

Module 5 Alcohols, Amines, Ethers and Epoxides

Lecture 10 Alcohols

5.1 Introduction

Alcohols are aliphatic organic compounds that contain hydroxyl (-OH) groups. They can be synthesized by a wide range of methods, and the hydroxyl group may be converted to other functional groups. The structure of an alcohol resembles the structure of water where one of the hydrogen atoms of water is replaced by alkyl group. Although both have sp^3 -hybridized oxygen atoms, the C-O-H bond angle in methanol (108.9°) is considerably larger than the H-O-H bond angle in water (104.5°) because the methyl group is much larger than a hydrogen atom (Figure 1)

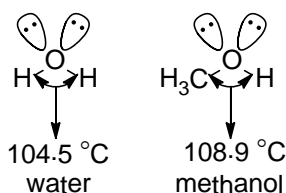
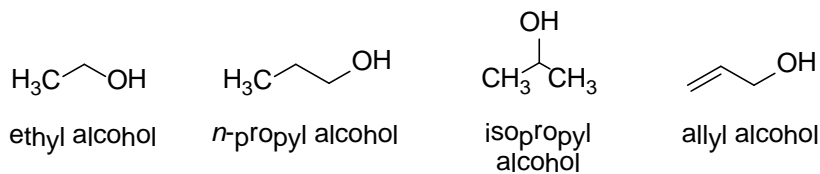


Figure 1

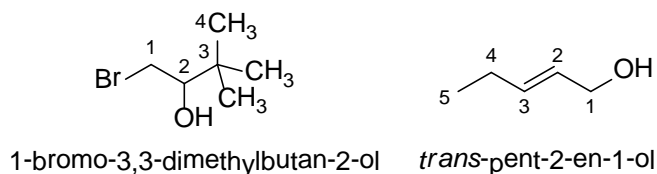
5.2 Nomenclature of Alcohols

- The common name of an alcohol is derived from the common name of the alkyl group and the word alcohol.

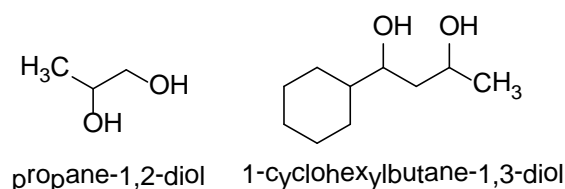


- Name the longest carbon chain that contains the carbon atom bearing the -OH group. Remove the final -e from the alkane name and add the suffix -ol to give the root name.
- Start numbering from the carbon which is nearest to the hydroxyl group, and use the appropriate number to indicate the position of the -OH group.

- Name all the substituents and give their numbers, as you would do for an alkane or an alkene



- Alcohols with two - OH groups are called diols or glycols. They are named like other alcohols except that the suffix *-diol* is used.



5.3 Physical Properties of Alcohols

Most of the common alcohols, up to about 11 or 12 carbon atoms, are liquids at room temperature. Ethyl alcohol and propane have similar molecular weights, yet their boiling points differ by about 120 °C. There is a large difference between the dipole moment of ethyl alcohol and propane. The polarized C-O and O-H bonds and the nonbonding electrons add to produce a dipole moment of 1.69 D in ethanol but the dipole moment of propane is only 0.08 D (Figure 2).

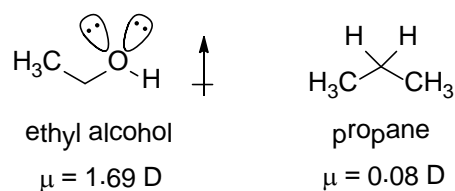


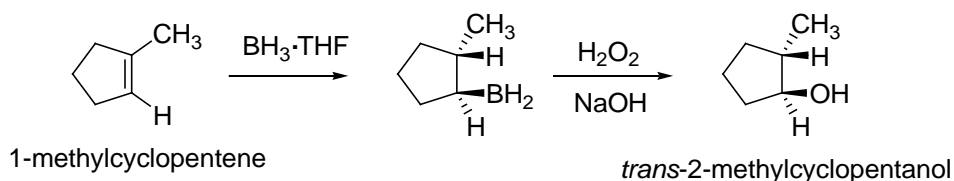
Figure 2

Hydrogen bonding is the major intermolecular attraction responsible for ethanol's high boiling point. The hydroxyl hydrogen of ethanol is strongly polarized forming a hydrogen bond with a pair of nonbonding electrons from the oxygen atom of another alcohol molecule.

Thus, several of the lower-molecular-weight alcohols are miscible with water and form hydrogen bond with water. Alcohols are much better solvents for polar substances. The water solubility decreases as the alkyl group becomes larger. Alcohols with one-, two-, or three-carbon alkyl groups are miscible with water. A four-carbon alkyl group is large enough to be immiscible. But *tert*-butyl alcohol is miscible as it has compact spherical shape.

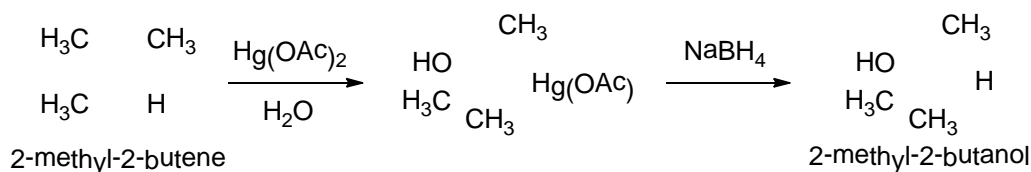
5.4 Synthesis of Alcohols

Hydroboration-oxidation of alkenes gives *anti*-Markovnikov alcohols with *syn*-stereochemistry. For example, hydroboration-oxidation of 1-methylcyclopentene leads to *syn*-addition to give *trans*-2-methylcyclopentanol (Scheme 1).



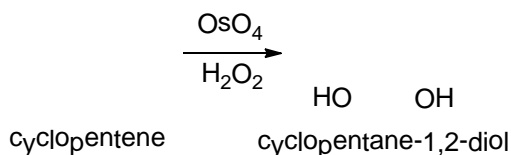
Scheme 1

Alcohols can also be prepared by oxymercuration-demercuration of alkenes, which gives the Markovnikov's products with *anti*-stereochemistry (Scheme 2).



Scheme 2

Diols can be prepared by *syn*-hydroxylation using osmium tetroxide (OsO_4). For example, the reaction of cyclopentene with OsO_4 gives cyclopentane-1,2-diol (Scheme 3).

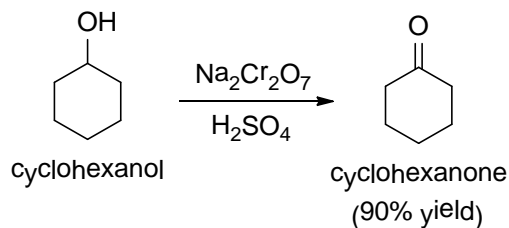


Scheme 3

5.5 Reactions of Alcohols

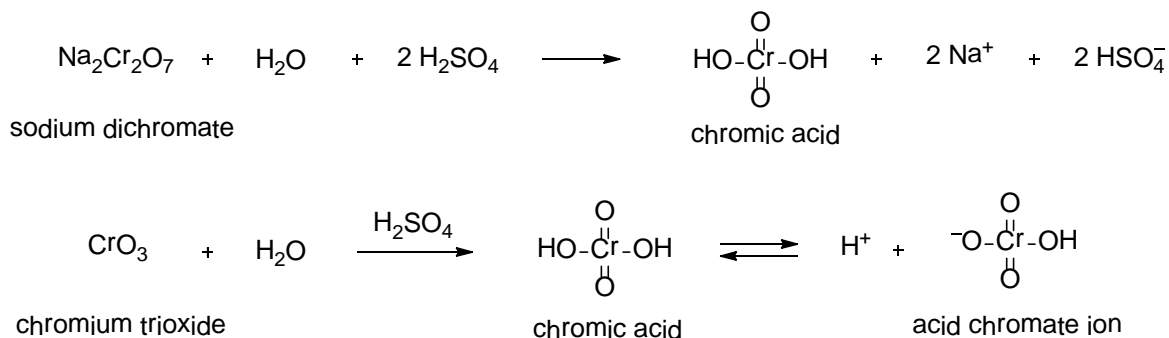
5.5.1 Oxidation

Primary and secondary alcohols are easily oxidized by reagents such as chromium oxides, permanganate, and nitric acid. Chromic acid is used to oxidize a secondary alcohol to give a ketone (Scheme 4).



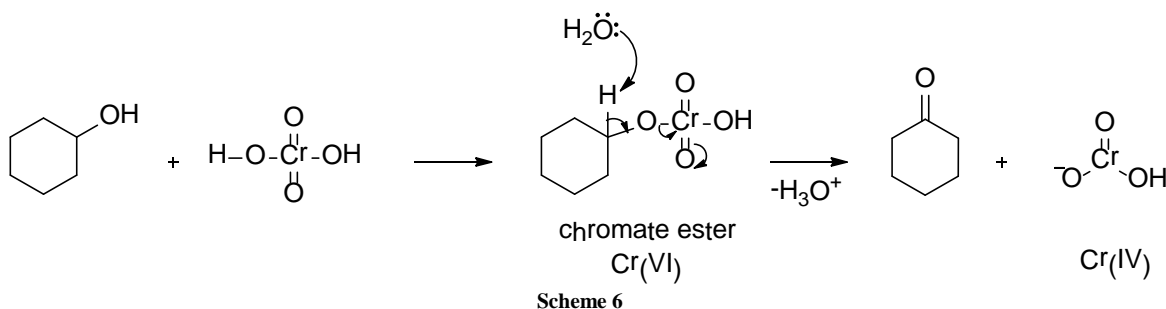
Scheme 4

The chromic acid reagent is prepared by dissolving sodium dichromate ($\text{Na}_2\text{Cr}_2\text{O}_7$) in a mixture of sulfuric acid and water, or by adding chromium trioxide (CrO_3) to dilute sulfuric acid (Scheme 5).

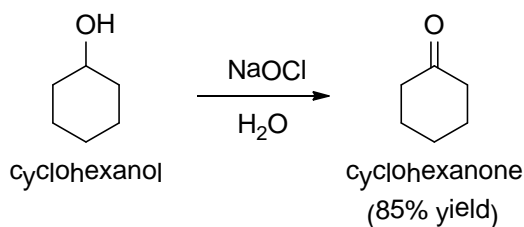


Scheme 5

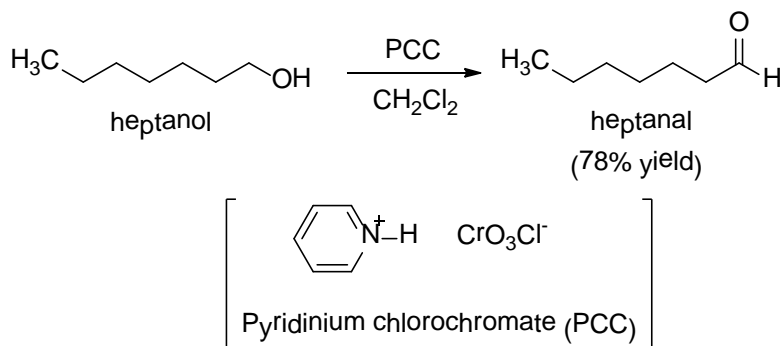
The mechanism of chromic acid oxidation probably involves the formation of a chromate ester. In the elimination, the carbinol carbon retains its oxygen atom but loses its hydrogen and makes the second bond to oxygen (Scheme 6). One can follow the progress of a chromic acid oxidation by observing the color change. The chromium(IV) species formed reacts further to give the stable reduced chromium(III) species. Both sodium dichromate and chromic acid are orange, but chromic ion (Cr^{3+}) is a deep blue.



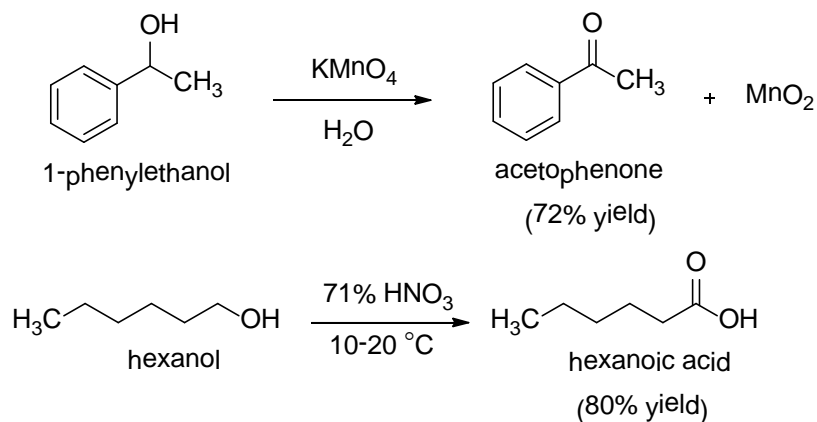
Chromium reagents produce hazardous byproducts that can be avoided by using simple oxidants such as sodium hypochlorite (Scheme 7).



In case of primary alcohols, the selective oxidation of primary alcohol to aldehydes can be accomplished using pyridinium chlorochromate (PCC) as a reagent (Scheme 8).

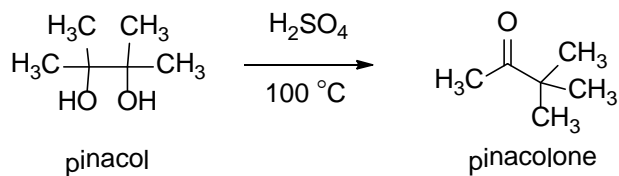


In contrast, the strong oxidizing agents such as permanganate and nitric acid oxidize secondary alcohols to ketones and primary alcohols to carboxylic acids (Scheme 11).



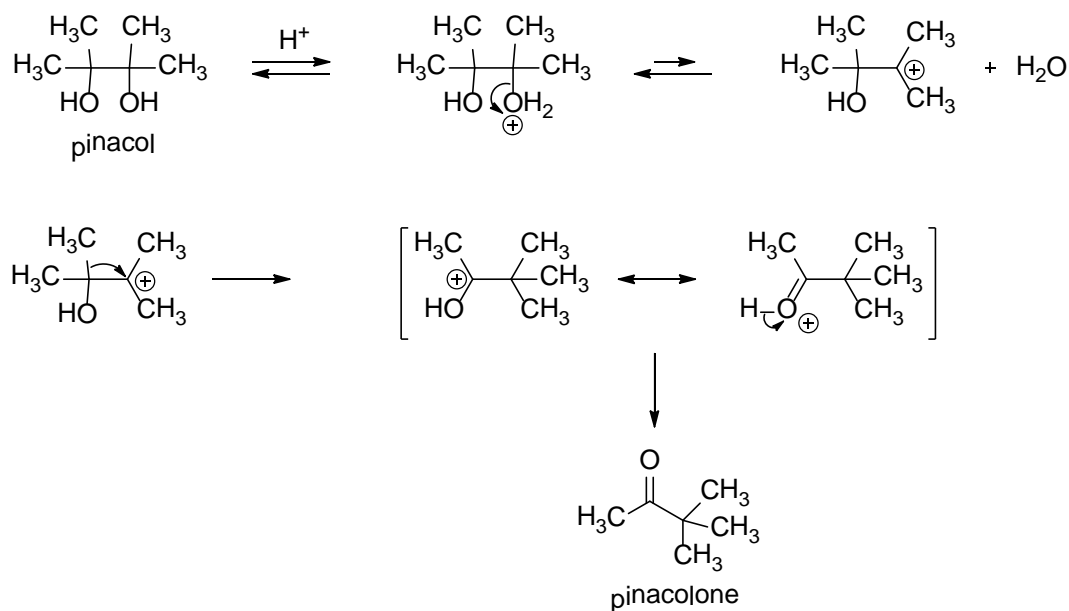
Scheme 11

The pinacol rearrangement is a unique reaction of diol (figure . Pinacol is heated to 100 °C in the presence of an acid to give pinacolone (Scheme 12).



Scheme 12

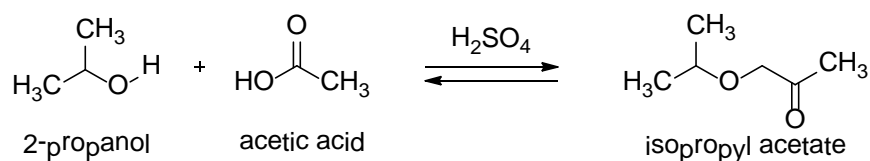
The first step is protonation of one of the hydroxyl oxygens. Loss of water gives a tertiary carbocation. Migration of a methyl group places the positive charge on the carbon atom bearing the second -OH group, where oxygen's nonbonding electrons help to stabilize the positive charge through resonance. This extra stability is the driving force for the rearrangement. Deprotonation of the resonance-stabilized cation gives the product, pinacolone (Scheme 13).



Scheme 13

5.5.2 Esterification

A carboxylic ester is formed by replacing the -OH group of a carboxylic acid with the -OR group of an alcohol. In the following example, isopropyl alcohol is mixed with acetic acid to give an ester where a drop of sulfuric acid is added as a catalyst (Scheme 14). Good yields can be obtained by adding a large excess of the alcohol or the acid which move the equilibrium towards right.



Scheme 14

Module 5 Alcohol, Amine, Ether and Epoxide

Lecture 11 Amines

5.6 Introduction

Amines are organic derivatives of ammonia in which the ammonia hydrogens are replaced by alkyl or aryl groups. Amine with one substituent called a primary amine. If it has two or three substituents, it is then called as secondary or tertiary amine (Figure 1).

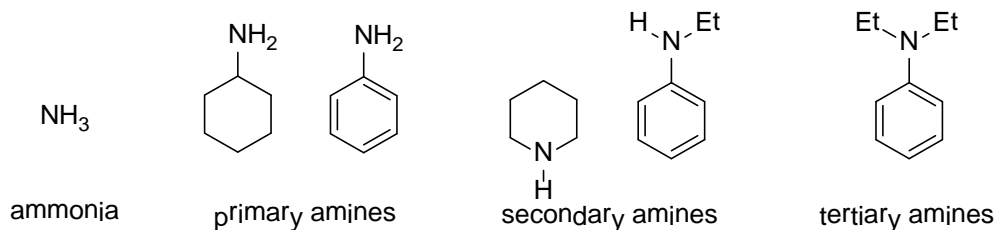


Figure 1

5.7 Nomenclature of Amines

A. Common Name

In common name, the suffix –amine is given after the names of the alkyl groups bonded to nitrogen. The prefixes *di-*, *tri-*, and *tetra-* are used to describe two, three, or four identical substituents. Aromatic and heterocyclic amines are known by historical names (Figure 2).

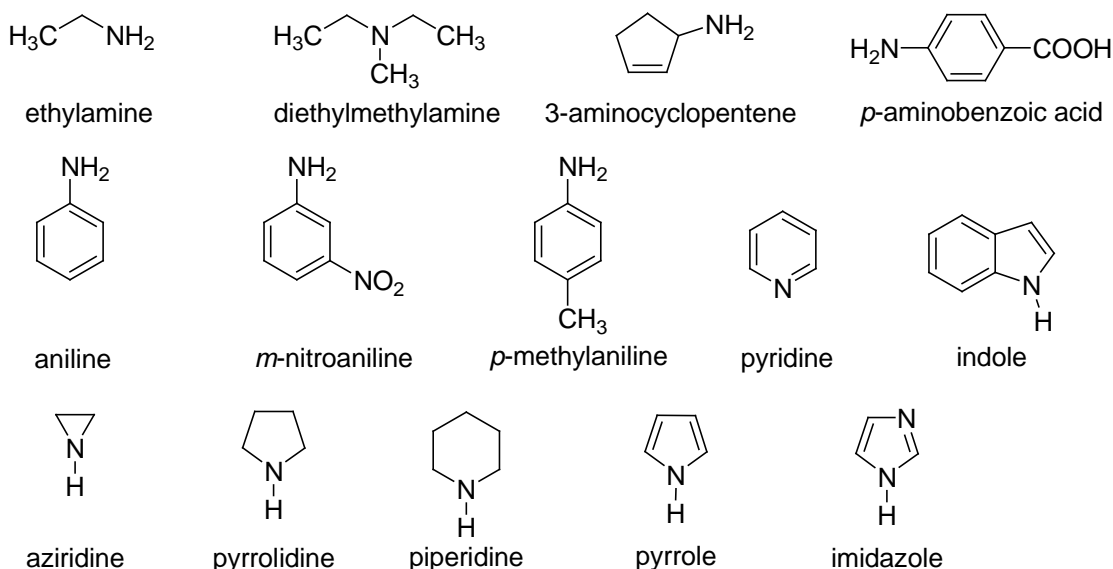
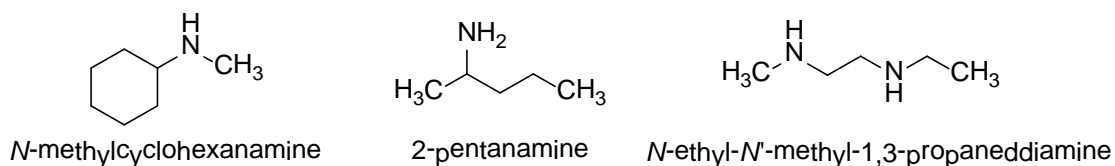


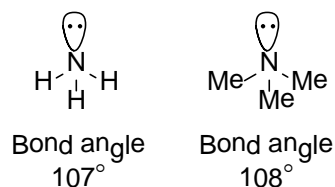
Figure 2

B. IUPAC name

- Find the longest continuous chain of carbon atoms and change the -e ending in the alkane to -amine
- Give the number to show the position of the amino group
- Prefix *N*- should be given for each substituent on nitrogen.

**5.8 Structure of Amines**

We know that ammonia has sp^3 hybridization and slightly distorted tetrahedral geometry (a pyramidal shape) where a lone pair of nonbonding electrons occupied one of the tetrahedral positions. The lone pair compresses the H-N-H bond angles from the ideal sp^3 bond angle of 109.5° to 107° . But substituted amines show less angle compression because the bulky substituents open the angle slightly. For example, bond angle of ammonia is 107° but it is 108° for trimethylamine (Figure 3).

**Figure 3**

Amine which has three different substituents is non-superimposable on its mirror image. So it appears to be chiral but its enantiomers cannot be resolved as they interconvert rapidly by nitrogen inversion. Lone pair on the nitrogen moves from one face of the molecule to the other. The nitrogen has sp^2 hybridized orbitals in the transition state, and the lone pair electrons occupy a p -orbital. Interconversion of (*R*)- and (*S*)-ethylmethylamine is given in Figure 4.

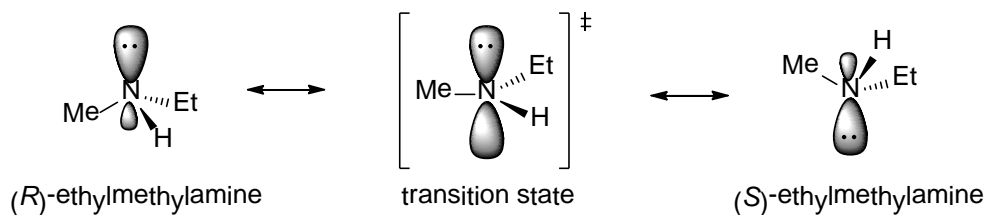


Figure 4

But in some cases enantiomers of amines can be resolved. For example, methyl ethyl isopropyl anilinium salt (a quaternary ammonium salt) can be resolved into enantiomers as there is no lone pair to undergo nitrogen inversion. Chiral aziridines may also be resolved into enantiomers. Such a compound has a higher activation energy for inversion and cannot attain the sp^2 hybrid transition state (Figure 5).

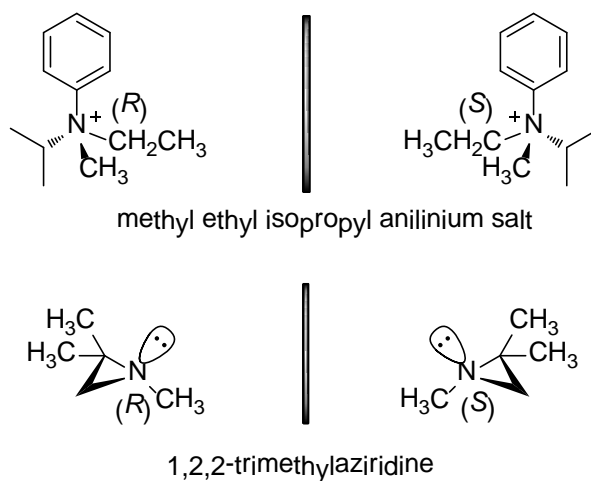
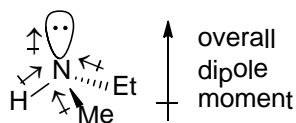


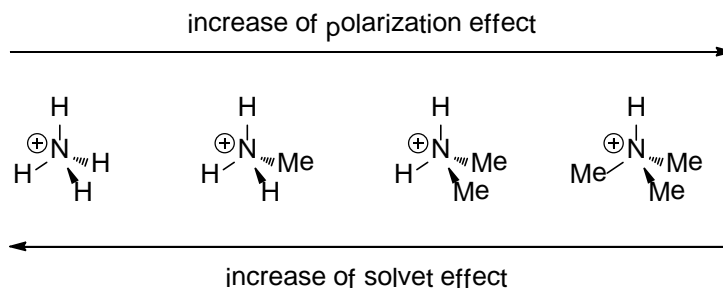
Figure 5

5.9 Physical Properties of Amines

Amines are strongly polar because they have large dipole moments. Primary and secondary amines do form hydrogen bonding but tertiary amines do not, because they have no N-H bonds. While comparing alcohols, amines form weaker hydrogen bond as nitrogen is less electronegative than oxygen. Tertiary amines have lower boiling points than primary and secondary amines of similar molecular weight. Amines, including tertiary amines, form hydrogen bonds with hydroxylic solvents such as water and alcohols. Therefore, amines tend to be soluble in alcohols, and the lower-molecular weight amines (up to six carbon atoms) are soluble in water.



Amines, like ammonia, are strong enough bases that they are completely protonated in dilute acid solutions. Basicity can be increased by increasing the availability of lone pair and stabilizing the resultant positive charge. When one hydrogen of ammonia is replaced by a methyl group, it stabilizes the resultant positive charge formed on protonation. Alkyl groups have the tendency to stabilize charge through a polarization effect. This effect increases on increasing numbers of the alkyl groups. There is another stabilizing effect called a solvent effect.



Every hydrogen attached directly to nitrogen can form hydrogen bond with solvent water and this also stabilizes the charge. This effect decreases with increasing numbers of alkyl groups. So the observed basicity is the combination of these two effects. Most of tertiary amines are less basic than that of primary amine because bulky groups in the tertiary amines make the lone pair less available. Lone pair held in an sp^2 or an sp orbital is much harder to protonate. So the basicity decreases from amine to imine to nitrile (Fig. 5.22).

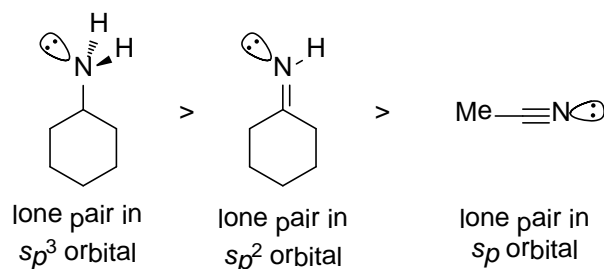


Figure 6

While comparing cyclohexanamine and aniline, aniline is a weak base because the lone pair can be delocalized into the benzene ring (Figure 7). In order for the lone pair to be fully conjugated with the benzene ring, the nitrogen would have to be sp^2 hybridized with the lone pair in the p -orbital. This is not found to be the case. Instead, the plane of the NH_2 group is about 40° away from the plane of the ring, which means the lone pair is partially conjugated into the ring.

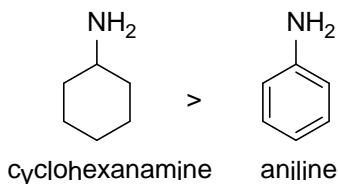
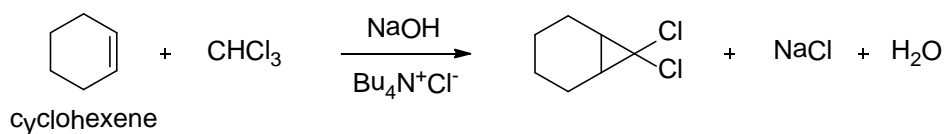


Figure 7

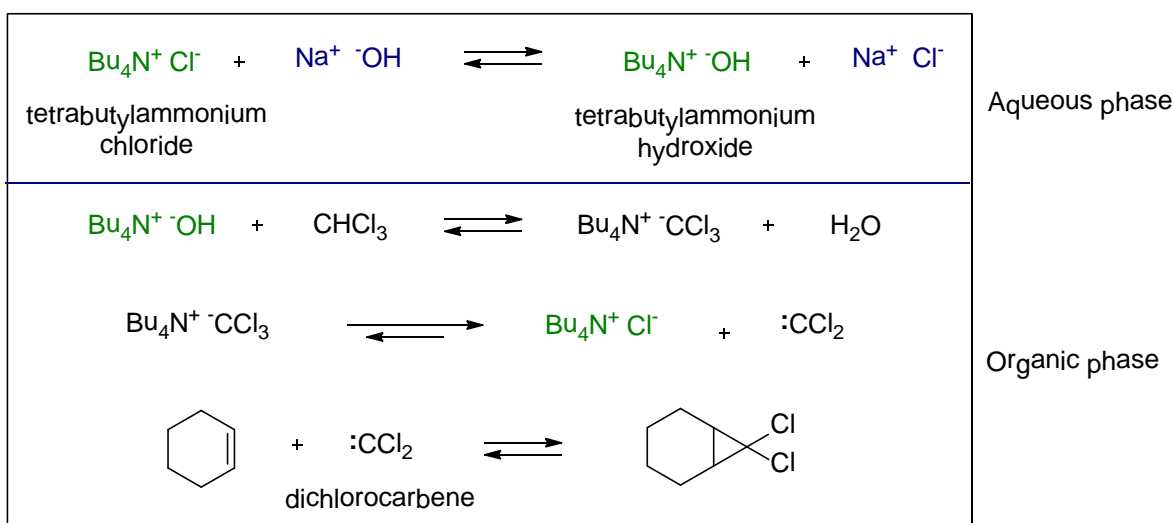
5.10 Phase-Transfer Catalysts

All four hydrogens of ammonium salt (NH_4^+) are replaced by alkyl or aryl groups. Such compounds are called quaternary ammonium salts, which are soluble in both water and non-polar organic solvents and can be used as Phase-Transfer catalyst. It is used to move ionic reagents into organic solvents. For example, dichlorocarbene adds to cyclohexene to form a cyclopropane ring (Scheme 1).



Scheme 1

In this case, sodium hydroxide dissolves in water but not in chloroform whereas cyclohexene dissolves in chloroform but not in water. Very little reaction occurs even at vigorous stirring. But reaction occurs easily after adding tetrabutylammonium chloride. Tetrabutylammonium chloride reacts with sodium hydroxide, in aqueous phase, to give tetrabutylammonium hydroxide which has large alkyl groups that enhance its solubility in organic solvents. Thus, tetrabutylammonium hydroxide migrates to organic phase where it reacts with chloroform to give dichlorocarbene, which reacts with cyclohexene to give the addition product (Scheme 2).

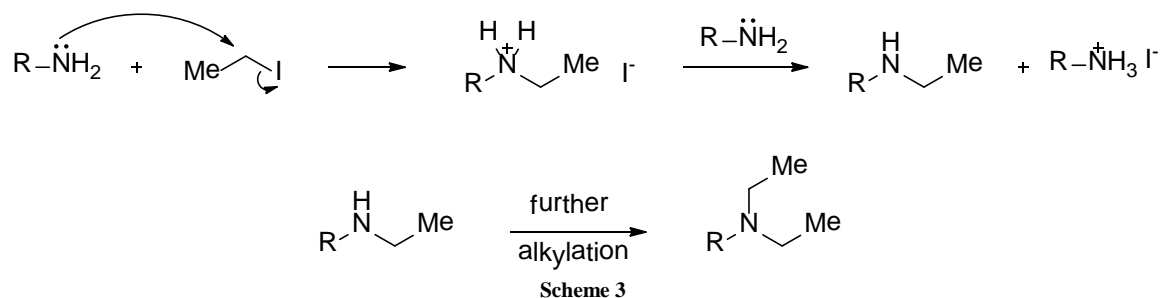


Scheme 2

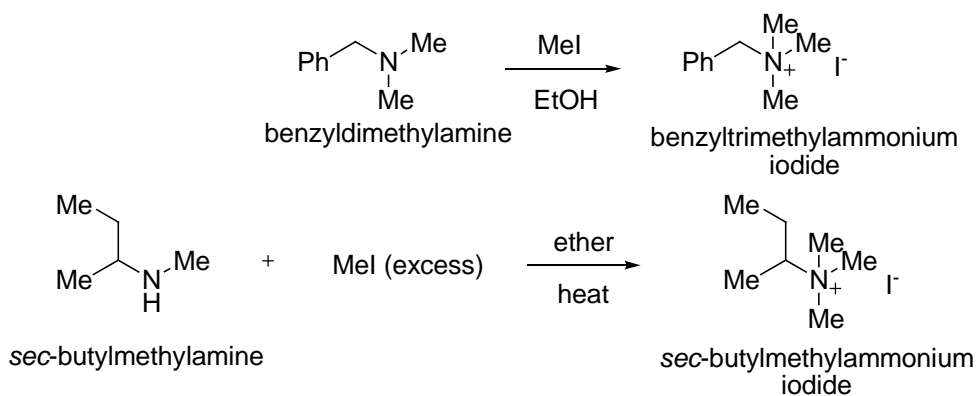
5.11 Reactions of Amines

5.11.1 Alkylation

Alkylation of amines with alkyl halides proceeds by S_N2 mechanism to give alkylammonium halides. If this alkylammonium halide has N-H bonds, further alkylation takes place which means that the reaction does not, usually, stop at one alkylation (Scheme 3).



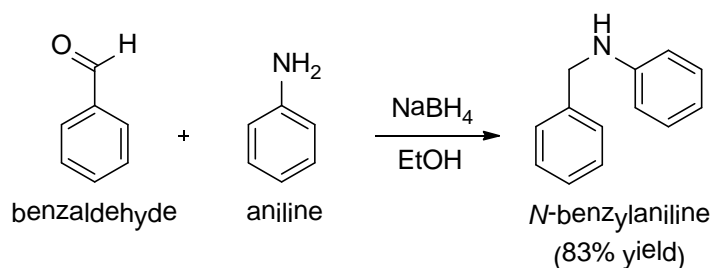
Amines can be converted into quaternary ammonium salts with excess alkyl halide under vigorous conditions. This process is called quaternization. When excess methyl iodide is used for this conversion, this process is called exhaustive methylation (Scheme 4).



Scheme 4

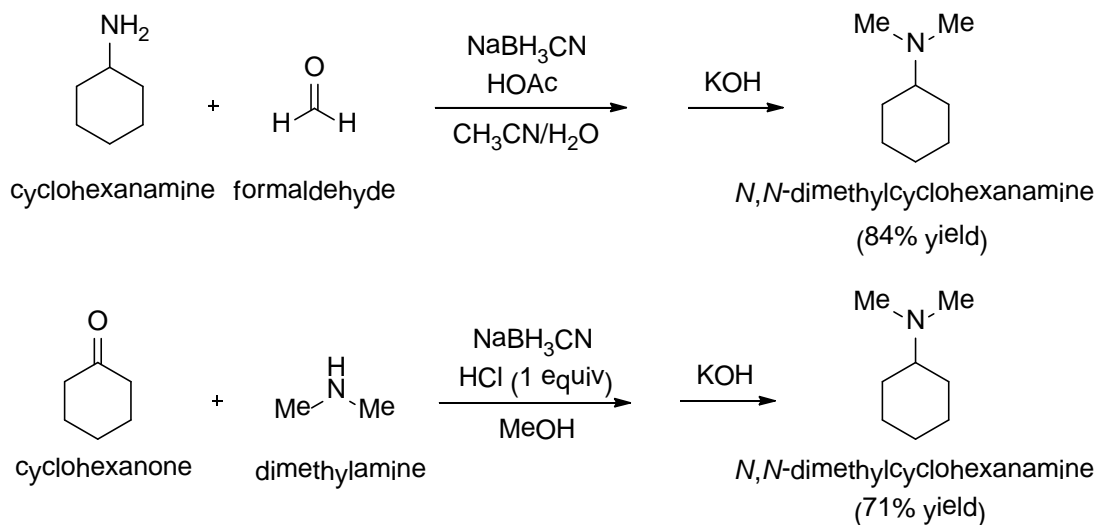
5.11.2 Condensation

Primary and secondary amines form imines and enamines when they react with either aldehydes or ketones. In the presence of a reducing agent such as sodium borohydride (NaBH_4) and sodium cyanoborohydride (NaBH_3CN), imines and enamines can be reduced to amines. Reduction of the $\text{C}=\text{N}$ double bond is similar to reduction of $\text{C}=\text{O}$ double bond. Nucleophilic substitution of aniline with benzaldehyde gives an imine which then reduced to *N*-benzylaniline by sodium borohydride (Scheme 5).



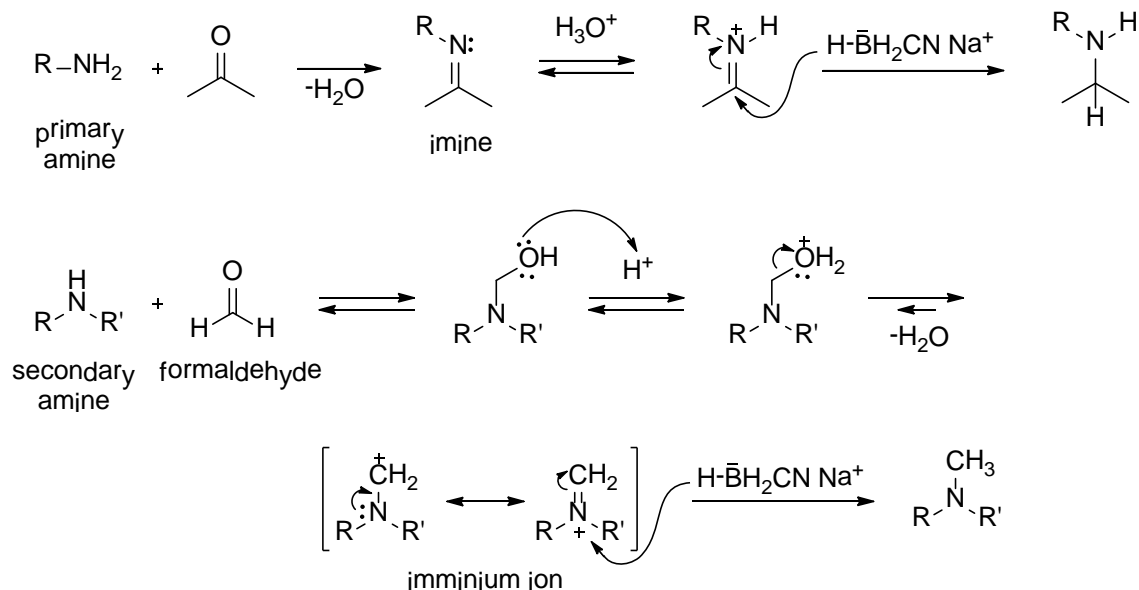
Scheme 5

Reductive amination with sodium cyanoborohydride is known as the **Borch reaction**. In the following example, both the reactions give the same product under given conditions (Scheme 6).



Scheme 6

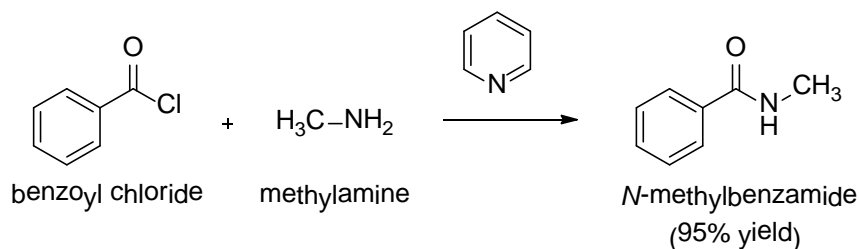
In the first case, primary amine forms an imine as an intermediate but in the second case, secondary amine forms an iminium ion as an intermediate which is rapidly attacked by hydride ion as shown in Scheme 7 .



Scheme 7

5.11.3 Acylation

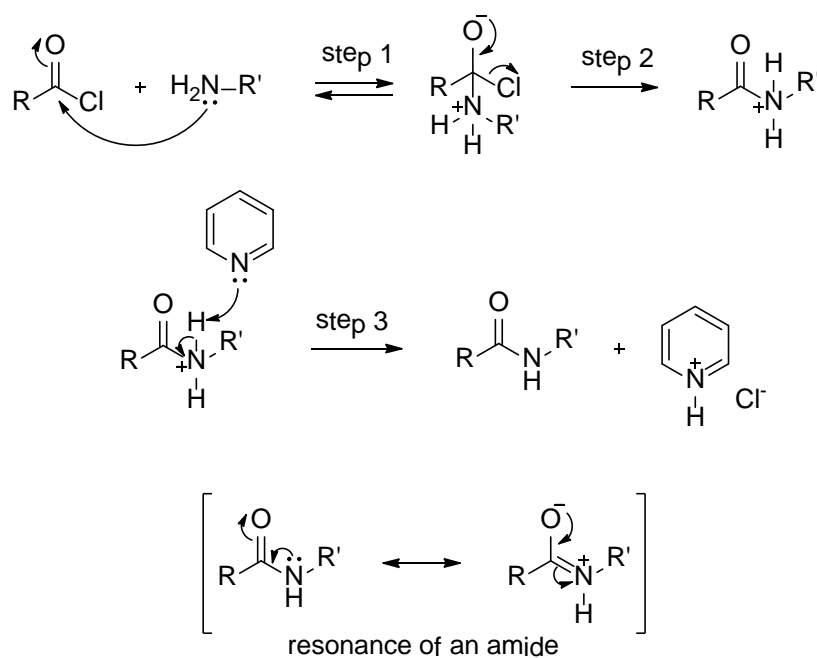
Primary and secondary amines react with acid halides to form amides. The acid chloride is more electrophilic and reactive than a ketone or an aldehyde because the electronegative chlorine atom attracts the electron density away from the carbonyl carbon. In the following example, benzoyl chloride reacts with methylamine to give *N*-methylbenzamide. A base such as pyridine or NaOH is often added to neutralize the HCl produced (Scheme 8).



Scheme 8

In the first step, amine attacks the electrophilic carbonyl group of the acid chloride to form a tetrahedral intermediate. Chloride ion is expelled from the tetrahedral intermediate in second step. Finally loss of a proton gives the amide (Scheme 9). The amide produced in this reaction usually does not undergo further acylation because amides are stabilized by a resonance structure that involves nitrogen's nonbonding electrons and places a

positive charge on nitrogen. As a result, amides are much less basic and less nucleophilic than amines.

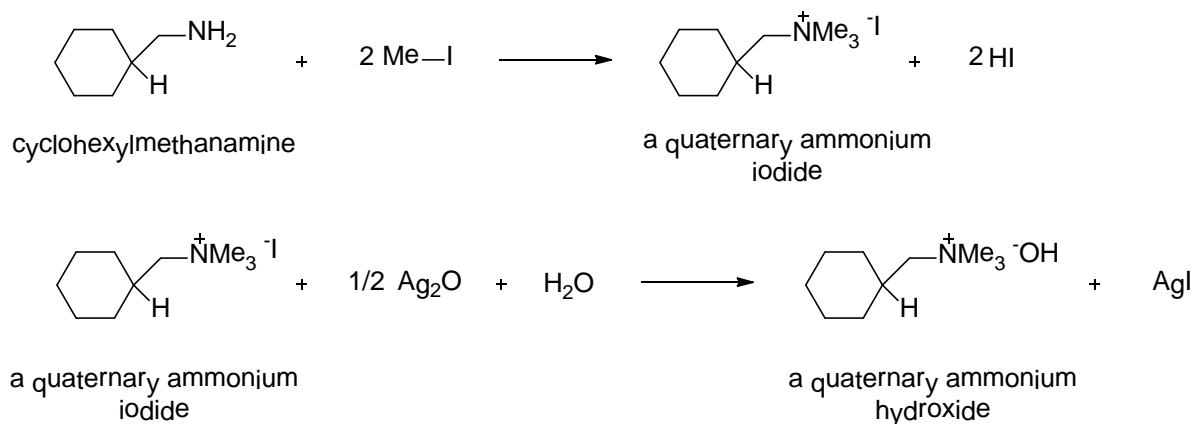


Scheme 9

5.11.4 Hofmann Elimination

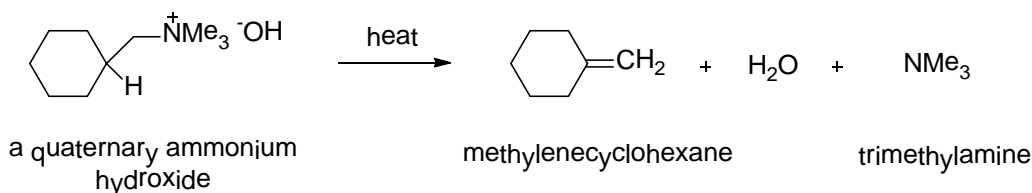
Alkenes can be prepared from amine by elimination reaction. Amines do not undergo elimination, however, because the leaving group would be an amide ion ($^-NH_2$) which is a poor leaving group. Exhaustive methylation of amino group converts it to a quaternary ammonium salt, a good leaving group, which can leave as a neutral amine. For example,

the exhaustive methylation by methyl iodide gives a quaternary ammonium iodide which can be converted to hydroxide salt by treatment with silver oxide (Scheme 10).



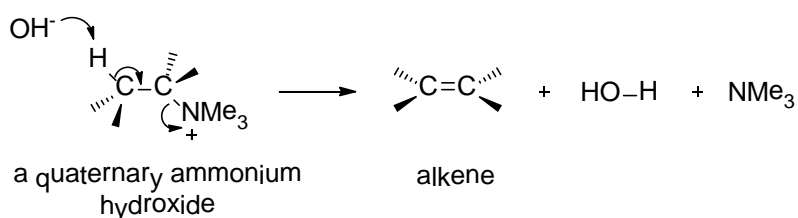
Scheme 10

When a quaternary ammonium hydroxide is heated, β -elimination reaction takes place to give an alkene (Scheme 11). This elimination reaction of a quaternary ammonium hydroxide is called the Hofmann elimination.



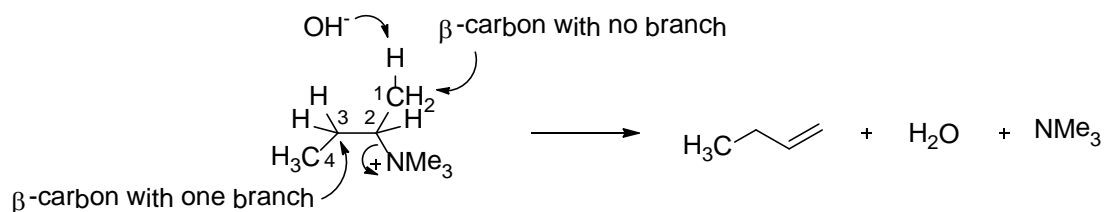
Scheme 11

The Hofmann elimination is an E2 elimination reaction where a proton and a tertiary amine are eliminated as shown in Scheme 12.



Scheme 12

The stereochemistry of Hofmann elimination can be explained by 2-butanamine. A base tends to abstract a proton from β -carbon. In 2-butanamine there are two β -carbon, one of them has one methyl branch and the other one has no such branch. Base abstracts a hydrogen from β -carbon which has no branch (Scheme 13).



Scheme 13

E2 elimination requires *anti*-coplanar arrangement of the proton and the leaving group. Consider the possible conformations of the transition state for elimination at the C2-C3 bond that give a minor product (a more substituted alkene). Although conformers **I** and **III** are suitable for *anti*-eliminations, they contain repulsion between methyl and trimethylammonium group. Conformer **II** does not have *anti*-coplanar arrangement of the proton and the leaving group (Figure 8). The relatively higher energy of these conformers causes the corresponding reactions to be relatively slow.

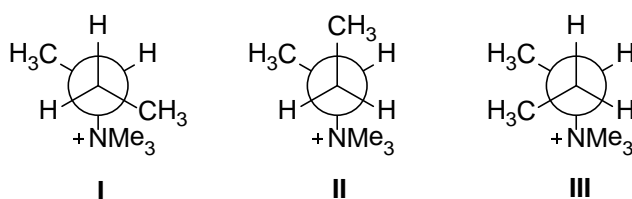


Figure 8

In contrast, elimination at the C1-C2 bond can occur with *anti*-stereochemistry because it has less steric repulsion and *anti*-coplanar arrangement of the hydrogen and the leaving group (Figure 9). The crowded conformations of the transition state (**I**, **II** and **III**) are required for Zaitsev elimination, which are relatively high energy. So the Hofmann product

predominates from lower energy conformer of the transition state. The Hofmann elimination is used to determine the structures of amines.

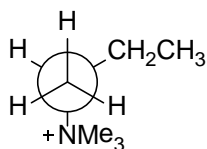
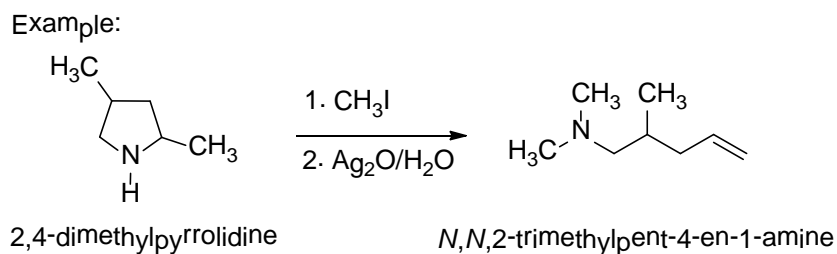
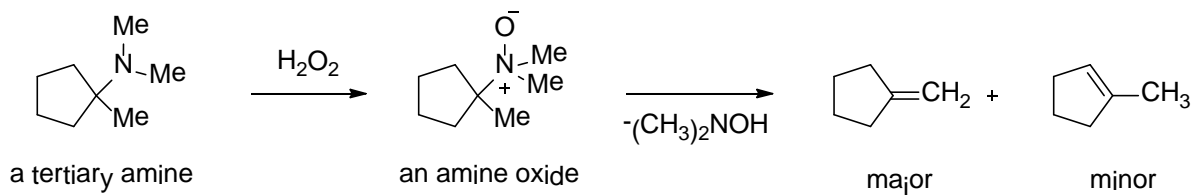


Figure 9



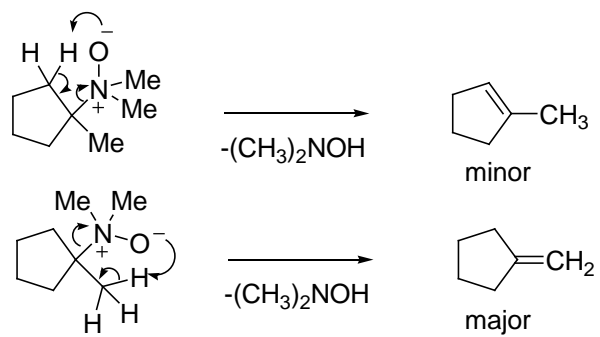
5.11.5 Oxidation

Tertiary amines can be oxidized to amine oxides by oxidizing agents such as H_2O_2 or a peroxyacid. This amine oxide can undergo the Cope elimination, much like the Hofmann elimination of a quaternary ammonium salt, because of the positive charge on nitrogen. The Cope elimination generally gives the same orientation as Hofmann elimination, resulting in the least-substituted alkene (Scheme 14).



Scheme 14

An internal elimination takes place, where amine oxide has both the base and the leaving group, through a cyclic transition state with *syn* stereochemistry. In this case, either alkenes can be formed, but the major product would be the alkene which is less substituted (Scheme 15).



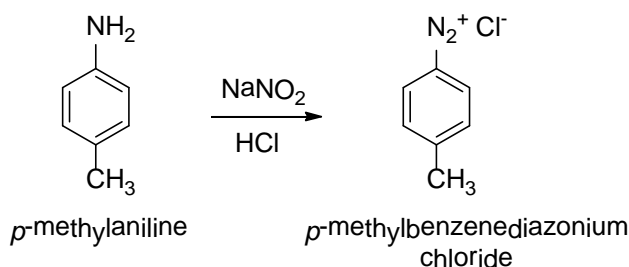
Scheme 15

Module 5 Alcohol, Amine, Ether and Epoxide

Lecture 12 Amine, Ether and Epoxide

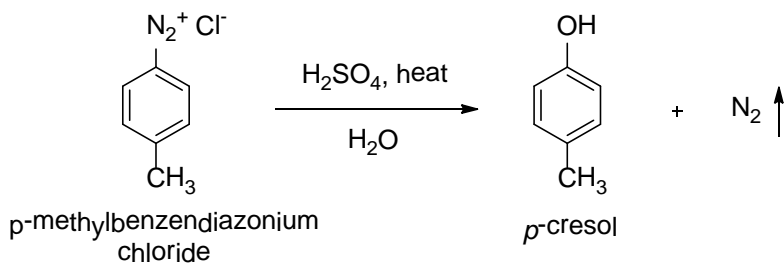
5.11.6 Diazotization

A primary amine reacts with nitrous acid to give a diazonium salt. This process is called diazotization. Both aliphatic and aromatic diazonium salts can be made but aromatic diazonium salts are relatively stable at 0-10 °C. Aryldiazonium salts are formed by diazotizing a primary aromatic amine. For example, *p*-methylaniline is diazotized to give *p*-methylbenzenediazonium chloride (Scheme 1). These reactions of diazonium salts are extremely useful in synthetic and material chemistry.



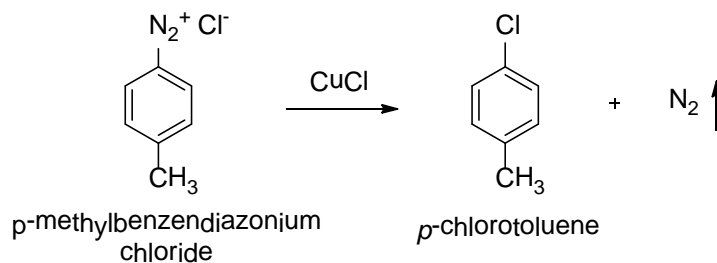
Scheme 1

When the acidic solution of this diazonium salt is warmed, the hydroxyl group of water replaces N₂ to give *p*-cresol (Scheme 2).



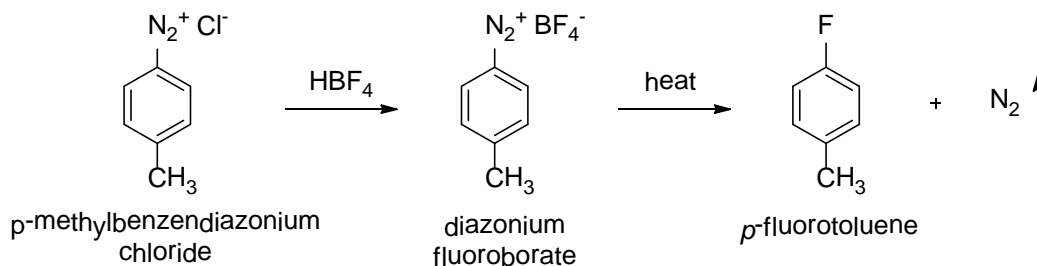
Scheme 2

Cuprous chloride reacts with diazonium salt to give *p*-chlorotoluene (Scheme 3). The use of cuprous salts to replace aryl diazonium group is called **Sandmeyer reaction**. Bromide and cyanide substituted aryl derivatives can be prepared by using cuprous bromide and cuprous cyanide, respectively.



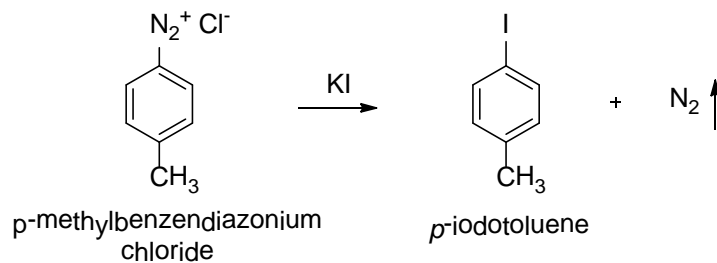
Scheme 3

Aryl diazonium salt with fluoroboric acid (HBF_4) gives the diazonium fluoroborate could be converted into *p*-fluorotoluene under heating (Scheme 4).



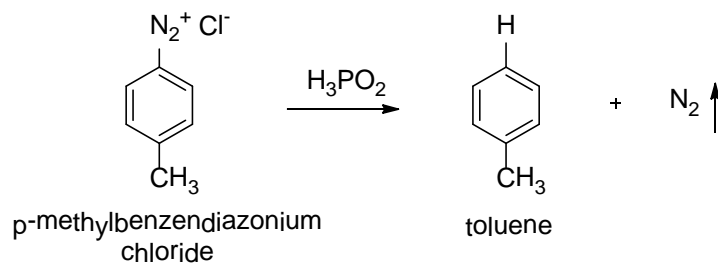
Scheme 4

Iodobenzene derivatives can be prepared by treating the diazonium salts with potassium iodide (Scheme 5).



Scheme 5

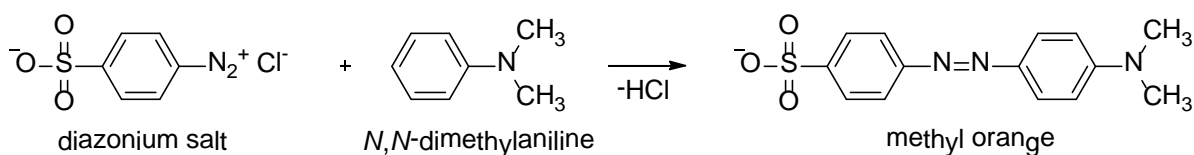
The diazonium group is replaced by hydrogen when it is treated with hypophosphorus acid (H_3PO_2) (Scheme 6).



Scheme 6

Diazonium salts react with strongly activated rings to give azo compounds (Scheme 7).

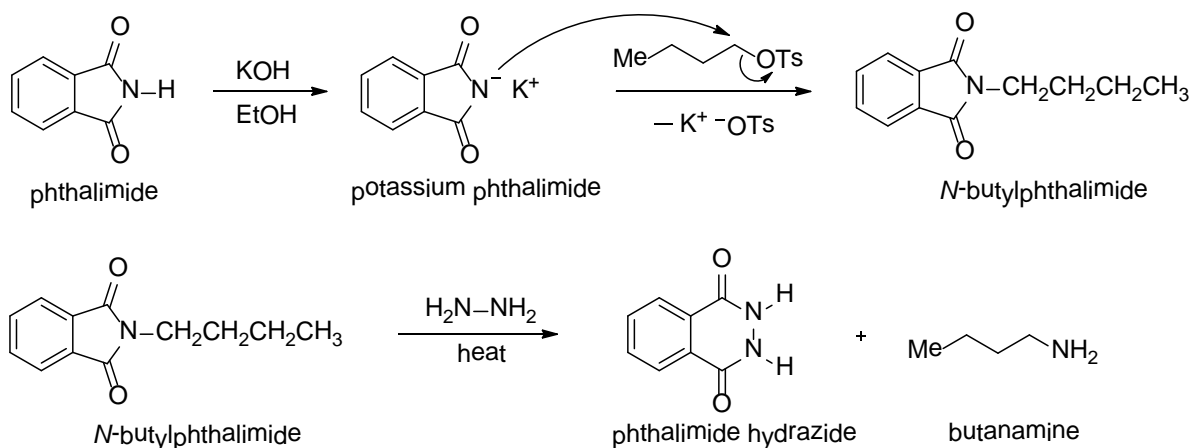
The reaction is called **dizazo coupling**.



Scheme 7

5.11.7 Gabriel Amine Synthesis

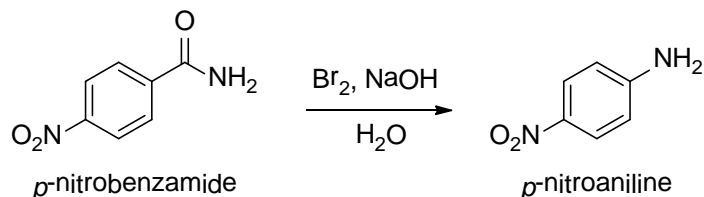
Phthalimide forms the phthalimide anion, when the acidic N-H proton is abstracted by potassium hydroxide (Scheme 8). The phthalimide anion is a strong nucleophile that displaces the tosylate ion. Thus, heating the *N*-alkyl phthalimide with hydrazine gives the primary amine and the phthalimide hydrazide.



Scheme 8

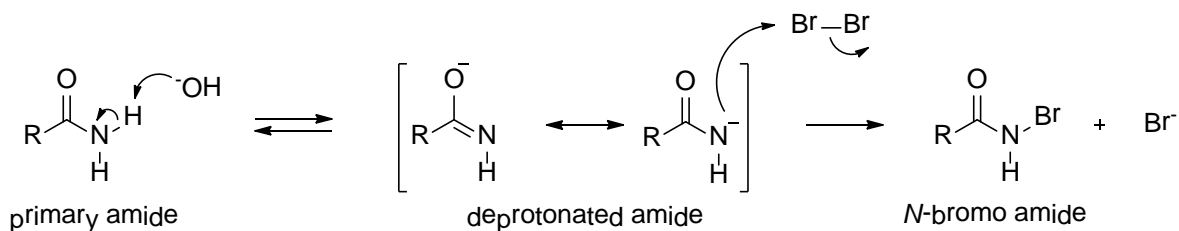
5.11.8 Hofmann Rearrangement

Primary amides react with chlorine or bromine, in the presence of a strong base, to form amines with loss of the carbonyl carbon atom. This reaction, called the **Hofmann rearrangement**, is used to synthesize primary amines. For example, rearrangement of *p*-nitrobenzamide gives *p*-nitroaniline (Scheme 9).

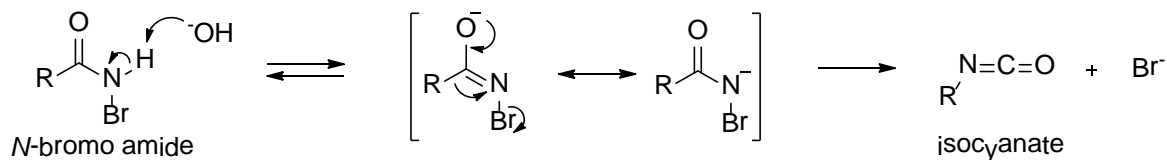


Scheme 9

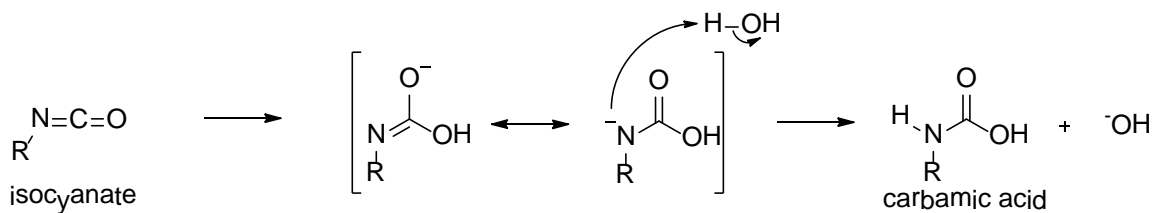
Step 1: The first step is the replacement of one of the hydrogens on nitrogen by a halogen. A strong base deprotonates N-H protons which are slightly acidic. The deprotonated amide is a strong nucleophile, and it attacks bromine to form the *N*-bromo amide.



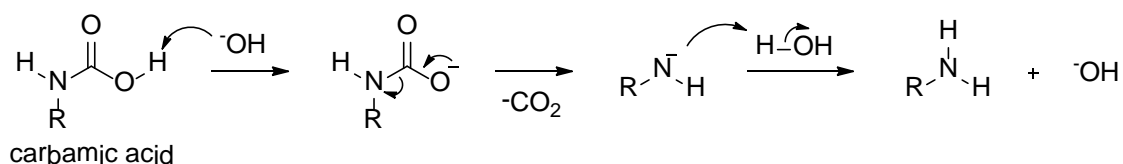
Step 2: The alkyl group migrates to nitrogen with retention of configuration and the leaving group leaves.



Step 3: Hydroxide ion from water attacks the carbonyl group of the isocyanate and gives a carbamic acid.

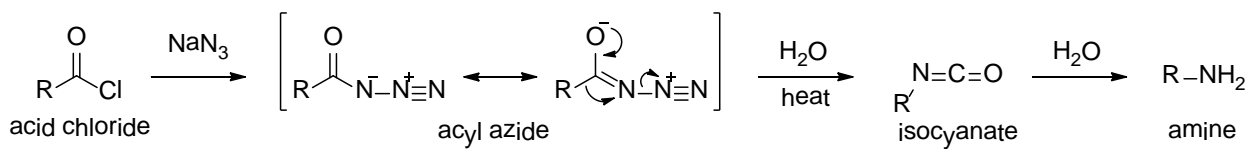


Step 4: Decarboxylation gives the amine.



5.11.9 Curtius Rearrangement

An acid chloride reacts with azide ion to give an acyl azide, which undergoes Curtius rearrangement on heating to give an amine. The Curtius rearrangement takes place by a similar mechanism.

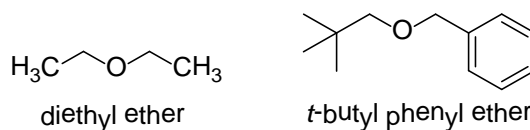


Scheme 10

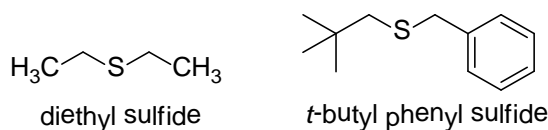
5.12 Ethers

5.12.1 Nomenclature

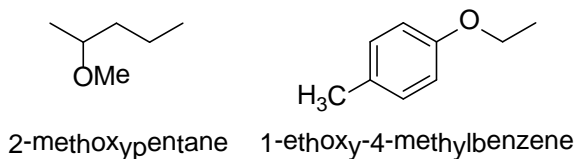
- The common name of an ether is given by citing the two groups attached to the ether oxygen in alphabetical order, followed by the word *ether*.



- A sulfide is named using the word sulfide.

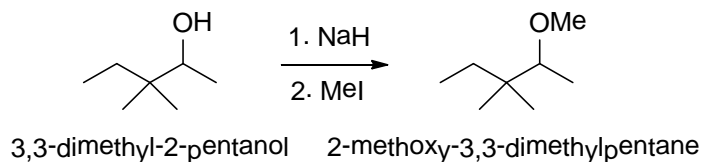


- In this IUPAC style, ethers are named as alkoxyalkanes, alkoxyalkenes, and alkoxyarenes.



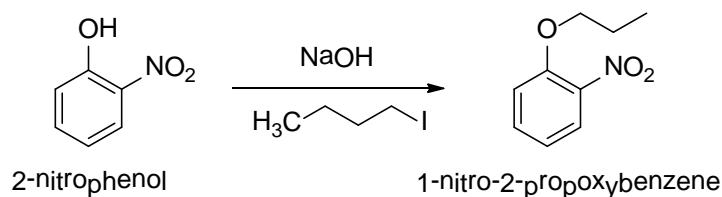
5.12.2 Synthesis

The most reliable ether synthesis is the **Williamson ether synthesis**. In this method, an alkoxide ion attack on a less hindered primary alkyl halide or tosylate, in $\text{S}_{\text{N}}2$ fashion.



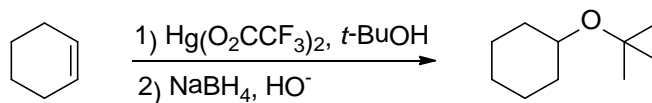
Scheme 11

Phenols are more acidic than aliphatic alcohols and sodium hydroxide is sufficiently basic to form the phenoxide ion (Scheme 12).



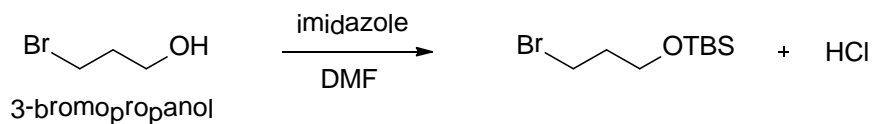
Scheme 12

We know that ethers can also be synthesized by alkoxymercuration–demercuration method (Scheme 13). The reaction of an alkene with an alcohol in the presence of a mercury salt leads to an alkoxymercury intermediate, which on reaction with sodium borohydride yields an ether.



Scheme 13

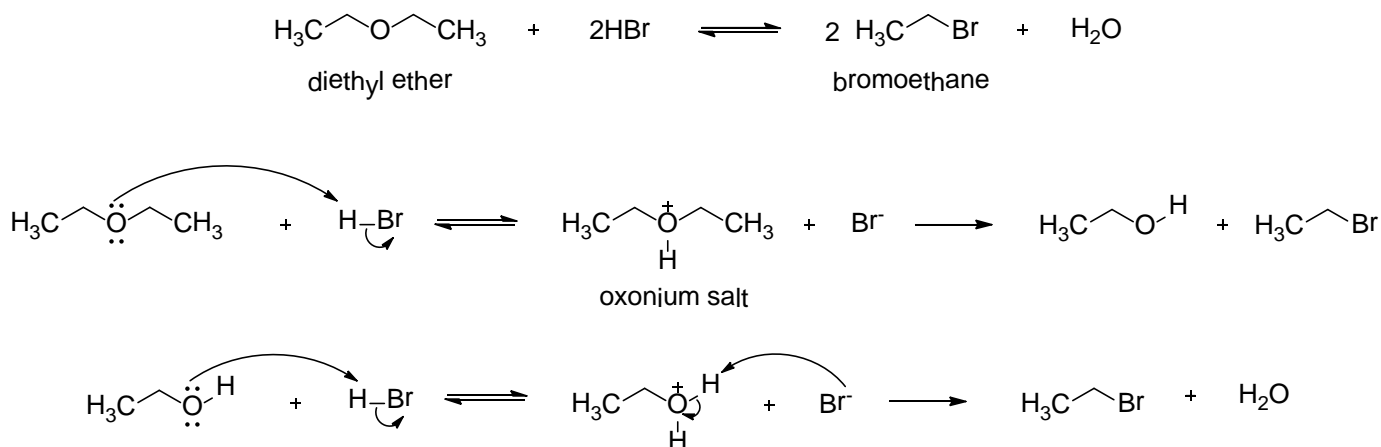
A *tert*-butyl ether can be used to “protect” the hydroxyl group of an alcohol, which can then be easily removed by treating the ether with dilute aqueous acid. A hydroxyl group can also be protected by converting it to a silyl ether group. Usually *tert*-butyldimethylsilyl chloride is used to convert an alcohol to the corresponding silyl ether, although triethylsilyl chloride, triisopropylsilyl chloride, *tert*-butyldiphenylsilyl chloride and others can also be used (Scheme 14).



Scheme 14

5.12.3 Reactions

Diethyl ether reacts with hot concentrated hydrobromic acid to give two molecular equivalents of bromoethane (Scheme 15). An oxonium cation is formed in the first step which is then attacked by a bromide ion to produce an ethanol and ethyl bromide. Excess HBr reacts with the ethanol to produce the second molar equivalent of ethyl bromide.



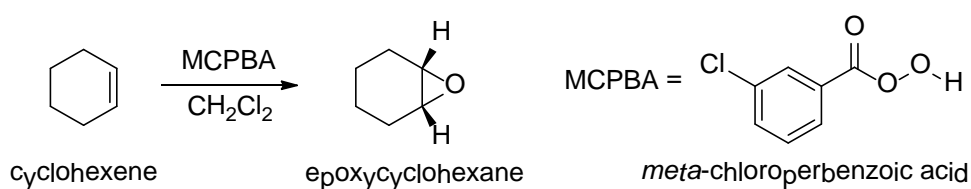
Scheme 15

5.13 Epoxides

Three-membered cyclic ethers are called as epoxides, also called oxiranes. Epoxides are easily made from alkenes and they undergo a variety of useful synthetic reactions.

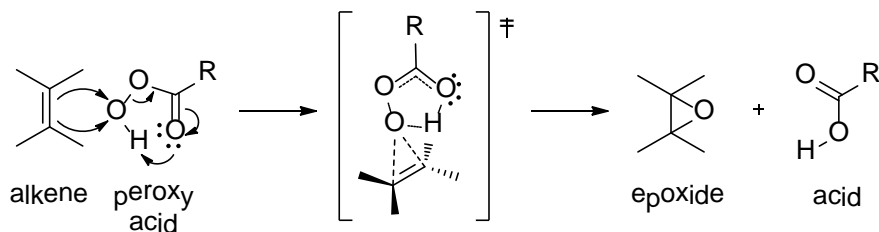
5.13.1 Synthesis

Alkenes can be converted to epoxides using peroxyacids (also called peracids) (Scheme 16). Use of strong acids should be avoided as it opens epoxides to give glycol. Because of this, *meta*-chloroperoxybenzoic acid (MCPBA) is often used for these epoxidations.



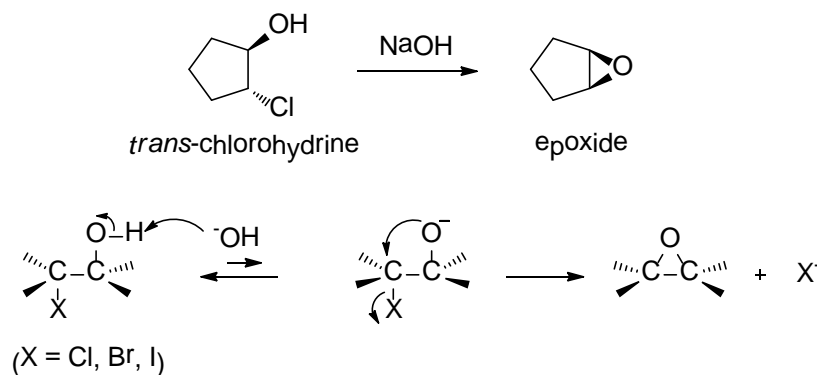
Scheme 16

The peroxy acid transfers an oxygen atom to the alkene in one one-step as shown below. The stereochemistry of alkene is maintained in the product (Scheme 17).



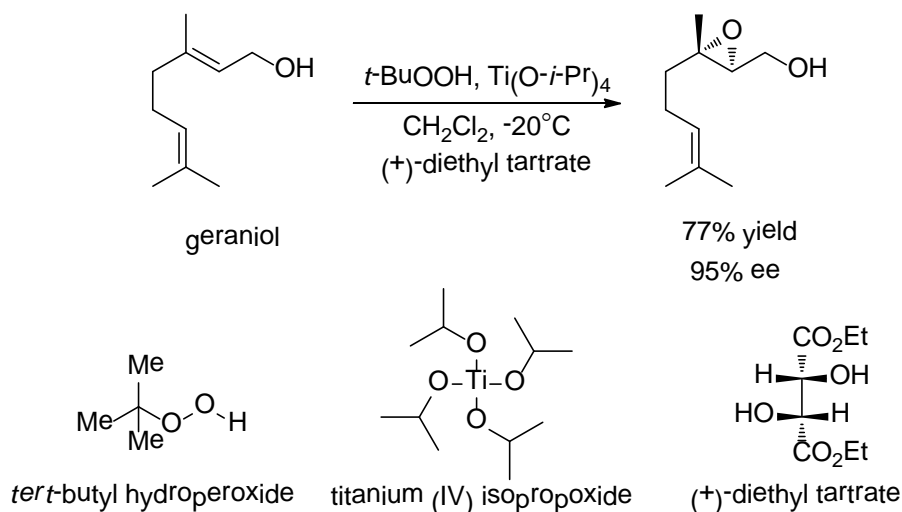
Scheme 17

Epoxides can also be obtained by the treatment of a halohydrin with a base. Treatment of the *trans*-chlorohydrin with aqueous sodium hydroxide gives the epoxide through the internal S_N2 reaction. This reaction can be used to synthesize cyclic ethers with larger rings (Scheme 18).



Scheme 18

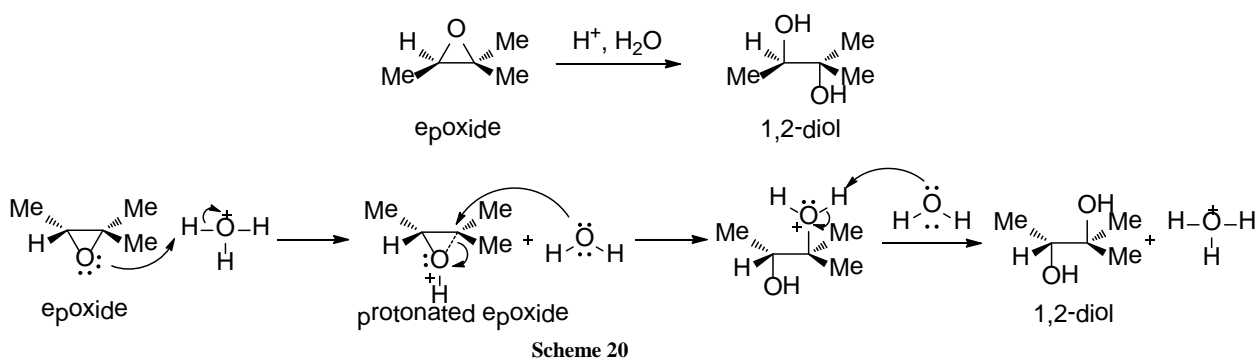
An allylic alcohols can be converted into a chiral epoxy alcohol by the method, called **the Sharpless asymmetric epoxidation**, with good enantioselectivity (Scheme 19). The Sharpless epoxidation uses *tert*-butyl hydroperoxide, titanium (IV) isopropoxide, and a (+)-diethyl tartrate ester as the reagents. One oxygen is transferred from *tert*-butyl hydroperoxide to the allylic alcohol to form the epoxide. The enantioselectivity results from the titanium complex where one of the ligands is the chiral (+)-diethyl tartrate. Opposite stereochemical product results when we use (-)-diethyl tartrate with good enantioselectivity.



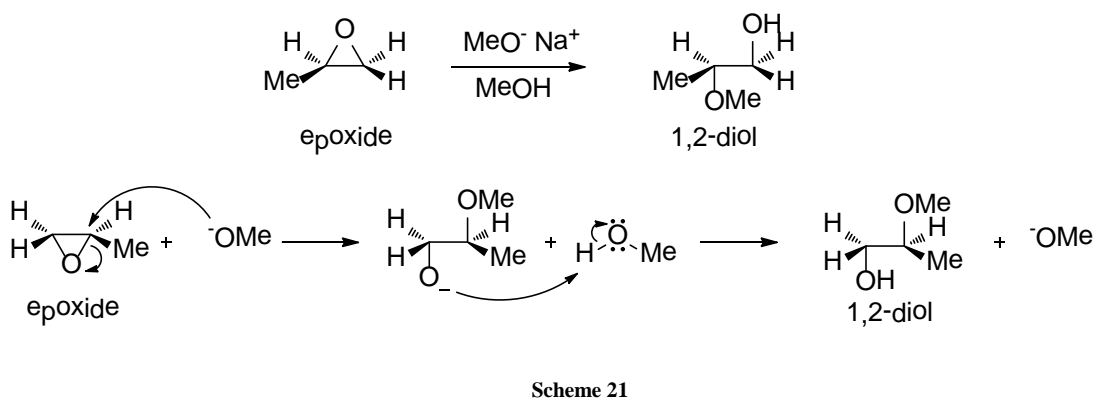
Scheme 19

5.13.2 Reactions

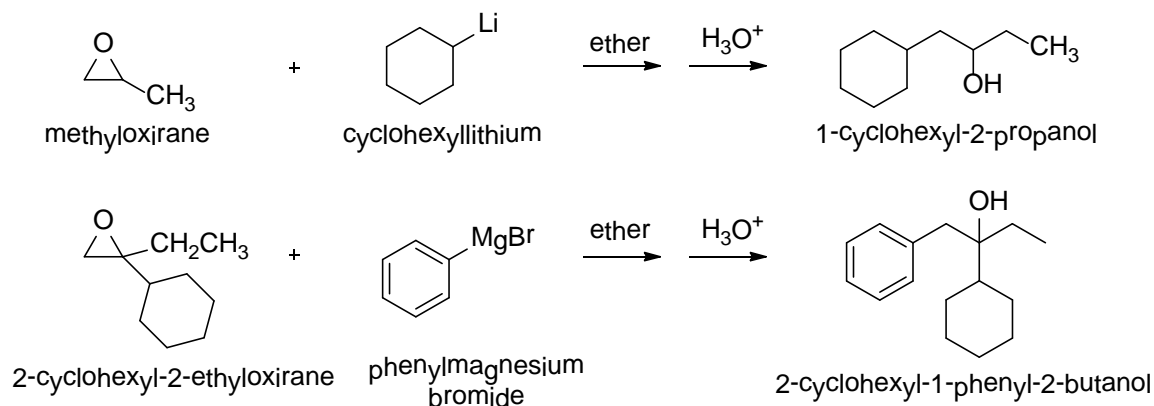
The highly strained three-membered ring of epoxides makes them much more reactive toward nucleophilic substitution (Scheme 20). Acid catalysis assists epoxide ring opening as shown below. In the acid-catalyzed ring opening of an unsymmetrical epoxide the nucleophile attacks primarily at the more substituted carbon atom and this is S_N1 like reaction. In the following example protonated epoxide is unsymmetrical which has a considerable positive charge on the more highly substituted carbon atom. The nucleophile, therefore, attacks this carbon atom even though it is more highly substituted.



Epoxides can also undergo base-catalyzed ring opening when react with strong nucleophiles such as an alkoxide ion or hydroxide ion (Scheme 21). In the base-catalyzed ring opening of an unsymmetrical epoxide the alkoxide ion attacks primarily at the less substituted carbon atom. This is S_N2 like reaction where a nucleophile at the less hindered carbon atom.



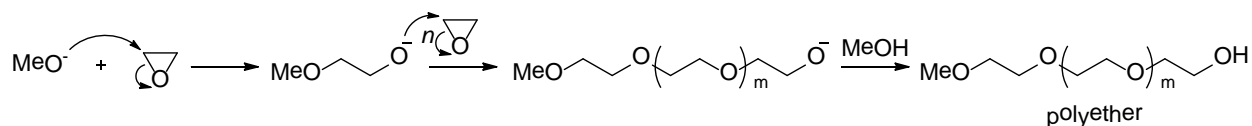
Like other nucleophiles, Grignard and organolithium reagents attack epoxides to give alcohols (Scheme 22). These nucleophiles usually attack the less hindered epoxide carbon atom. Organolithium reagents are more selective than Grignard reagents in attacking the less hindered epoxide carbon atom. Grignard reagents may give mixtures of products unless one of the carbons atom is strongly hindered.



Scheme 22

Polyether is formed when we treat ethylene oxide with sodium methoxide (Scheme 23).

The alkoxide group at the end of the chain is protonated by methanol.



Scheme 23