyl compound having two alkyl groups bonded to the C = O carbon is called a ketone.



Internal alkynes undergo hydration with concentrated acid, whereas terminal alkynes require the presence of an additional Hg^{2+} catalyst usually $HgSO_4$ to yield methyl ketones by Markovnikov addition of H_2O.

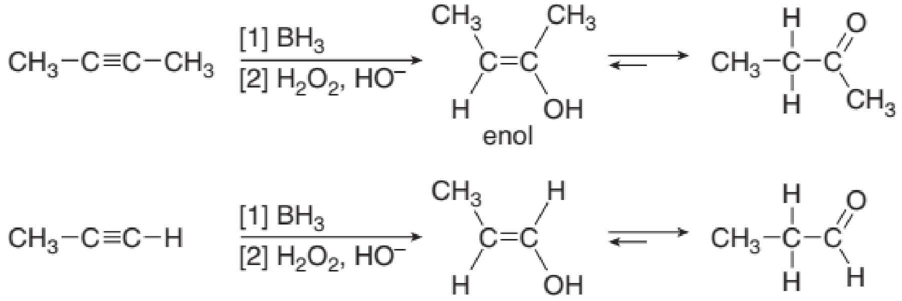
Hydroboration–Oxidation

Hydroboration–oxidation is a two-step reaction sequence that converts an alkyne to a carbonyl compound.



Addition of borane forms an organoborane. Oxidation with basic H_2O_2 forms an enol. Tautomerization of the enol forms a carbonyl compound. The overall result is addition of H_2O to a triple bond.

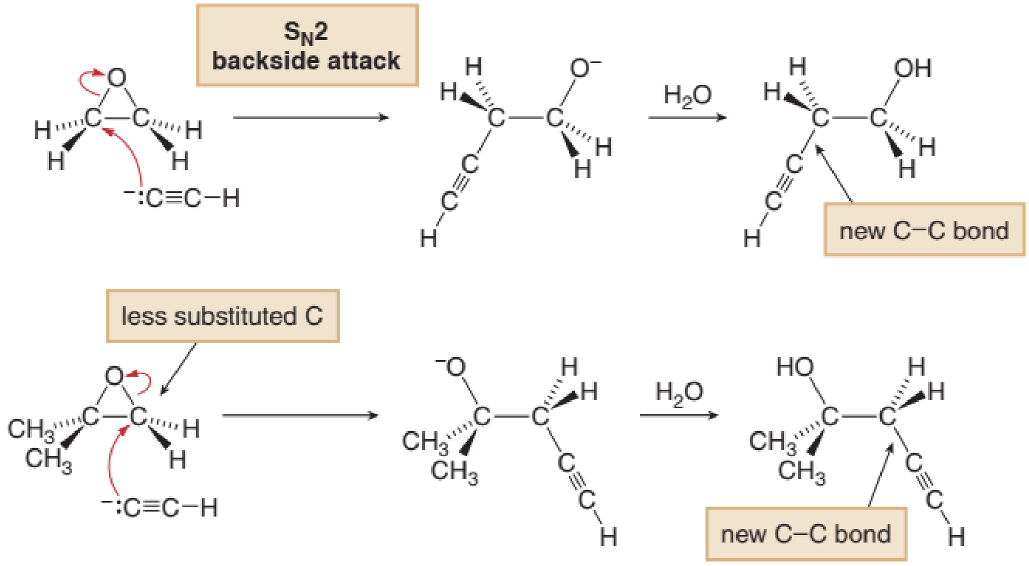
Hydroboration–oxidation of an internal alkyne forms a ketone. Hydroboration of a terminal alkyne adds BH_2 to the less substituted, terminal carbon. After oxidation to the enol, tautomerization yields an aldehyde, a carbonyl compound having a hydrogen atom bonded to the carbonyl carbon.



Addition of H_2O using H_2O, $H2SO4$, and $HgSO_4$ forms methyl ketones from terminal alkynes. Addition of H_2O using $BH3$, then H_2O_2, HO– forms aldehydes from terminal alkynes.

Reaction of Acetylide Anions with Epoxides

Acetylide anions are strong nucleophiles that open epoxide rings by an SN2 mechanism. This reaction also results in the formation of a new carbon–carbon bond. Backside attack occurs at the less substituted end of the epoxide.

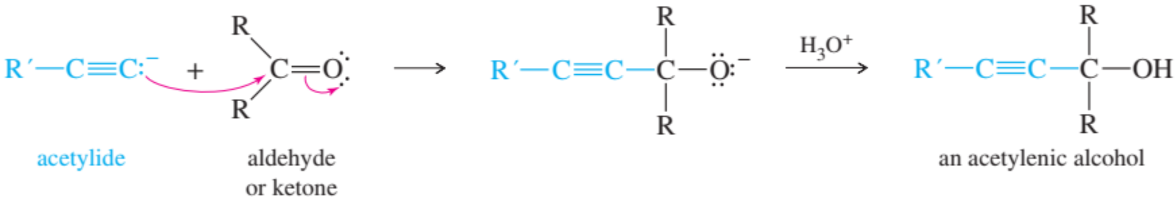


Addition of Acetylide Ions to Carbonyl Groups

Acetylide ions are strong nucleophiles and strong bases. In addition to displacing halide ions in reactions, they can add to carbonyl groups. Because oxygen is more electronegative than carbon, the double bond is polarized. The oxygen atom has a partial negative charge balanced by an equal amount of positive charge on the carbon atom. An acetylide ion can serve as the nucleophile in this addition to a carbonyl group.

The acetylide ion adds to the carbonyl group to form an alkoxide ion. Addition

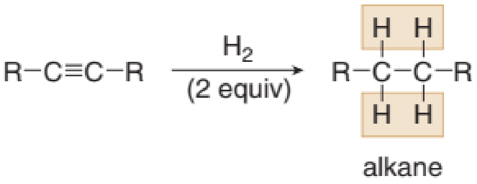
of dilute
acid (in a separate step) protonates the alkoxide to give the alcohol.

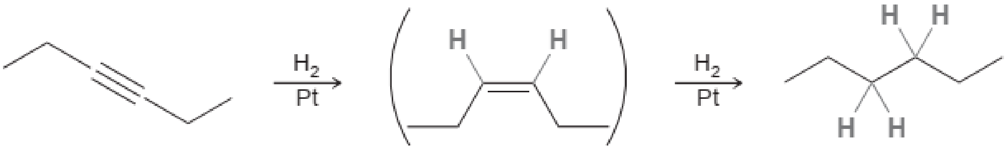


Addition to formaldehyde gives primary alcohol, addition to higher aldehyde gives secondary alcohol, addition to ketone gives secondary alcohol

Reduction of Alkynes

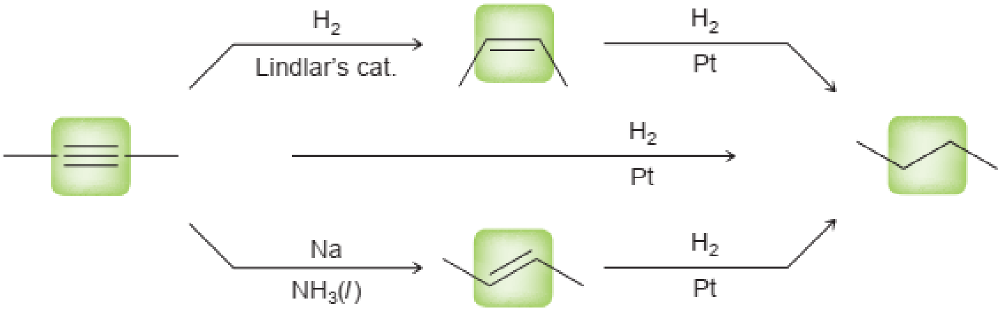
Reduction of an alkyne adds H_2 to one or both of the π bonds. There are three different ways by which the elements of H_2 can be added to a triple bond. Adding two equivalents of H_2 forms an alkane. Adding one equivalent of H_2 in an anti fashion forms a trans alkene.





Alkynes can also be reduced to trans alkenes via an entirely different reaction called
dissolving metal reduction.

To produce an alkane, an alkyne can be treated with H_2 in the presence of a metal catalyst, such as Pt, Pd, or Ni. To produce a cis alkene, an alkyne can be treated with H_2 in the presence of a poisoned catalyst, such as Lindlar's catalyst or Ni_2B. To produce a trans alkene, an alkyne can be treated with sodium in liquid ammonia

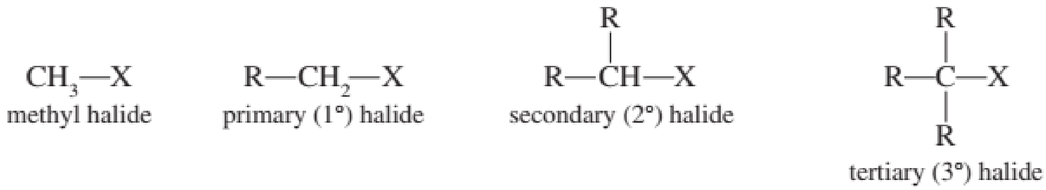


Spectroscopy Of Alkynes

IR: C-H Stretch for sp C-H usually occurs near 3300 cm^{-1}.C-C triple bond Stretch occurs near 2150 cm^{-1}; conjugation moves stretch to lower frequency. Disubstituted or symmetrically substituted triple bonds give either no absorption or weak absorption.

Alkyl halide (organohalides)

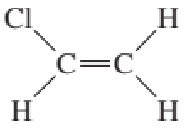
Alkyl halides are organic molecules containing a halogen atom X bonded to an carbon atom. Alkyl halides are classified as primary (1°), secondary (2°), or tertiary (3°) depending on the number of carbons bonded to the carbon with the halogen. The classes of halogenated organic compounds: the alkyl halides, simply has a halogen atom bonded to one of the carbon atoms of an alkyl group; the vinyl halides, has a halogen atom bonded to one of the carbon atoms of an alkene; the aryl halides has a halogen atom bonded to one of the carbon atoms of an aromatic ring. The chemistry of vinyl halides and aryl halides is different from that of alkyl halides because their bonding and hybridization are different; Allylic halides have X bonded to the carbon atom adjacent to a carbon–carbon double bond; and benzylic halides have X bonded to the carbon atom adjacent to a benzene ring.



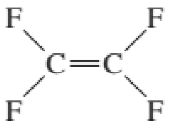
Alkyl halides

$CHCl_3$	$CHClF_2$	$CCl_3—CH_3$	$CF_3—CHClBr$
chloroform	Freon-22®	1,1,1-trichloroethane	Halothane
solvent	refrigerant	cleaning fluid	nonflammable anesthetic

Vinyl halides

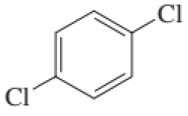


vinyl chloride
monomer for poly(vinyl chloride)

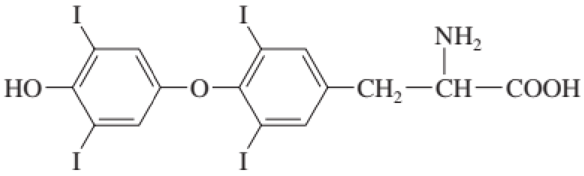


tetrafluoroethylene (TFE)
monomer for Teflon®

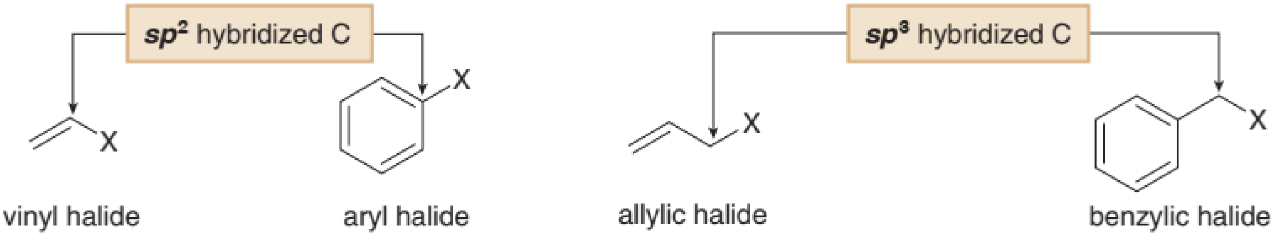
Aryl halides



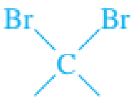
para-dichlorobenzene
mothballs



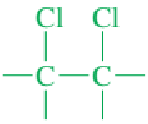
thyroxine
thyroid hormone



A geminal dihalide (Latin, geminus, “twin”) has the two halogen atoms bonded to the same carbon atom. A vicinal dihalide (Latin, vicinus, “neighboring”) has the two halogens bonded to adjacent carbon atoms.



a geminal dibromide



a vicinal dichloride

In an alkyl halide, the halogen atom is bonded to an carbon atom. The halogen is more electronegative than carbon, and the bond is polarized with a partial positive charge on carbon and a partial negative charge on the halogen. The electronegativities of the halogens increase in the order:

F > Cl > Br > I

These two effects oppose each other, with the larger halogens having longer bonds but weaker electronegativities. The overall result is that the bond dipole moments increase in the order

$$\underset{1.29\ \text{D}}{\text{C—I}} \quad < \quad \underset{1.48\ \text{D}}{\text{C—Br}} \quad < \quad \underset{1.51\ \text{D}}{\text{C—F}} \quad < \quad \underset{1.56\ \text{D}}{\text{C—Cl}}$$

The chemistry of alkyl halides is determined by this polar C – X bond.

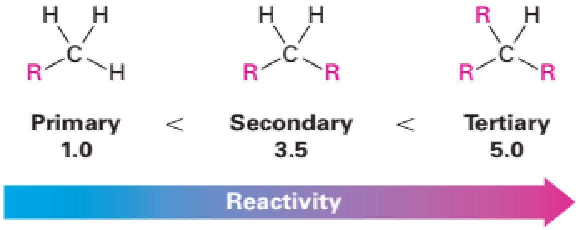
Synthesis of alkyl halides

Free-Radical Halogenation of alkane

Free-radical halogenation is rarely an effective method for the synthesis of alkyl halides. It usually produces mixtures of products because there are different kinds of hydrogen atoms that can be abstracted. Also, more than one halogen atom may react, giving multiple substitutions. For example, the chlorination of propane can give a messy mixture of products.

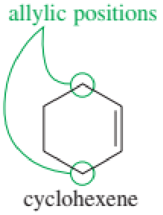
$$CH_3—CH_2—CH_3 \quad + \quad Cl_2 \quad \xrightarrow{h\nu} \quad \left\{\begin{array}{l} CH_3—CH_2—CH_2Cl \quad + \quad CH_3—CHCl—CH_3 \\ + \quad CH_3—CHCl—CH_2Cl \quad + \quad CH_3—CCl_2—CH_3 \\ + \quad CH_3—CH_2—CHCl_2 \quad + \quad \text{others} \end{array}\right.$$

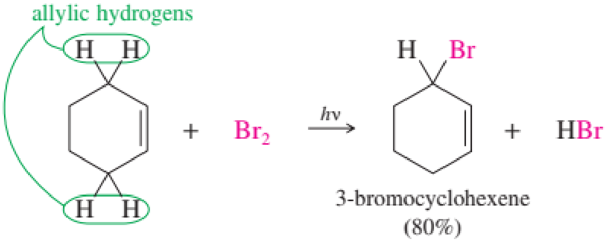
The reactivity order of alkane hydrogens toward radical chlorination, which, can be explained by looking at the bond dissociation energies.



Allylic Bromination

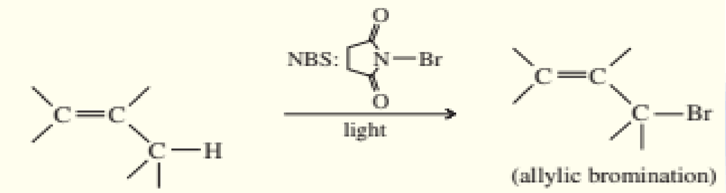
Free-radical bromination of alkenes can be carried out in a highly selective manner. Allylic intermediates (cations, radicals, and anions) are stabilized by resonance with the double bond, allowing the charge or radical to be delocalized. bromination is highly selective, with only the most stable radical being formed. If there is an allylic hydrogen, the allylic radical is usually the most stable of the radicals that might be formed. For efficient allylic bromination, a large concentration of bromine must be avoided because bromine can also add to the double bond.

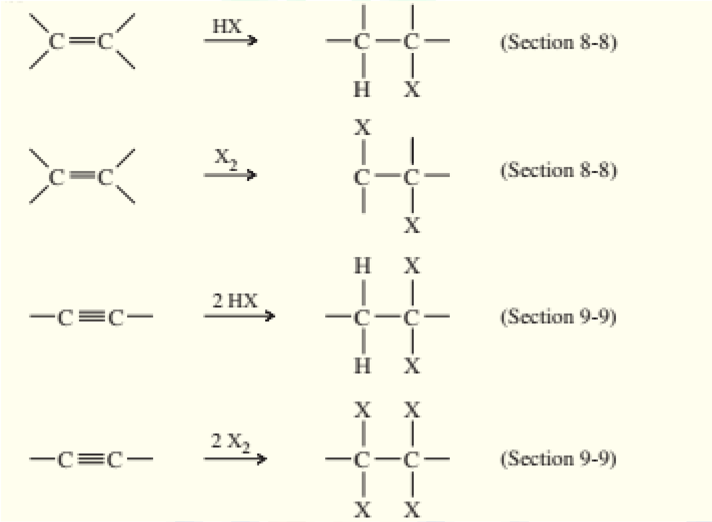




Preparation alkyl halides from alkene and alkyne

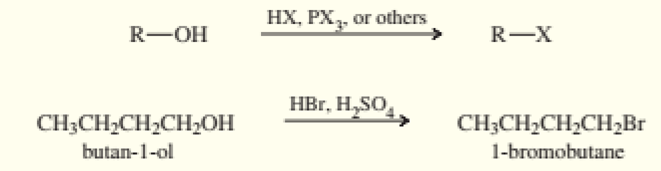
The details of these preparation methods are mention above.



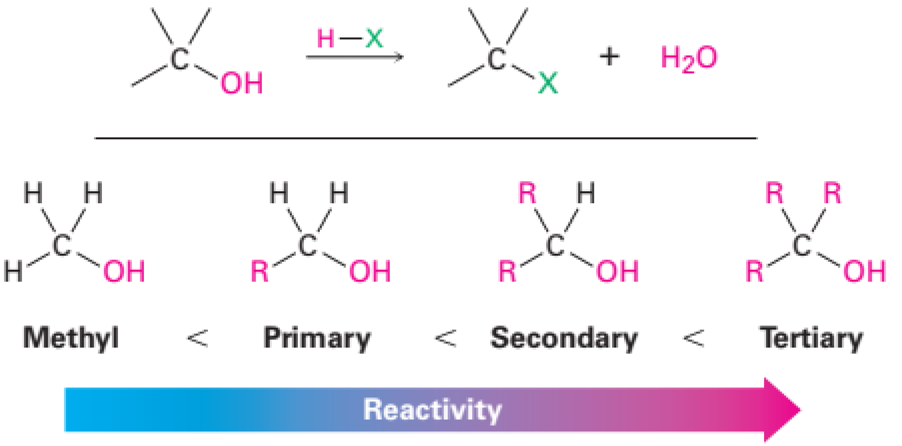


Preparation alkyl halide from alcohol

The most generally useful method for preparing alkyl halides is to make them
from alcohols, by treat the alcohol with HCl, HBr, or HI.



the reaction works best with tertiary alcohols, R3COH. Primary and secondary alcohols react much more slowly and at higher temperatures.

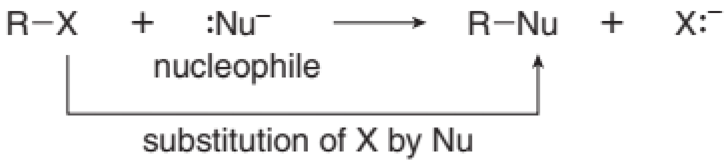


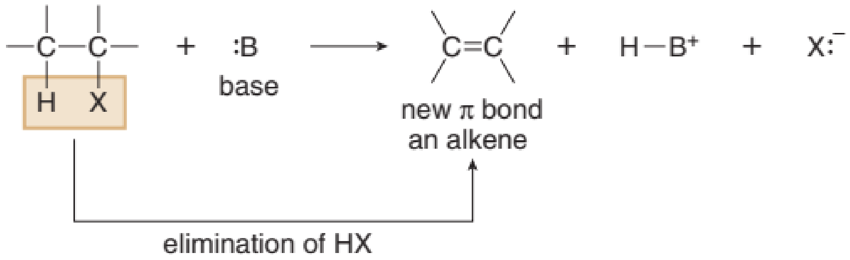
Reaction of alkyl halides

the kinds of reactions they undergo nucleophilic substitutions and eliminations are encountered frequently. Because alkyl halides contain an electrophilic carbon, they
react with electron-rich reagents—Lewis bases (nucleophiles) and Brønsted–Lowry bases.

Alkyl halides are easily converted to many other functional groups. The halogen atom can leave with its bonding pair of electrons to form a stable halide ion; we say that a halide is a good leaving group. When another atom replaces the halide ion, the reaction is a substitution. When the halide ion leaves with another atom or ion (often) and forms a new π bond, the reaction is an elimination. In many eliminations, a molecule of is lost from the alkyl halide to give an alkene. These eliminations are called
dehydrohalogenations because a hydrogen halide has been removed from the alkyl
halide. Substitution and elimination reactions often compete with each other.

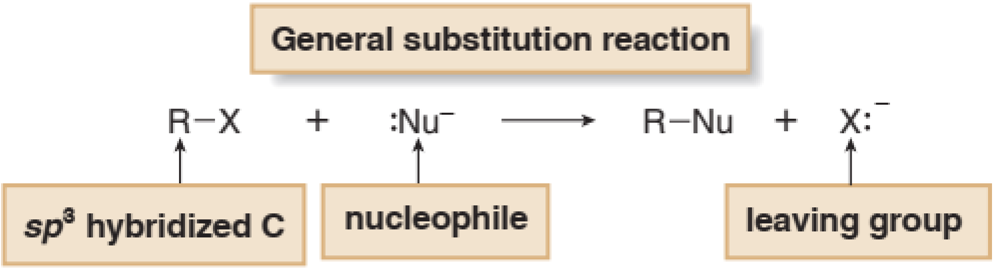
In a substitution reaction of RX, the halogen X is replaced by an electron-rich nucleophile :Nu⁻. The C – X σ bond is broken and the C – Nu σ bond is formed.



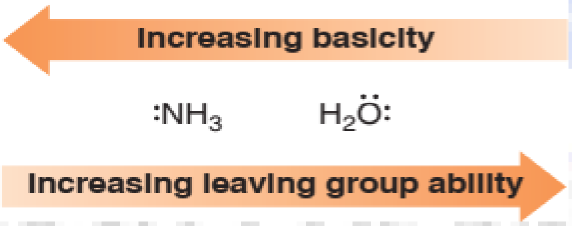


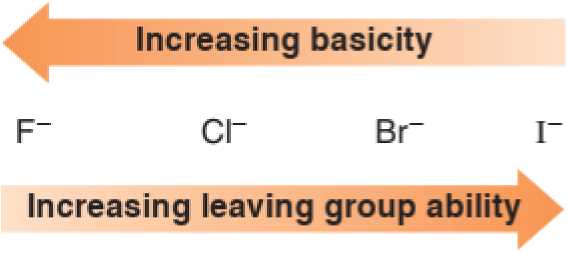
Nucleophilic substitution reactions

Nucleophilic substitutions are Lewis acid–base reactions. The nucleophile donates its electron pair, the alkyl halide (Lewis acid) accepts it, and the C – X bond is heterolytically cleaved. Curved arrow notation can be used to show the movement of electron pairs. In a nucleophilic substitution reaction of R– X, the C– X bond is heterolytically cleaved, and the leaving group departs with the electron pair in that bond, forming (X:⁻).

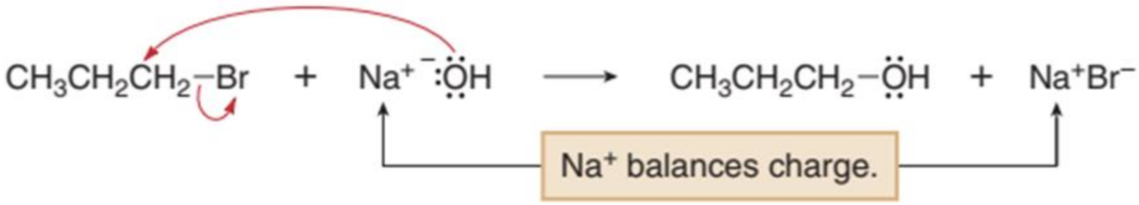


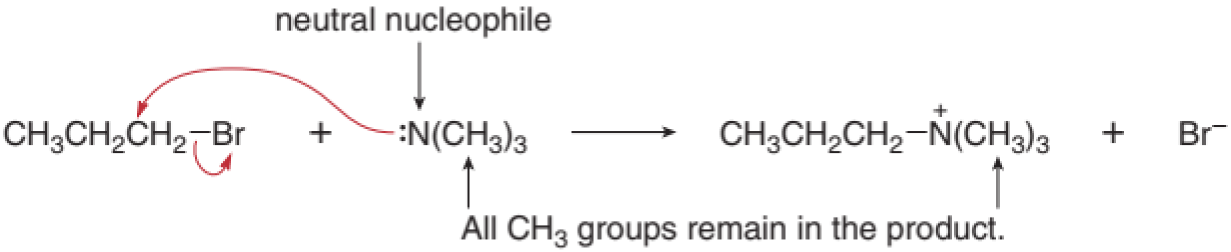
X: An atom X (or a group of atoms) called a leaving group, which is able to accept the electron density in the C – X bond. The most common leaving groups are halide anions (X–), but H_2O (from ROH_2^+) and N_2 (from RN_2^+) are also encountered. The more stable the leaving group X:–, the better able it is to accept an electron pair, and the better leaving group is the weaker base.

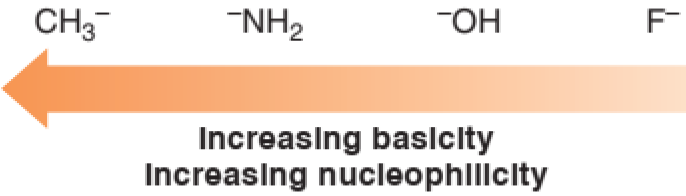




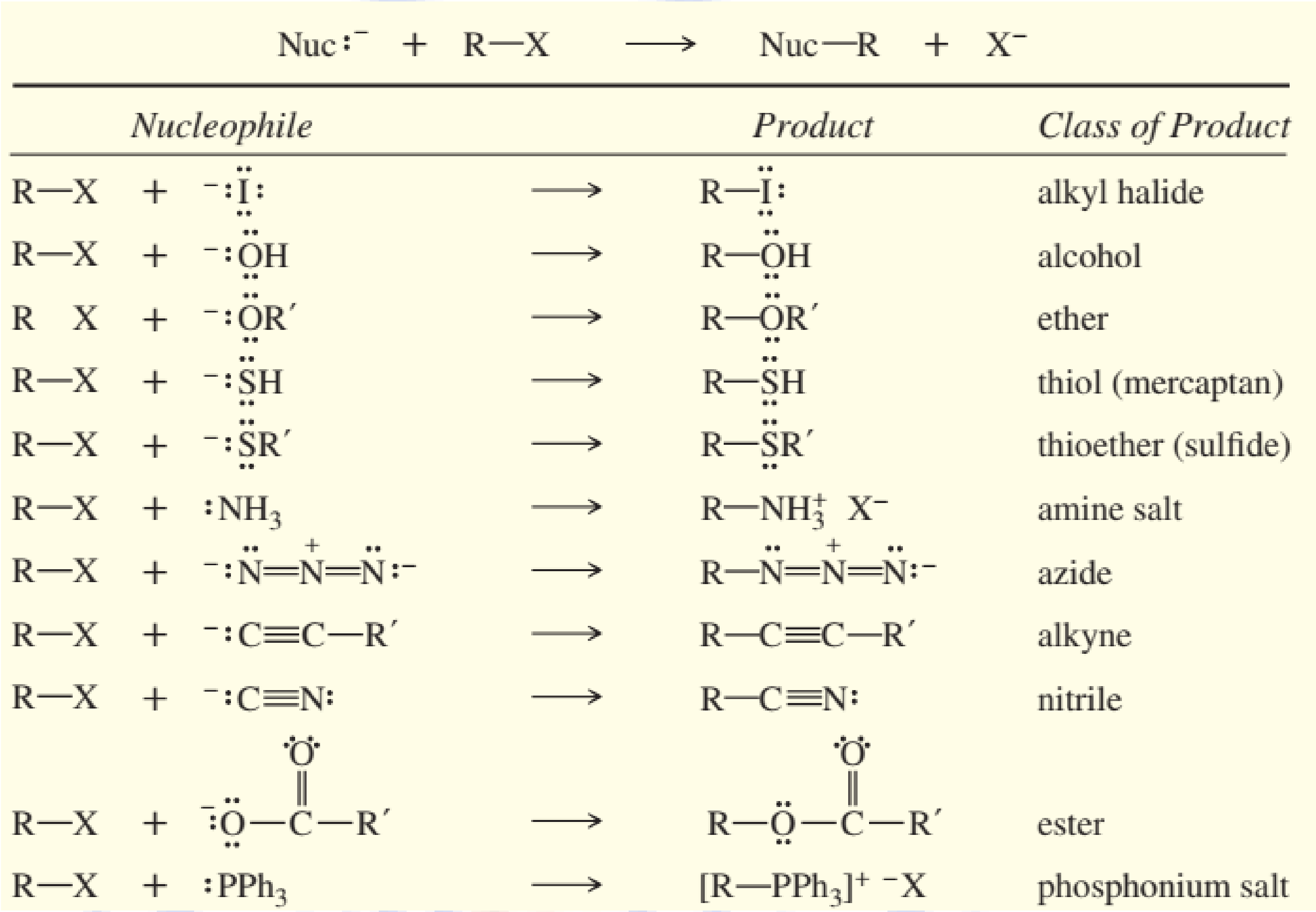
Nu:$^-$ **:**A nucleophile. Nucleophiles contain a lone pair or a π bond but not necessarily a negative charge. Negatively charged nucleophiles like –OH and –SH are used as salts with Li+, Na+, or K+ counterions to balance charge. The identity of the cation is usually inconsequential, and therefore it is often omitted from the chemical equation. neutral nucleophile is used, the substitution product bears a positive charge. Note that all atoms originally bonded to the nucleophile stay bonded to it after substitution occurs. All three CH_3 groups stay bonded to the N atom in the given example.







Many useful reactions take place by the mechanism. The reaction of an alkyl halide, such as methyl iodide, with hydroxide ion gives an alcohol. Other nucleophiles convert alkyl halides to a wide variety of functional groups. The following table summarizes some of the types of compounds that can be formed by nucleophilic displacement of alkyl halides.



$$\mathrm{Nuc}:^{-} \;+\; \mathrm{R{-}X} \;\longrightarrow\; \mathrm{Nuc{-}R} \;+\; \mathrm{X}^{-}$$

Nucleophile				*Product*	*Class of Product*
R—X	+	$^{-}:\ddot{\mathrm{I}}:$	$\longrightarrow$	$\mathrm{R{-}\ddot{I}}:$	alkyl halide
R—X	+	$^{-}:\ddot{\mathrm{O}}\mathrm{H}$	$\longrightarrow$	$\mathrm{R{-}\ddot{O}H}$	alcohol
R X	+	$^{-}:\ddot{\mathrm{O}}\mathrm{R'}$	$\longrightarrow$	$\mathrm{R{-}\ddot{O}R'}$	ether
R—X	+	$^{-}:\ddot{\mathrm{S}}\mathrm{H}$	$\longrightarrow$	$\mathrm{R{-}\ddot{S}H}$	thiol (mercaptan)
R—X	+	$^{-}:\ddot{\mathrm{S}}\mathrm{R'}$	$\longrightarrow$	$\mathrm{R{-}\ddot{S}R'}$	thioether (sulfide)
R—X	+	$:\mathrm{NH_3}$	$\longrightarrow$	$\mathrm{R{-}NH_3^+\ X^-}$	amine salt
R—X	+	$^{-}:\ddot{\mathrm{N}}{=}\overset{+}{\mathrm{N}}{=}\ddot{\mathrm{N}}:^{-}$	$\longrightarrow$	$\mathrm{R{-}\ddot{N}{=}\overset{+}{N}{=}\ddot{N}:^{-}}$	azide
R—X	+	$^{-}:\mathrm{C{\equiv}C{-}R'}$	$\longrightarrow$	$\mathrm{R{-}C{\equiv}C{-}R'}$	alkyne
R—X	+	$^{-}:\mathrm{C{\equiv}N}:$	$\longrightarrow$	$\mathrm{R{-}C{\equiv}N}:$	nitrile
R—X	+	$^{-}:\ddot{\mathrm{O}}{-}\overset{\overset{\ddot{\mathrm{O}}}{\Vert}}{\mathrm{C}}{-}\mathrm{R'}$	$\longrightarrow$	$\mathrm{R{-}\ddot{O}{-}\overset{\overset{\ddot{O}}{\Vert}}{C}{-}R'}$	ester
R—X	+	$:\mathrm{PPh_3}$	$\longrightarrow$	$[\mathrm{R{-}PPh_3}]^{+}\ {}^{-}\mathrm{X}$	phosphonium salt

Halogen Exchange Reactions

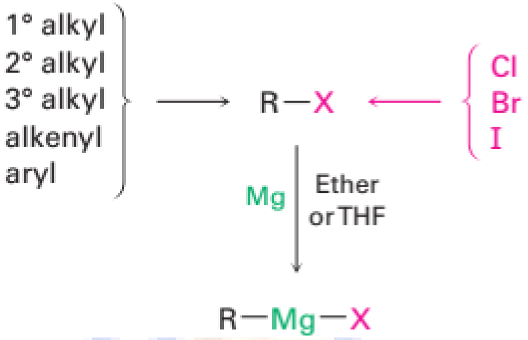
The reaction provides a useful method for synthesizing alkyl iodides and fluorides, which are more difficult to make than alkyl chlorides and bromides. Halides can be converted to other halides by halogen exchange reactions, in which one halide displaces another. Iodide is a good nucleophile, and many alkyl chlorides react with sodium iodide to give alkyl iodides. Alkyl fluorides are difficult to synthesize directly, and they are often made by treating alkyl chlorides or bromides with KF.

$$R{-}X + I^- \longrightarrow R{-}I + X^-$$

$$R{-}X + KF \xrightarrow[CH_3CN]{\text{18-crown-6}} R{-}F + KX$$

Preparation of alkyl halides by organometallic

Alkyl halides, RX, react with magnesium metal in ether or tetrahydrofuran (THF) solvent to yield alkylmagnesium halides, RMgX. The products, called Grignard reagents after their discoverer, Victor Grignard, are examples of organometallic compounds because they contain a carbon–metal bond. In addition to alkyl halides, Grignard reagents can also be made from alkenyl (vinylic) and aryl (aromatic) halides. The halogen can be Cl, Br, or I, although chlorides are less reactive than bromides and iodides. Organofluorides rarely react with magnesium.



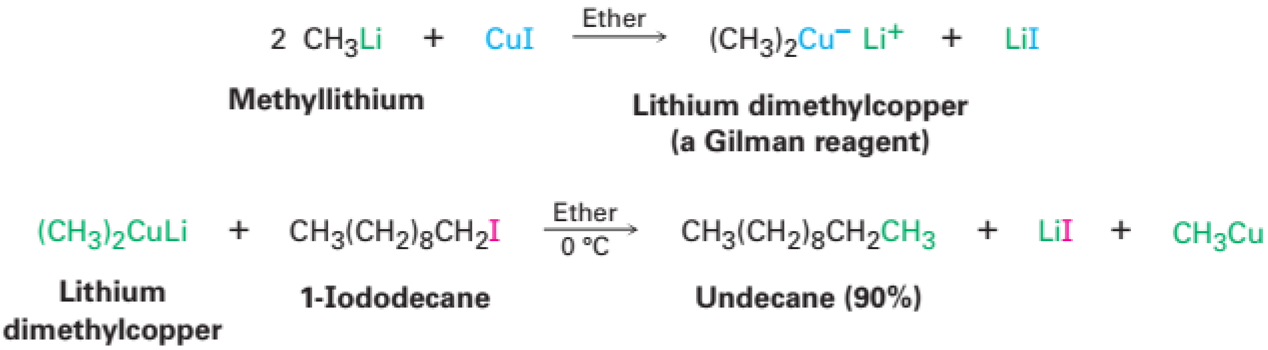
Organometallic Coupling Reactions

Many other kinds of organometallic compounds can be prepared in a manner similar to that of Grignard reagents. For instance, alkyllithium reagents(R-Li) can be prepared by the reaction of an alkyl halide with lithium metal. Alkyl-lithiums are both nucleophiles and strong bases, and their chemistry is similar in many respects to that of alkyl-magnesium halides.

$$CH_3CH_2CH_2CH_2Br \xrightarrow[\text{Pentane}]{2\ Li} CH_3CH_2CH_2CH_2Li + LiBr$$

1-Bromobutane **Butyllithium**

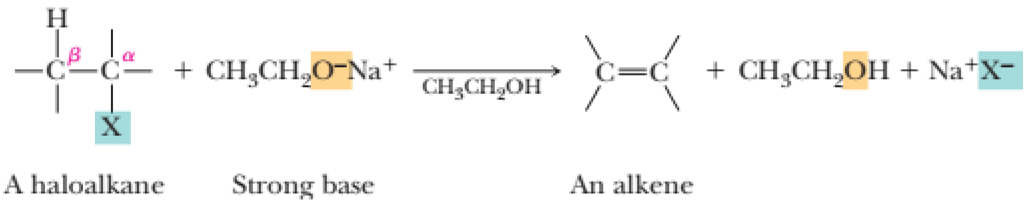
One particularly valuable reaction of alkyl-lithiums is in making lithium diorgano-copper compounds, R2CuLi, by reaction with copper(I) iodide in diethyl ether as solvent. Called Gilman reagents, lithium diorganocopper compounds are useful because they undergo a coupling reaction with organochlorides, bromides, and iodides (but not fluorides). One of the alkyl groups from the Gilman reagent replaces the halogen of the organohalide, forming a new carbon– carbon bond and yielding a hydrocarbon product. Lithium dimethylcopper, forinstance, reacts with 1-iododecane to give undecane in 90% yield.



Elimination Reaction

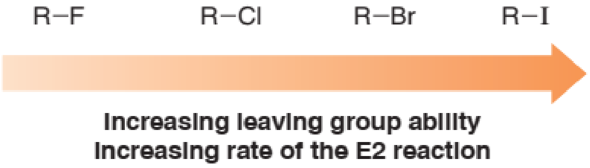
Introduce π bonds into organic compounds, so they can be used to synthesize alkenes and alkynes hydrocarbons that contain one and two π bonds, respectively. Like nucleophilic substitution, elimination reactions can occur by two different pathways, depending on the conditions. All elimination reactions involve loss of elements from the starting material to form a new π bond in the product. Alkyl halides undergo elimination reactions with Brønsted–Lowry bases. The elements of HX are lost and an alkene is formed.

Dehydrohalogenation: Removal of -H and -X from adjacent carbons in presence of base. Dehydrohalogenation is an example of a elimination, because it involves loss of elements from two adjacent atoms: the ` carbon bonded to the leaving group X, and the a carbon adjacent to it.

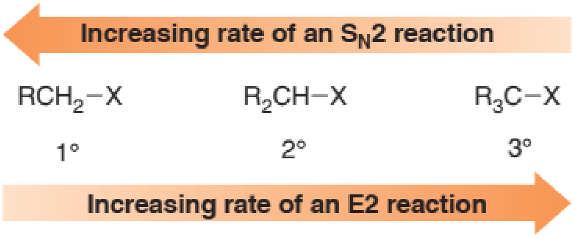


The most common bases used in elimination reactions are negatively charged oxygen compounds such as NaOH , KOH, $NaOCH_3$, $NaOCH_2CH_3$, and $KOC(CH_3)_3$. Note that the solvent used is commonly the conjugate acid of the base used in the elimination.

Because the bond to the leaving group is partially broken in the transition state, the better the leaving group the faster the E2 reaction.

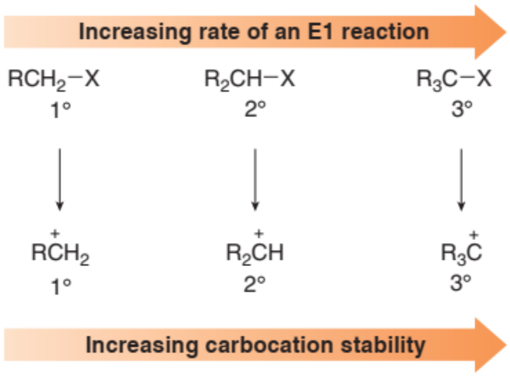


As the number of R groups on the carbon with the leaving group increases, the rate of the E2 reaction increases.

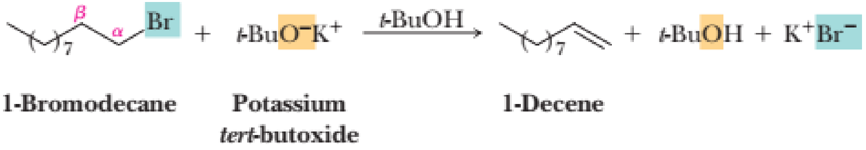


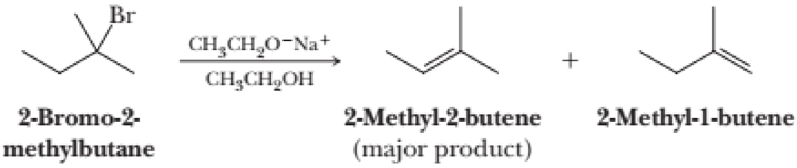
At one extreme, breaking of the C-LG bond to give a carbocation is complete before any reaction occurs with the base to lose a hydrogen and form the carboncarbon double bond. This mechanism is designated an E1 reaction, where E stands for elimination and 1 stands for unimolecular. One species, in this case the haloalkane, is involved in the rate-determining step. The mechanism of an E1 reaction is illustrated here by the reaction of 2-bromo-2-methylpropane to form 2-methylpropene.

So, in an E1 reaction, the leaving group comes off before the a proton is removed, and the reaction occurs in two steps. In an E2 reaction, the leaving group comes off as the a proton is removed, and the reaction occurs in one step.



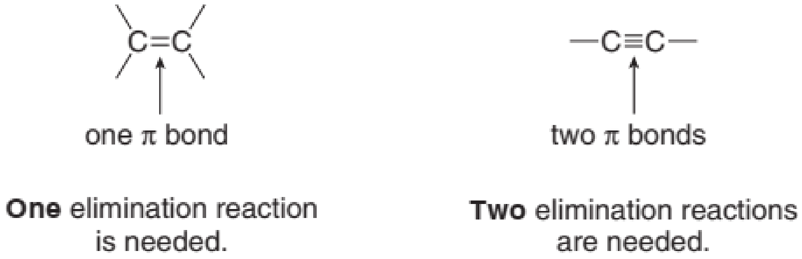
Alkene Formation





E2 Reactions and Alkyne Synthesis

A single elimination reaction produces the π bond of an alkene. Two consecutive elimination reactions produce the two π bonds of an alkyne.



Spectroscopy of alkyl halides

C-F: Stretch (strong) at 1400–1000 cm^{-1}. C-Cl Stretch (strong) in aliphatic chlorides occurs in the range 785–540 cm^{-1}, and Bend (wagging) at 1300–1230 cm^{-1}. C-Br Stretch (strong) in aliphatic bromides occurs at 650–510 cm^{-1}, and Bend (wagging) at 1250–1190 cm^{-1}. C-I Stretch (strong) in aliphatic iodides occurs at 600–485 cm^{-1}, and Bend (wagging) at 1200–1150 cm^{-1}.

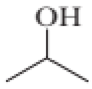
Alcohols

Alcohols contain a hydroxy group (OH group) bonded to an carbon atom. Alcohols are classified as primary (1°), secondary (2°), or tertiary (3°) based on the number of carbon atoms bonded to the carbon with the OH group.

Compounds with a hydroxyl group bonded directly to an aromatic (benzene) ring are called phenols. Phenols have many properties similar to those of alcohols, while other properties derive from their aromatic character.

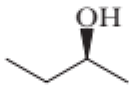
Alcohols are important because they can be converted into many other types of compounds, including alkenes, haloalkanes, aldehydes, ketones, carboxylic acids, and esters. Not only can alcohols be converted to these compounds, but these compounds can also be converted to alcohols. Thus, alcohols play a central role in the interconversion of organic functional groups.

1-Propanol
(Propyl alcohol)

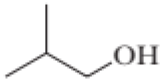


2-Propanol
(Isopropyl alcohol)

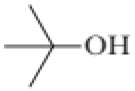
1-Butanol
(Butyl alcohol)



(*S*)-2-Butanol
((*S*)-*sec*-Butyl alcohol)



2-Methyl-1-propanol
(Isobutyl alcohol)



2-Methyl-2-propanol
(*tert*-Butyl alcohol)

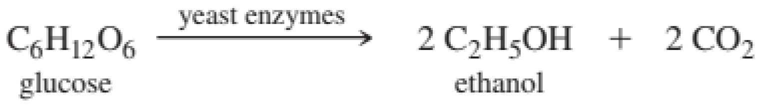
Synthesis of alcohols

From synthesis gas

Methanol is synthesized by a catalytic reaction of carbon monoxide with hydrogen. This reaction uses high temperatures and pressures and requires large, complicated industrial reactors.

$$\underset{\text{synthesis gas}}{CO + 2\,H} \xrightarrow[CuO-ZnO/Al_2O_3]{300-400\ ^\circ C,\ 200-300\ atm\ H_2} CH_3OH$$

Ethanol can be produced by the fermentation of sugars and starches from many different sources.



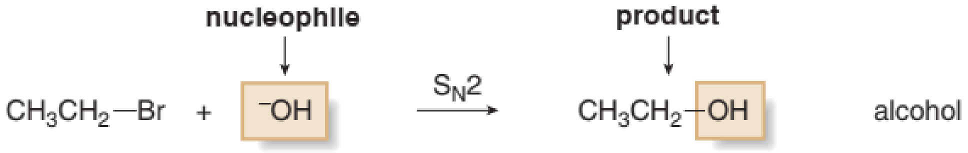
$$C_6H_{12}O_6 \xrightarrow{\text{yeast enzymes}} 2\,C_2H_5OH + 2\,CO_2$$

industrial ethanol has been synthesized directly by the catalyzed high-temperature, high-pressure, gas-phase reaction of water with ethylene. This process uses catalysts such as tungsten oxide, or various specially treated clays.

$$H_2C{=}CH_2 + H_2O \xrightarrow[\text{catalyst}]{100-300\text{ atm, }300\text{ °C}} CH_3{-}CH_2{-}OH$$

Alkyl halides

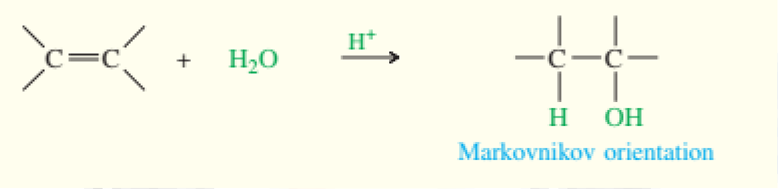
Alcohols and ethers are both common products of nucleophilic substitution. They are synthesized from alkyl halides by SN2 reactions using strong nucleophiles. As in all SN2 reactions, highest yields of products are obtained with unhindered methyl and 1° alkyl halides.



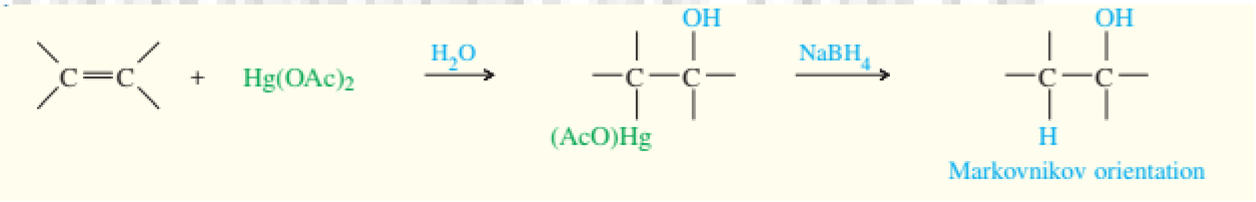
$$CH_3CH_2{-}Br + \boxed{^{-}OH} \xrightarrow{S_N2} CH_3CH_2{-}\boxed{OH}$$

Synthesis of Alcohols from Alkenes

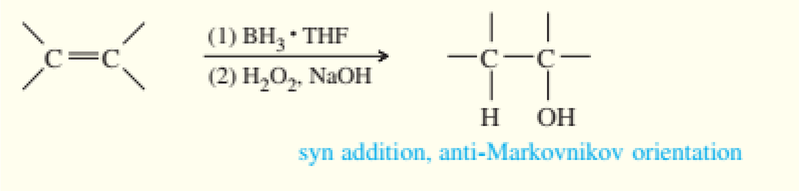
Acid-catalyzed hydration



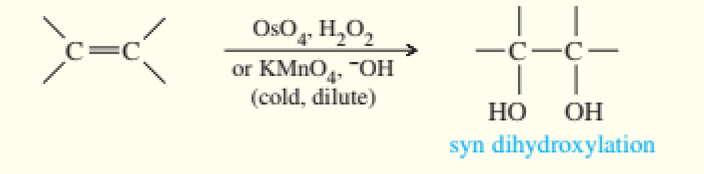
Oxymercuration–demercuration



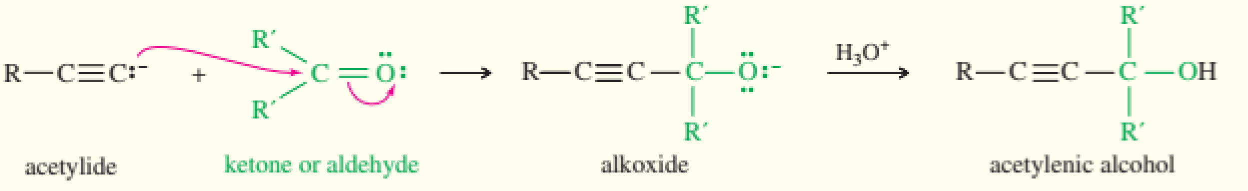
Hydroboration–oxidation



Dihydroxylation: synthesis of 1,2-diols from alkenes

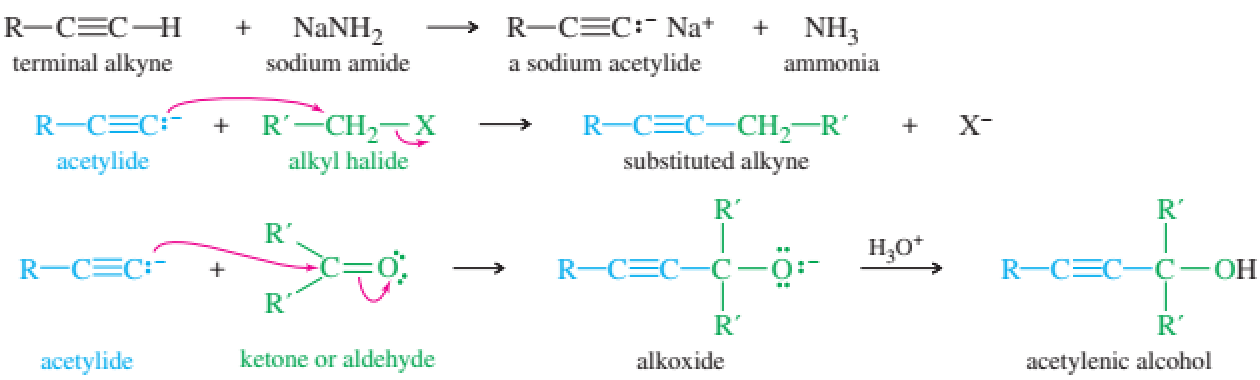


Addition of acetylides to carbonyl compounds



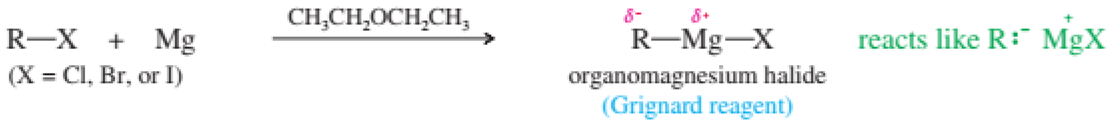
organometallic reagent

Terminal alkynes are weakly acidic, and they are converted to sodium acetylides by treatment with an unusually strong base, sodium amide. These sodium acetylides are useful nucleophiles, reacting with alkyl halides and carbonyl compounds to form new carbon–carbon bonds.



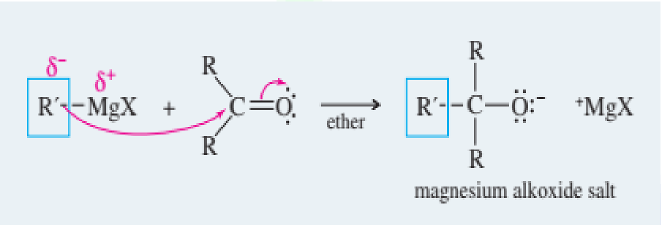
lithium and magnesium are frequently used for the synthesis of alcohols.

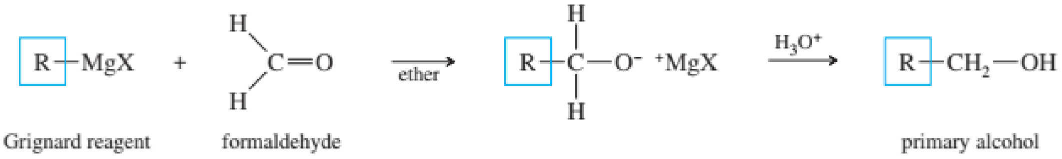
Grignard reagents may be made from primary, secondary, and tertiary alkyl halides, as well as from vinyl and aryl halides. Alkyl iodides are the most reactive halides, followed by bromides and chlorides. Alkyl fluorides generally do not react.



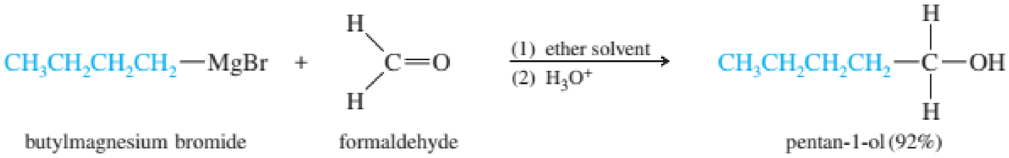
reactivity: R—I > R—Br > R—Cl ≫ R—F

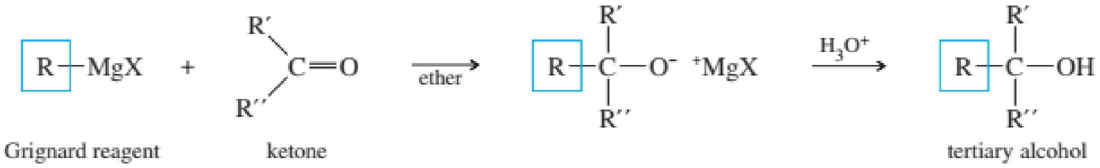
Because they resemble carbanions, Grignard and organolithium reagents are strong
nucleophiles and strong bases. Their most useful nucleophilic reactions are additions
to carbonyl groups, much like we saw with acetylide ions





For example,

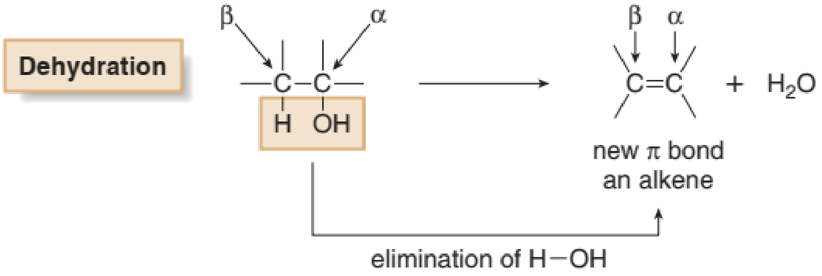




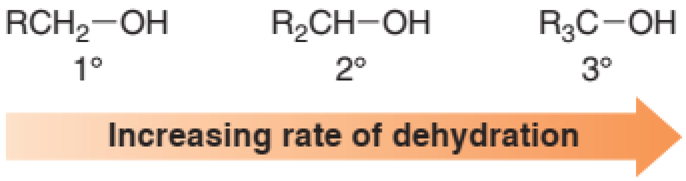
Alcohol reaction

Dehydration of Alcohols to Alkenes

The dehydrohalogenation of alkyl halides, is one way to introduce a π bond into a molecule. Another way is to eliminate water from an alcohol in a dehydration. reaction. Dehydration, like dehydrohalogenation, is a β elimination reaction in which the elements of OH and H are removed from the α and β carbon atoms, respectively.

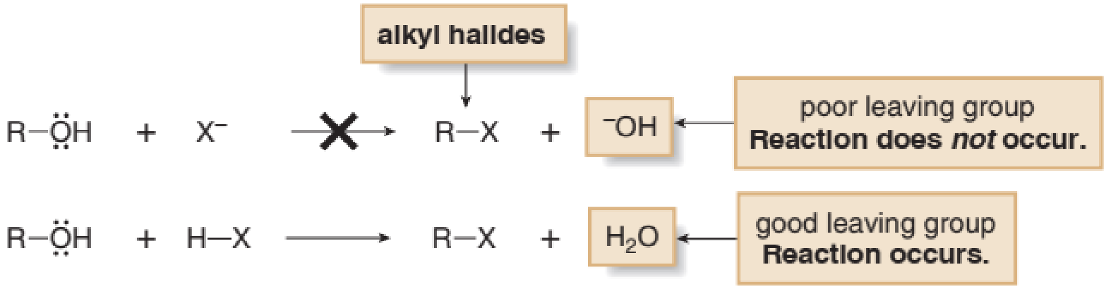


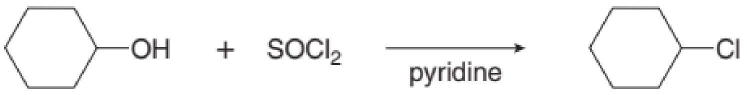
Dehydration is typically carried out using H_2SO_4 and other strong acids, or phosphorus oxychloride ($POCl_3$) in the presence of an amine base. We consider dehydration in acid first, followed by dehydration with $POCl_3$.

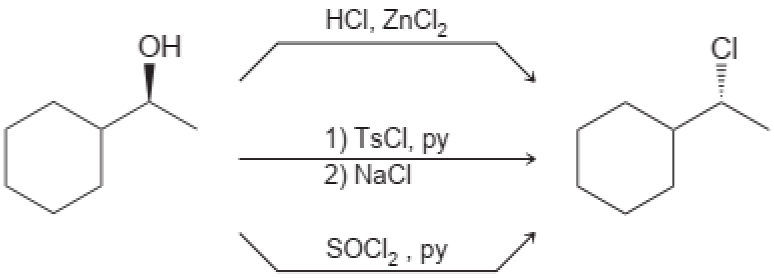


Conversion of Alcohols to Alkyl Halides with HX

Alcohols undergo nucleophilic substitution reactions only if the OH group is converted into a better leaving group before nucleophilic attack. Thus, substitution does not occur when an alcohol is treated with X– because –OH is a poor leaving group, but substitution does occur on treatment of an alcohol with HX because H_2O is now the leaving group. The reaction of alcohols with HX (X = Cl, Br, I) is a general method to prepare 1°, 2°, and 3° alkyl halides. $SOCl_2$ (thionyl chloride) converts alcohols into alkyl chlorides. PBr_3 (phosphorus tribromide) converts alcohols into alkyl bromides.

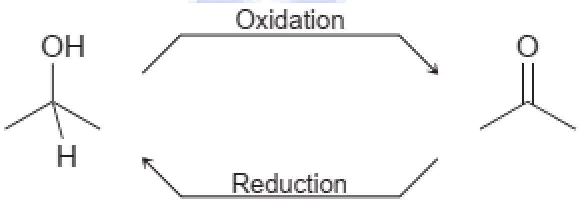




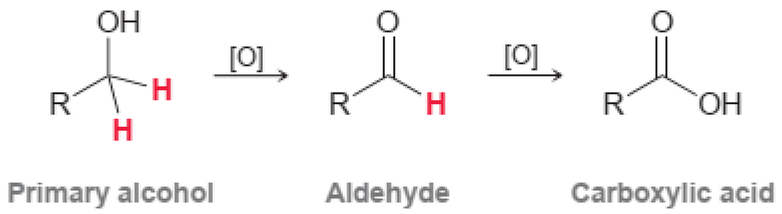


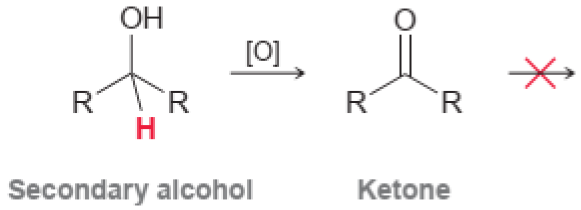
Oxidation of Alcohols:

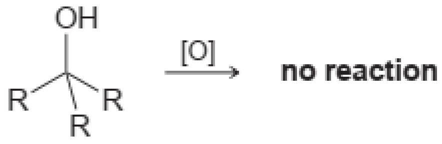
oxidation, which involves an increase in oxidation state



The outcome of an oxidation process depends on whether the starting alcohol is primary, secondary, or tertiary. primary alcohol has two protons at the α position (the carbon atom bearing the hydroxyl group). As a result, primary alcohols can be oxidized twice. Secondary alcohols only have one proton at the α position so they can only be oxidized once, forming a ketone. Tertiary alcohols do not have any protons at the α position, and as a result, they generally do not undergo oxidation.

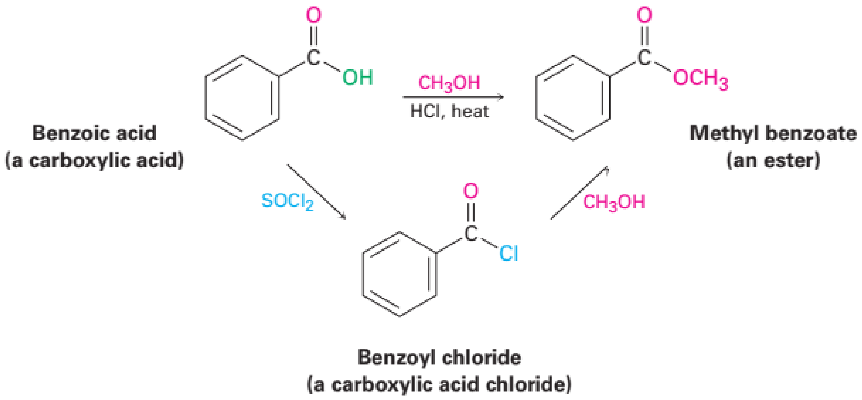


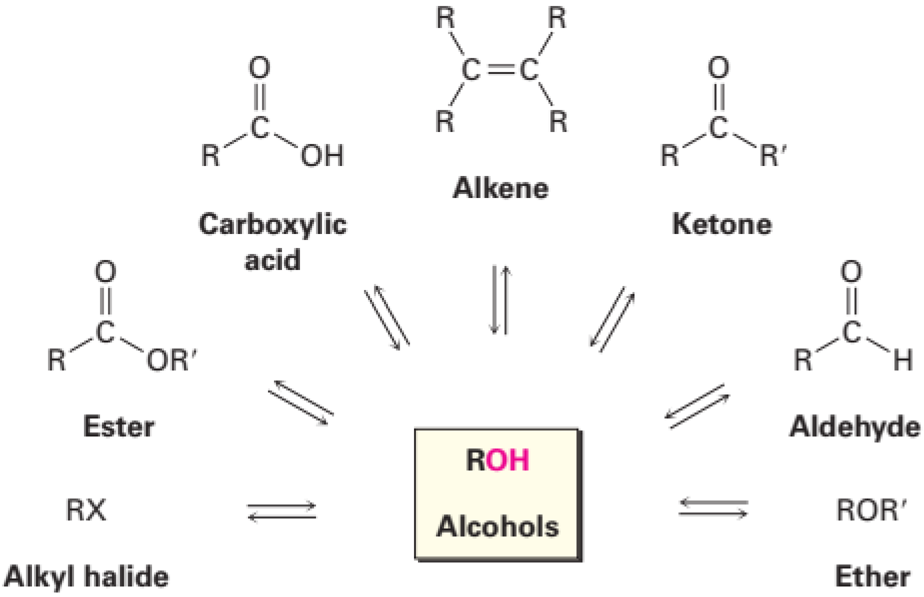




Ester formation

Alcohols react with carboxylic acids to give esters, a reaction that is common in
both the laboratory and living organisms. In the laboratory, the reaction can be carried out in a single step if a strong acid is used as catalyst. More frequently, though, the reactivity of the carboxylic acid is enhanced by first converting it into a carboxylic acid chloride, which then reacts with the alcohol.



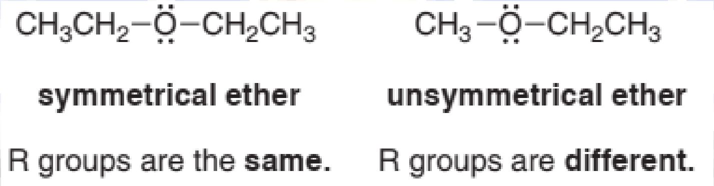


Spectroscopy Of Alcohols

The free O-H stretch is a sharp peak at 3650–3600 cm^{-1}. The hydrogen-bonded O-H band is a broad peak at 3400–3300 cm^{-1}. C-O-H bending appears as a broad and weak peak at 1440–1220 cm^{-1}, C-O stretching vibration usually occurs in the range 1260–1000 cm^{-1}.

Ethers

Ether have two alkyl groups bonded to an oxygen atom. An ether is symmetrical if the two alkyl groups are the same, and unsymmetrical if they are different. Both alcohols and ethers are organic derivatives of H_2O, formed by replacing one or both of the hydrogens on the oxygen atom by R groups, respectively.



$CH_3CH_2-\ddot{\underset{\cdot\cdot}{O}}-CH_2CH_3$ $CH_3-\ddot{\underset{\cdot\cdot}{O}}-CH_2CH_3$

symmetrical ether **unsymmetrical ether**

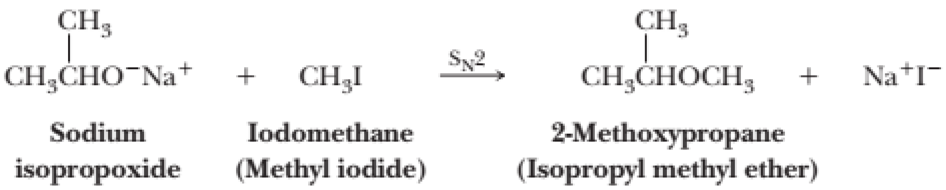
R groups are the **same.** R groups are **different.**

Preparation of Ethers

Williamson Ether Synthesis

The most common general method for the synthesis of ethers, the

Williamson ether synthesis, involves nucleophilic displacement of a halide ion or other good leaving group by an alkoxide ion. Williamson ether synthesis, it is essential to use a combination of reactants that maximizes nucleophilic substitution and minimizes any competing β-elimination. Yields of ether are highest when the halide to be displaced is on a methyl or a primary carbon. Yields are low in the displacement from secondary halides (because of competing β-elimination), and the Williamson ether synthesis fails altogether with tertiary halides (because β-elimination by an E2 mechanism is the exclusive reaction).



$$CH_3CH(CH_3)O^-Na^+ + CH_3I \xrightarrow{S_N2} CH_3CH(CH_3)OCH_3 + Na^+I^-$$

Sodium isopropoxide **Iodomethane (Methyl iodide)** **2-Methoxypropane (Isopropyl methyl ether)**

Acid-Catalyzed Dehydration of Alcohols

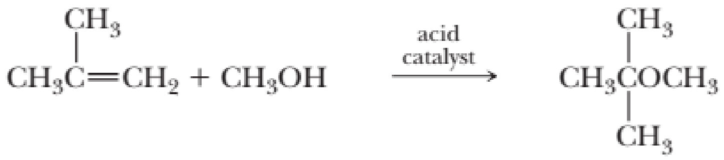
Diethyl ether and several other commercially available ethers are synthesized on an industrial scale by the acid-catalyzed dehydration of primary alcohols. Intermolecular dehydration of ethanol for example, gives diethyl ether.

$$2\ CH_3CH_2OH \xrightarrow[140°C]{H_2SO_4} CH_3CH_2OCH_2CH_3 + H_2O$$

Ethanol **Diethyl ether**

Acid-Catalyzed Addition of Alcohols to Alkenes

Under suitable conditions, alcohols can be added to the carbon-carbon double bond of an alkene to give an ether. The usefulness of this method of ether synthesis is limited to the interaction of alkenes that form stable carbocations and methanol or primary alcohols. An example is the commercial synthesis of tert-butyl methyl ether (MTBE). 2-Methylpropene and methanol are passed over an acid catalyst to give the ether.



$$CH_3\overset{\overset{\displaystyle CH_3}{|}}{C}{=}CH_2 + CH_3OH \xrightarrow[]{\text{acid catalyst}} CH_3\underset{\underset{\displaystyle CH_3}{|}}{\overset{\overset{\displaystyle CH_3}{|}}{C}}OCH_3$$

2-Methoxy-2-methylpropane
(*tert*-Butyl methyl ether)

Reactions of Ethers

Ethers resemble hydrocarbons in their resistance to chemical reaction. They do not react with oxidizing agents such as potassium dichromate or potassium permanganate. They are stable toward even very strong bases, and, except for tertiary alkyl ethers, they are not affected by most weak acids at moderate temperatures. Because of their good solubilizing properties and general inertness to chemical reaction, ethers are excellent solvents in which to carry out many organic reactions.

Acid-Catalyzed Cleavage by Concentrated HX

Cleavage of di-alkyl ethers requires both a strong acid and a good nucleophile, hence the use of concentrated aqueous HI (57%) or HBr (48%). Dibutyl ether, for example, reacts with hot concentrated HBr to give two molecules of 1-bromobutane.

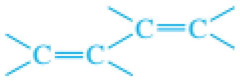
Dibutyl ether **1-Bromobutane**

Spectroscopy Of Ether

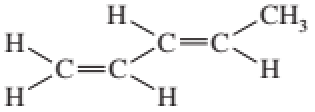
The most prominent band is that due to CIO stretch, 1300–1000 cm^{-1}.

Conjugated system

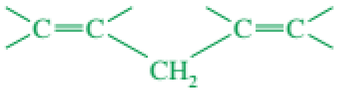
Double bonds can interact with each other if they are separated by just one single bond. Such interacting double bonds are said to be conjugated. Double bonds with two or more single bonds separating them have little interaction and are called isolated double bonds. For example, penta-1,3-diene has conjugated double bonds, while penta-1,4-diene has isolated double bonds. Because of the interaction between the double bonds, systems containing conjugated double bonds tend to be more stable than similar systems with isolated double bonds. double bonds with no intervening single bonds are called cumulated double bonds. Consider penta-1,2-diene, which contains cumulated double bonds. Such 1,2-diene systems are also called allenes.



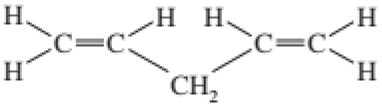
conjugated double bonds
(more stable than isolated double bonds)



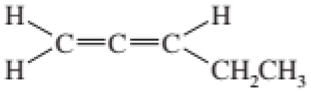
penta-1,3-diene



isolated double bonds

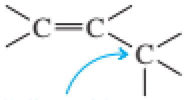


penta-1,4-diene



penta-1,2-diene (ethylallene)

Conjugated compounds undergo a variety of reactions, many of which involve intermediates that retain some of the resonance stabilization of the conjugated system. Common intermediates include allylic systems, particularly allylic cations and radicals. Allylic cations and radicals are stabilized by delocalization.



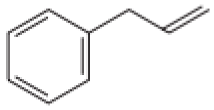
allylic position

$H_2C{=}CH{-}CH_2Br$

allyl bromide

$H_2C{=}CH{-}CH_2OH$

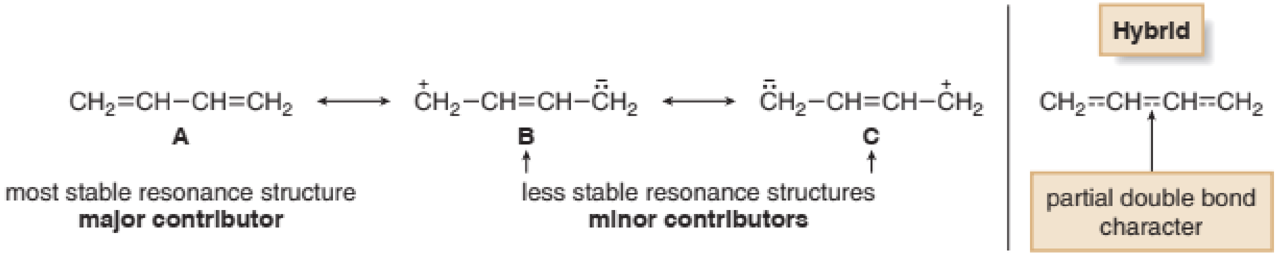
allyl alcohol



allylbenzene

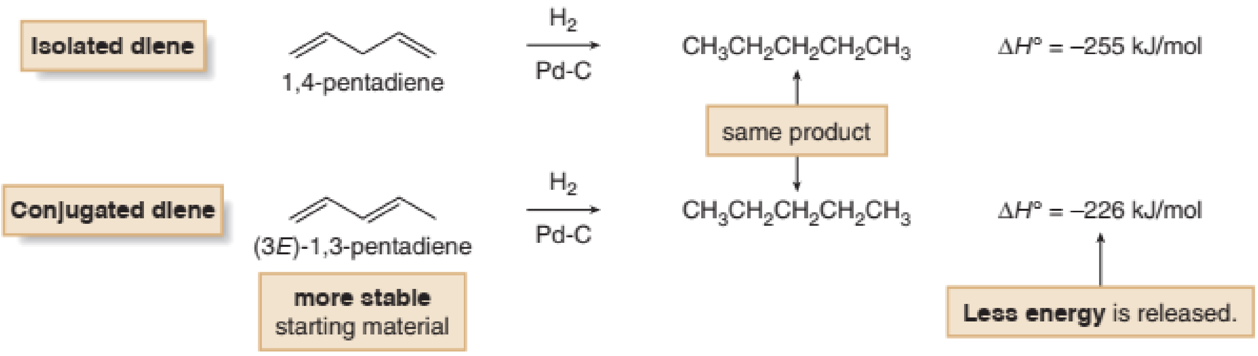
1,2 And 1,4- Addition To Conjugated Diene

Conjugated diene compounds having two double bonds joined by one σ bond. Conjugated dienes are also called 1,3-dienes. 1,3-Butadiene ($CH_2=CH-CH=CH_2$) is the simplest conjugated diene. The bond length of the carbon–carbon double bonds in 1,3-butadiene is similar to an isolated double bond, but the central carbon–carbon single bond is shorter than the C – C bond in ethane. This is due to the resonance. Based on resonance, the central C – C bond in 1,3-butadiene is shorter because it has partial double bond character.



1,3-butadiene is a conjugated molecule with four overlapping p orbitals on adjacent atoms. As a result, the π electrons are not localized between the carbon atoms of the double bonds, but rather delocalized over four atoms. This places more electron density between the central two carbon atoms of 1,3-butadiene than would normally be present. This shortens the bond. Drawing resonance structures illustrates this delocalization.

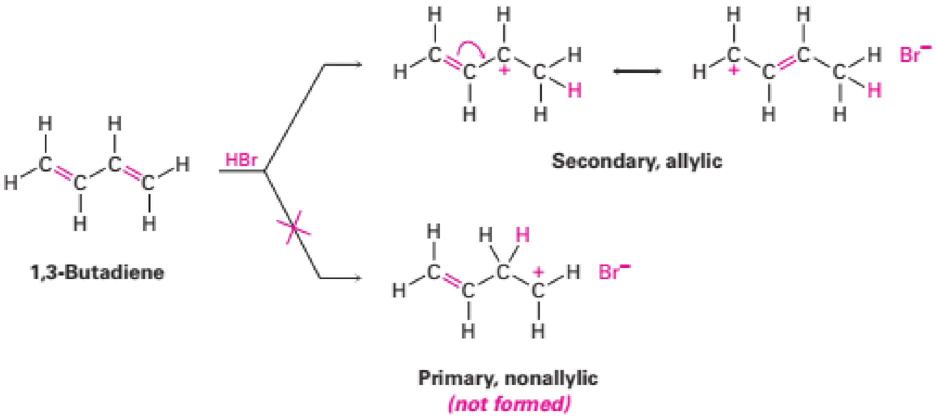
the heat of hydrogenation, can be used as a measure of alkene stability. When hydrogenation gives the same alkane from two dienes, the more stable diene has the smaller heat of hydrogenation. Therefore, conjugated diene is more stable than isolated. Because a conjugated diene has overlapping p orbitals on four adjacent atoms, its π electrons are delocalized over four atoms. This delocalization, which cannot occur in an isolated diene, is illustrated by drawing resonance structures.



The π bonds in conjugated dienes undergo addition reactions, too, but they differ in two ways from the addition reactions to isolated double bonds. Electrophilic addition in conjugated dienes gives a mixture of products. Conjugated dienes undergo a unique addition reaction not seen in alkenes or isolated dienes.

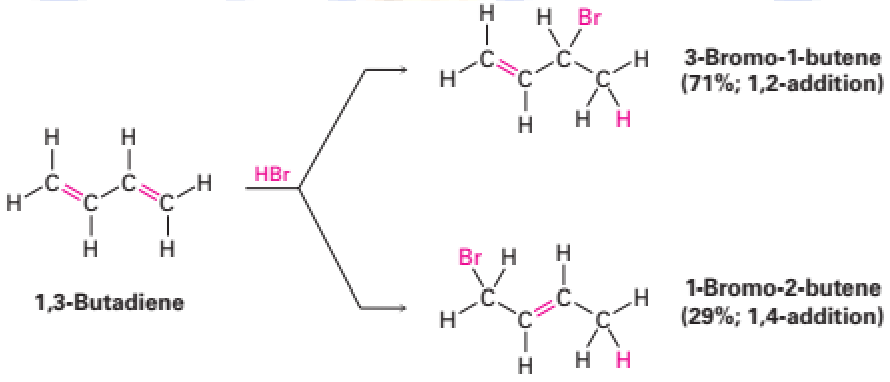
Electrophilic additions to conjugated dienes usually involve allylic cations as intermediates. Unlike simple carbocations, an allylic cation can react with a nucleophile at either of its positive centers. This leads to a mixtures of products are invariably obtained.

When 1,3-butadiene reacts with an electrophile such as H^+, two carbocation intermediates are possible a primary nonallylic carbocation and a secondary allylic cation. Because an allylic cation is stabilized by resonance between two forms, it is more stable and forms faster than a nonallylic carbocation. When the allylic cation reacts with Br_2 to complete the electrophilic addition, reaction can occur either at C1 or at C3 because both carbons share the positive charge. Thus, a mixture of 1,2- and 1,4-addition products results.



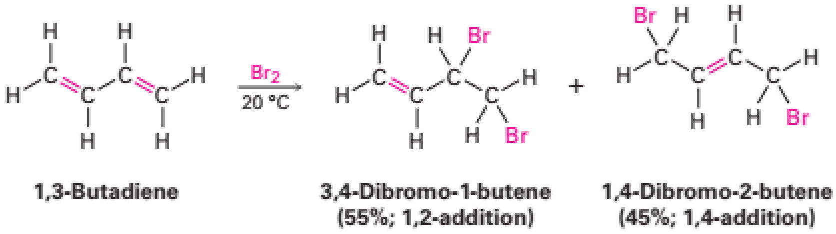
Addition of HX

Addition of HBr to 1,3-butadiene, for instance, yields a mixture of two products (not counting cis–trans isomers). The 1,2-addition product results from Markovnikov addition of HBr across two adjacent carbon atoms (C1 and C2) of the diene. The 1,4-addition product results from addition of HBr to the two end carbons (C1 and C4) of the diene. 1,4-Addition is also called conjugate addition.



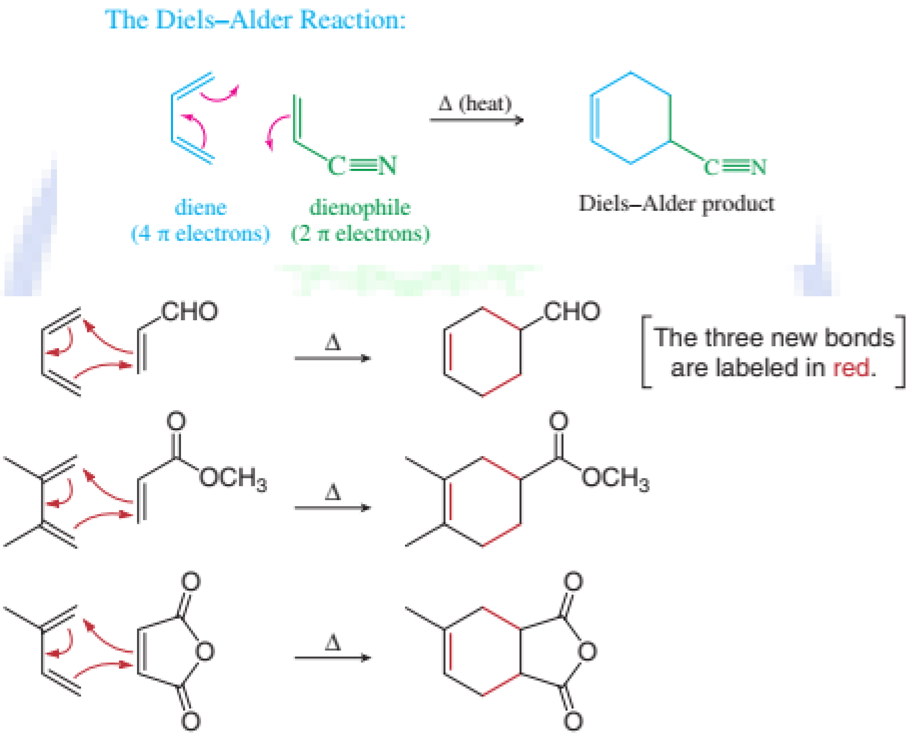
Addition of X_2

Halide adds to 1,3-butadiene to give a mixture of 3,4-dibromo-1-butene and 1,4-dibromo-2-butene.



The Diels–Alder Reaction

The Diels–Alder reaction, named for German chemists Otto Diels and Kurt Alder, is an addition reaction between a 1,3-diene and an alkene called a dienophile, to form a new six-membered ring. The Diels–Alder reaction forms new carbon–carbon bonds, so it can be used to synthesize larger, more complex molecules from smaller ones.

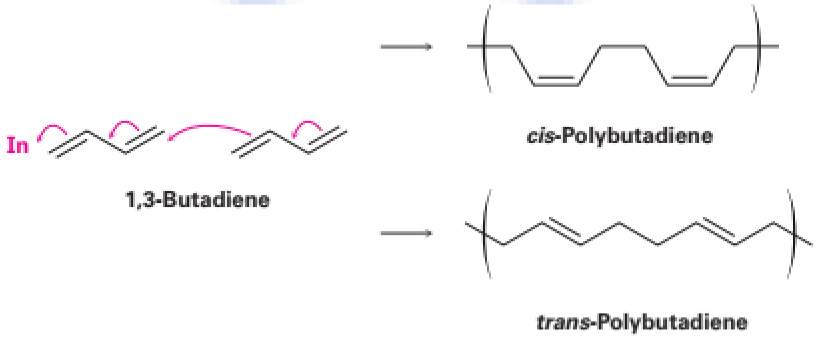


Diene Reactivity, The diene can react only when it adopts the s-cis conformation.
Dienophile Reactivity, Electron-withdrawing substituents in the dienophile increase the reaction rate.

In a Diels–Alder reaction, the conjugated diene acts as a nucleophile and the dienophile acts as an electrophile. As a result, electron-withdrawing groups make the dienophile more electrophilic (and, thus, more reactive) by withdrawing electron density from the carbon–carbon double bond.

Diene Polymers

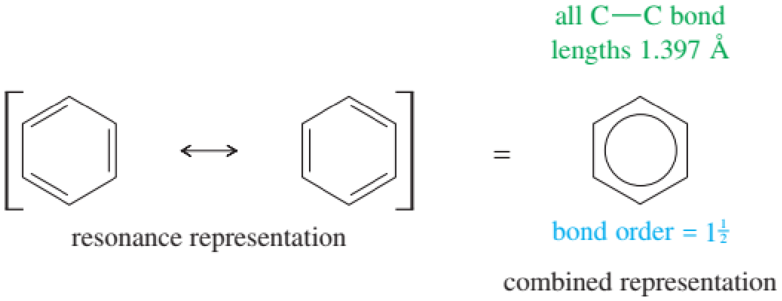
Conjugated dienes can be polymerized just as simple alkenes can, are structurally more complex than simple alkene polymers, though, because double bonds remain every four carbon atoms along the chain, leading to the possibility of cis–trans isomers. The initiator (In) for the reaction can be either a radical, as occurs in ethylene polymerization, or an acid. Note that the polymerization is a 1,4 addition of the growing chain to a conjugated diene monomer.



Aromatic Compound (Arenes)

A term used initially to classify benzene and its derivatives. More accurately, it is used to classify any compound that meets the Hückel criteria for aromaticity. So, Aromatic compounds resemble benzene they are unsaturated, conjugated, planar ring accompanied by delocalized π electrons clouds. These compounds do not undergo the addition reactions characteristic of alkenes. As the unusual stability of aromatic compounds was investigated, the term aromatic came to be applied to compounds with this stability, regardless of their odors.

Benzene (C_6H_6) is the simplest aromatic hydrocarbon. It has four degrees of unsaturation, making it a highly unsaturated hydrocarbon. is much less reactive than typical alkenes and fails to undergo typical alkene addition reactions. Because the ring is planar and the carbon nuclei are positioned at equal distances, the two Kekulé structures must differ only in the positioning of the π electrons. Benzene is actually a resonance hybrid of the two Kekulé structures. This representation implies that the pi electrons are delocalized, with a bond order of between adjacent carbon atoms. The carbon–carbon bond lengths in benzene are shorter than typical single-bond lengths, yet longer than typical double-bond lengths.

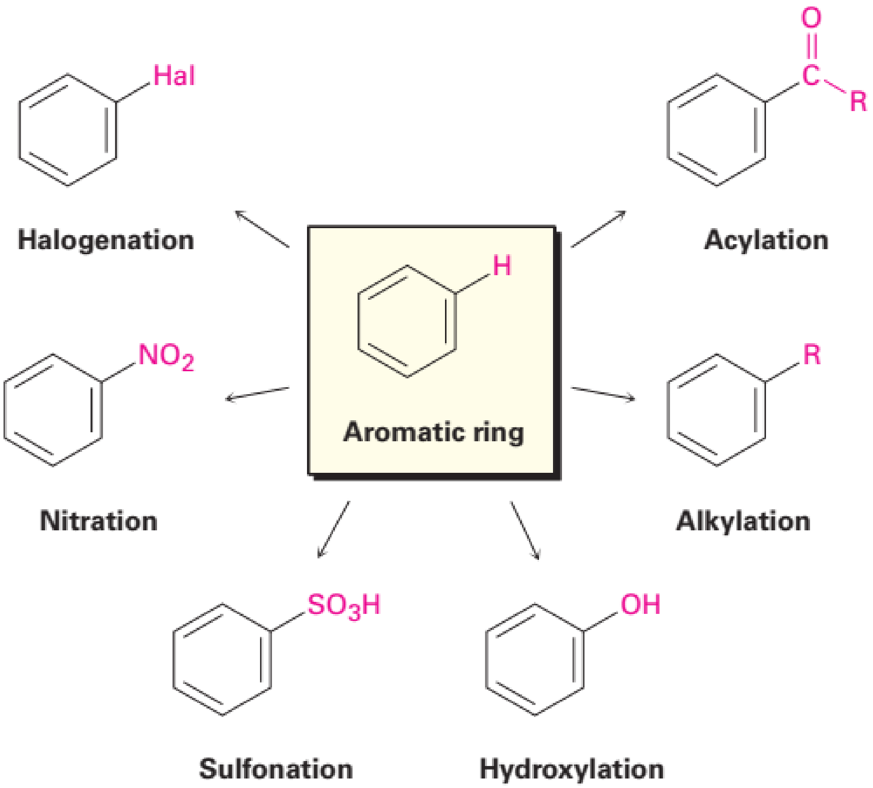


Reactions of Benzene

Benzene is actually much more stable than we would expect from the simple resonance-delocalized picture. Both the Kekulé structure and the resonance-delocalized picture show that benzene is a cyclic conjugated triene. We might expect benzene to undergo the typical reactions of polyenes. Benzene's six π electrons make it electron rich and so it readily reacts with electrophiles. In fact, its reactions are quite unusual. Thus, any structure proposed for benzene must account for its high degree of unsaturation and its lack of reactivity towards electrophilic addition.

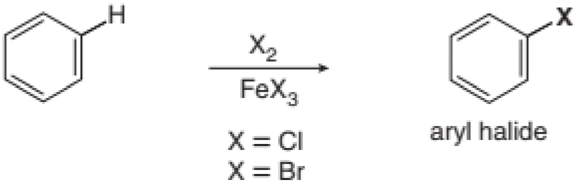
Electrophilic substitution of aromatic compounds

the characteristic reaction of benzene is electrophilic aromatic substitution a hydrogen atom is replaced by an electrophile. The reaction is characteristic of all aromatic rings, not just benzene and substituted benzenes. In fact, the ability of a compound to undergo electrophilic substitution is a good test of aromaticity.



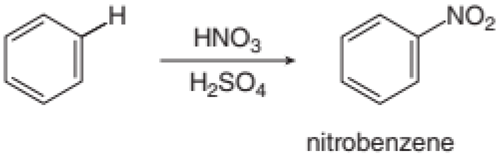
Halogenation

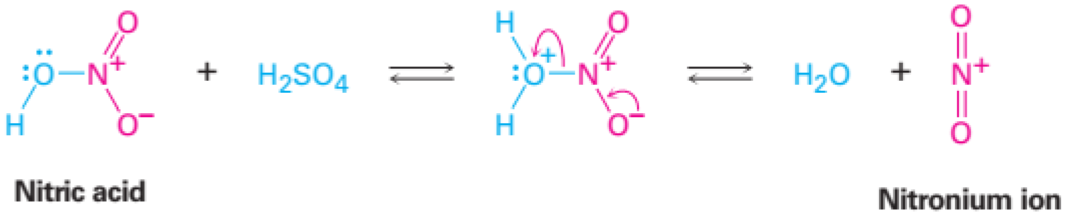
For halogenation of benzene to take place, a catalyst such as FeX_3 is needed. The catalyst makes the X_2 molecule more electrophilic by polarizing it to give an FeX^-X^+ species that reacts as if it were X^+. The polarized X_2 molecule then reacts with the nucleophilic benzene ring to yield a nonaromatic carbocation intermediate that is doubly allylic and has three resonance forms.

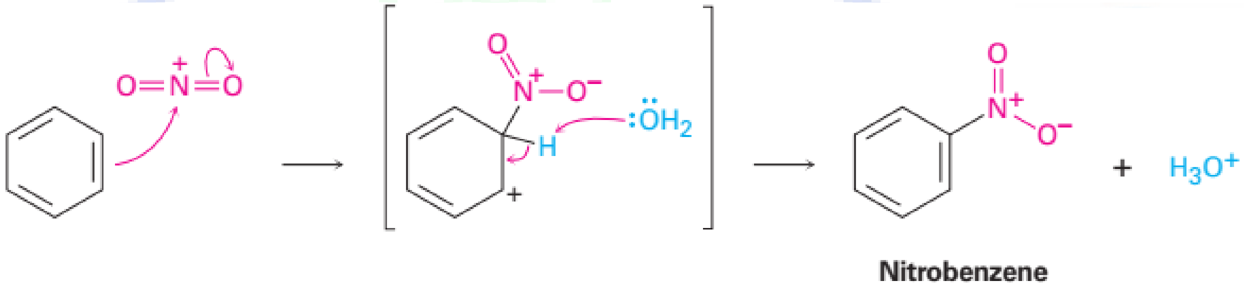


Nitration

Aromatic rings are nitrated by reaction with a mixture of concentrated nitric and sulfuric acids. The electrophile is the nitronium ion, NO_2+, which is formed from HNO_3 by protonation and loss of water. The nitronium ion reacts with benzene to yield a carbocation intermediate, and loss of H+ from this intermediate gives the neutral substitution product, nitrobenzene.

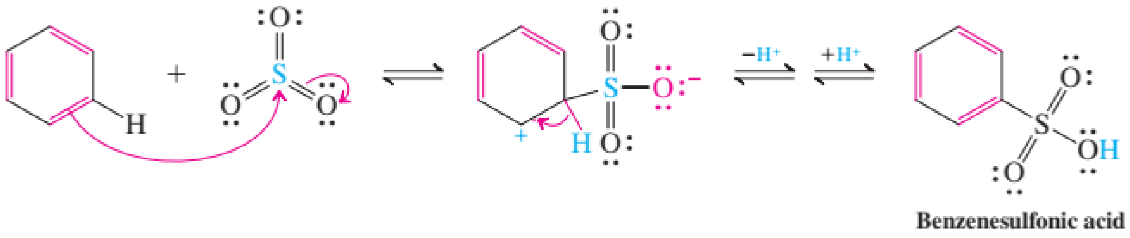






Sulfonation

Concentrated sulfuric acid does not sulfonate benzene at room temperature. However, a more reactive form, called fuming sulfuric acid, permits electrophilic attack by SO_3. Commercial fuming sulfuric acid is made by adding about 8% of sulfur trioxide, SO_3, to the concentrated acid. Because of the strong electron-withdrawing effect of the three oxygens, the sulfur in SO_3 is electrophilic enough to attack benzene directly. Subsequent proton transfer results in the sulfonated product, benzenesulfonic acid. Aromatic sulfonation is readily reversible. The reaction of sulfur trioxide with water to give sulfuric acid is so exothermic that heating benzenesulfonic acid in dilute aqueous acid completely reverses sulfonation.

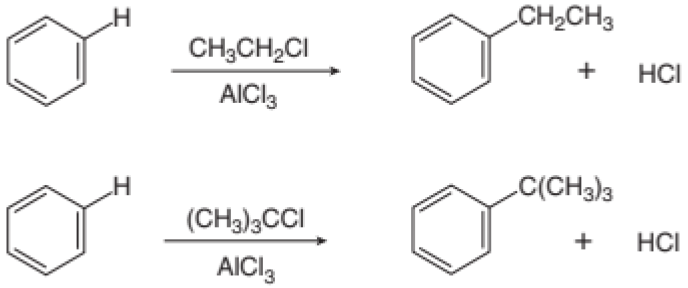


Reverse Sulfonation: Hydrolysis

Friedel–Crafts Alkylation and Friedel–Crafts Acylation

In Friedel–Crafts alkylation, treatment of benzene with an alkyl halide and a Lewis acid ($AlCl_3$) forms an alkyl benzene. This reaction is an alkylation because it results in transfer of an alkyl group from one atom to another (from Cl to benzene).

In Friedel–Crafts acylation, a benzene ring is treated with an acid chloride (RCOCl) and $AlCl_3$ to form a ketone. Because the new group bonded to the benzene ring is called an acyl group, the transfer of an acyl group from one atom to another is an acylation.



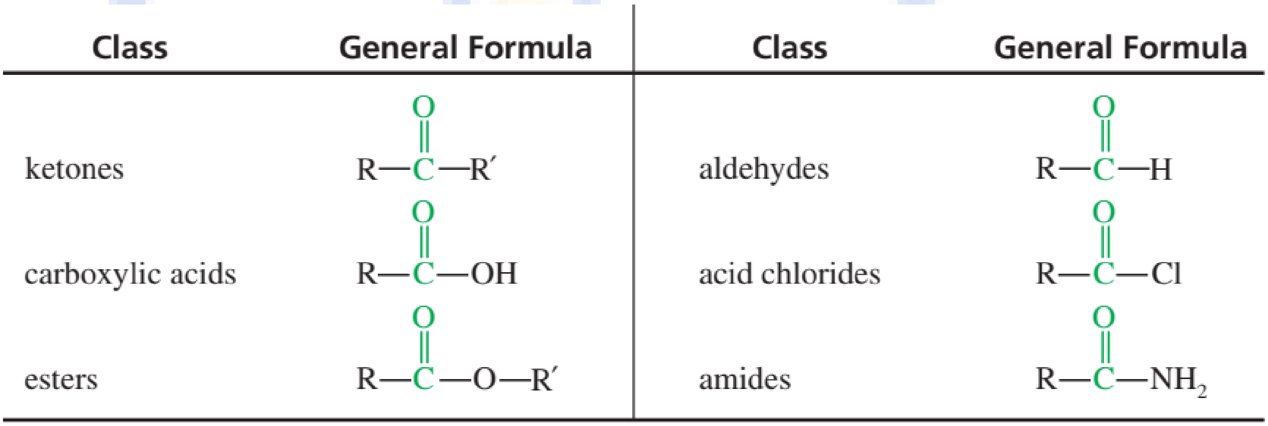
Vinyl halides and aryl halides do not react in Friedel–Crafts alkylation. Rearrangements can occur, For CH_3Cl and 1° RCl, the Lewis acid–base complex itself serves as the electrophile for electrophilic aromatic substitution. With 2° and 3° RCl, the Lewis acid–base complex reacts further to give a 2° or 3° carbocation, which serves as the electrophile. Carbocation formation occurs only with 2° and 3° alkyl chlorides, because they afford more stable carbocations. Other functional groups that form carbocations can also be used as starting materials.

Spectroscopy Of Aromatic Compounds

=C-H stretch for sp2 CIH occurs at values greater than 3000 cm^{-1} (3050–3010 cm^{-1}). =C-H out-of-plane (oop) bending occurs at 900–690 cm^{-1}. These bands can be used with great utility to assign the ring substitution pattern. C=C ring stretch absorptions often occur in pairs at 1600 cm^{-1} and 1475 cm^{-1}. Overtone/combination bands appear between 2000 and 1667 cm^{-1}. These weak absorptions can be used to assign the ring substitution pattern.

Carbonyl Compounds

Carbonyl compounds are compounds that contain carbonyl group (C=O). There are many different kinds of carbonyl compounds, aldehydes, ketones, acid halides, esters, amides, and carboxylic acids. The carbonyl group is perhaps the most important functional group in organic chemistry, because its electron-deficient carbon and easily broken π bond make it susceptible to a wide variety of useful reactions.

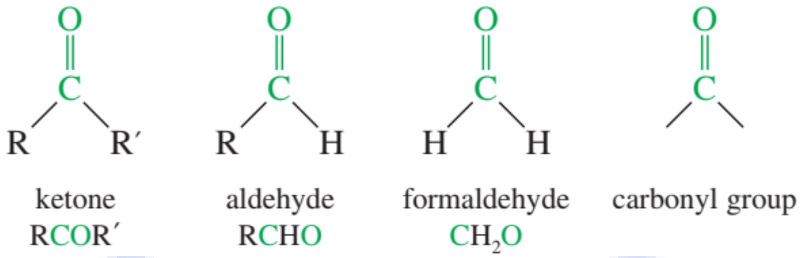


Class	General Formula	Class	General Formula
ketones	$R-\overset{\overset{O}{\Vert}}{C}-R'$	aldehydes	$R-\overset{\overset{O}{\Vert}}{C}-H$
carboxylic acids	$R-\overset{\overset{O}{\Vert}}{C}-OH$	acid chlorides	$R-\overset{\overset{O}{\Vert}}{C}-Cl$
esters	$R-\overset{\overset{O}{\Vert}}{C}-O-R'$	amides	$R-\overset{\overset{O}{\Vert}}{C}-NH_2$

The double bond of the carbonyl group has a large dipole moment because oxygen is more electronegative than carbon, and the bonding electrons are not shared equally. In particular, the less tightly held pi electrons are pulled more strongly toward the oxygen atom, giving ketones and aldehydes larger dipole moments than most alkyl halides and ethers.

Aldehyde and ketone

Compounds that have only carbon and hydrogen atoms bonded to the carbonyl group. An aldehyde has at least one H atom bonded to the carbonyl group, while, a ketone has two alkyl or aryl groups bonded to the carbonyl group. The double bond of the carbonyl group has a large dipole moment because oxygen is more electronegative than carbon, and the bonding electrons are not shared equally. In particular, the less tightly held pi electrons are pulled more strongly toward the oxygen atom, giving ketones and aldehydes larger dipole moments than most alkyl halides and ethers.

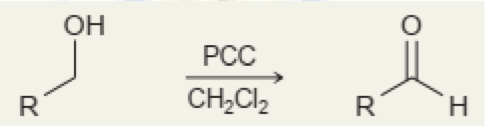


Ketones and aldehydes are similar in structure, and they have similar properties. There are some differences, however, particularly in their reactions with oxidizing agents and with nucleophiles. In most cases, aldehydes are more reactive than ketones, for reasons we discuss shortly.

Synthesis Of Aldehyde And Ketone

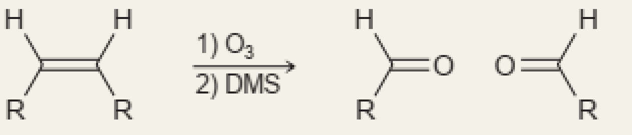
Oxidation of Primary Alcohols

When treated with a strong oxidizing agent, primary alcohols are oxidized to carboxylic acids. Formation of an aldehyde requires an oxidizing agent, such as PCC, that will not further oxidize the resulting aldehyde.



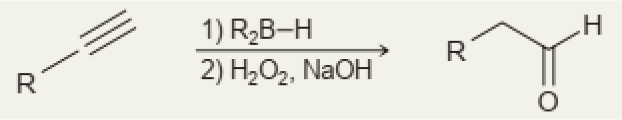
Ozonolysis of Alkenes

Ozonolysis will cleave a C=C double bond. If either carbon atom bears a hydrogen atom, an aldehyde will be formed.



Hydroboration-Oxidation of Terminal Alkynes

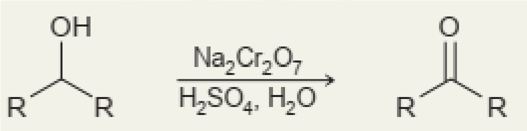
Hydroboration-oxidation results in an anti-Markovnikov addition of water across a π bond, followed by tautomerization of the resulting enol to form an aldehyde.



Synthesis of ketones

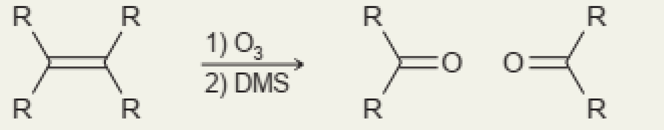
Oxidation of Secondary Alcohols

A variety of strong or mild oxidizing agents can be used to oxidize secondary alcohols. The resulting ketone does not undergo further oxidation.



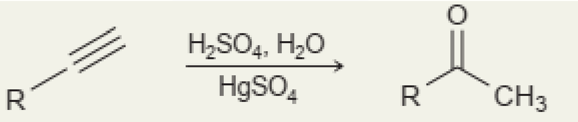
Ozonolysis of Alkenes

Tetrasubstituted alkenes are cleaved to form ketones



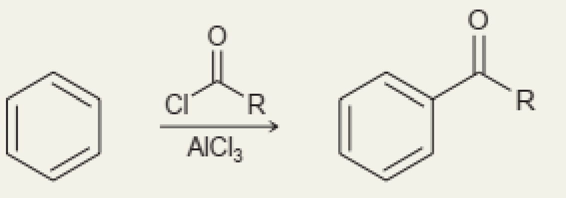
Acid-Catalyzed Hydration of Terminal Alkynes

This procedure results in a Markovnikov addition of water across the p bond, followed by tautomerization to form a methyl ketone.



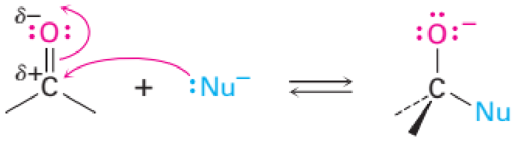
Friedel-Crafts Acylation

Aromatic rings that are not too strongly deactivated will react with an acid halide in the presence of a Lewis acid to produce an aryl ketone.



Reaction of aldehyde and ketone

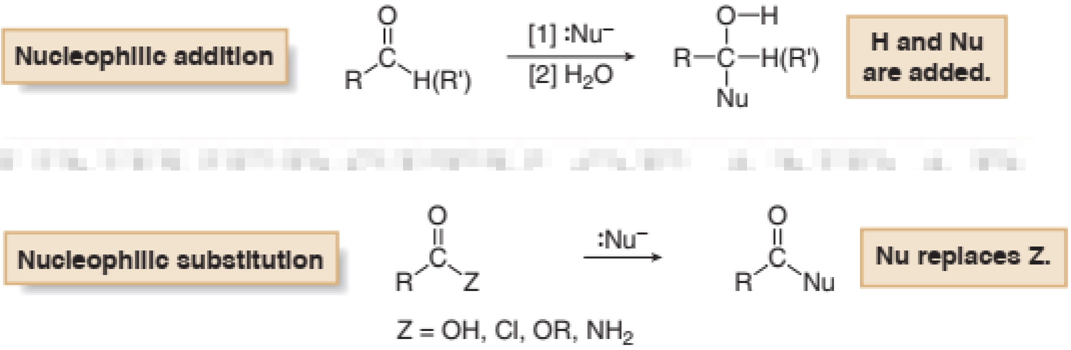
The most common reaction of aldehydes and ketones is the nucleophilic addition reaction, in which a nucleophile (:Nu-) adds to the electrophilic carbon of the carbonyl group. Since the nucleophile uses an electron pair to form a new bond to carbon, two electrons from the carbon–oxygen double bond must move toward the electronegative oxygen atom to give an alkoxide anion. The carbonyl carbon rehybridizes from sp2 to sp3 during the reaction, and the alkoxide ion product therefore has tetrahedral geometry.



A carbonyl compound (sp^2-hybridized carbon)

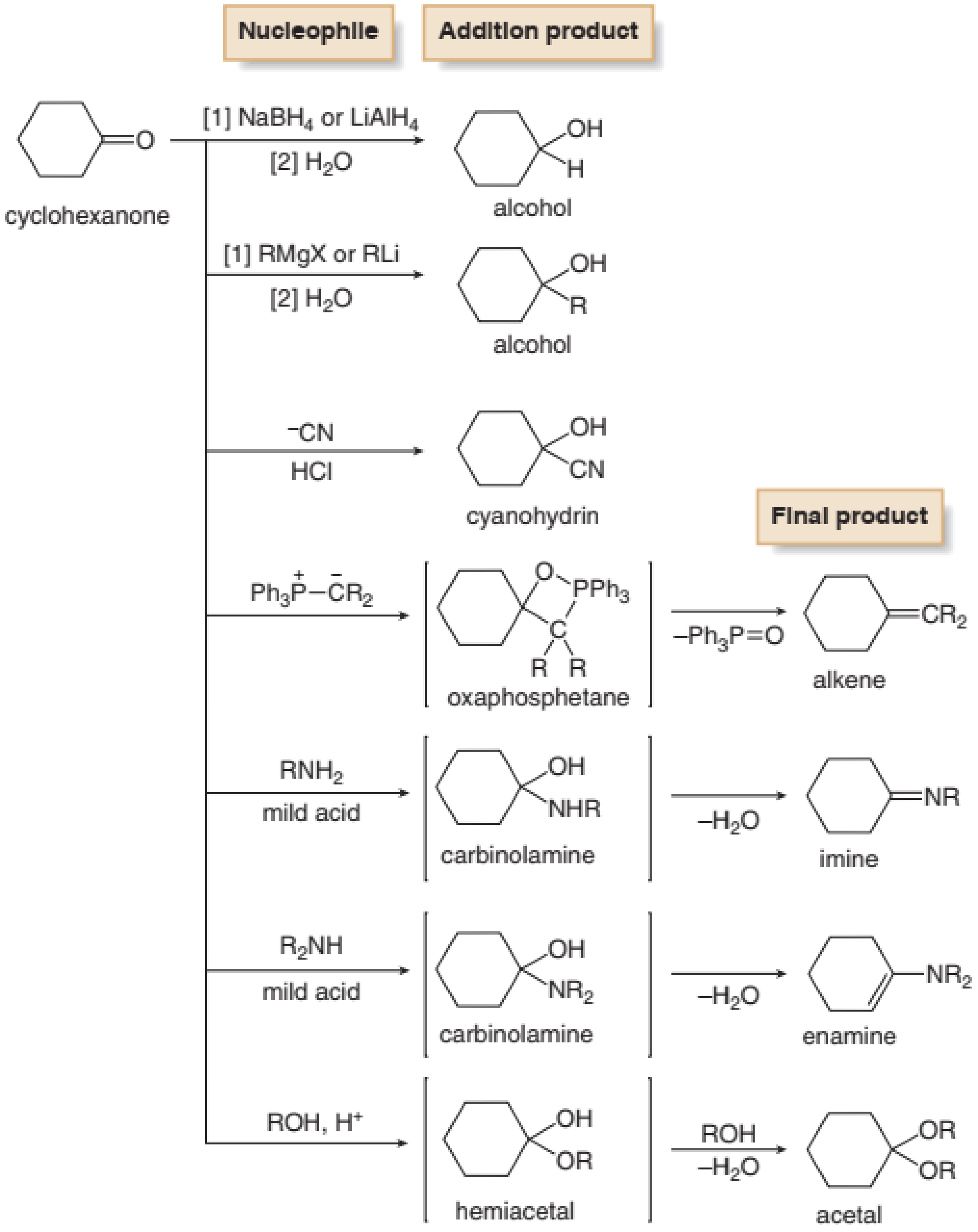
A tetrahedral intermediate (sp^3-hybridized carbon)

Once formed, and depending on the nature of the nucleophile, the tetrahedral alkoxide intermediate can undergo either of two further reactions. Often, the tetrahedral alkoxide intermediate is simply protonated by water or acid to form an alcohol product. Alternatively, the tetrahedral intermediate can be protonated and expel the oxygen to form a new double bond between the carbonyl carbon and the nucleophile.



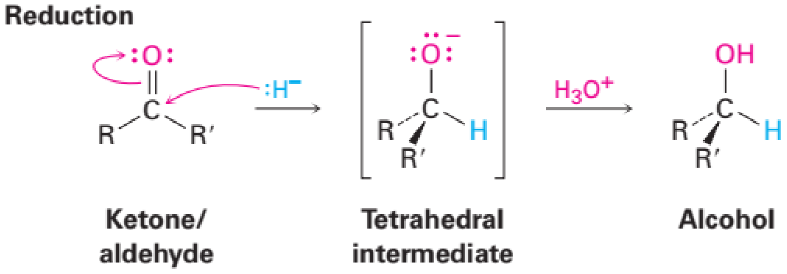
Aldehydes and ketones react with nucleophiles at the carbonyl carbon. Aldehydes and ketones form enolates that react with electrophiles at the α-carbon

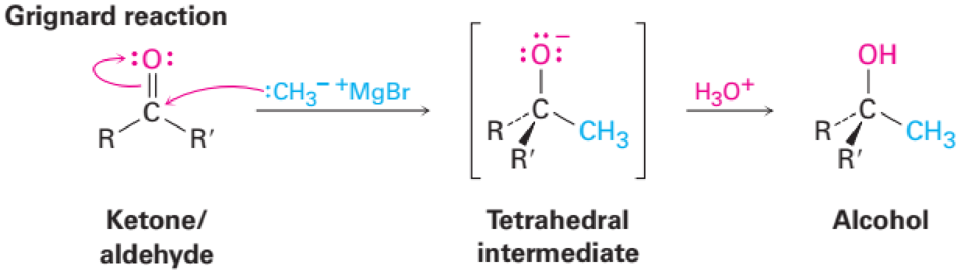
Nucleophilic Addition



Formation of an Alcohol

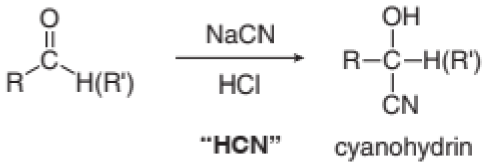
The simplest reaction of a tetrahedral alkoxide intermediate is protonation to yield an alcohol. Such as, reduction of aldehydes and ketones with hydride reagents such as $NaBH_4$ and $LiAlH_4$ and during Grignard reactions. During a reduction, the nucleophile that adds to the carbonyl group is a hydride ion, (H:-), while during a Grignard reaction, the nucleophile is a carbanion, (R_3C:-).





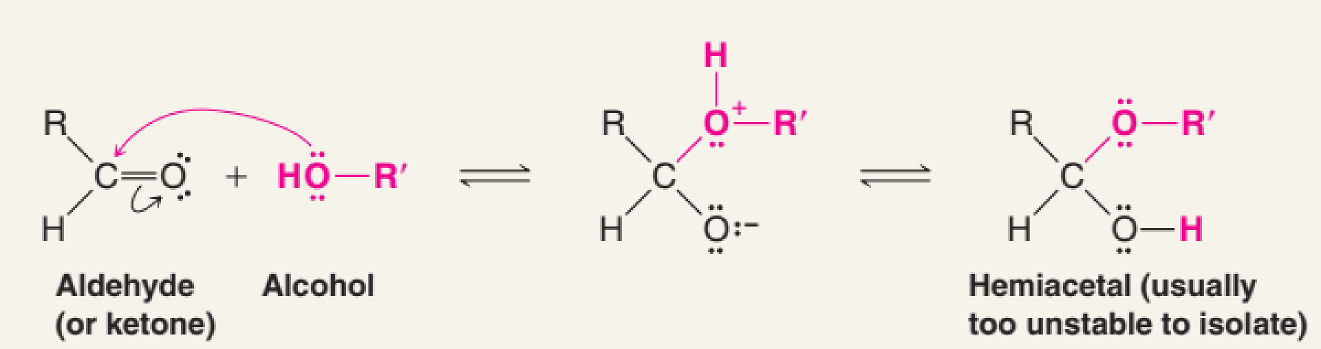
Formation of cyanohydrin

Treatment of an aldehyde or ketone with NaCN and a strong acid such as HCl adds the elements of HCN across the carbon–oxygen π bond, forming a cyanohydrin. This reaction adds one carbon to the aldehyde or ketone, forming a new carbon–carbon bond.

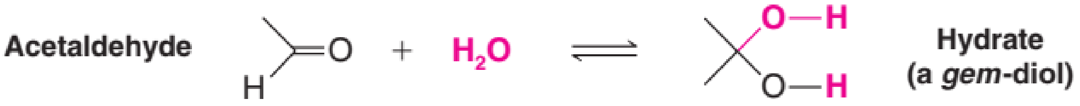


Formation of Hemiacetals and Acetals

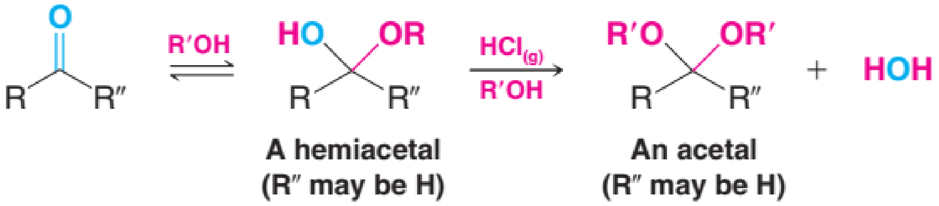
Aldehydes and ketones react with alcohols to form hemiacetals and acetals by an equilibrium reaction. The essential structural features of a hemiacetal are an OH and an OR group attached to the same carbon atom. The hemiacetal results by nucleophilic addition of an alcohol oxygen to the carbonyl carbon of an aldehyde or ketone.



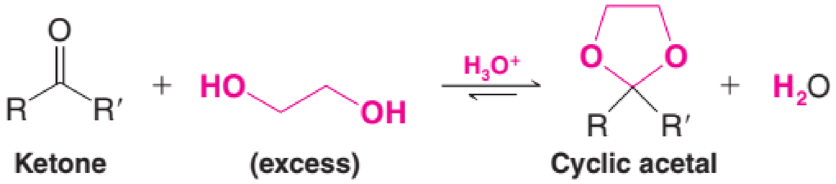
Aldehyde Hydrates, gem-Diols Dissolving an aldehyde such as acetaldehyde in water causes the establishment of an equilibrium between the aldehyde and its hydrate. This hydrate is in actuality a 1,1-diol, called a geminal diol (or simply a gem-diol). The gem-diol results from a nucleophilic addition of water to the carbonyl group of the aldehyde.



An acetal has two OR groups attached to the same carbon atom. If we take an alcohol solution of an aldehyde (or ketone) and pass into it a small amount of gaseous HCl, a hemiacetal forms, and then the hemiacetal reacts with a second molar equivalent of the alcohol to produce an acetal.

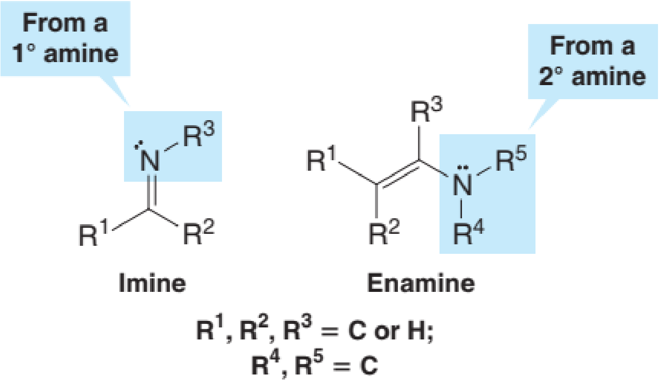


Cyclic acetal formation is favored when a ketone or an aldehyde is treated with an excess of a 1,2-diol and a trace of acid

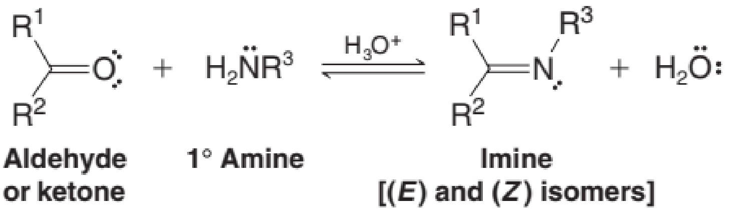


Reactions of Aldehydes and Ketones with Derivatives of Ammonia

Aldehydes and ketones react with primary amines to form imines and with secondary amines to form enamines. Imines have a carbon–nitrogen double bond. Enamines have an amino group joined to a carbon–carbon double bond (they are alkeneamines).



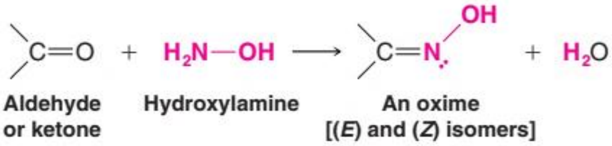
A general equation for the formation of an imine from a primary amine and an aldehyde or ketone is shown here. Imine formation is acid catalyzed, and the product can form as a mixture of (E) and (Z) isomers. Imine formation generally takes place fastest between pH 4 and 5 and is slow at very low or very high pH.



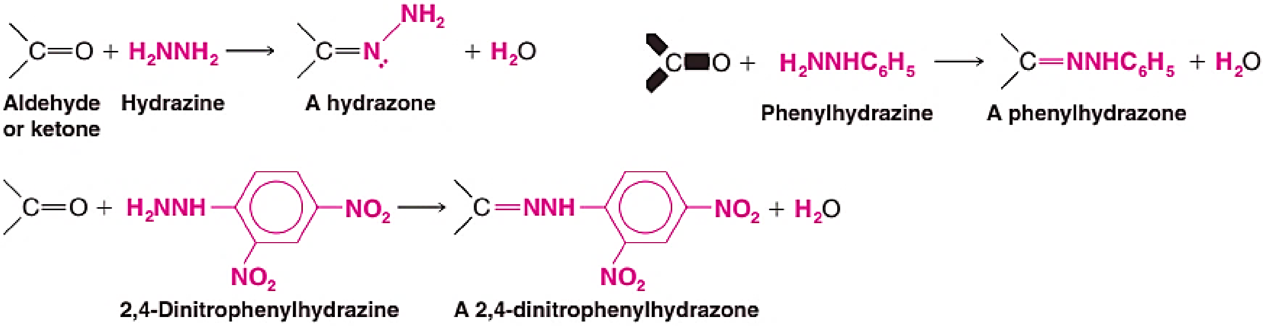
Oximes and Hydrazones, Compounds such as hydroxylamine (NH_2OH), hydrazine (NH_2NH_2), and substituted hydrazines such as phenylhydrazine ($C_6H_5NHNH_2$) and 2,4-dinitrophenylhydrazine, form C=N derivatives of aldehydes and ketones. The reactions of aldehydes and ketones with derivatives of ammonia are summarized below

1. Imine formation—reaction with a primary amine

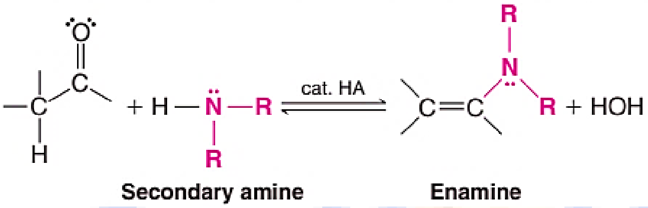
2. Oxime formation—reaction with hydroxylamine



3. Hydrazone and substituted hydrazone formation—reactions with hydrazine, phenylhydrazine, and 2,4-dinitrophenylhydrazine [each derivative can form as an (E) or (Z) isomer]

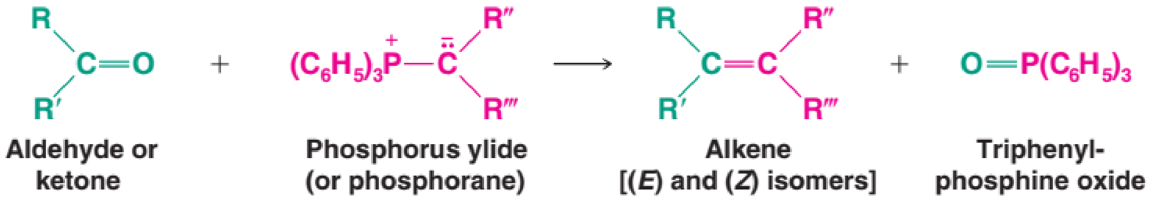


4. Enamine formation—reaction with a secondary amine



The Wittig Reaction

Aldehydes and ketones react with phosphorus ylides to yield alkenes and triphenyl-phosphine oxide (a by-product). This reaction is known as the Wittig reaction. The Wittig reaction uses a carbon nucleophile, the Wittig reagent, to form alkenes. When a carbonyl compound is treated with a Wittig reagent, the carbonyl oxygen atom is replaced by the negatively charged alkyl group bonded to the phosphorus—that is, the C = O is converted to a C = C. The ylide required for the reaction is a molecule with no net charge but which has a negative carbon atom adjacent to a positive heteroatom, which in the Wittig reaction is a phosphorus atom. Phosphorus ylides are also called phosphoranes.



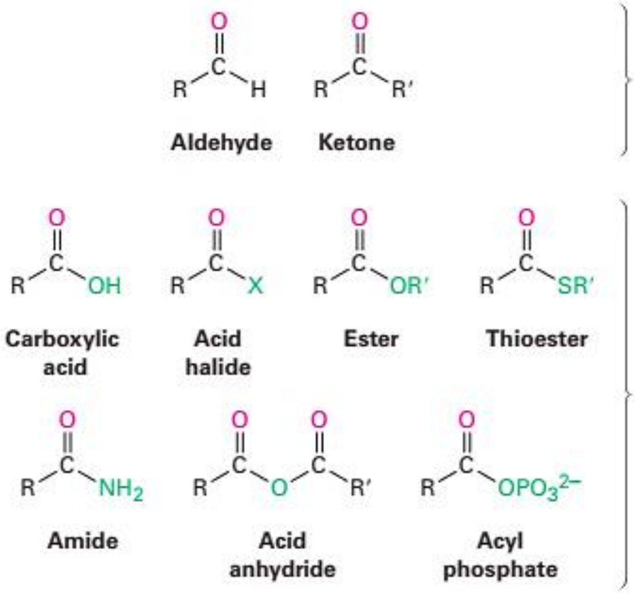
Spectroscopy of aldehyde and ketone

Aldehyde: C-H stretch, aldehyde hydrogen (-CHO), consists of a pair of weak bands, one at 2860–2800 cm^{-1} and the other at 2760–2700 cm^{-1}. C= O stretch appears in the range 1740–1725 cm^{-1} for normal aliphatic aldehydes.

Ketone: C=O stretch appears in the range 1720–1708 cm^{-1} for normal aliphatic ketones. C-CO-C Bending appears as a medium-intensity peak in the range 1300–1100 cm^{-1}.

Carboxylic Acids and Their Derivatives

Compounds that contain an electronegative atom bonded to the carbonyl group. These include carboxylic acids, acid chlorides, esters, and amides. Each of these compounds contains an electronegative atom (Cl, O, or N) capable of acting as a leaving group. Acid chlorides, esters, and amides are often called carboxylic acid derivatives, because they can be synthesized from carboxylic acids. Since each compound contains an acyl group (RCO^-), they are also called acyl derivatives.

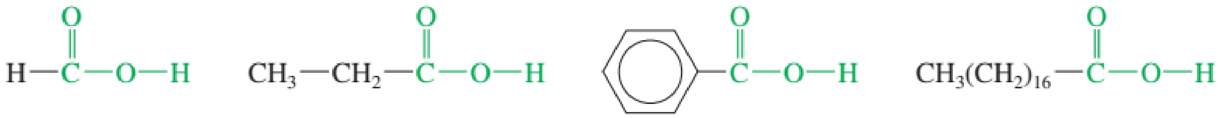


The –R′ and –H in these compounds *can't* act as leaving groups in nucleophilic substitution reactions.

The –OH, –X, –OR′, –SR, $-NH_2$, –OCOR′, and $-OPO_3^{2-}$ in these compounds *can* act as leaving groups in nucleophilic substitution reactions.

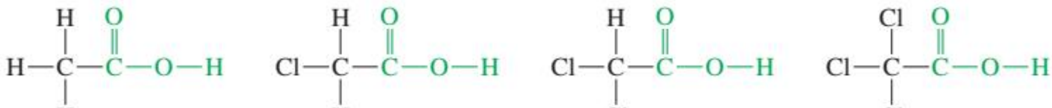
Carboxylic acid

Compounds of a carbonyl group and a hydroxyl on the same carbon atom is called a carboxyl group. Compounds containing the carboxyl group are distinctly acidic and are called carboxylic acids (with -COOH moiety). These compounds are abundant in nature, where they are responsible for some familiar odors. Carboxylic acids are classified according to the substituent bonded to the carboxyl group. An aliphatic acid has an alkyl group bonded to the carboxyl group, and an aromatic acid has an aryl group.

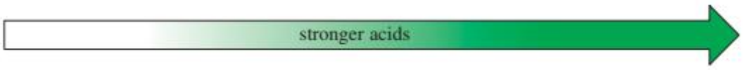


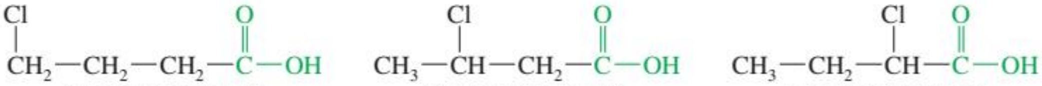
formic acid | propionic acid (an aliphatic acid) | benzoic acid (an aromatic acid) | stearic acid (a fatty acid)

A carboxylic acid donates protons by heterolytic cleavage of the acidic bond to give a proton and a carboxylate ion. Although carboxylic acids are not as strong as most mineral acids, they are still much more acidic than other functional groups we have studied. Electronegative atoms enhance the strength of an acid by withdrawing electron density from the carboxylate ion. This inductive effect can be quite large if one or more strongly electron-withdrawing groups are present on the a carbon atom. The magnitude of a substituent effect depends on its distance from the carboxyl group. Substituents on the carbon atom are most effective in increasing acid strength.



acetic acid $pK_a = 4.74$ | chloroacetic acid $pK_a = 2.86$ | dichloroacetic acid $pK_a = 1.26$ | trichloroacetic acid $pK_a = 0.64$



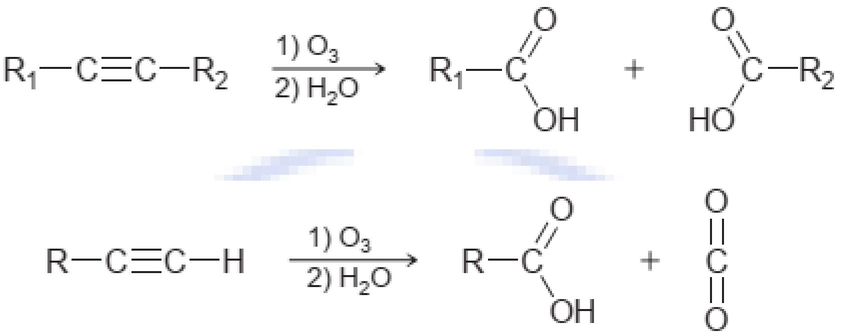


4-chlorobutanoic acid $pK_a = 4.52$ | 3-chlorobutanoic acid $pK_a = 4.05$ | 2-chlorobutanoic acid $pK_a = 2.86$

Preparation of Carboxylic Acids

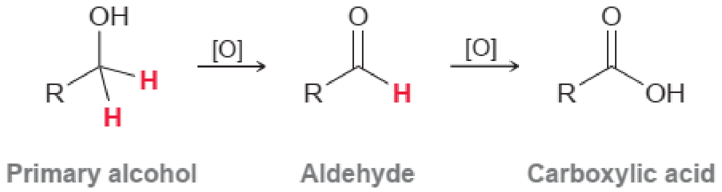
Oxidative Cleavage Of Alkynes

When treated with ozone followed by water, alkynes undergo oxidative cleavage to produce carboxylic acids. When a terminal alkyne undergoes oxidative cleavage, the terminal side is converted into carbon dioxide.



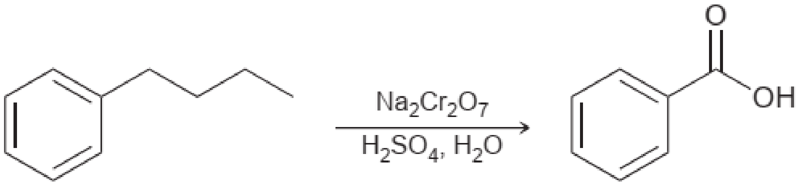
Oxidation of Alcohols

The outcome of an oxidation process depends on whether the starting alcohol is primary, secondary, or tertiary. Let's first consider the oxidation of a primary alcohol. Primary alcohols can be oxidized twice. The first oxidation produces an aldehyde, and then oxidation of the aldehyde produces a carboxylic acid.



Oxidation Of Alkylbenzenes

Any alkyl group on an aromatic ring will be completely oxidized to give benzoic acid, provided that the benzylic position has at least one hydrogen atom.

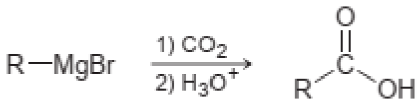


Hydrolysis of Nitriles

When treated with aqueous acid, a nitrile (a compound with a cyano group) can be converted into a carboxylic acid.

Carboxylation of Grignard Reagents

Carboxylic acids can also be prepared by treating a Grignard reagent with carbon dioxide.

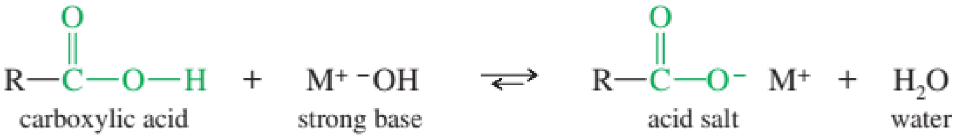


Reaction of Carboxylic Acid

Carboxylic acid undergo nucleophilic substitution reaction. The carbonyl group in carboxylic acids shows reactivity similar to that in aldehydes and ketones: It is subject to attack by nucleophiles at carbon and electrophiles at oxygen. However, the presence of the carboxy OH group in the structure adds another dimension to the chemical function of carboxylic acids: Just as in alcohols, this OH may be converted into a leaving group. As a result, after nucleophilic addition to the carbonyl carbon takes place, the leaving group may depart, resulting in a net substitution process and a new carbonyl compound. This section introduces this process and the general mechanisms by which it takes place. This type of reactivity is observed in the carboxylic acids and the carboxylic acid derivatives, substances with the general formula RCOL (L stands for leaving group).

Reaction With Base

Carboxylic acids exhibit mildly acidic protons. Treatment of a carboxylic acid with a strong base, such as sodium hydroxide, yields a carboxylate salt. Because mineral acids are stronger than carboxylic acids, addition of a mineral acid converts a carboxylic acid salt back to the original carboxylic acid.

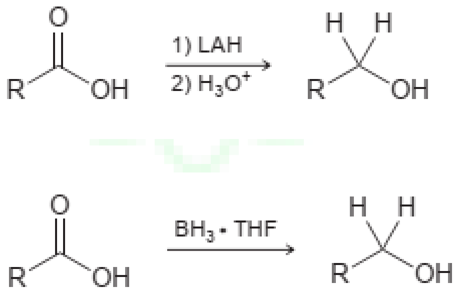


$$R-\overset{\overset{\large O}{\|}}{C}-O-H + M^{+}\,{}^{-}OH \rightleftarrows R-\overset{\overset{\large O}{\|}}{C}-O^{-}\;M^{+} + H_2O$$

$$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-O-H + Na^+\,{}^-OH \rightleftharpoons CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-O^- \; Na^+ + H_2O$$

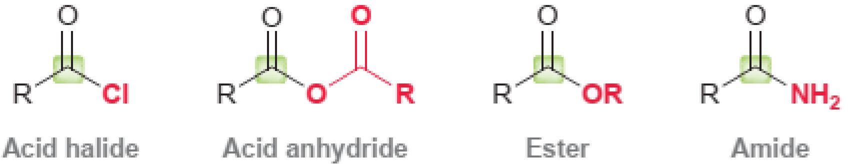
Redaction of Carboxylic Acids

Carboxylic acids are reduced to alcohols upon treatment with lithium aluminum hydride. An alternative method for reducing carboxylic acids involves the use of borane (BH_3).



Convert Carboxylic Acid to It Is Derivative

Carboxylic acids also undergo many other reactions that do not involve a change in oxidation state. Nucleophilic acyl substitution is the most common method for interconverting these derivatives. Replacement of the OH group with a different group (Z) does not involve a change in oxidation state if Z is a heteroatom (Cl, O, N, etc.). Compounds of this type are called carboxylic acid derivatives, and they will be the focus of the remainder of this chapter. The four most common types of carboxylic acid derivatives are shown below.

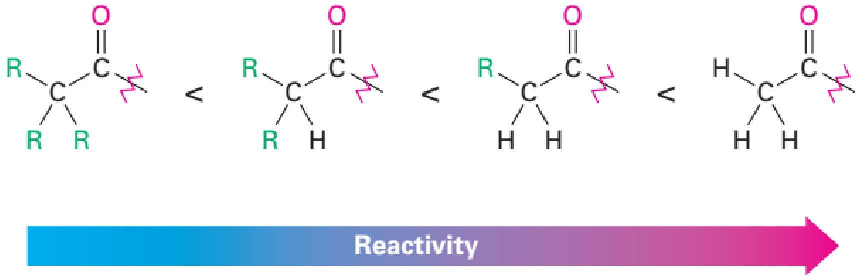


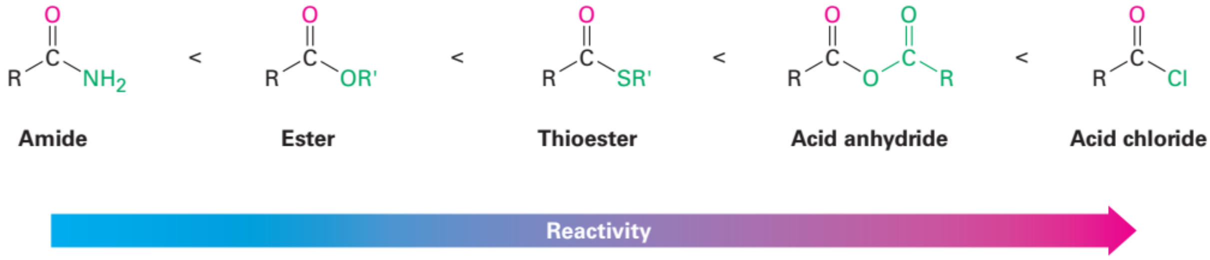
Spectroscopy Of Carboxylic Acid

O-H stretch, usually very broad (strongly H-bonded), at 3400–2400 cm^{-1}. C=O stretch, broad, occurs at 1730 –1700 cm^{-1}. C-O stretch occurs in the range 1320 –1210 cm^{-1}

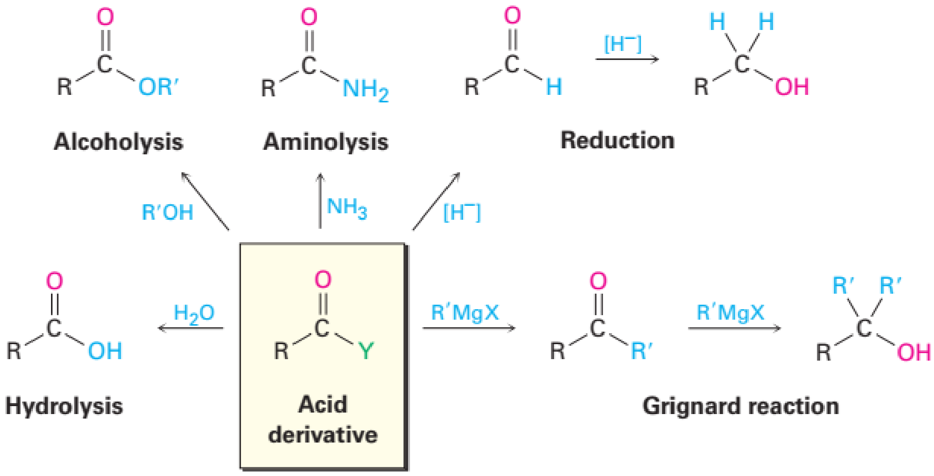
Carboxylic Acids Derivative

Steric and electronic factors are both important in determining reactivity. Sterically, we find within a series of similar acid derivatives that unhindered, accessible carbonyl groups react with nucleophiles more readily than do sterically hindered groups. Electronically, the strongly polarized acyl compounds react more readily than less polar ones. Thus, acid chlorides are the most reactive because the electronegative chlorine atom withdraws electrons from the carbonyl carbon, whereas amides are the least reactive. The reactivity order is.





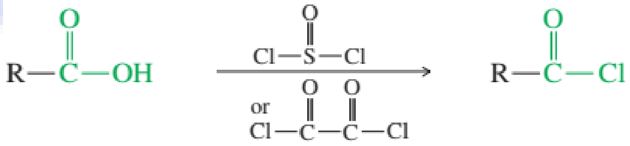
General reaction of acids derivative



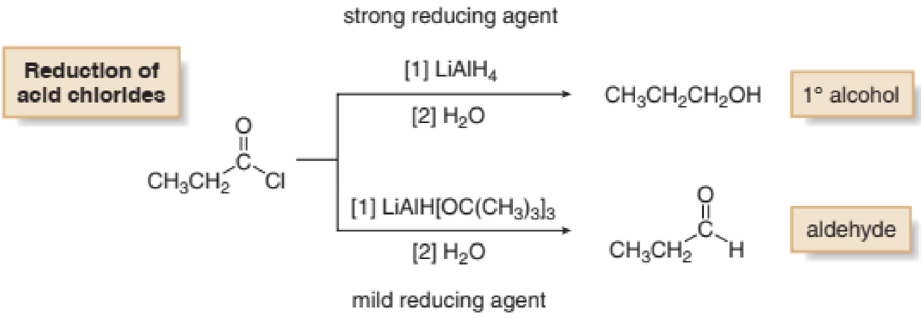
Acid Chlorides

Halide ions are excellent leaving groups for nucleophilic acyl substitution.

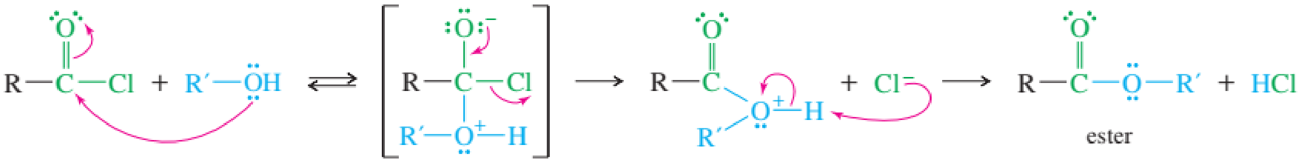
Therefore, acyl halides are useful intermediates for making acid derivatives. In particular, acid chlorides (acyl chlorides) are easily made and are commonly used as an activated form of a carboxylic acid. Acid chlorides react with a wide range of nucleophiles, generally through the addition–elimination mechanism of nucleophilic acyl substitution. The best reagents for converting carboxylic acids to acid chlorides are thionyl chloride and oxalyl chloride because they form gaseous by-products that do not contaminate the product. Oxalyl chloride is particularly easy to use because it boils at 62 °C and any excess is easily evaporated from the reaction mixture.



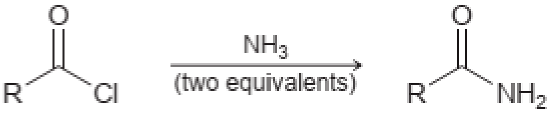
Acid chlorides can be reduced to either aldehydes or 1° alcohols, depending on the reagent. $LiAlH_4$ converts RCOCl to 1° alcohols. A milder reducing agent (DIBAL-H or $LiAlH[OC(CH_3)_3]_3$) converts RCOCl to RCHO at low temperatures.

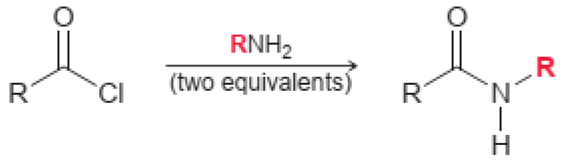


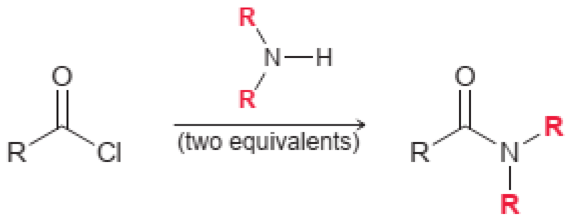
Acid chlorides react with alcohols to give esters through a nucleophilic acyl substitution by the addition–elimination mechanism



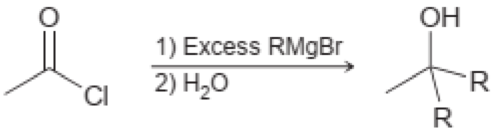
Aminolysis: Ammonia and amines react with acid chlorides to give amides







When (RCOCl) treated with a Grignard reagent, acid chlorides are converted into alcohols, with the introduction of two alkyl groups.

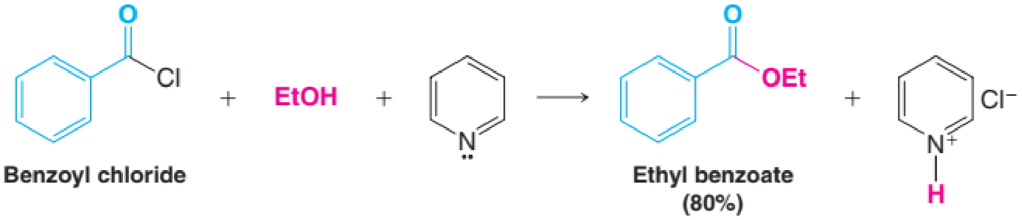


Spectroscopy Of Acid Chloride

C=O stretch occurs in the range 1810–1775 cm^{-1}. C-Clstretch occurs in the range 730–550 cm^{-1}.

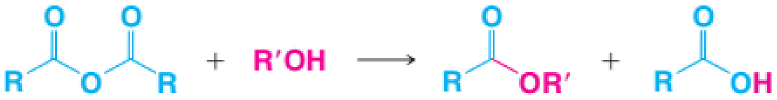
Ester

Carboxylic acid (and acid chloride) react with alcohol to form an ester

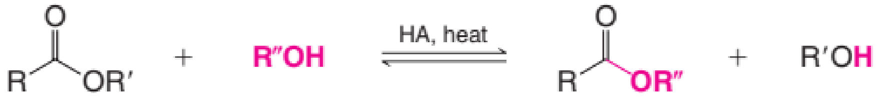


Benzoyl chloride

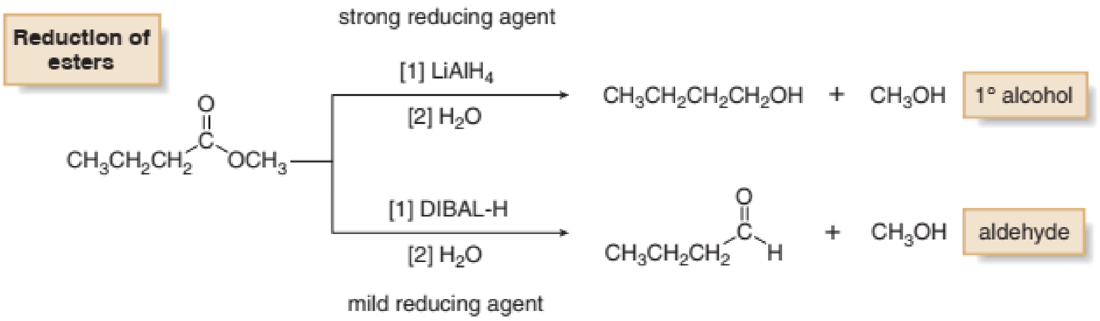
Ethyl benzoate (80%)



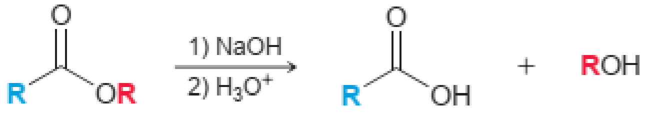
Esters can also be synthesized by transesterification



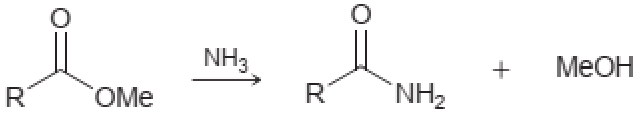
esters can be reduced to either aldehydes or 1° alcohols, depending on the reagent (like acid chloride).



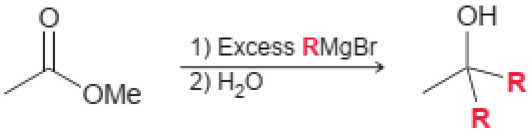
Esters can be converted into carboxylic acids by treatment with sodium hydroxide followed by an acid. This process is called saponification



Esters react slowly with amines to yield amides. This process has little practical utility, because preparation of amides is achieved more efficiently from the reaction between acid chlorides and ammonia or primary or secondary amines.



When treated with a Grignard reagent, esters are reduced to yield alcohols with the introduction of two alkyl groups.

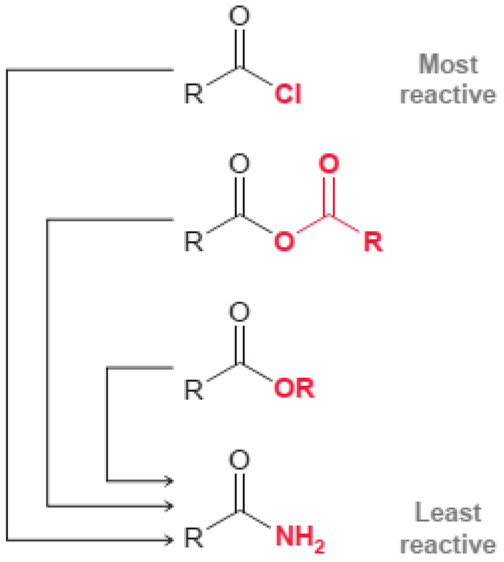


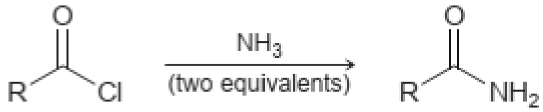
Spectroscopy Of Ester

C=O stretch appears in the range 1750–1735 cm^{-1}. C-O Stretch in two or more bands, one stronger and broader than the other, occurs in the range 1300–1000 cm^{-1}

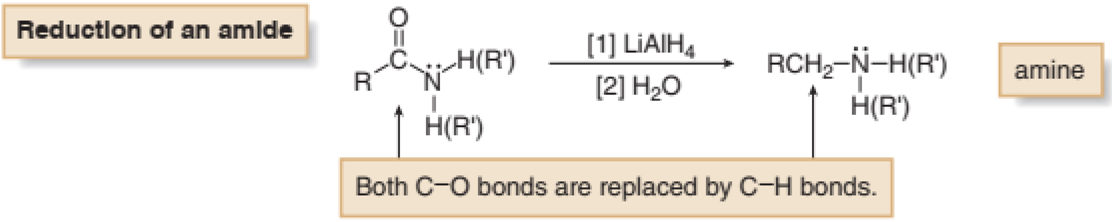
Amides

Amides can be prepared from any of the carboxylic acid derivatives. Although they can be prepared in a variety of ways, amides are most efficiently prepared from acid chlorides.

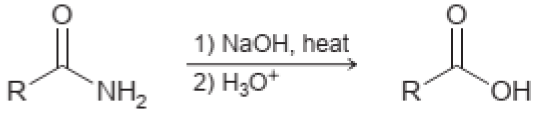




Redaction Of Amide By Lialh$_4$ Forms Amines.



Amides undergo hydrolysis to yield carboxylic acids plus ammonia or an amine on heating in either aqueous acid or aqueous base.

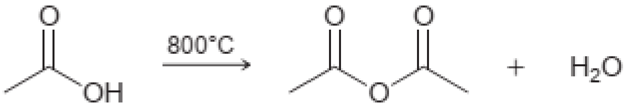


Spectroscopy Of Amide

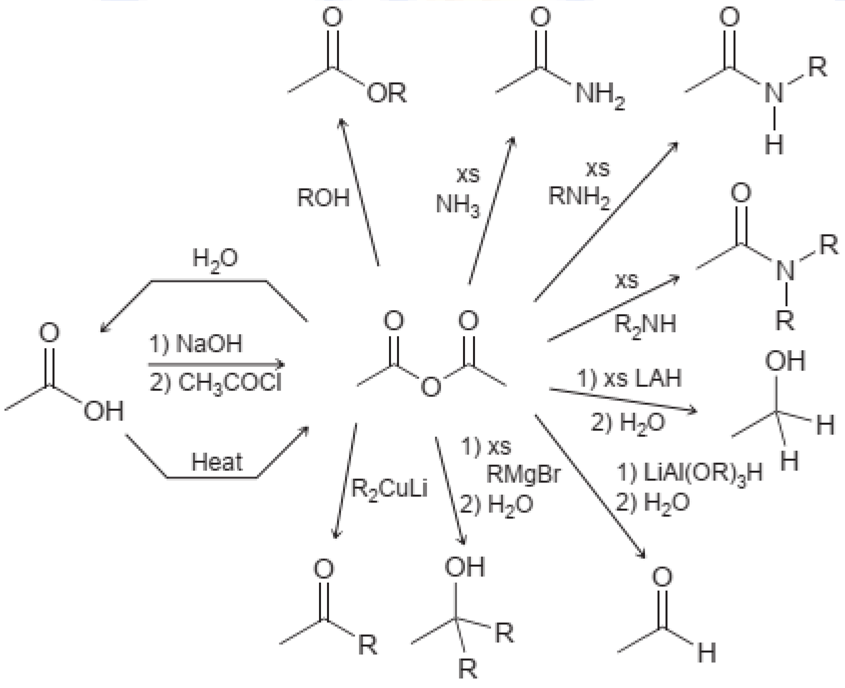
C=O stretch occurs at approximately 1700-1640 cm^{-1}. N-H stretch in primary amides (-NH_2) gives two bands near 3350 and 3180 cm^{-1}. Secondary amides have one band (INH) at about 3300 cm^{-1}. N-H bending occurs around 1640–1550 cm^{-1} for primary and secondary amides.

Acid Anhydrides

Carboxylic acids can be converted into acid anhydrides with excessive heating. This method is only practical for acetic acid, as most other acids cannot survive the excessive heat. An alternative method for preparing acid anhydrides involves treating an acid chloride with a carboxylate ion, which functions as a nucleophile.



The reactions of anhydrides are directly analogous to the reactions of acid chlorides. The only difference is in the identity of the leaving group. With an acid anhydride, the leaving group is a carboxylate ion, and the by product is therefore a carboxylic acid.



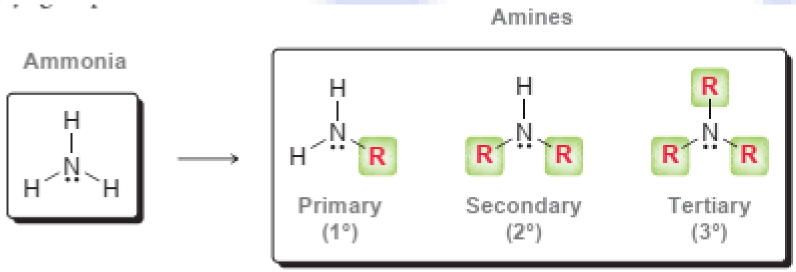
Each of these reactions produces acetic acid as a by-product. From a synthetic point of view, the use of anhydrides (rather than acid chlorides) involves the loss of half of the starting material, which is inefficient. For this reason, acid chlorides are more efficient as starting materials than acid anhydrides.

Spectroscopy Of Acid Anhydrides

C=O stretch always has two bands, 1830–1800 cm^{-1} and 1775–1740 cm^{-1}. C-O stretch (multiple bands) occurs in the range 1300–900 cm^{-1}.

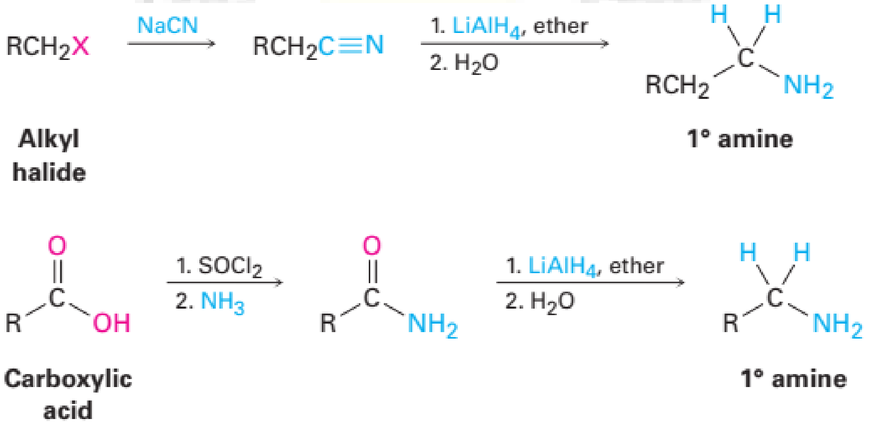
Amines

Amines are derivatives of ammonia in which one or more of the protons has been replaced with alkyl or aryl groups. Amines are classified as primary, secondary, or tertiary, depending on the number of groups attached to the nitrogen atom. Note that these terms have a different meaning than when they were used in naming alcohols. A tertiary alcohol has three groups attached to the α carbon, while a tertiary amine has three groups attached to the nitrogen atom.

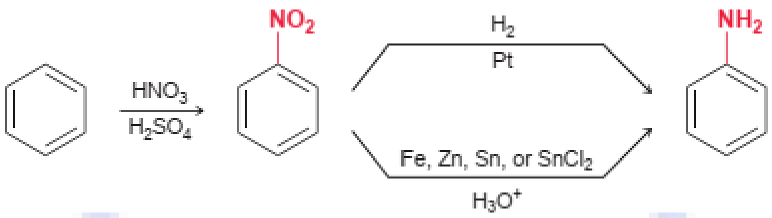


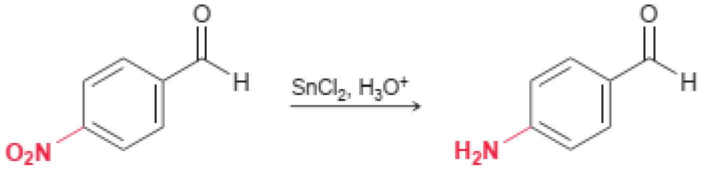
Synthesis of Amines

Reduction of nitriles, amides, and nitro compounds. Amines can be prepared by reduction of nitriles and amides with LiAlH4. The two-step sequence of S_N2 displacement with CN- followed by reduction thus converts an alkyl halide into a primary alkylamine having one more carbon atom. Amide reduction converts carboxylic acids and their derivatives into amines with the same number of carbon atoms.

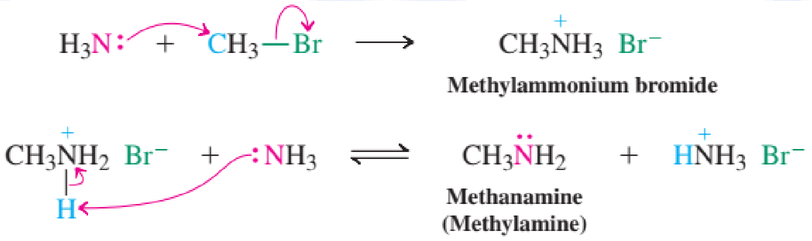


Aryl amines, such as aniline, can be prepared from benzene using the following approaches. Several reagents can be used to accomplish this reduction, including hydrogenation in the presence of a catalyst or reduction with iron, zinc, tin, or tin(II) chloride ($SnCl_2$) in the presence of aqueous acid.

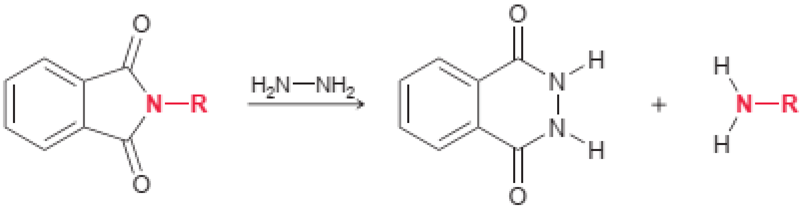




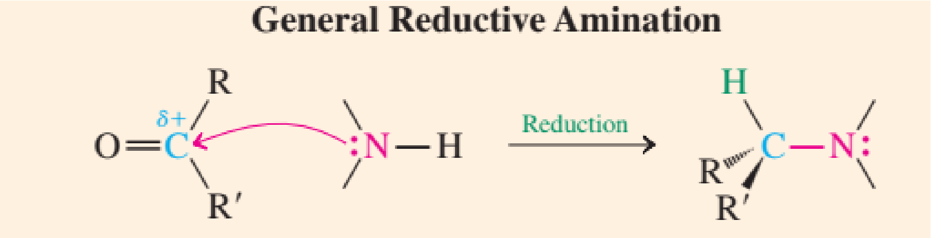
Ammonia is a very good nucleophile and will readily undergo alkylation when treated with an alkyl halide.

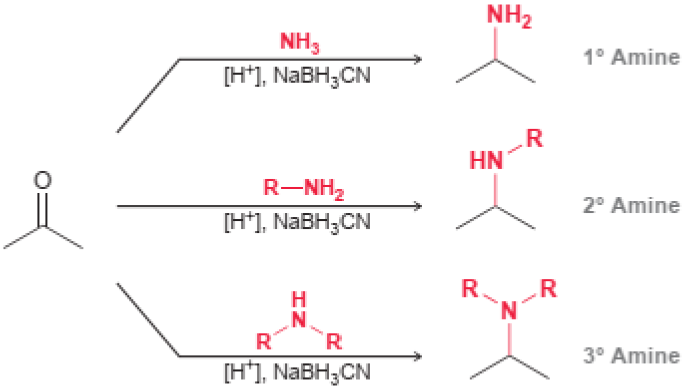


The Gabriel synthesis is another method for preparing primary amines while avoiding formation of secondary and tertiary amines. The key reagent is potassium phthalimide, which is prepared by treating phthalimide with potassium hydroxide. The reaction best with primary alkyl halides. It can be performed with secondary alkyl halides in many cases, but tertiary alkyl halides cannot be used. Acid-catalyzed or base-catalyzed hydrolysis is then performed to release the amine. Acidic conditions are more common than basic conditions.



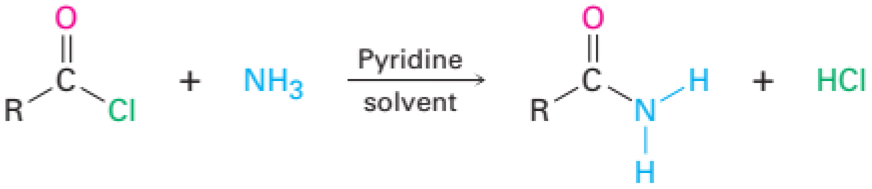
A more general method of amine synthesis, called reductive amination of aldehydes and ketones, allows the construction of primary, secondary, and tertiary amines. In this process, the carbonyl compound is exposed to an amine containing at least one N – H bond (NH_3, primary, secondary amines) and a reducing agent to furnish a new alkylated amine directly (a primary, secondary, or tertiary amine, respectively). The new C – N bond is formed to the carbonyl carbon of the aldehyde or ketone.


General Reductive Amination

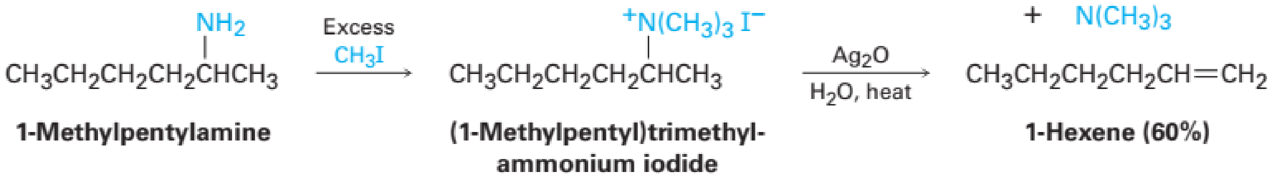


Reactions of Amines

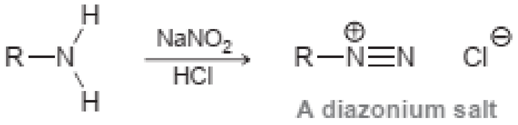
Alkylation and Acylation are the two most general reactions of amines. primary, secondary, and tertiary amines can be alkylated by reaction with a primary alkyl halide. Alkylations of primary and secondary amines are difficult to control and often give mixtures of products, but tertiary amines are cleanly alkylated to give quaternary ammonium salts. Primary and secondary (but not tertiary) amines can also be acylated by nucleophilic acyl substitution reaction with an acid chloride or an acid anhydride to yield an amide.

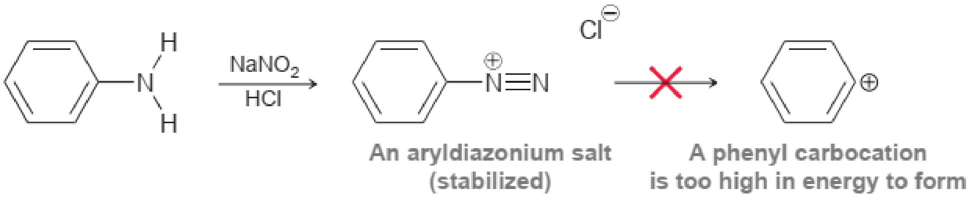


Amines can be converted into alkenes by an elimination reaction. But because an amide ion, NH_2^-, is such a poor leaving group, it must first be converted into a better leaving group. In the Hofmann elimination reaction, an amine is completely methylated by reaction with an excess amount of iodomethane to produce the corresponding quaternary ammonium salt. This salt then undergoes elimination to give an alkene on heating with a base, typically silver oxide Ag_2O.

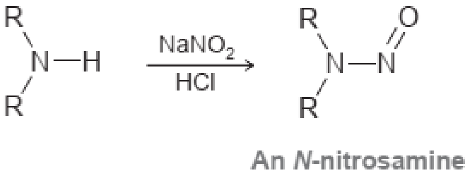


Amines are treated with in situ prepared nitrous acid The outcome of the reaction depends on whether the amine is primary or secondary. We will explore these possibilities separately, beginning with secondary amines. When a primary amine is treated with sodium nitrite and HCl, the reaction produces a diazonium salt This process is called diazotization. If, however, the primary amine is an aryl amine, then the resulting aryldiazonium salt is stable enough to be isolated. It does not liberate nitrogen gas, because that would involve formation of an aryl cation, which is too high in energy to form.





When a secondary amine is treated with sodium nitrite and HCl, the reaction produces an N-nitrosamine.



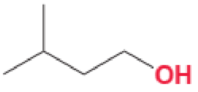
Spectroscopy Of Amine

N-H stretch occurs in the range 3500–3300 cm^{-1}. Primary amines have two bands. Secondary amines have one band. N-H bend in primary amines results in a broad band in the range 1640–1560 cm^{-1}, secondary amines absorb near 1500 cm^{-1}. C-N stretch occurs in the range 1350–1000 cm^{-1}.

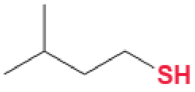
Thiols and Thioethers (Sulfides)

Sulfur is directly below oxygen in the periodic table (in the same column), and therefore, many oxygen-containing compounds have sulfur analogs. Sulfur analogs of alcohols contain an SH group in place of an OH group and are called thiols. The nomenclature of thiols is similar to that of alcohols, but the suffix of the name is “thiol” instead of “ol”: When another functional group is present in the compound, the SH group is named as a substituent and is called a mercapto group.

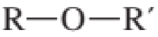
Thioethers, also called sulfides, are ethers with a sulfur atom replacing the oxygen atom of an ether, just like the sulfur in a thiol replaces the oxygen atom of an alcohol. The chemistry of thioethers is much like the chemistry of ethers, except that thioethers can undergo oxidation and alkylation of the sulfur atom. Sulfides are much more reactive than ethers.



3-Methyl-1-butanol



3-Methyl-1-butanethiol

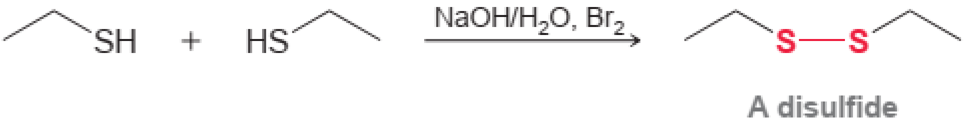


ether

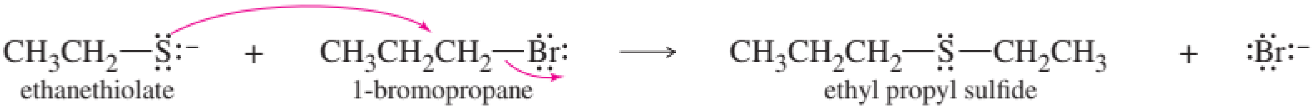
thioether
(sulfide)

Thiols can be prepared via an SN2 reaction between sodium hydrosulfide (NaSH) and a suitable alkyl halide. This reaction can occur even at secondary substrates without competing E2 reactions, because the hydrosulfide ion (HS-) is an excellent nucleophile and a poor base. When this nucleophile attacks a chirality center, inversion of configuration is observed.

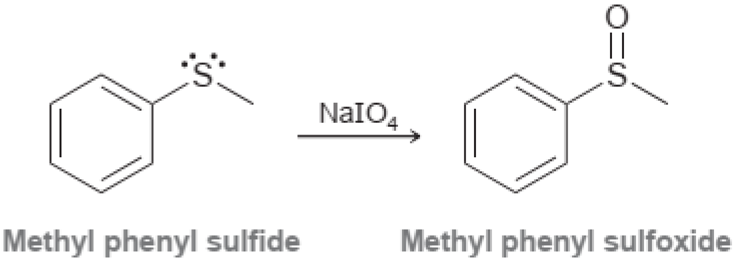
Thiols easily undergo oxidation to produce disulfides. The conversion of thiols into disulfides requires an oxidizing reagent, such as bromine in aqueous hydroxide.

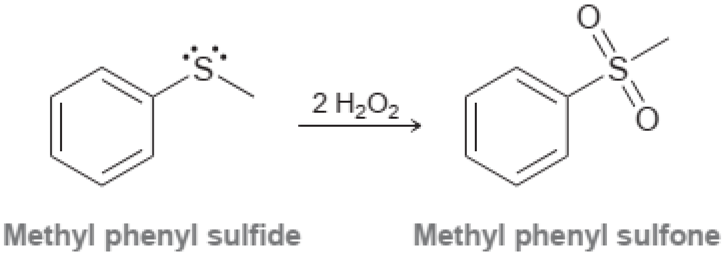


Sulfides are easily synthesized by the Williamson ether synthesis, using a thiolate ion as the nucleophile.

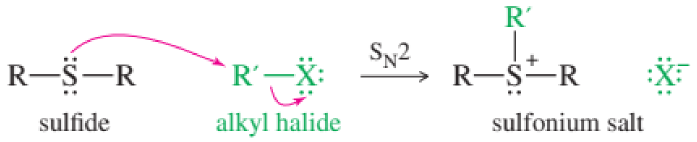


Sulfides also undergo oxidation to give sulfoxides and then sulfones. The initial product is a sulfoxide. If the oxidizing agent is strong enough and present in excess, then the sulfoxide is oxidized further to give the sulfone. For good yields of the sulfoxide without further oxidation to the sulfone, it is necessary to use an oxidizing reagent that will not oxidize the sulfoxide. Many such reagents are available, including sodium meta-periodiate, $NaIO_4$.

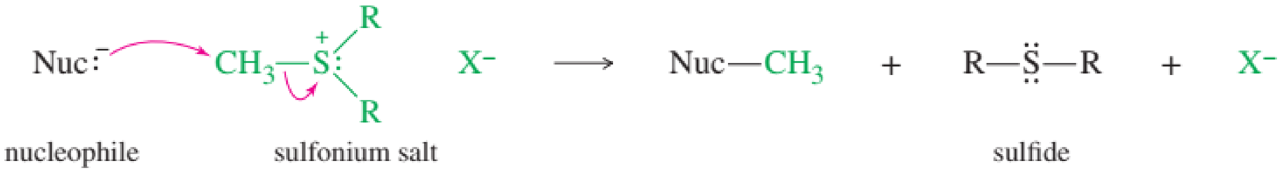




Sulfur compounds are more nucleophilic than the corresponding oxygen compounds, because sulfur is larger and more polarizable and its electrons are less tightly held in orbitals that are farther from the nucleus. Although ethers are weak nucleophiles, sulfides are relatively strong nucleophiles. Sulfides attack unhindered alkyl halides to give sulfonium salts.



Sulfonium salts are strong alkylating agents because the leaving group is an uncharged sulfide. Sulfur's polarizability enhances partial bonding in the transition state, lowering its energy.



Spectroscopy

S-H stretch, one weak band, occurs near 2550 cm $^{-1}$

Reference:

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2- Organic chemistry, 10th Ed, T. W. Craham Solomon & Craig B. fryhle
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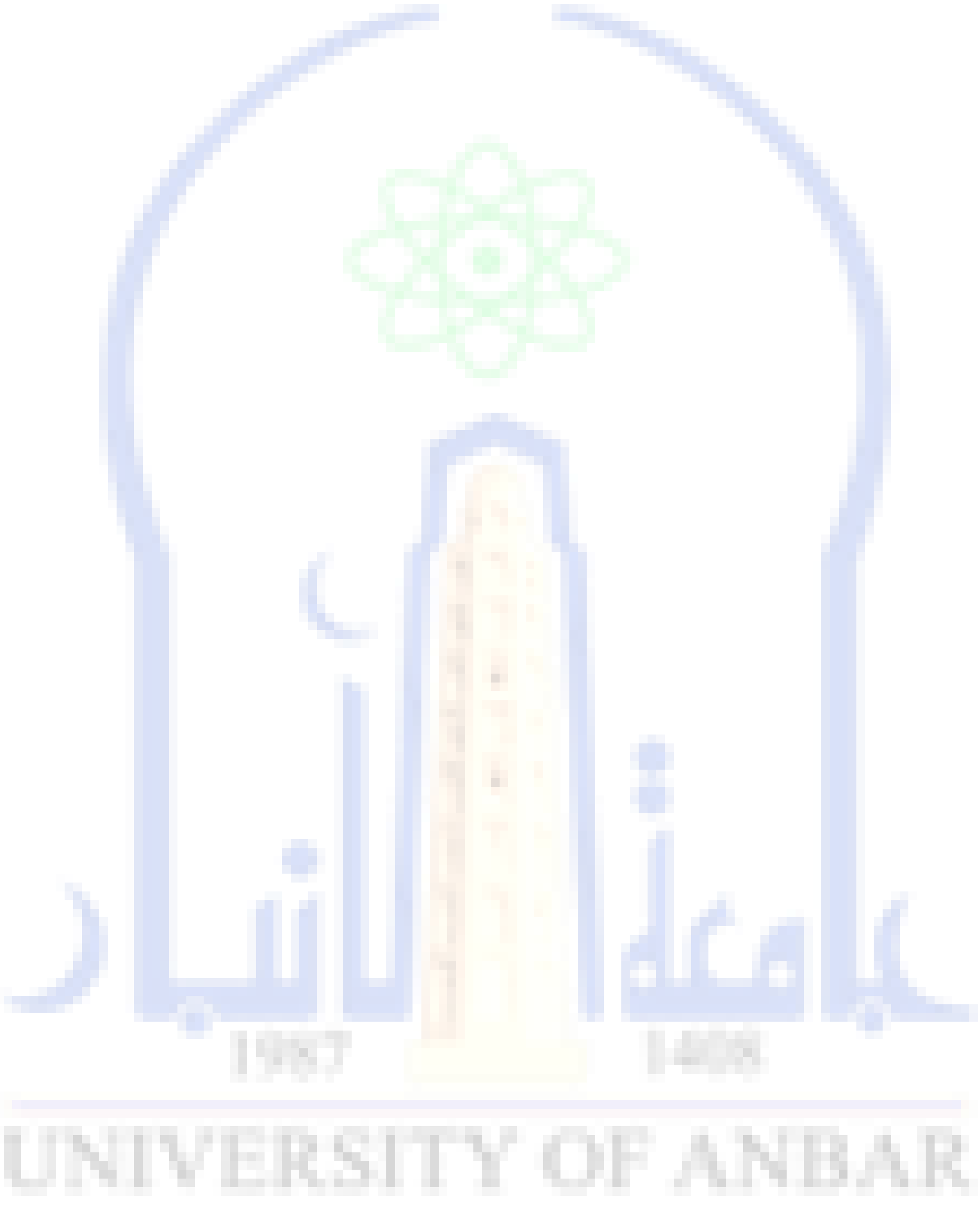
9- Organic Chemistry, 6th Ed, R. T. Morrison & R. N. Boyd
10- Introduction To Spectroscopy, 5th Ed, Donald L. Pavia, Gary M. Lampman, George S. Kriz, & James R. Vyvyan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