CHEM 208

Final Exam

Notes & Reactions

Notes

Aromatic compounds

The structural facts:

- Benzene is planar
- All bond angles are 120°
- All carbons are sp^2 hybridized
- Each carbon has a half filled 2p orbital that can participate in π bonding the six π electrons are delocalized over all six carbons
- Aromaticity is attributed to this cyclic delocalization of the conjugated system of six π electrons
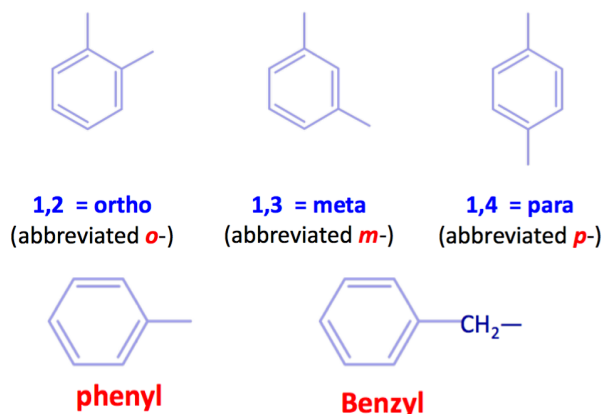
Common names of some monosubstituted derivatives of benzene

Benzaldehyde

Benzoic acid

Acetophenone

Phenol

Anisole

Aniline

Styrene
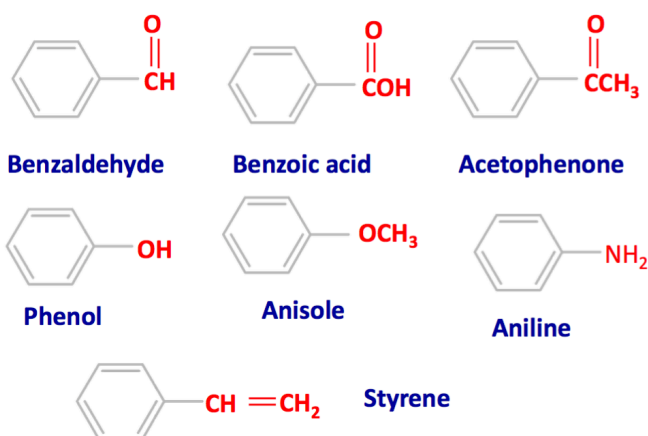
Disubstituted benzene

alternative locants for disubstituted derivatives of benzene

Ortho, Meta, and Para

1,2 = ortho (abbreviated *o*-)

1,3 = meta (abbreviated *m*-)

1,4 = para (abbreviated *p*-)

phenyl

Benzyl

Oxidation of alkyl benzenes

- Alkanes and benzene are not oxidized by an oxidizing agent alkyl side chain on a benzene ring is oxidized using a strong oxidizing agent such as chromic acid H_2CRO_4 which can be prepared by adding sulfuric acid to sodium dichromate
- Alkyl groups, regardless of their chain length, are converted to carboxyl groups ($—CO_2H$)
- Tert-alkyl groups ($—CR_3$) are not susceptible to oxidation because they lack benzylic hydrogens
- Arenes undergo electrophilic substitution reactions

Electrophilic aromatic substitutions include:
1. Nitration
2. Sulfonation
3. Halogenation
4. Friedel-crafts alkylation
5. Friedel-crafts acylation

Notes

Generalizations

- Activating substituents increase the rate of EAS compared to that of benzene.
- Deactivating substituents decrease the rate of EAS compared to benzene.
- All activating substituents are ortho-para directors.
- Halogen substituents are slightly deactivating but ortho-para directing.
- Deactivating substituents are meta directors.

Activating groups

- Are electron releasing or donating groups
- They stabilize the intermediate carbocation
- The intermediates formed from ortho and para attack are stabilized more than the intermediate formed from the meta attack
- All alkyl groups are activating, ortho para directors
- Any group with at least one unshared electron pair on the atom directly attached to the ring is activating

Substituents in which nitrogen is directly attached to the ring are more strongly activating than oxygen because:

3. Nitrogen is less electronegative than oxygen
4. It is a better electron donor
5. Stabilize the intermediate to a greater extent

Deactivating groups

- Are electron withdrawing
- They destabilize a carbocation intermediate
- Are meta directors
- Attack at the meta position leads to a more stable intermediate than attack at either the ortho or the para positions, the meta substitution predominates

Deactivating groups are electron withdrawing the atom directly attached to the benzene ring has:

- Either a partial or a full positive charge
- Is multiply bonded to a more electronegative atom
- Many EWGS have a carbonyl group attached directly to the ring
- F, Cl, Br, and I are ortho-para directing, but deactivating
- Halogens are electronegative
- Electron donation through resonance stabilizes the intermediates from the ortho and para attacks
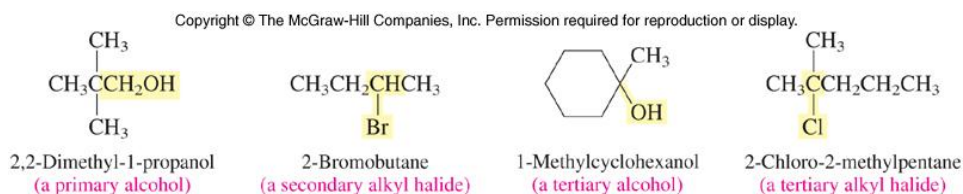
Notes

Alkyl Halides Structures and Preparation from Alcohols and Alkanes

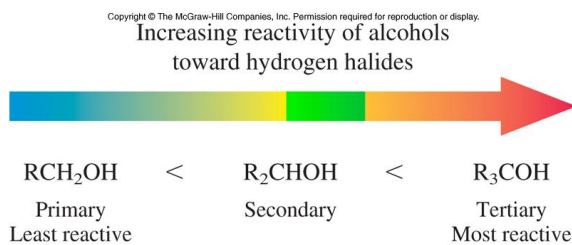Halogen and alkyl groups are of equal rank when it comes to numbering the chain.

- Number the chain in the direction that gives the lowest number to the group (halogen or alkyl) that appears first.
- If the substituents have the same numbering, use alphabetical order
- Hydroxyl groups outrank alkyl groups when it comes to numbering the chain.
- Number the chain in the direction that gives the lowest number to the carbon that bears the OH group

Alcohols and alkyl halides are classified as

- Primary secondary tertiary according to their "degree of substitution."
- Degree of substitution is determined by counting the number of carbon atoms directly attached to the carbon that bears the halogen or hydroxyl group.

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CH_3		CH_3	CH_3
CH_3CCH_2OH	$CH_3CH_2CHCH_3$	$\overset{|}{\bigcirc}$	$CH_3CCH_2CH_2CH_3$
CH_3	Br	OH	Cl
2,2-Dimethyl-1-propanol	2-Bromobutane	1-Methylcyclohexanol	2-Chloro-2-methylpentane
(a primary alcohol)	(a secondary alkyl halide)	(a tertiary alcohol)	(a tertiary alkyl halide)

- Order of reactivity of hydrogen halides parallels their acidity: HI > hbr> hcl > HF
- Order of reactivity of alcohols:

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Increasing reactivity of alcohols
toward hydrogen halides

RCH_2OH < R_2CHOH < R_3COH

Primary	Secondary	Tertiary
Least reactive		Most reactive

- Primary alcohols react by a mechanism called S_N2

Free Radicals: are species that contain unpaired electrons or an odd number of electrons
Alkyl Radicals

- Most free radicals in which carbon bears the unpaired electron are too unstable to be isolated.
- Alkyl radicals are classified as primary, secondary, or tertiary in the same way that carbocations are.

Notes

Structure of Methyl Radical

- Methyl radical is planar
- Carbon is sp^2 hybridized
- The unpaired electron is in a p orbital.

Stability of Alkyl Radicals

The stability of a free radical is similar to that of carbocation

- The order of stability of free radicals can be determined by measuring bond strengths.
- "bond strength" means the energy required to break a covalent bond.
- A chemical bond can be broken in two different ways— heterolytically or homolytically

Heterlolytic
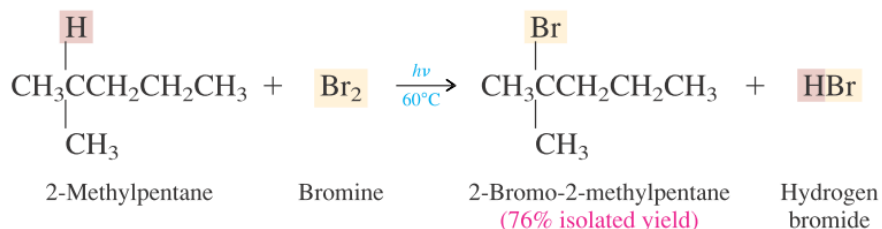- In a **heterolytic cleavage**, one atom retains both electrons

Homolytic

- In a **homolytic bond cleavage**, the two electrons in the bond are divided equally between the two atoms. One electron goes with one atom, the second with the other atom.
- The species formed by a homolytic bond cleavage of a neutral molecule are free radicals. Therefore, measure enthalpy cost of homolytic bond cleavage to gain information about stability of free radicals.
- The more stable the free-radical products, the weaker the bond, and the lower the bond-dissociation energy.
- Chlorine is non-polar -homolytic cleavage

Reaction of chlorine radical is less regioselective

$$CH_3CH_2CH_2CH_3 \xrightarrow[hv,\ 35°C]{Cl_2} CH_3CH_2CH_2CH_2Cl \ + \ CH_3CHCH_2CH_3$$
$$\underset{Cl}{|}$$
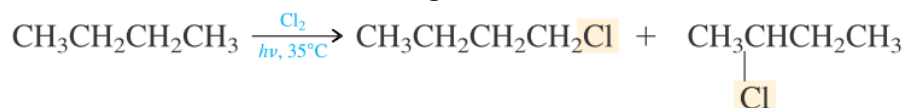
Free Radical Bromination of alkanes unlike chlorination is very selective
Tertiary Alkanes is Regiospecific; only tertiary hydrogen is replaced

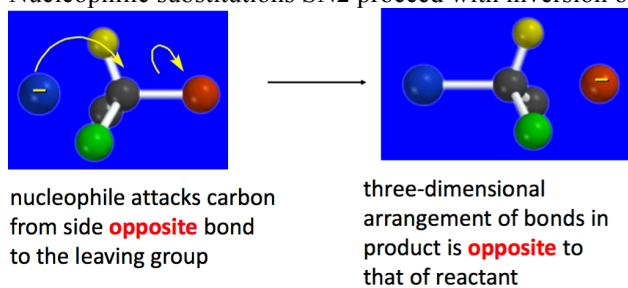2-Methylpentane   Bromine   2-Bromo-2-methylpentane   Hydrogen
                                              (76% isolated yield)   bromide

Notes

Nucleophilic Substitution

- Nucleophile is an electron-pair donor
- Often negatively charged and used as Na$^+$ or K$^+$ salt substrate is usually an alkyl halide
- **Compounds in which the halogen is attached to an sp^2-hybridized carbon are unreactive under these conditions.**
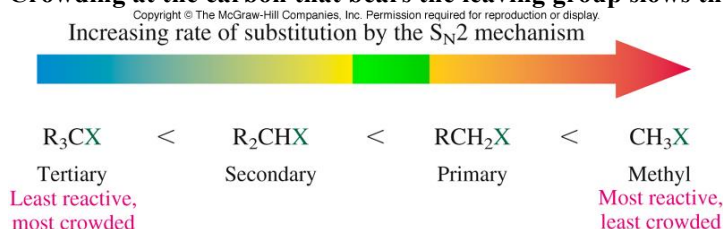
SN2 reaction:

- Occurs in one single step; concerted process
- Both the nucleophile and the alkyl halide are involved in the only step
- Bimolecular

Nucleophilic substitutions SN2 proceed with inversion of configuration.

nucleophile attacks carbon from side **opposite** bond to the leaving group

three-dimensional arrangement of bonds in product is **opposite** to that of reactant

Crowding at the carbon that bears the leaving group slows the rate of SN2:

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Increasing rate of substitution by the S_N2 mechanism

R_3CX	<	R_2CHX	<	RCH_2X	<	CH_3X
Tertiary		Secondary		Primary		Methyl
Least reactive, most crowded						Most reactive, least crowded

Nucleophiles can be negatively charged or neutral:

1. A negatively charged nucleophile is always a more reactive nucleophile than its conjugate acid. **HO⁻ is a stronger nucleophile than H2O**.
2. Nucleophile Strength Increases Down the Group
3. Right-to-left-across a row of the periodic table, nucleophilicity increases (parallel basicity)

Tertiary alkyl halides are very unreactive in substitutions that proceed by the SN2 mechanism. Do they undergo nucleophilic substitution at all?

- Yes. But by a mechanism different from SN2.
- The most common examples are seen in solvolysis reactions.
- In **Solvolysis** reactions the solvent is the nucleophile, solvents are weak nucleophiles.

Notes

Partial racemization occurs when leaving group is located at a stereogenic center

Summary of S$_N$2 reactions

Kinetics	• Second-order kinetics; rate = k[RX][:Nu⁻]
Mechanism	• One step
Stereochemistry	• Backside attack of the nucleophile • Inversion of configuration at a stereogenic center
Alkyl Halide	• Unhindered halides react fastest. • Rate: $CH_3X > RCH_2X > R_2CHX > R_3CX$

Summary of S$_N$1 reactions

Kinetics	• First-order kinetics; rate = k[RX]
Mechanism	• Two steps
Stereochemistry	• Trigonal planar carbocation intermediate • Racemization at a single stereogenic center
Alkyl Halide	• More substituted halides react fastest. • Rate: $R_3CX > R_2CHX > RCH_2X > CH_3X$

Summary of Factors in predicting S$_N$1 vs S$_N$2 mechanisms:

Nucleophile:
S$_N$1 - Weak Nucleophile- Lone Pair

S$_N$2 -Needs a stronger nucleophile, usually negatively charged

Alkyl Halides:

S$_N$1 - $3^o > 2^o$ (Require dissociation to carbocation before reaction)

S$_N$2 - $CH_3 > 1^o > 2^o$ (Less sterically hindered favors reaction)

Alkyl halides can react with bases/nucleophiles by nucleophilic substitution and/or elimination. How can we tell which reaction pathway is followed for a particular alkyl halide?
The two most important factors are:

1. The structure of the alkyl halide
2. The basicity of the anion

Overall Summary of S$_N$1, S$_N$2, E1 ,E2

CH$_3$X Methyl	RCH$_2$X 1º	R$_2$CHX 2º	R$_3$CX 3º
Gives S$_N$2 reactions only	No S$_N$1 Gives mainly S$_N$2 **except** with hindered, bulky strong bases e.g (CH$_3$)$_3$CO⁻ then gives mainly E2	Mainly S$_N$2 with weak bases Γ, CN⁻, RCO$_2^-$ And mainly E2 with strong bases RO⁻	No S$_N$2 In solvolysis gives S$_N$1/E1, at lower temperatures S$_N$1 is favored And mainly E2 with strong bases RO⁻

Note: Check table 9.2 for a comparison between S$_N$2 and S$_N$1 mechanisms

Notes

Oxygen Containing Functional groups

		O ‖	O ‖	O ‖
ROH	ROR′	RCH	RCR′	RCOH
Alcohol	Ether	Aldehyde	Ketone	Carboxylic acid
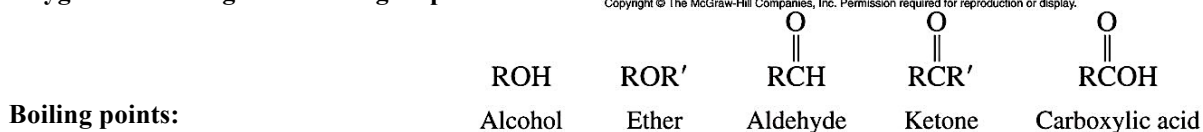
Boiling points:

- Alkane has the lowest boiling point because it has weak intermolecular forces, only intermolecular forces are induced dipole-induced dipole
- Alkyl halides are polar, and as a result have higher boiling points than alkanes.
  - As the number of chlorine atoms increase, the induced dipole –induced dipole attractive forces increase the boiling points increase.
- Alcohols are also polar compounds, they have higher boiling point than alkyl halides because they have the strongest intermolecular attractive forces.
  - Hydrogen bonding is stronger than other dipole-dipole attractions.
  - Hydrogen bonding occur in compounds that have a hydrogen bonded to an electronegative element such as O or N
- Aldehydes and ketones have
  - **higher** boiling points than alkenes because they are **more** polar
  - **Lower** boiling points than alcohols because they **can't** form **hydrogen bonds** to each other
- Carboxylic acids have the highest boiling point
  - Intermolecular forces, especially hydrogen bonding, are stronger in carboxylic acids than in other compounds of similar shape and molecular weight

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Alkane < Alkyl Halides < Aldehydes and Ketones < Alcohols < Carboxylic Acids

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Solubility in water

- Alkyl halides are insoluble in water.
- Methanol, ethanol, isopropyl alcohol are completely miscible with water.
  - The solubility of an alcohol in water decreases with increasing number of carbons (compound becomes more hydrocarbon-like).
- Aldehydes and ketones are **more** soluble in water than alkenes because they can form **hydrogen bonds** with the OH of water but are **less** soluble than alcohols.
- Carboxylic acids are similar to alcohols in respect to their solubility in water
  - Form hydrogen bonds to water

Alkyl Halides < Aldehydes and Ketones < Alcohol ≤ Carboxylic Acids

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Density

- Alkyl fluorides and alkyl chlorides are less dense than water.
- Alkyl bromides and alkyl iodides are more dense than water.
- All liquid alcohols have densities of about 0.8 g/ml.

Notes

Acidity

- Carboxylic acids are weak acids but they are the most acidic class of compounds that contain only carbon, hydrogen and oxygen.
- Carboxylic acids are far more acidic than alcohols
- Electronegative substituents increase the acidity of carboxylic acids.
- Electronegative substituents withdraw electrons from carboxyl group; increase K for loss of H^+
- The order of acidity increases with an increasing number of electron-withdrawing groups.

Oxidation and Reduction

Reduction

- An increase in the number of carbon-hydrogen bonds
- Or a decrease in the number of carbon-oxygen bonds

Reducing agents:

1. Catalytic hydrogenation H_2, **Pt, Pd, Ni, Ru**
2. Metal hydride; sodium borohydride **NABH$_4$**
3. Lithium aluminum hydride **LiAlH$_4$**

Selective reduction of a carbonyl group: **NaBH$_4$ and LiAlH$_4$**
- Reduce carbonyls to the corresponding alcohol
- Do not reduce carbon-carbon double bonds
- Catalytic hydrogenation reduces both carbonyls and carbon-carbon double bonds

Reduction of an aldehyde gives a primary alcohol
Reduction of a ketone gives a secondary alcohol

Oxidation:

- An increase in the number of carbon-oxygen bonds
- Or a decrease in the number of carbon-hydrogen bonds

Oxidizing agents:

- KMnO4
- H2Cr2O4
- H2Cr2O7

Primary alcohols can be oxidized to aldehydes using:

1. PCC
2. PDC

Secondary alcohols are oxidized to the ketone.

Tertiary alcohols have no hydrogen on their hydroxyl bearing carbon and do not undergo oxidation readily.

Notes

Ethers

- Contain a C-O-C unit.
- Are relatively unreactive, they undergo few reactions
- They are mainly used cyclic ethers have their oxygen as part of the ring, they are heterocyclic compounds
- **Epoxides (3 membered) cyclic ethers** are named are derivatives of alkanes as solvents
- Epoxidation with peroxy acids is a syn addition to the double bond.
- Aldehydes and Ketones react with alcohols to yield acetals
    o **Hemiacetal (OH & OR** on the **same** carbon) is formed by nucleophilic addition of the alcohol to the carbonyl
    o Hemiacetal reacts further in acid to yield an **acetal (two OR** groups on the **same** carbon)

Carboxylic Acids:

Sources of Carboxylic Acids

- Side-chain oxidation of alkylbenzenes
- Oxidation of primary alcohols
- Oxidation of aldehydes

Reactions

ALCOHOLS AND ALKYL HALIDES

An alcohol can be converted into an alkyl halide by the following reaction:

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$$R-OH + H-X \longrightarrow R-X + H-OH$$

Alcohol   Hydrogen halide   Alkyl halide   Water
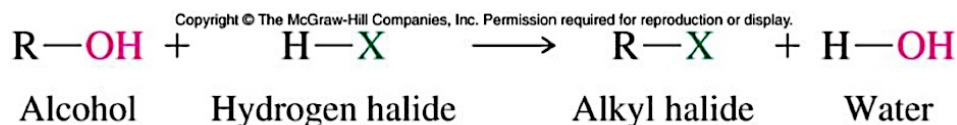
Peroxide effect:

Addition of HBr in the absence of peroxides:

$$CH_2=CHCH_2CH_3 + HBr \xrightarrow{\text{no peroxides}} CH_3\underset{\underset{Br}{|}}{C}HCH_2CH_3$$

1-Butene   Hydrogen bromide   2-Bromobutane
(only product; 90% yield)
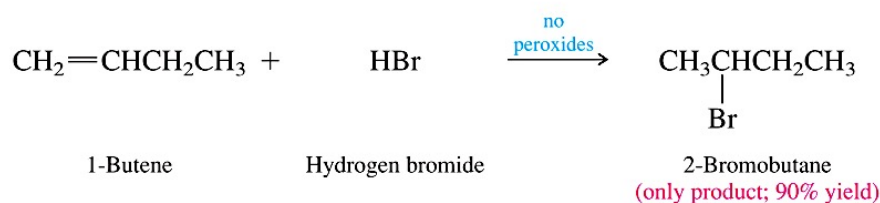
Addition of HBr in the presence of peroxides:

$$CH_2=CHCH_2CH_3 + HBr \xrightarrow{\text{peroxides}} BrCH_2CH_2CH_2CH_3$$

1-Butene   Hydrogen bromide   1-Bromobutane
(only product; 95% yield)
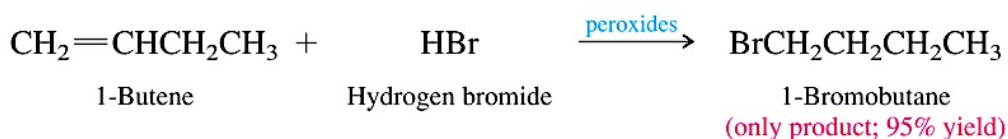
ALCOHOLS, ETHERS

Oxygen Containing Functional groups
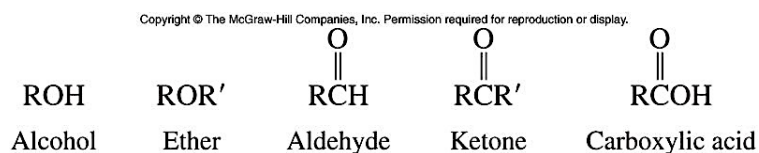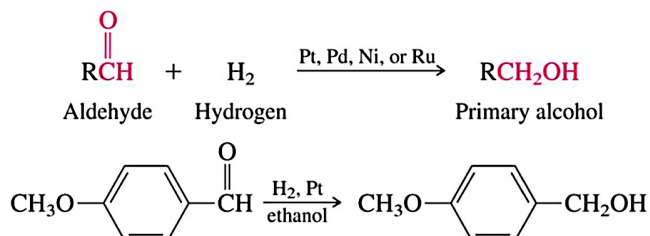
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ROH	ROR′	$\overset{\displaystyle O}{\overset{\|}{RCH}}$	$\overset{\displaystyle O}{\overset{\|}{RCR′}}$	$\overset{\displaystyle O}{\overset{\|}{RCOH}}$
Alcohol	Ether	Aldehyde	Ketone	Carboxylic acid

Reduction of an **aldehyde** gives a **primary alcohol**

$$\overset{\displaystyle O}{\overset{\|}{RCH}} + H_2 \xrightarrow{\text{Pt, Pd, Ni, or Ru}} RCH_2OH$$

Aldehyde   Hydrogen   Primary alcohol

$$CH_3O-\underset{}{\bigcirc}-\overset{\displaystyle O}{\overset{\|}{CH}} \xrightarrow[\text{ethanol}]{H_2,\ Pt} CH_3O-\bigcirc-CH_2OH$$

Selective reduction of a carbonyl group:

$NaBH_4$ and $LiAlH_4$ reduce carbonyls to the corresponding alcohol **do not** reduce carbon-carbon double bonds.

Note: Catalytic hydrogenation (H+) reduces both carbonyls **and** carbon-carbon double bonds

Reactions

Reduction of a **ketone** gives a **secondary alcohol**

$$\underset{\text{Ketone}}{\overset{\overset{\displaystyle O}{\|}}{RCR'}} + \underset{\text{Hydrogen}}{H_2} \xrightarrow{\text{Pt, Pd, Ni, or Ru}} \underset{\text{Secondary alcohol}}{\overset{\displaystyle RCHR'}{\underset{\displaystyle OH}{|}}}$$

$$\xrightarrow[\text{methanol}]{H_2,\ Pt}$$

H   OH

Reactions of Alcohols:

1. Reaction with hydrogen halides (8.5)

$$\underset{\text{Alcohol}}{ROH} + \underset{\text{Hydrogen halide}}{HX} \longrightarrow \underset{\text{Alkyl halide}}{RX} + \underset{\text{Water}}{H_2O}$$
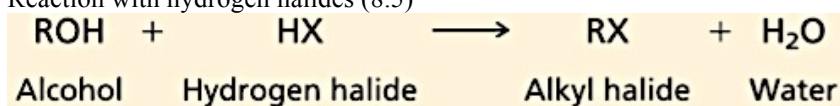
2. Acid-catalyzed dehydration (5.7)

$$\underset{\text{Alcohol}}{\overset{\displaystyle R_2CCHR_2}{\underset{\displaystyle OH}{|}}} \xrightarrow[\text{heat}]{H^+} \underset{\text{Alkene}}{R_2C{=}CR_2} + \underset{\text{Water}}{H_2O}$$
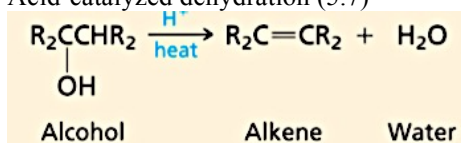
3. Oxidation of Alcohols

Primary alcohols can be oxidized to **aldehydes** using
1. Pyridinium chlorochromate **PCC**
2. Pyridinium dichromate **PDC**

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$$\underset{\text{Primary alcohol}}{RCH_2OH} \xrightarrow{\text{oxidize}} \underset{\text{Aldehyde}}{\overset{\overset{\displaystyle O}{\|}}{RCH}} \xrightarrow{\text{oxidize}} \underset{\text{Carboxylic acid}}{\overset{\overset{\displaystyle O}{\|}}{RCOH}}$$
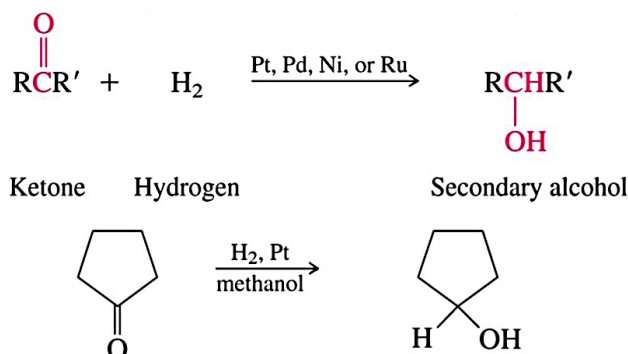
Secondary **alcohols** are oxidized to the **ketone**

$$\underset{\text{Secondary alcohol}}{\overset{\displaystyle OH}{\underset{\displaystyle RCHR'}{|}}} \xrightarrow{\text{oxidize}} \underset{\text{Ketone}}{\overset{\overset{\displaystyle O}{\|}}{RCR'}}$$

$$\xrightarrow[\text{H}_2\text{SO}_4,\ \text{H}_2\text{O}]{\text{Na}_2\text{Cr}_2\text{O}_7}$$

Cyclohexanol   Cyclohexanone
                                        (85%)
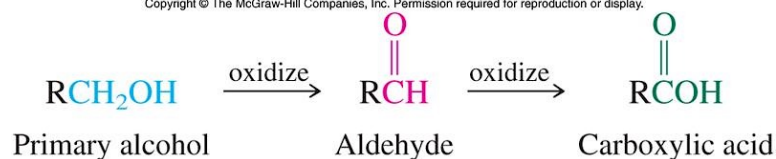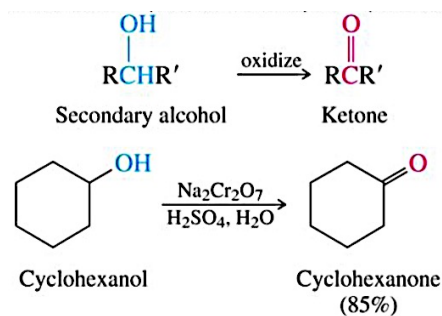
Reactions

Tertiary alcohols have no hydrogen on their hydroxyl bearing carbon and **do not** undergo oxidation readily.

$$\overset{\displaystyle R'}{\underset{\displaystyle R''}{R-\overset{|}{\underset{|}{C}}-OH}} \xrightarrow{\text{oxidize}} \text{no reaction except under forcing conditions}$$
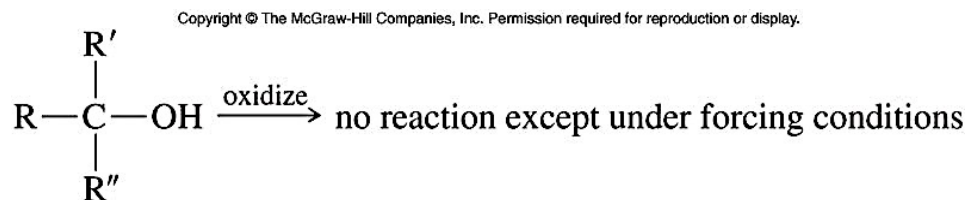
Preparation of Ethers: Williamson Ether Synthesis

- Alkyl halide must be primary
- Alkoxide ion can be derived from primary, secondary, or   tertiary alcohol

$$R\ddot{O}\colon^- \quad R'-\ddot{X}\colon \xrightarrow{S_N2} R\ddot{O}R' \;+\; \colon\ddot{X}\colon^-$$

| Alkoxide ion | Alkyl halide | Ether | Halide ion |
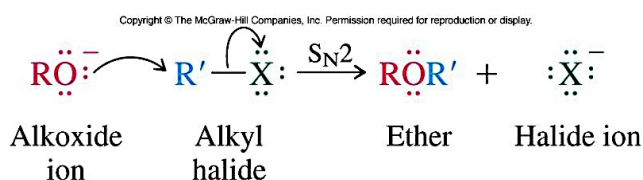
Preparation of Epoxides
Epoxidation of Alkenes

$$\overset{}{C}{=}\overset{}{C} \;+\; RC\overset{O}{\overset{\|}{O}}OH \longrightarrow \overset{}{C}\underset{O}{-}\overset{}{C} \;+\; RC\overset{O}{\overset{\|}{}}OH$$

Alkene   Peroxy acid   Epoxide   Carboxylic acid

$$R_2C{=}CR_2 \;+\; R'C\overset{O}{\overset{\|}{}}OOH \longrightarrow R_2C\underset{O}{-}CR_2 \;+\; R'C\overset{O}{\overset{\|}{}}OH$$

Alkene   Peroxy acid   Epoxide   Carboxylic acid

Reactions

ALDEHYDES AND KETONES

Synthesis of Aldehydes and Ketones

1. From alkynes hydration (via enol)
2. From arenes friedel-crafts acylation
3. From alcohols oxidation

1. Hydration of alkynes:

2. From arenes friedel-crafts acylation

3. From alcohols oxidation

Summary of Alcohol Oxidations		
To Oxidize	*Product*	*Reagent*
2° alcohol	ketone	chromic acid (or PCC)
1° alcohol	aldehyde	PCC
1° alcohol	acid	chromic acid

Cyanohydrin Formation

| Aldehyde or ketone | Hydrogen cyanide | | Cyanohydrin |

Reactions

Hydration of Aldehydes and Ketones
Aldehydes and ketones react with water in a rapid equilibrium
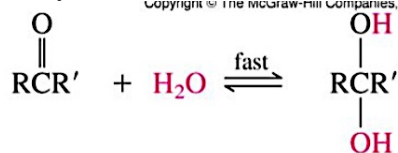
Aldehyde   Water   Geminal diol
or ketone   (hydrate)

Acetal Formation

Aldehyde   Hemiacetal   Acetal   Water

Benzaldehyde   Ethanol   Benzaldehyde diethyl acetal   Water
(66%)
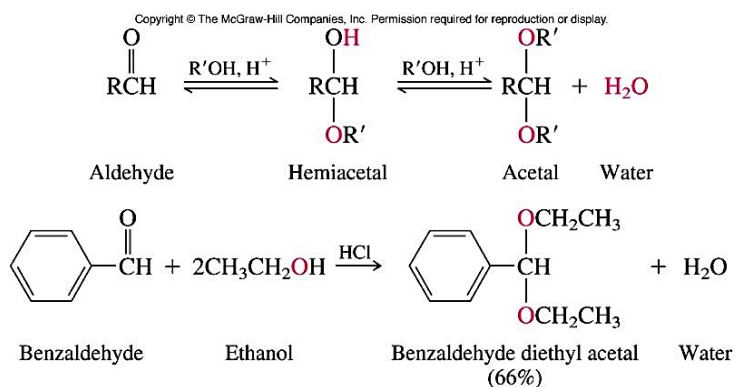
Reaction with Primary Amines: Imines

Aldehydes and ketones react with primary amines such as: RNH_2 and $ArNH_2$
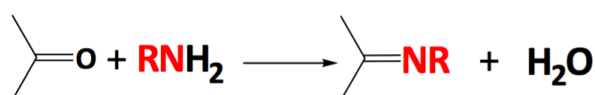
The reaction occurs in **two** steps:

1. The amine adds to the carbonyl to give the **carbinolamine**

2. The carbinolamine undergoes dehydration to give the **imine**
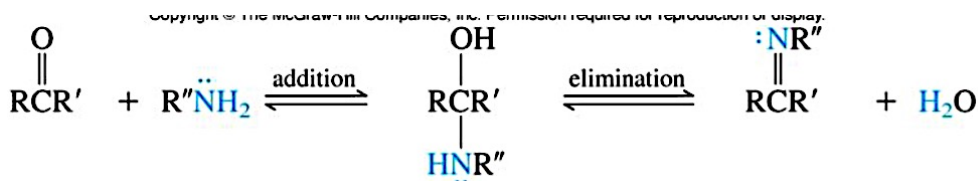
Reactions

CARBOXYLIC ACIDS

Sources of Carboxylic Acids
Synthesis of Carboxylic Acids
1. Side-chain oxidation of alkylbenzenes

$$ArCHR_2 \xrightarrow[K_2Cr_2O_7, H_2SO_4]{KMnO_4 \text{ or}} ArCO_2H$$

Alkylbenzene   Arenecarboxylic acid

3-Methoxy-4-nitrotoluene $\xrightarrow[\text{2. } H^+]{\text{1. } KMnO_4, HO^-}$ 3-Methoxy-4-nitrobenzoic acid (100%)

2. Oxidation of primary alcohols

$$RCH_2OH \xrightarrow[K_2Cr_2O_7, H_2SO_4]{KMnO_4 \text{ or}} RCO_2H$$

Primary alcohol   Carboxylic acid

$$(CH_3)_3CCHC(CH_3)_3 \xrightarrow[H_2O, H_2SO_4]{H_2CrO_4} (CH_3)_3CCHC(CH_3)_3$$

CH₂OH   CO₂H

2-*tert*-Butyl-3,3-dimethyl-1-butanol   2-*tert*-Butyl-3,3-dimethylbutanoic acid (82%)

3. Oxidation of aldehydes

$$RCH \xrightarrow{\text{oxidizing agent}} RCO_2H$$

Aldehyde   Carboxylic acid

Furan-2-carbaldehyde (furfural) $\xrightarrow[H_2SO_4, H_2O]{K_2Cr_2O_7}$ Furan-2-carboxylic acid (furoic acid) (75%)

1. Preparation of nitriles

$$:\ddot{X}-R + :\bar{C}\equiv N: \xrightarrow{S_N2} RC\equiv N + :\ddot{X}:^-$$

Primary or   Cyanide ion   Nitrile   Halide ion
secondary alkyl   (alkyl cyanide)
halide

2. Hydrolysis of nitriles
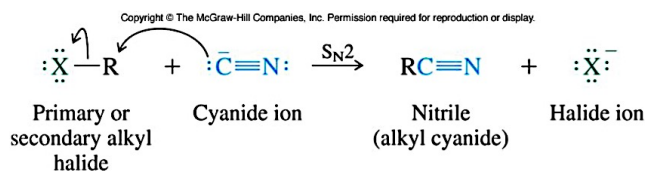
Synthesis of Carboxylic Acids by the Preparation and Hydrolysis of Nitriles

$$RC\equiv N + 2H_2O + H^+ \xrightarrow{heat} RCOH + NH_4^+$$

Nitrile   Water   Carboxylic   Ammonium
                           acid   ion
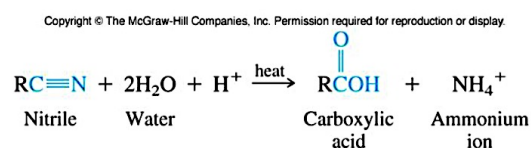
Reactions

Dicarboxylic Acid

$$BrCH_2CH_2CH_2Br \xrightarrow[H_2O]{NaCN} NCCH_2CH_2CH_2CN \xrightarrow[heat]{H_2O, HCl} HOC\overset{\displaystyle O}{\overset{\|}{}}CH_2CH_2CH_2C\overset{\displaystyle O}{\overset{\|}{}}OH$$

1,3-Dibromopropane   1,5-Pentanedinitrile   1,5-Pentanedioic acid
                                          (77–86%)   (83–85%)

via Cyanohydrin

$$CH_3\overset{\displaystyle O}{\overset{\|}{C}}CH_2CH_2CH_3 \xrightarrow[2.\ H_3O^+]{1.\ NaCN} CH_3\overset{\displaystyle OH}{\underset{\underset{\displaystyle CN}{|}}{C}}CH_2CH_2CH_3 \xrightarrow[heat]{H_2O, HCl} CH_3\overset{\displaystyle OH}{\underset{\underset{\displaystyle CO_2H}{|}}{C}}CH_2CH_2CH_3$$

2-Pentanone   2-Pentanone   2-Hydroxy-2-methyl-
                                  cyanohydrin   pentanoic acid
                                                                    (60% from 2-pentanone)
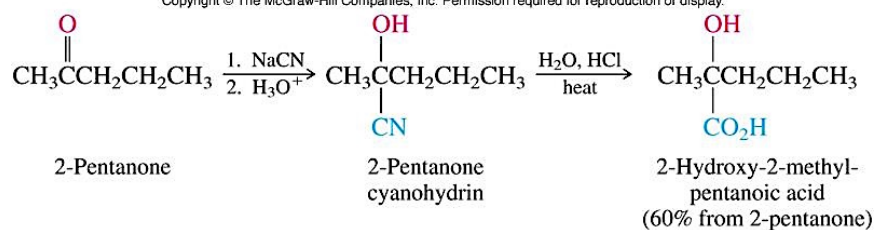
Reactions of Carboxylic Acids

1. **Reduction of Carboxylic Acids Gives Primary Alcohols**

$$RC\overset{\displaystyle O}{\overset{\|}{}}OH \xrightarrow[2.\ H_2O]{1.\ LiAlH_4, diethyl ether} RCH_2OH$$

Carboxylic acid   Primary alcohol
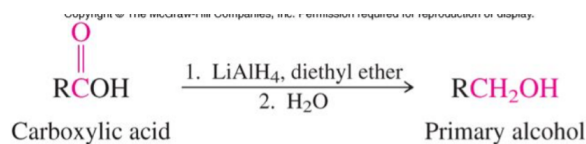
<u>Lithium aluminum hydride is the only effective reducing agent !</u>

2. **Reaction with Thionyl Chloride to yield Acyl Chlorides**

$$RC\overset{\displaystyle O}{\overset{\|}{}}OH + SOCl_2 \longrightarrow RC\overset{\displaystyle O}{\overset{\|}{}}Cl + SO_2 + HCl$$

Carboxylic   Thionyl   Acyl   Sulfur   Hydrogen
    acid   chloride   chloride   dioxide   chloride
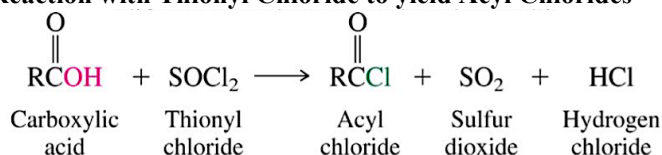
3. **Reaction with Alcohols to yield Esters**

$$ROH + R'C\overset{\displaystyle O}{\overset{\|}{}}OH \underset{}{\overset{H^+}{\rightleftharpoons}} R'C\overset{\displaystyle O}{\overset{\|}{}}OR + H_2O$$

Alcohol   Carboxylic acid   Ester   Water

Reactions

$C = C$

$\xrightarrow[\text{Electrophilic Addition}]{Hx}$ $\underset{X}{\overset{H}{C} - C}$

$\xrightarrow[\text{Electrophilic Addition}]{HBr}$ $\underset{Br}{\overset{H}{C} - C}$

$\xrightarrow[\text{Addition of Halogens}]{X_2}$ $\underset{X}{\overset{X}{C} - C}$ (anti–addition)

$\xrightarrow[\text{Halohydrin formation}]{X_2/H_2O}$ $\underset{X}{\overset{HO}{C} - C}$ (anti–addition)

$\xrightarrow[\text{Alcohol formation.}]{H^+/H_2O}$ $\underset{OH}{\overset{H}{C} - C}$

$\xrightarrow[\text{Alkane formation}]{H_2 \, Pt.}$ $\overset{H}{C} - \overset{H}{C}$ (syn addition)

Dehydration $\underset{}{\overset{OH}{C} - \overset{H}{C}}$ $\xrightarrow{Acid}$ $C = C$

Dehydrohalogenation $\overset{X}{C} - \overset{H}{C}$ $\xrightarrow{Base}$ $C = C$

Reactions

$R - C \equiv C - H$

$\xrightarrow{2HX}$ $R - \underset{X}{\overset{X}{\underset{|}{\overset{|}{C}}}} - \underset{H}{\overset{H}{\underset{|}{\overset{|}{C}}}} - H$

$\xrightarrow{2X_2}$ $R - \underset{X}{\overset{X}{\underset{|}{\overset{|}{C}}}} - \underset{X}{\overset{H}{\underset{|}{\overset{|}{C}}}} - X$

$\xrightarrow[\substack{\text{Hydrogenation} \\ \text{of alkynes to alkanes}}]{2H_2, Pt}$ $R - \underset{H}{\overset{H}{\underset{|}{\overset{|}{C}}}} - \underset{H}{\overset{H}{\underset{|}{\overset{|}{C}}}} - H$

$\xrightarrow[\substack{\text{Hydrogenation of} \\ \text{alkynes to Alkenes.}}]{H_2, \text{ Lindlar's}}$ $\underset{R}{\overset{H}{>}} C = C \underset{H}{\overset{H}{<}}$ (syn addition)

$\xrightarrow[\substack{\text{Metal-ammonia} \\ \text{reduction}}]{Na, NH_3(liq)}$ $\underset{R}{\overset{H}{>}} C = C \underset{H}{\overset{R'}{<}}$ (anti-addition).

$\xrightarrow[\substack{RCH_2X \\ \text{Alkylation of} \\ \text{Acetylene.}}]{NaNH_2, NH_3}$ $R - C \equiv C - CH_2R$

$\xrightarrow[\substack{HgSO_4 \\ \text{Acid catalyzed} \\ \text{hydration}}]{H^+/H_2O}$ $\underset{R}{\overset{:\ddot{O}:}{\underset{|}{\overset{||}{C}}}} - \underset{H}{\overset{H}{\underset{|}{\overset{|}{C}}}} - H$ (Ketone).