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OpenCourseWare (2023)

CHEMISTRY II

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ORGANIC COMPOUNDS WITH OTHER FUNCTIONALITIES

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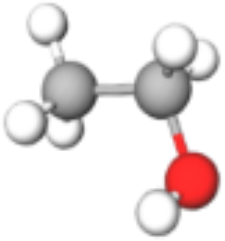
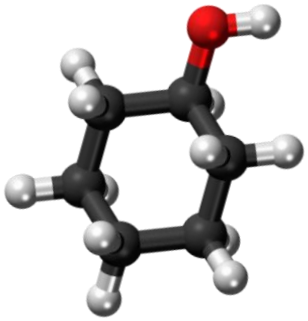
Contents

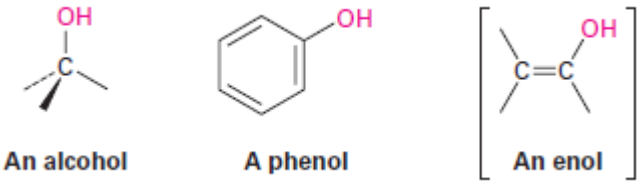
Introduction



Ethanol



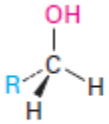
Phenol



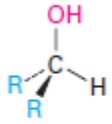
An alcohol **A phenol** **An enol**

Alcohols and phenols can be thought of as organic derivatives of water in which one of the water hydrogens is replaced by an organic group

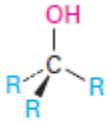
Naming Alcohols and Phenols



A primary (1°) alcohol



A secondary (2°) alcohol

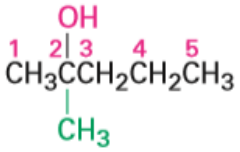


A tertiary (3°) alcohol

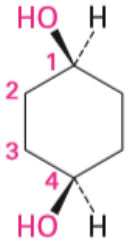
Rule 1. Select the longest carbon chain containing the hydroxyl group, and derive the parent name by replacing the ***e*** *ending of the corresponding alkane with* ***ol****. The e is deleted to prevent the occurrence of two adjacent vowels: propanol rather than propaneol, for example.*

Rule 2. Number the alkane chain beginning at the end nearer the ***hydroxyl group****.*

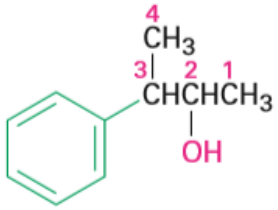
Rule 3. *Number the substituents according to their position on the chain, and write the name, listing the* ***substituents*** *in alphabetical order and identifying the position to which the -OH is bonded.*



2-Methyl-2-pentanol
(New: 2-Methylpentan-2-ol)



***cis*-1,4-Cyclohexanediol**
(New: *cis*-Cyclohexane-1,4-diol)



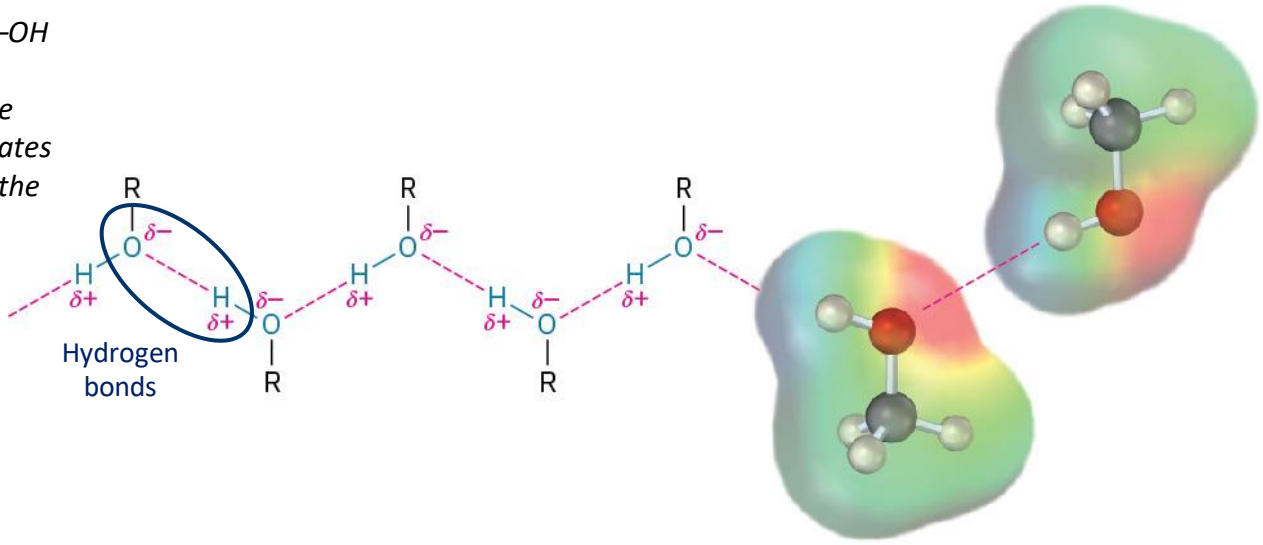
3-Phenyl-2-butanol
(New: 3-Phenylbutan-2-ol)

Physical Properties

Boiling Points of Alcohols

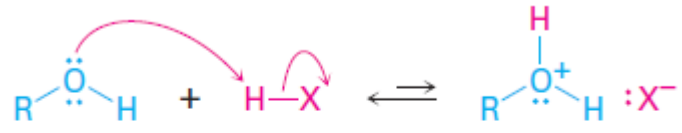
1-Propanol (MW = 60), butane (MW = 58), and chloroethane (MW = 65) have similar molecular weights, yet **1-propanol boils at 97 °C**, compared with **20.5 °C for the alkane** and **12.5 °C for the chloroalkane**, Why?

Hydrogen bonding *in alcohols and phenols. The interaction between a positively charged –OH hydrogen and a negatively charged oxygen is responsible for holding molecules together. The electrostatic potential map of methanol illustrates the positive charge on the –OH hydrogen and the negative charge on oxygen.*

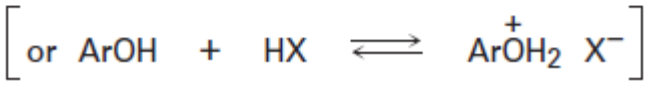


Acidity of Alcohols and Phenols

Weak base

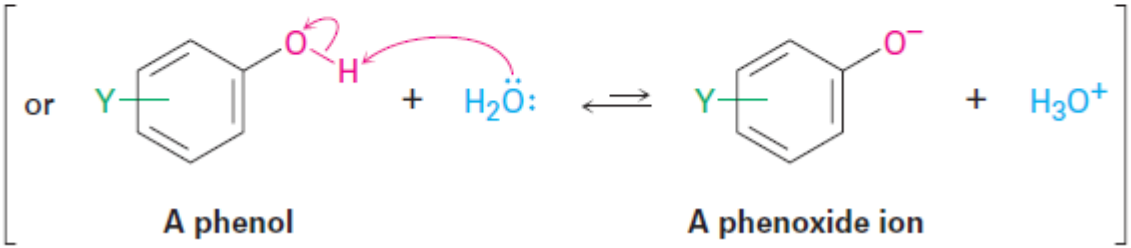


An alcohol **An oxonium ion**



Weak acid

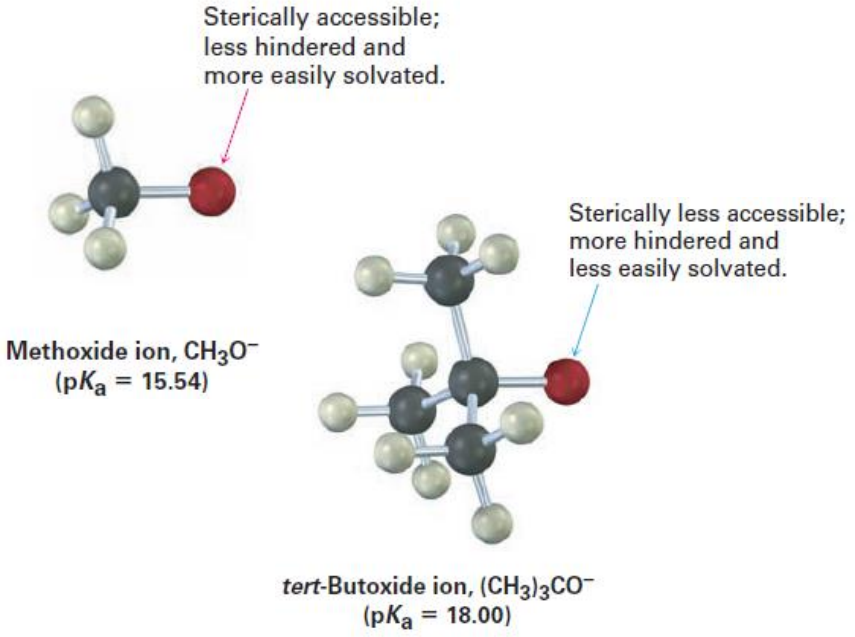
An alcohol **An alkoxide ion**

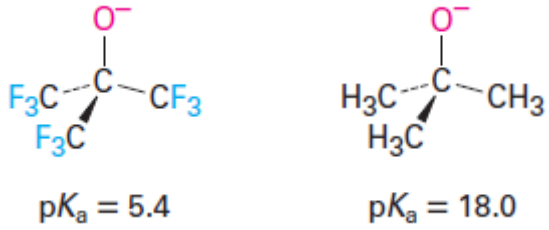


A phenol **A phenoxide ion**

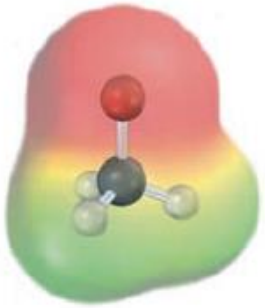
Acidity Constants of Some Alcohols and Phenols

Compound	pK_a	
$(CH_3)_3COH$	18.00	Weaker acid
CH_3CH_2OH	16.00	
H_2O	15.74	
CH_3OH	15.54	
CF_3CH_2OH	12.43	
p-Aminophenol	10.46	
CH_3SH	10.3	
p-Methylphenol	10.17	
Phenol	9.89	
p-Chlorophenol	9.38	
p-Nitrophenol	7.15	Stronger acid

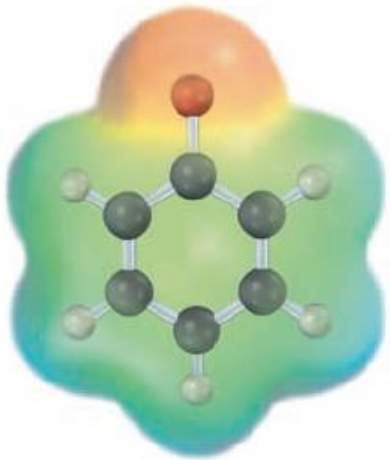




Electron-withdrawing groups *stabilize the alkoxide ion and lower the pKa.*



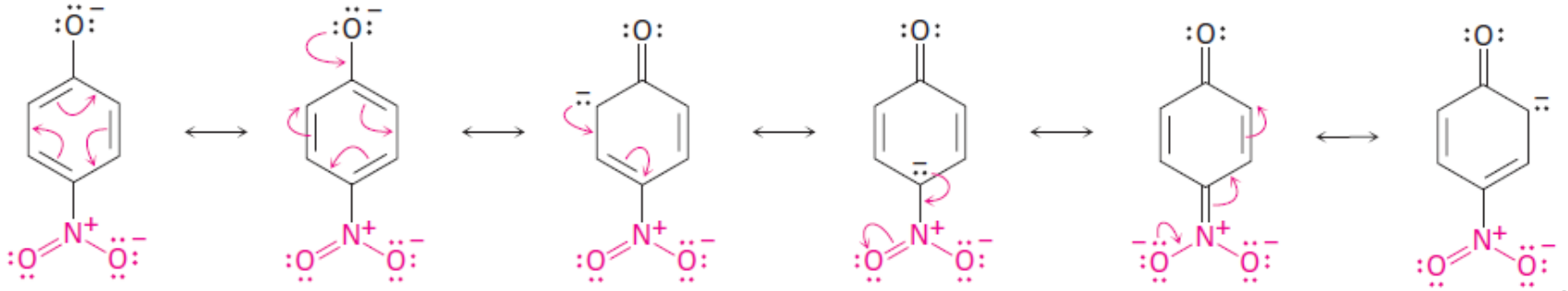
CH_3O^-



$C_6H_5O^-$

*The resonance-stabilized phenoxide ion is more stable than an alkoxide ion. Electrostatic potential maps show how the **negative charge** is concentrated on oxygen in the methoxide ion but is spread over the aromatic ring in the phenoxide ion.*

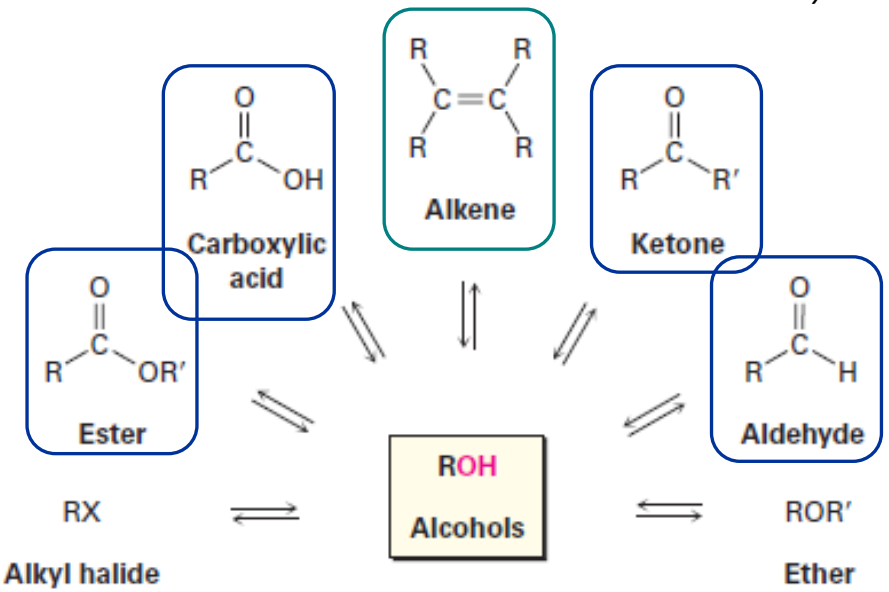
***Substituted phenols**: Phenols with an **electron-withdrawing substituent** are more acidic and phenols with an electron-donating substituent are less acidic.*



Synthesis of alcohols

Hydroxylation of an alkene *(Through an epoxide)*

Hydration of alkenes *(oxymercuration–demercuration yields the product of Markovnikov hydration).*

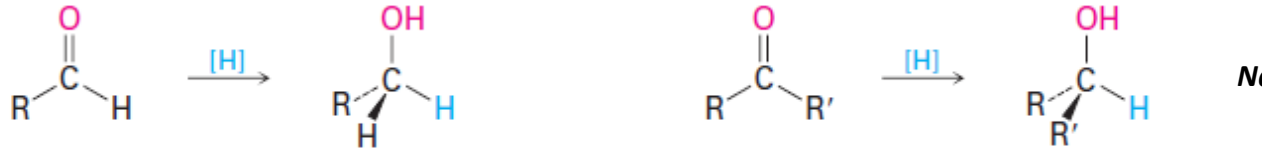


Reduction of Carbonyl Compounds

From ***Carbonyl Compounds: Grignard Reaction***

The central position of alcohols in organic chemistry.
Alcohols can be prepared from, and converted into, many other kinds of compounds.

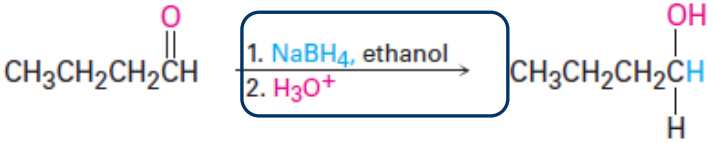
Alcohols from Carbonyl Compounds: Reduction



An aldehyde — A primary alcohol — A ketone — A secondary alcohol

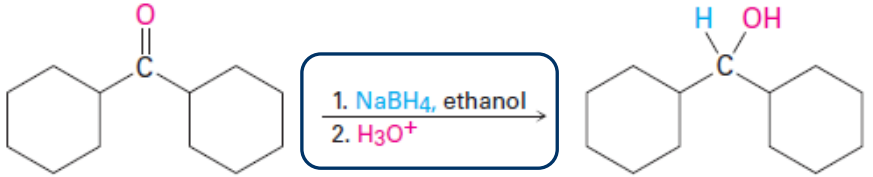
$NaBH_4$ *and* $LiAlH_4$ *are reducing agents*

Aldehyde reduction



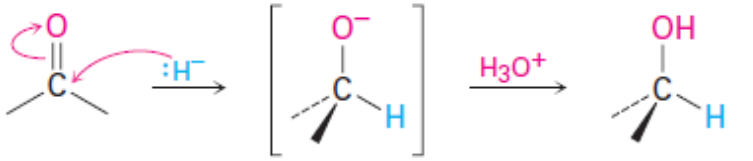
Butanal — 1-Butanol (85%) (a 1° alcohol)

Ketone reduction

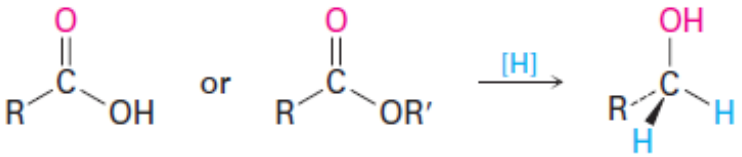


Dicyclohexyl ketone — Dicyclohexylmethanol (88%) (a 2° alcohol)

Mechanism



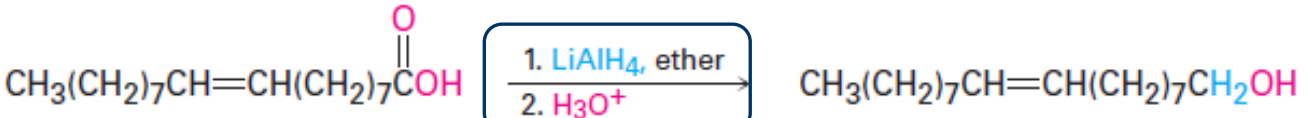
A carbonyl compound — An alkoxide ion intermediate — An alcohol



A carboxylic acid **An ester** **A primary alcohol**

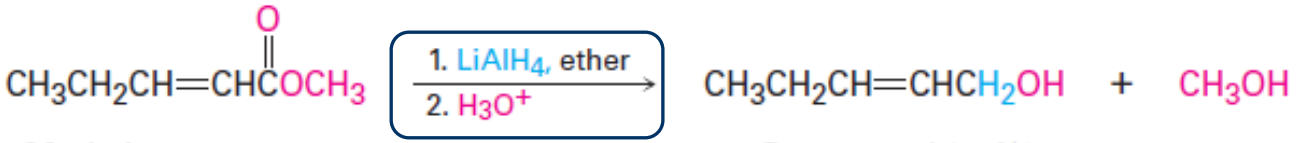
*$NaBH_4$ and **$LiAlH_4$** are reducing agents*

Carboxylic acid reduction



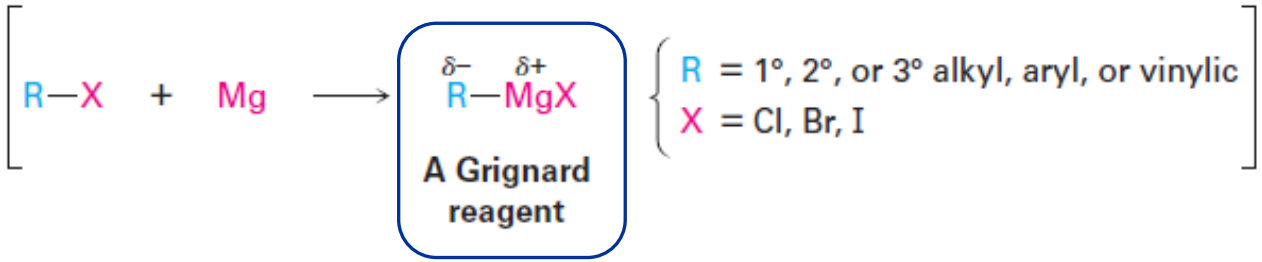
9-Octadecenoic acid (oleic acid) **9-Octadecen-1-ol (87%)**

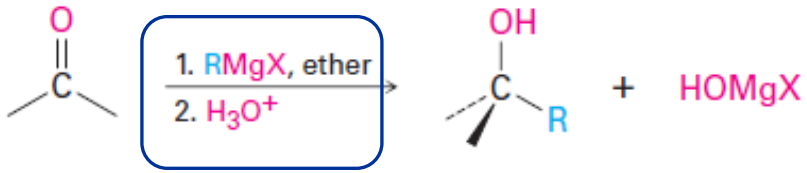
Ester reduction



Methyl 2-pentenoate **2-Penten-1-ol (91%)**

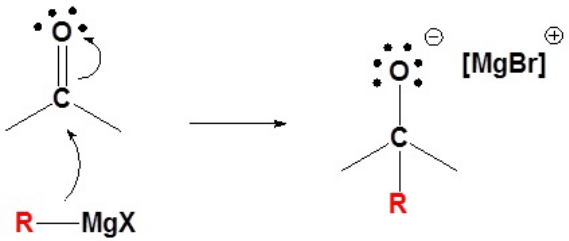
Alcohols from Carbonyl Compounds: Grignard Reaction





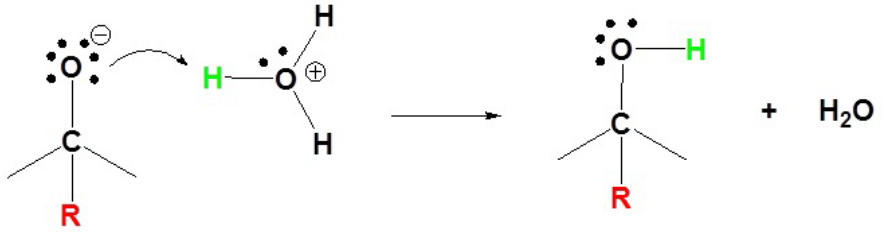
Mechanism

1. Nucleophilic reaction



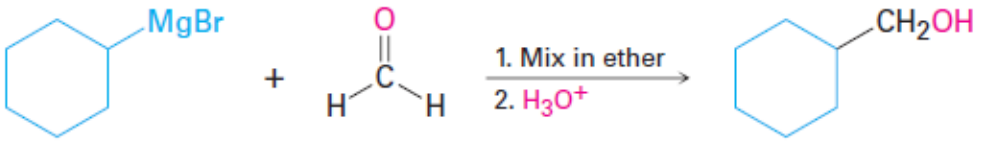
Alcoxide ion intermediate

2. Protonation



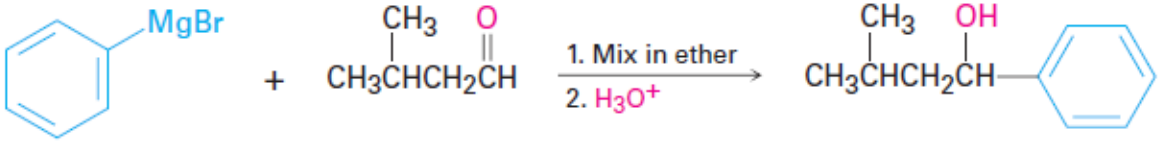
Examples

Formaldehyde reaction



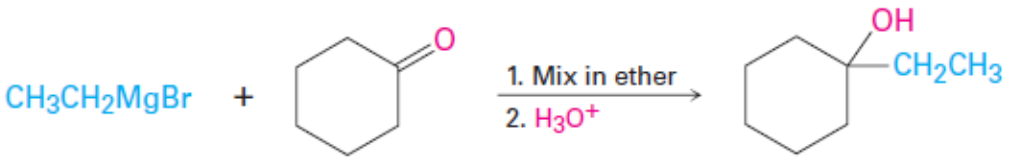
Cyclohexyl-magnesium bromide + **Formaldehyde** → **Cyclohexylmethanol (65%) (a 1° alcohol)**

Aldehyde reaction



Phenylmagnesium bromide + **3-Methylbutanal** → **3-Methyl-1-phenyl-1-butanol (73%) (a 2° alcohol)**

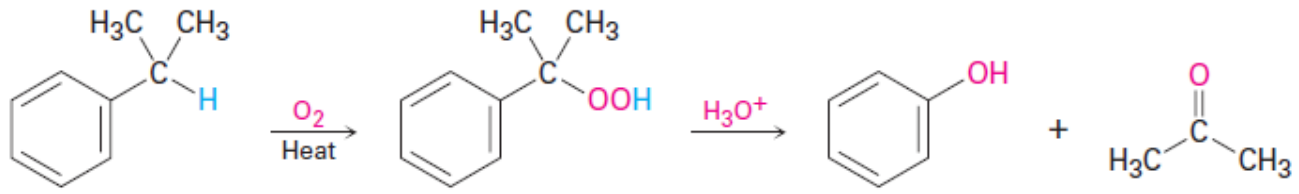
Ketone reaction



Ethylmagnesium bromide + **Cyclohexanone** → **1-Ethylcyclohexanol (89%) (a 3° alcohol)**

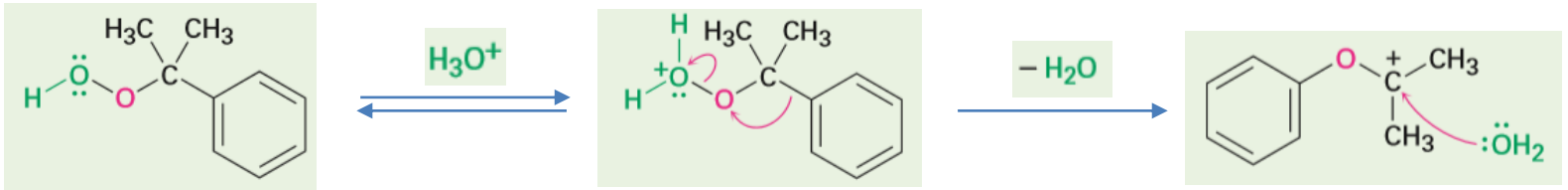
Synthesis of phenols

Benzylic oxidation
Reaction with air at high temperature



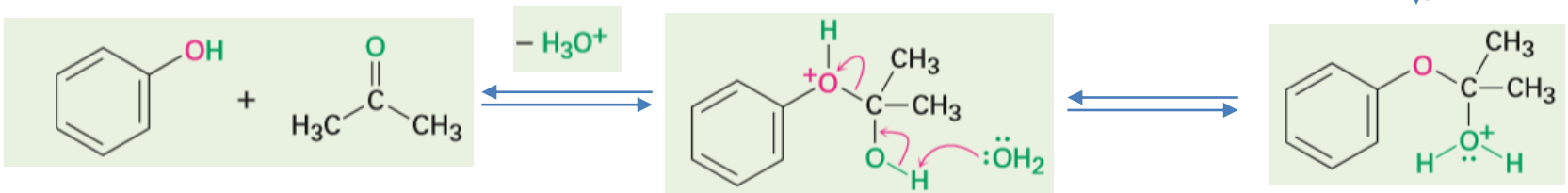
Cumene (isopropylbenzene) → **Cumene hydroperoxide** → **Phenol** + **Acetone**

Mechanism



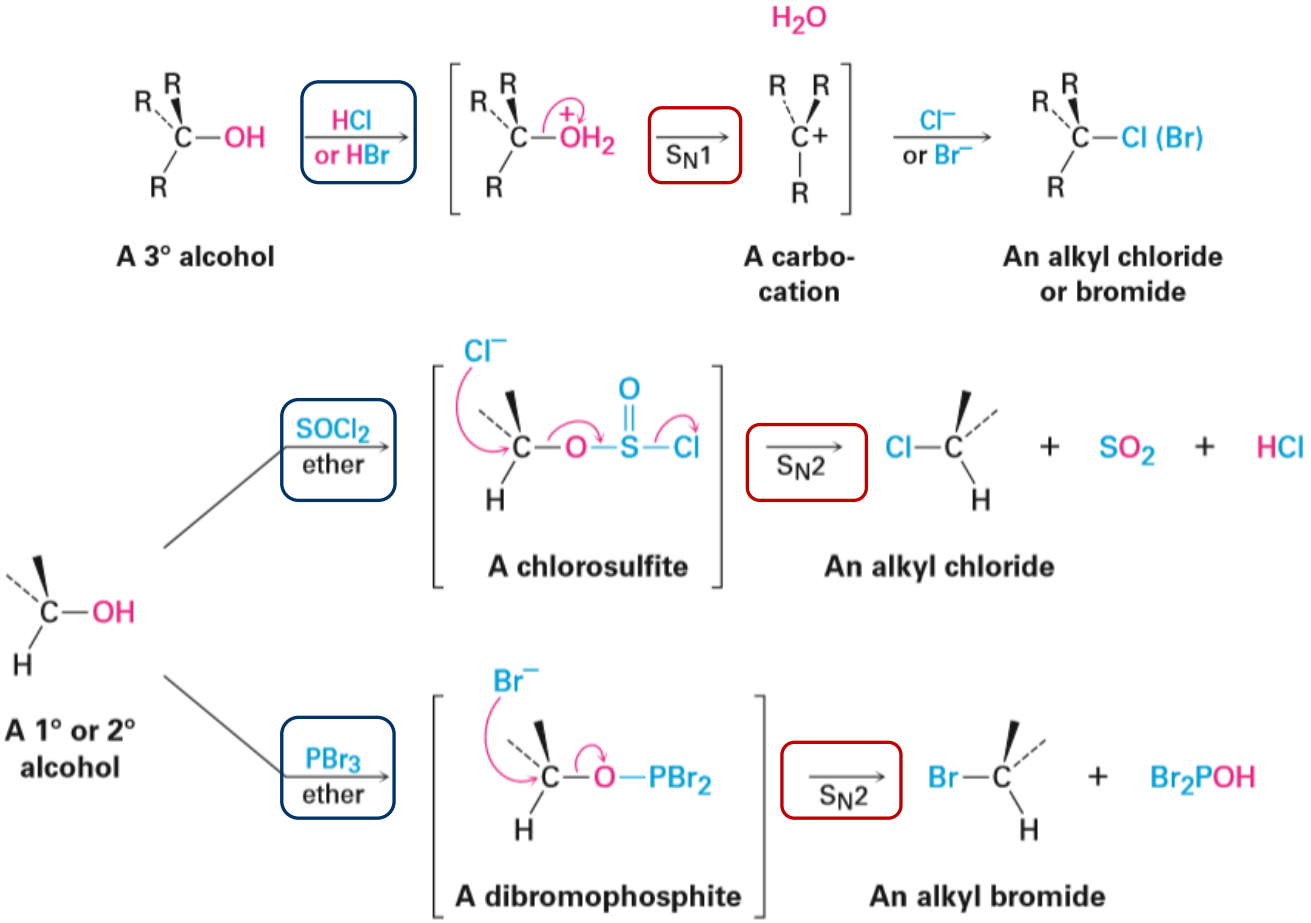
Protonation of the hydroperoxy group

Migration of the phenyl ring from carbon to oxygen

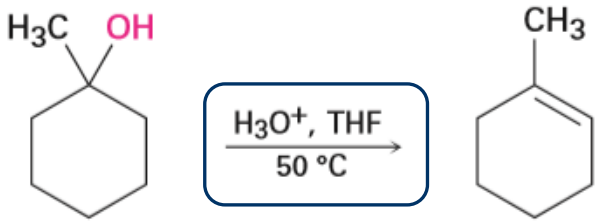


Reactivity of Alcohols

Conversion of Alcohols into Alkyl Halides

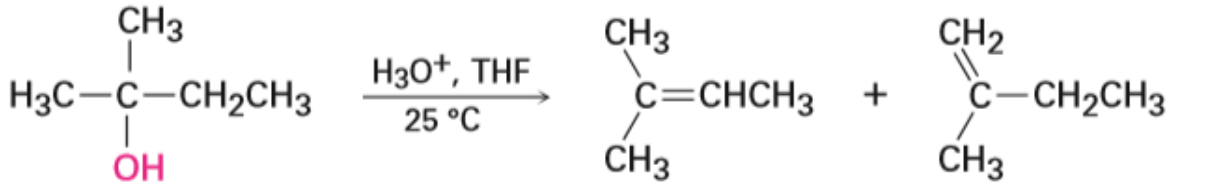


Dehydration of Alcohols to Yield Alkenes



1-Methylcyclohexanol 1-Methylcyclohexene (91%)

Acid catalyzed reaction



2-Methyl-2-butanol

2-Methyl-2-butene (trisubstituted) — **Major product**

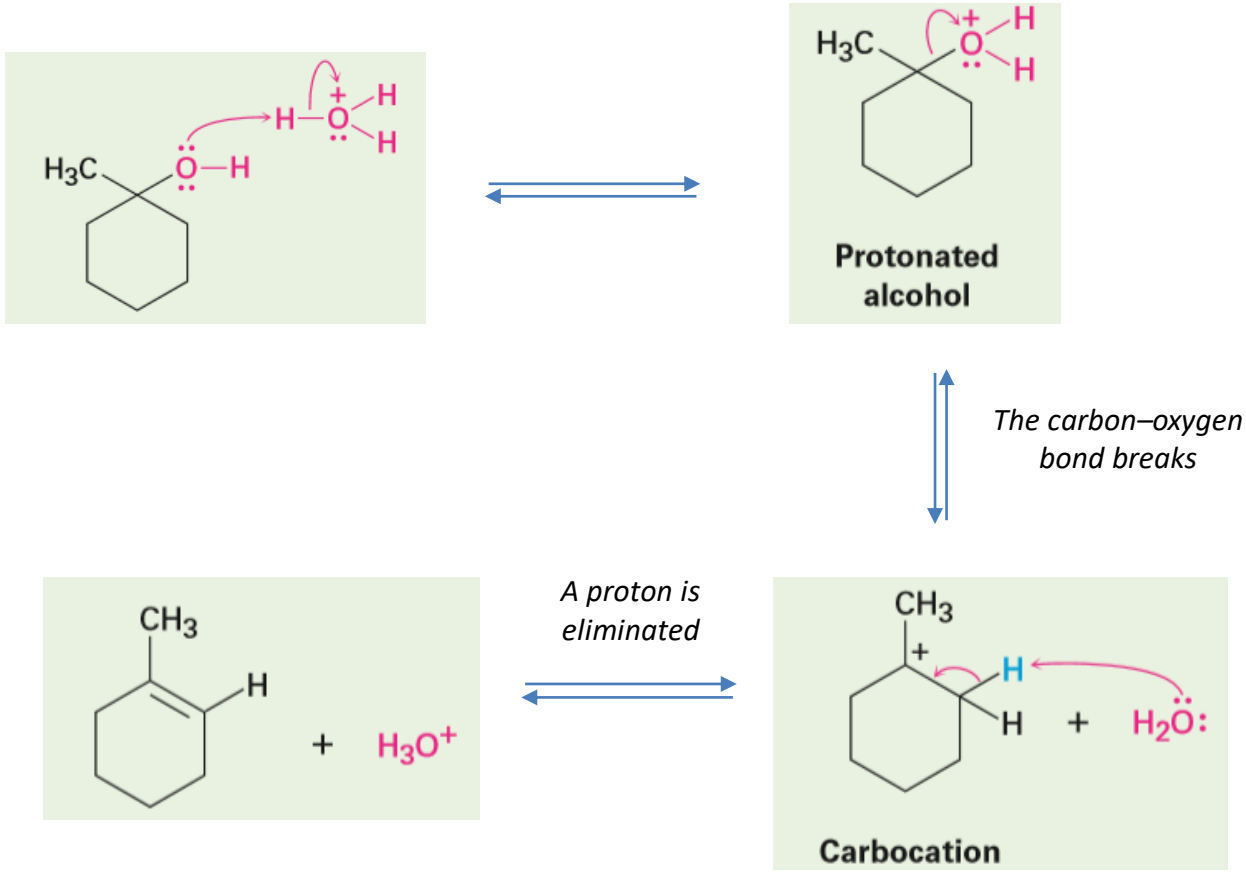
2-Methyl-1-butene (disubstituted) — **Minor product**

*Acid catalyzed dehydrations usually follow **Zaitsev's rule** and yield the more stable alkene as the major product*

Mechanism

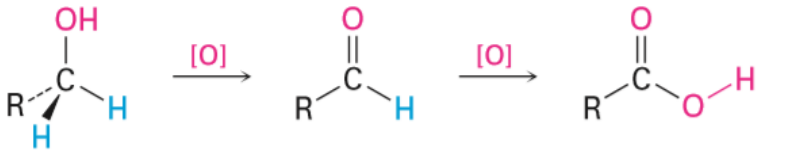
Mechanism of the acid-catalyzed dehydration of a tertiary alcohol to yield an alkene.

*The process is an **E1 reaction** and involves a carbocation intermediate*

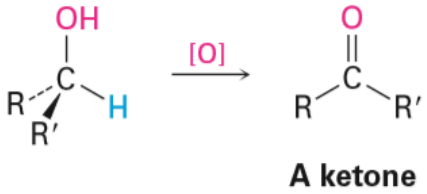


Oxidation of Alcohols

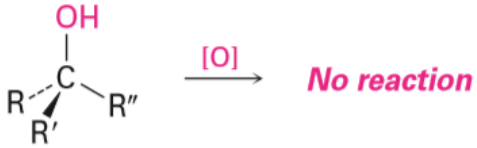
Primary alcohol



Secondary alcohol

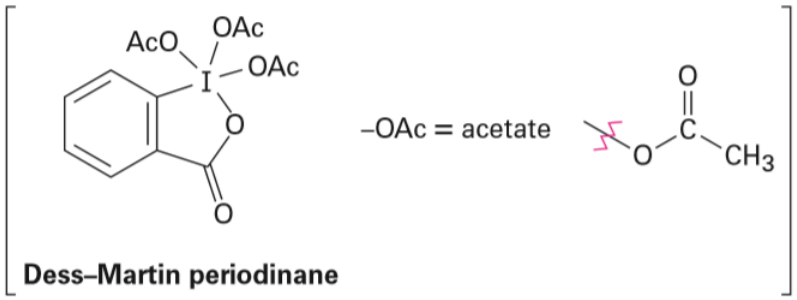


Tertiary alcohol



The oxidation of a primary or secondary alcohol can be accomplished by any of a large number of reagents, including ***$KMnO_4$, CrO_3,*** *and* ***$Na_2Cr_2O_7$***

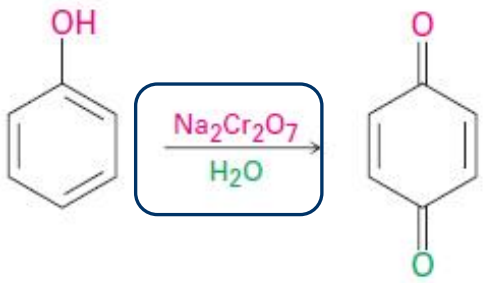
To prepare an aldehyde from a primary alcohol in the laboratory is to use the I(V) containing **Dess–Martin periodinane** in dichloromethane solvent.



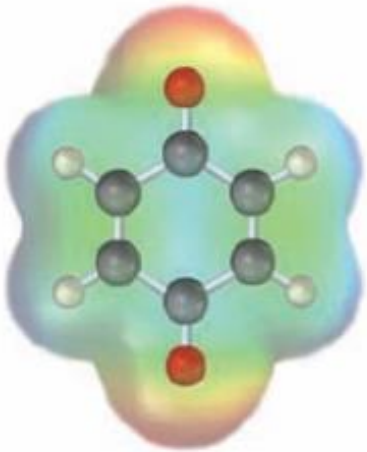
Reactivity of phenols

Oxidation of Phenols: Quinones

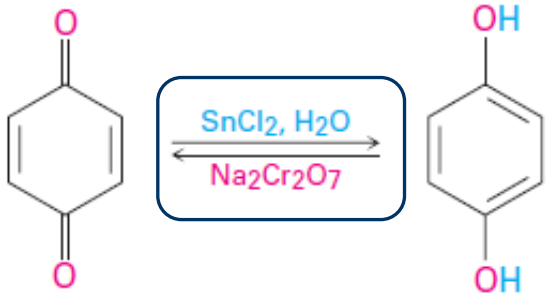
Oxidation



Phenol **Benzoquinone (79%)**

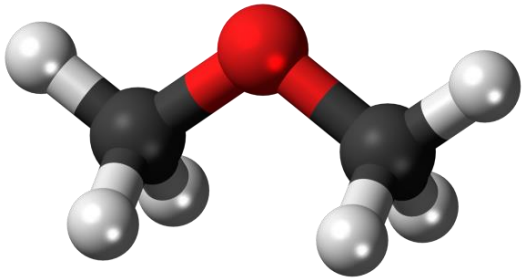


Reduction

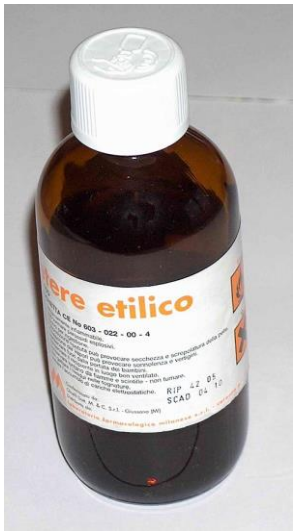


Benzoquinone **Hydroquinone**

Introduction



Diethyl Ether

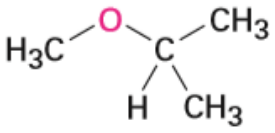


Industrial use as a solvent

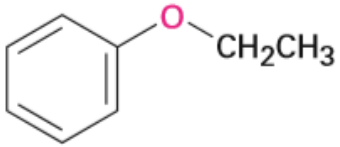
Ether as an anesthetic

Naming Ethers

Simple ethers with no other functional groups are named by identifying the two organic substituents and adding the word ***ether****.*

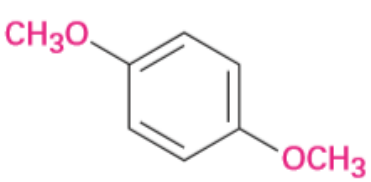


Isopropyl methyl ether

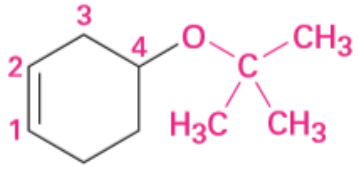


Ethyl phenyl ether

If other functional groups are present, the ether part is considered an ***alkoxy*** *substituent.*

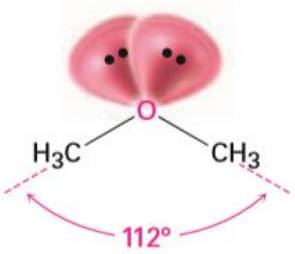


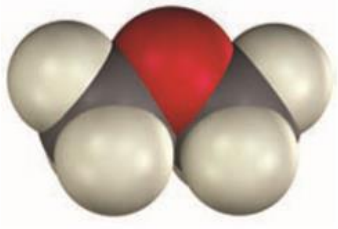
***p*-Dimethoxybenzene**

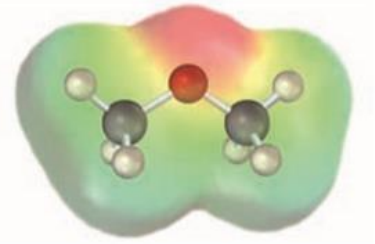


4-*tert*-Butoxy-1-cyclohexene

Physical Properties



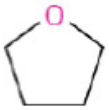
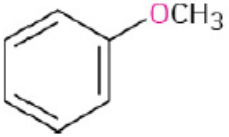
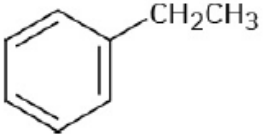




The R-O-R bonds have an approximately tetrahedral bond angle (112° in dimethyl ether), and the oxygen atom is **sp³-hybridized**.

The electronegative oxygen atom gives ethers a **slight dipole moment**, and the boiling points of ethers are often slightly higher than the boiling points of comparable alkanes.

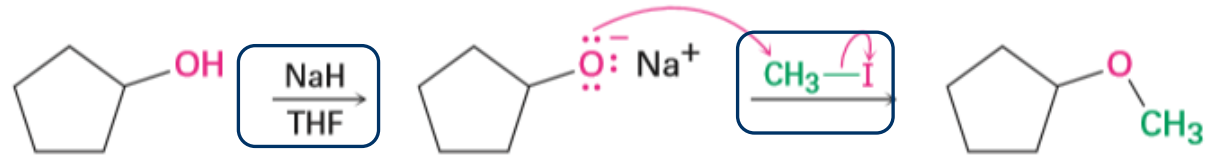
Comparison of Boiling Points of Ethers and Hydrocarbons

Ether	Boiling point °C	Hydrocarbon	Boiling point °C
CH_3OCH_3	−25	$CH_3CH_2CH_3$	−45
$CH_3CH_2OCH_2CH_3$	34.6	$CH_3CH_2CH_2CH_2CH_3$	36
	65		49
	158		136

Ethers:
Higher boiling points

Synthesis of Ethers

The Williamson Ether Synthesis

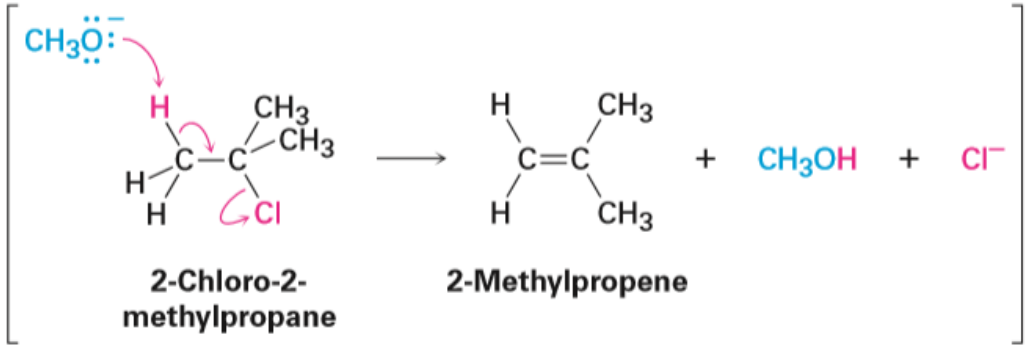


Cyclopentanol **Alkoxide ion** **Cyclopentyl methyl ether (74%)**

S_N2 Reaction

***tert*-Butoxide** **Iodomethane** ***tert*-Butyl methyl ether**

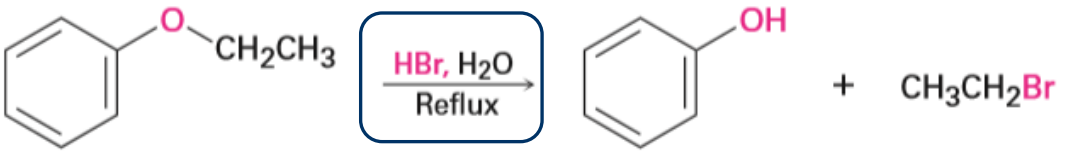
*Primary halides work best because **competitive E2 elimination** can occur with more hindered substrates.*



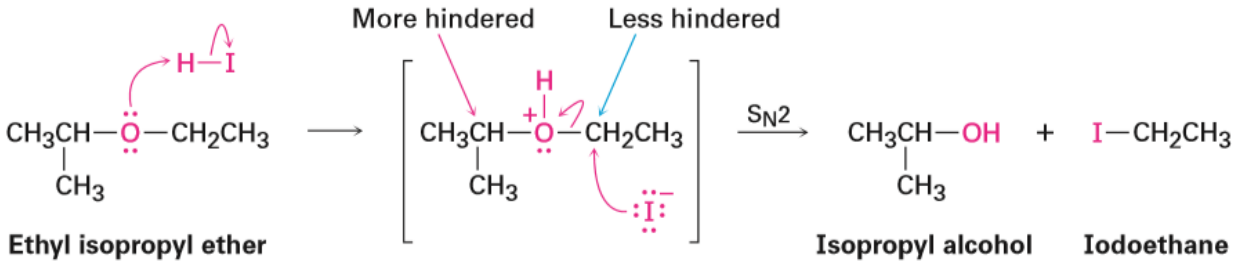
2-Chloro-2-methylpropane **2-Methylpropene**

Reactivity of Ethers

Acidic Cleavage

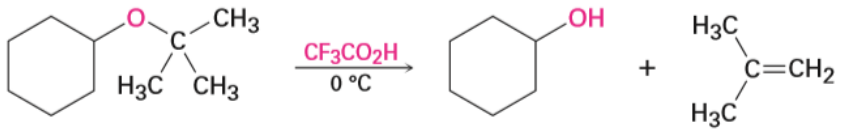


Ethyl phenyl ether **Phenol** **Bromoethane**



Ethyl isopropyl ether **Isopropyl alcohol** **Iodoethane**

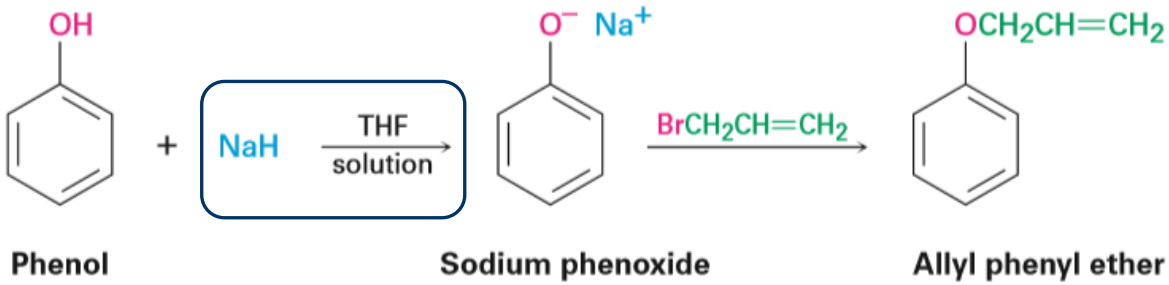
*Ethers with only primary and secondary alkyl groups react by an **S_N2** mechanism*

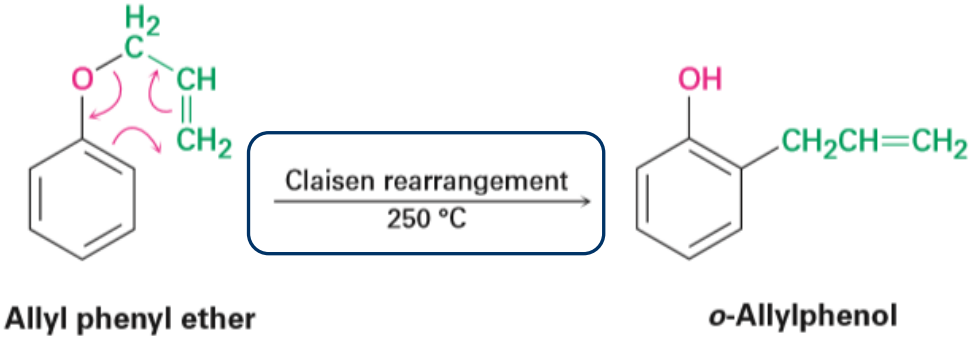


***tert*-Butyl cyclohexyl ether** **Cyclohexanol (90%)** **2-Methylpropene**

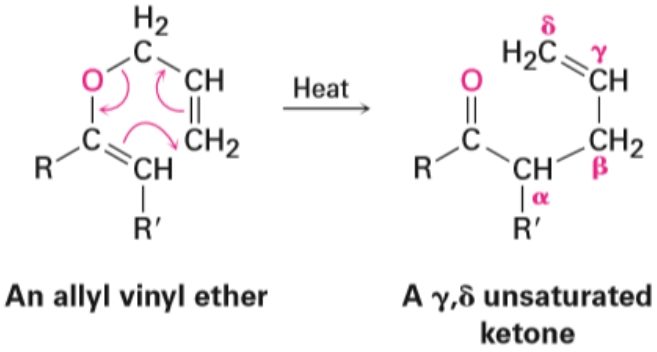
*Ethers with a tertiary, benzylic, or allylic group cleave by either an **S_N1** or **E1** mechanism*

Claisen Rearrangement

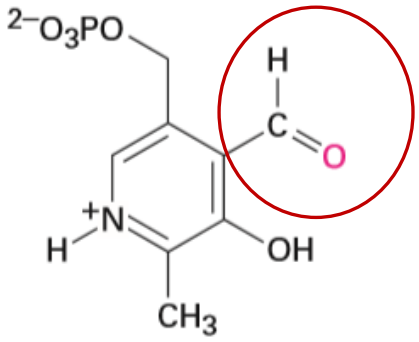




*Alkylation of the phenol in an **ortho** position*

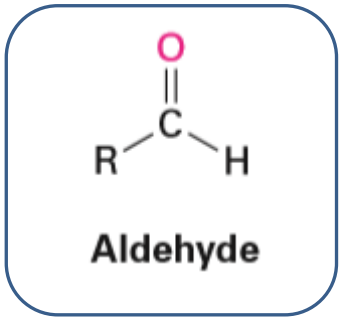


Introduction

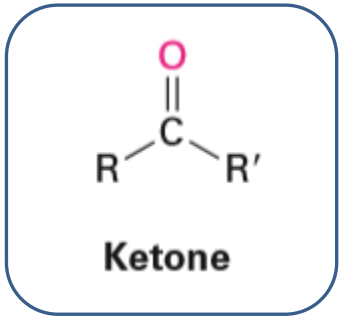


Pyridoxal phosphate (PLP)

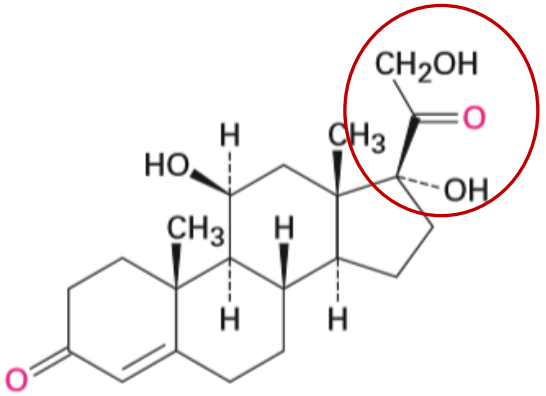
Pyridoxal phosphate is a coenzyme involved in a large number of metabolic reactions



Aldehyde



Ketone

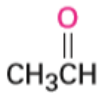


Hydrocortisone

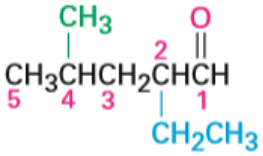
The ketone hydrocortisone is a steroid hormone secreted by the adrenal glands to regulate fat, protein, and carbohydrate metabolism

Naming Carbonyl Compounds

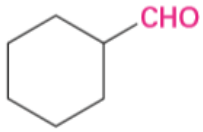
Aldehydes are named by replacing the terminal **-e** of the corresponding alkane name with **–al**. For cyclic aldehydes in which the -CHO group is directly attached to a ring, the suffix **-carbaldehyde** is used.



Ethanal
(acetaldehyde)

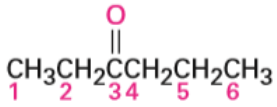


2-Ethyl-4-methylpentanal

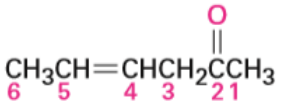


Cyclohexanecarbaldehyde

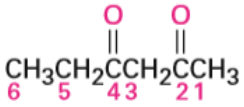
Ketones are named by replacing the terminal **-e** of the corresponding alkane name with **-one**. If other functional groups are present and the doubly bonded oxygen is considered a substituent on a parent chain, the prefix **oxo-** is used.



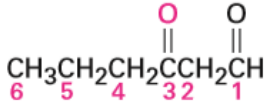
3-Hexanone
(New: Hexan-3-one)



4-Hexen-2-one
(New: Hex-4-en-2-one)

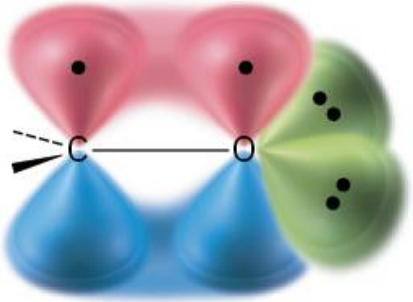


2,4-Hexanedione
(New: Hexane-2,4-dione)

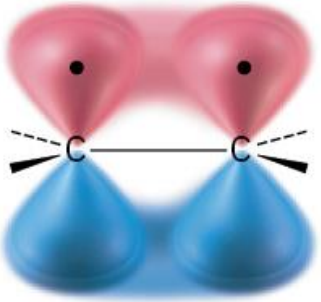


3-Oxohexanal

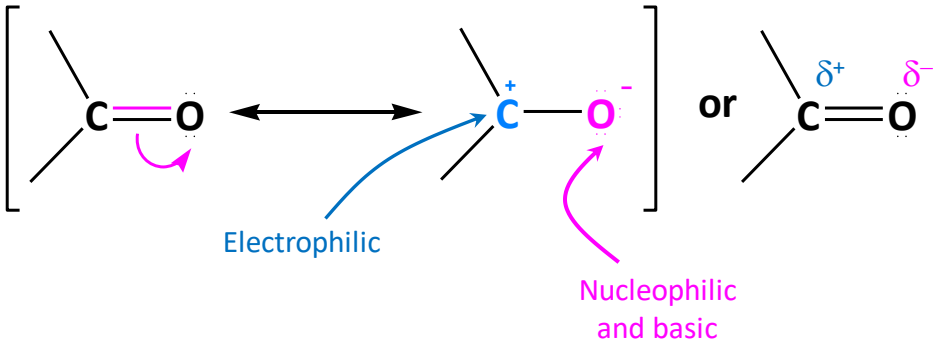
Structure of the Carbonyl Group

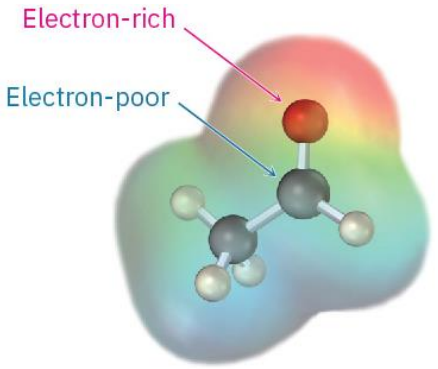


Carbonyl group



Alkene





Structure of acetaldehyde

Physical Properties

Boiling Points of Aldehydes and Ketones

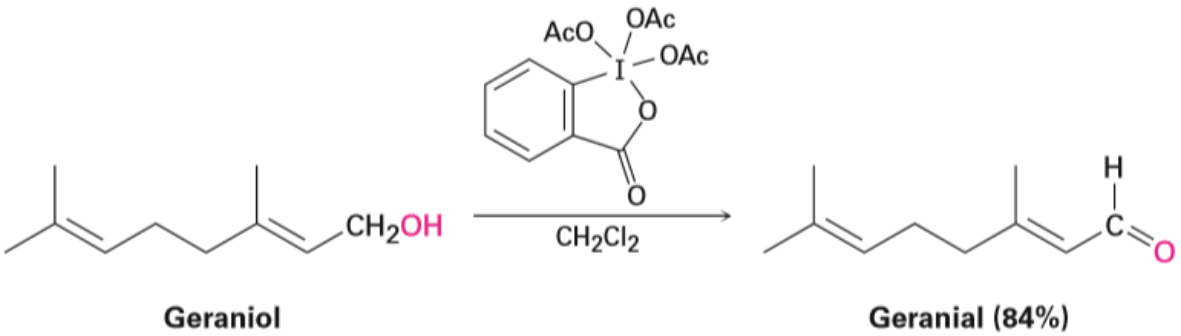
Compound	Boiling point (ºC)
Formaldehyde	-21
Acetaldehyde	21
Propanal	49
Acetone	56
Butanal	76
Butanone	80
Pentanal	102
2-Pentanone	102
3-Pentanone	102

*The **polarization of the carbonyl group** makes the boiling points of aldehydes and ketones higher than those of hydrocarbons of similar size and molecular weight*

Pentane
Boiling Point = 36.1 ºC

Synthesis of Ketones and Aldehydes

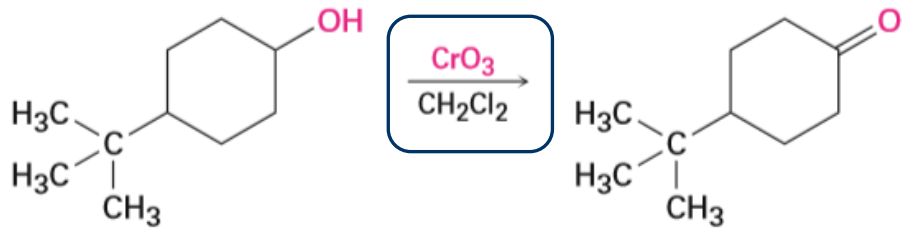
Preparing Aldehydes: Oxidation of Primary Alcohols



Geraniol → **Geranial (84%)**

Dess–Martin periodinane *reagent as an oxidant*

Preparing Ketones: Oxidation of Secondary Alcohols

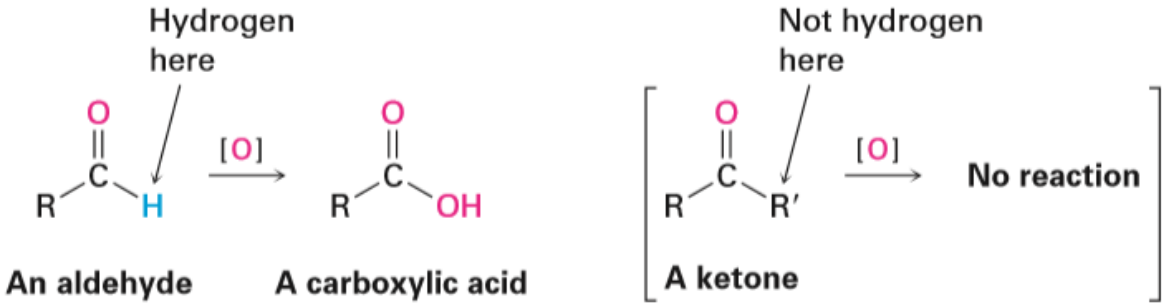


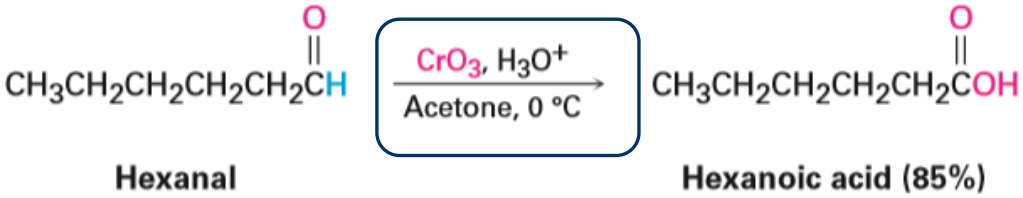
4-*tert*-Butylcyclohexanol → **4-*tert*-Butylcyclohexanone (90%)**

Dess–Martin periodinane reagent or ***CrO_3*** *as an oxidant*

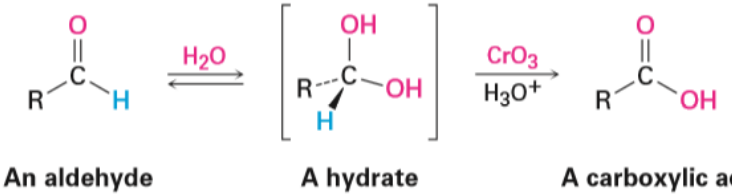
Reactivity of Ketones and Aldehydes

Oxidation of Ketones and Aldehydes





Oxidation of aldehydes: Mechanism



Nucleophilic Addition Reactions

Mechanism

An electron pair from the nucleophile adds to the electrophilic carbon of the carbonyl group, pushing an electron pair from the C=O bond onto oxygen. The carbonyl carbon rehybridizes from sp^2 to sp^3.

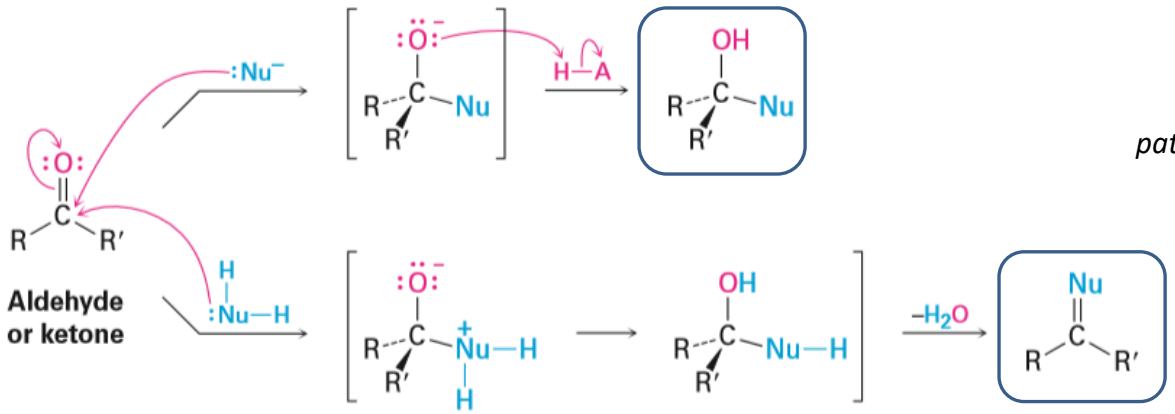
Protonation of the alkoxide anion intermediate gives the neutral alcohol addition product

Some negatively charged nucleophiles

- $H\ddot{O}:^-$ (hydroxide ion)
- $H:^-$ (hydride ion)
- $R_3C:^-$ (a carbanion)
- $R\ddot{O}:^-$ (an alkoxide ion)
- $N{\equiv}C:^-$ (cyanide ion)

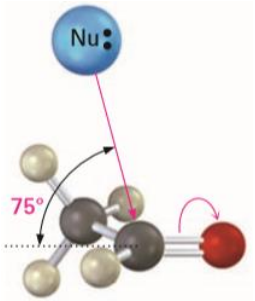
Some neutral nucleophiles

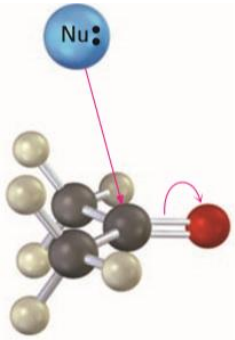
- $H\ddot{O}H$ (water)
- $R\ddot{O}H$ (an alcohol)
- $H_3N:$ (ammonia)
- $R\ddot{N}H_2$ (an amine)



The top pathway leads to an alcohol product; the bottom pathway leads to a product with a C=Nu double bond

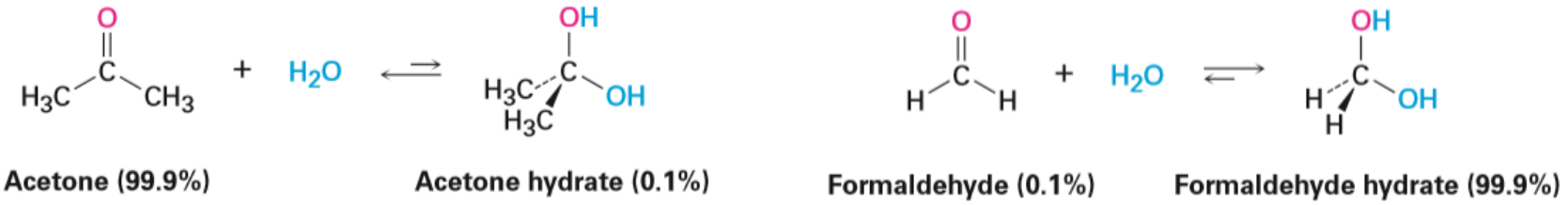
In an aldehyde, reaction is sterically less hindered





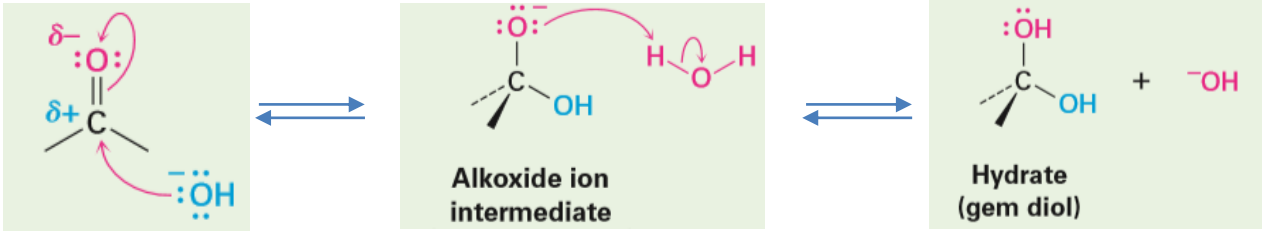
A ketone has two large substituents and is more hindered.

Nucleophilic Addition of H_2O: Hydration

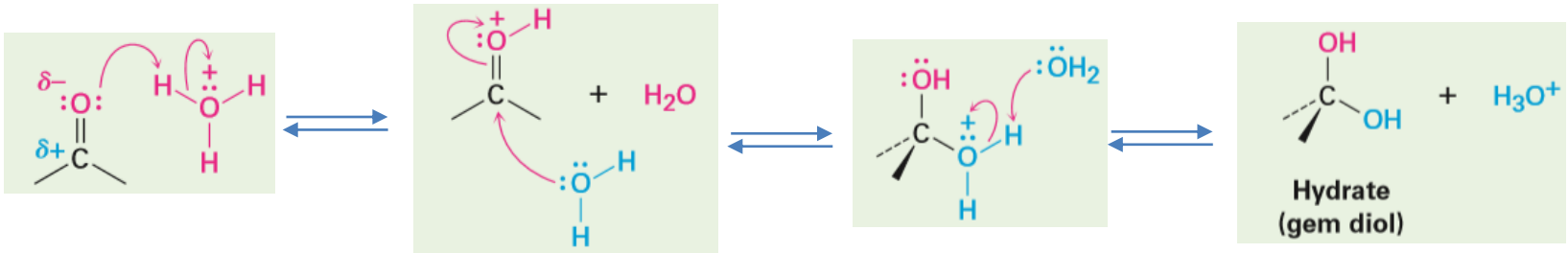


The nucleophilic addition of water to an aldehyde or ketone is slow under neutral conditions but is catalyzed by both base and acid.

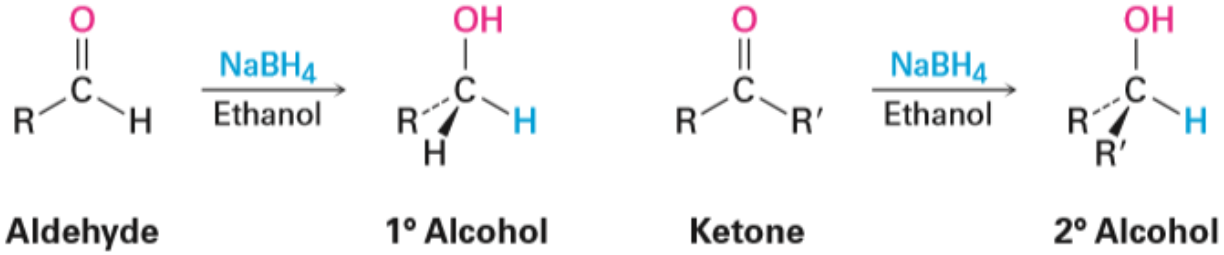
Basic



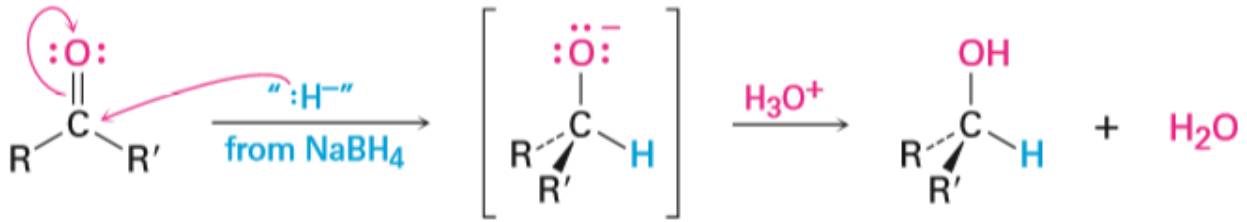
Acid



Nucleophilic Addition of Hydride: Reduction



Aldehydes are reduced with sodium borohydride ($NaBH_4$) to give primary alcohols, and ketones are reduced similarly to give secondary alcohols

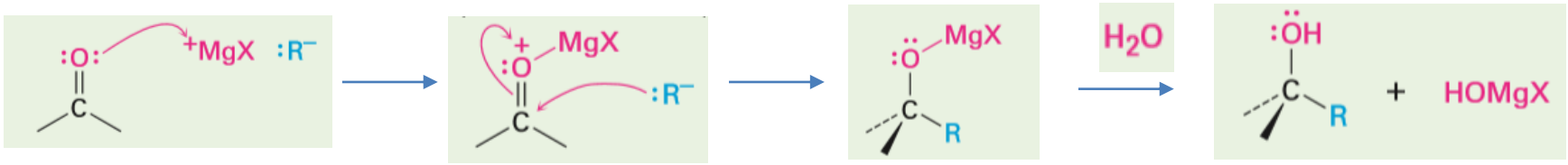


$LiAlH_4$ *and* ***$NaBH_4$*** *act as if they were donors of hydride ion nucleophile, $:H^-$, and the initially formed alkoxide ion intermediate is then protonated by addition of aqueous acid*

Nucleophilic Addition of Grignard Agents

Aldehyde **2° Alcohol** **Ketone** **3° Alcohol**

Mechanism

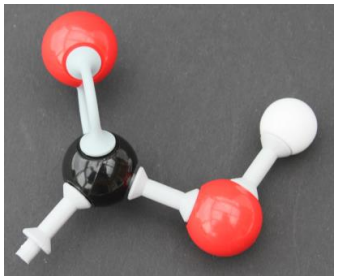


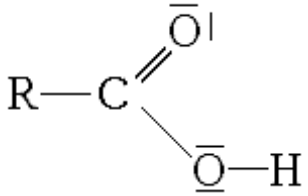
Acid–base complex

Tetrahedral magnesium alkoxide intermediate

Alcohol

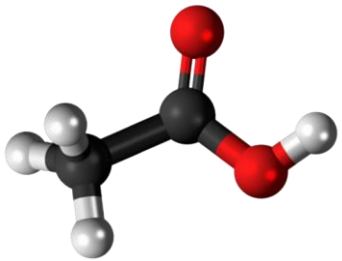
Introduction



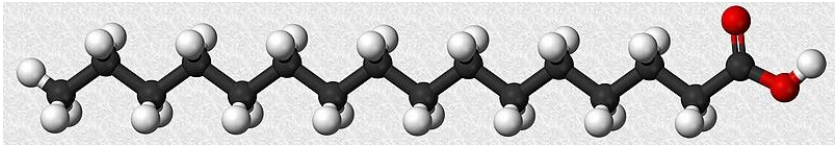


Carboxy Group

It is a major component of the oil from the fruit of oil palm



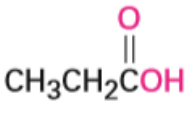
Acetic Acid



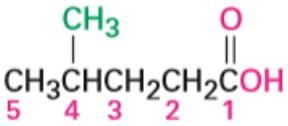
Palmitic Acid

Naming Carboxylic Acids

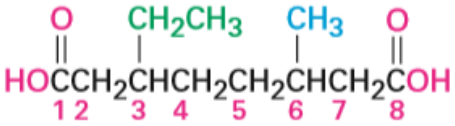
Simple carboxylic acids derived from open-chain alkanes are systematically named by replacing the terminal ***-e*** *of the corresponding alkane name with* ***-oic acid****. The -CO_2H carbon atom is numbered* ***C1****.*



Propanoic acid

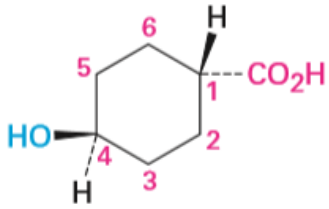


4-Methylpentanoic acid



3-Ethyl-6-methyloctanedioic acid

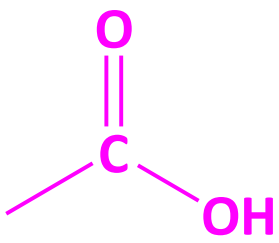
Compounds that have a -CO_2H group bonded to a ring are named using the suffix ***-carboxylic acid****. The CO_2H carbon is attached to* ***C1*** *in this system and is not itself numbered. As a substituent, the CO_2H group is called a carboxyl group.*



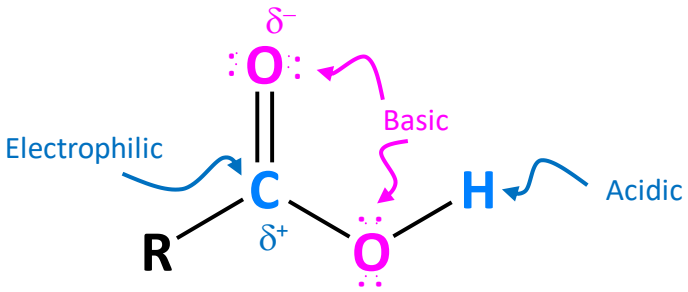
***trans*-4-Hydroxycyclohexanecarboxylic acid**

1-Cyclopentenecarboxylic acid

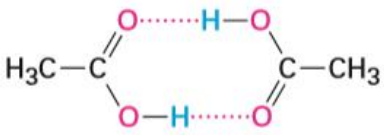
Physical properties: The Carboxy Group



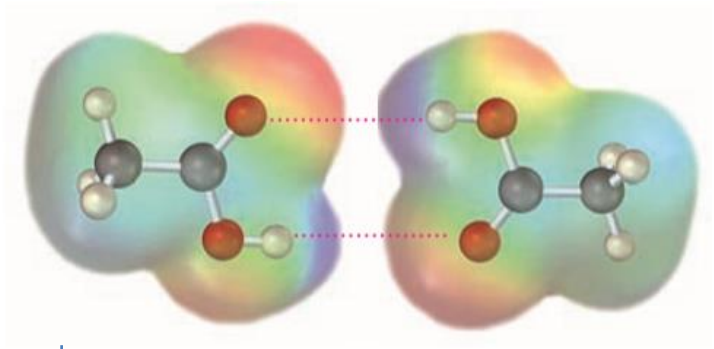
Carboxy group



Hydrogen Bonding



Acetic acid dimer



Melting and Boiling Points

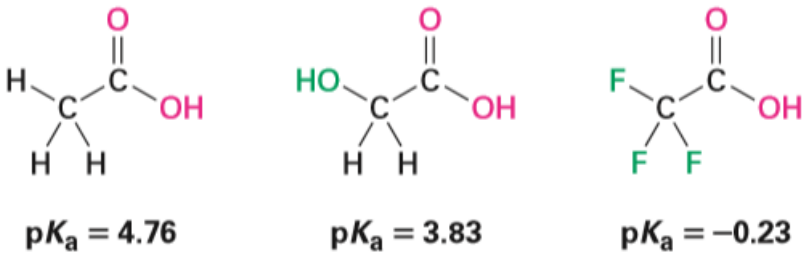
Acidity and Solubility

$$K_a = \frac{[RCO_2^-][H_3O^+]}{[RCO_2H]} \quad \text{and} \quad pK_a = -\log K_a$$

Acidity of Some Carboxylic Acids

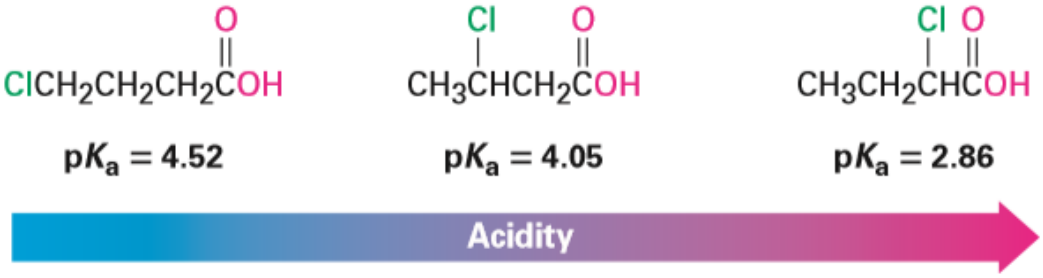
Structure	K_a	pK_a	
CF_3CO_2H	0.59	0.23	Stronger acid
HCO_2H	1.77×10^{-4}	3.75	
$HOCH_2CO_2H$	1.5×10^{-4}	3.84	
$C_6H_5CO_2H$	6.46×10^{-5}	4.19	
$H_2C{=}CHCO_2H$	5.6×10^{-5}	4.25	
CH_3CO_2H	1.75×10^{-5}	4.76	
$CH_3CH_2CO_2H$	1.34×10^{-5}	4.87	
CH_3CH_2OH (ethanol)	(1.00×10^{-16})	(16.00)	Weaker acid

Substituent Effects on Acidity

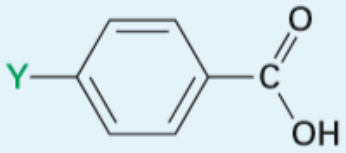


*Three **electron-withdrawing** fluorine atoms delocalize the negative charge in the trifluoroacetate anion, thereby stabilizing the ion and increasing the acidity of CF_3CO_2H.*

***Inductive effects** operate through sigma bonds and are dependent on distance, the effect of halogen substitution decreases as the substituent moves farther from the carboxyl.*

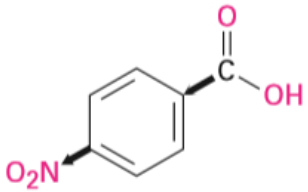


Substituent Effects on Acidity of p-Substituted Benzoic Acids

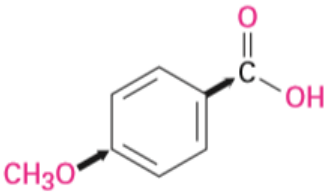


	Y	$K_a \times 10^{-5}$	pK_a	
Stronger acid	$-NO_2$	39	3.41	Deactivating groups
	$-CN$	28	3.55	
	$-CHO$	18	3.75	
	$-Br$	11	3.96	
	$-Cl$	10	4.0	
	$-H$	6.46	4.19	
	$-CH_3$	4.3	4.34	Activating groups
	$-OCH_3$	3.5	4.46	
Weaker acid	$-OH$	3.3	4.48	

The carboxylate anion is stabilized



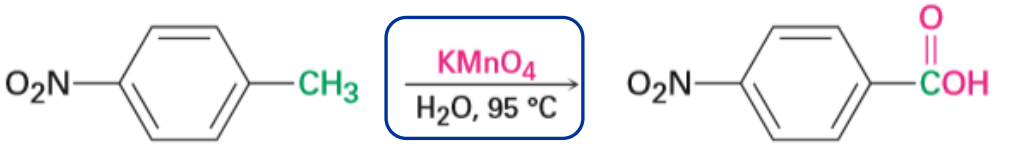
***p*-Nitrobenzoic acid**
(pK_a = 3.41)



***p*-Methoxybenzoic acid**
(pK_a = 4.46)

Synthesis of carboxylic acids

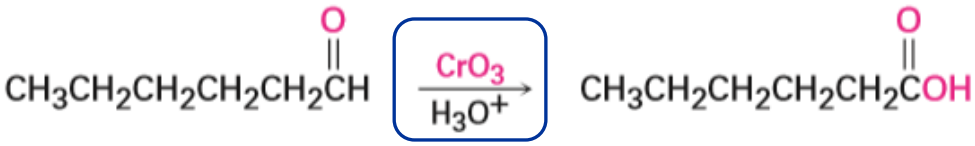
Oxidation Reactions



p-Nitrotoluene **p-Nitrobenzoic acid (88%)**

Oxidation of a substituted alkylbenzene gives a substituted benzoic acid

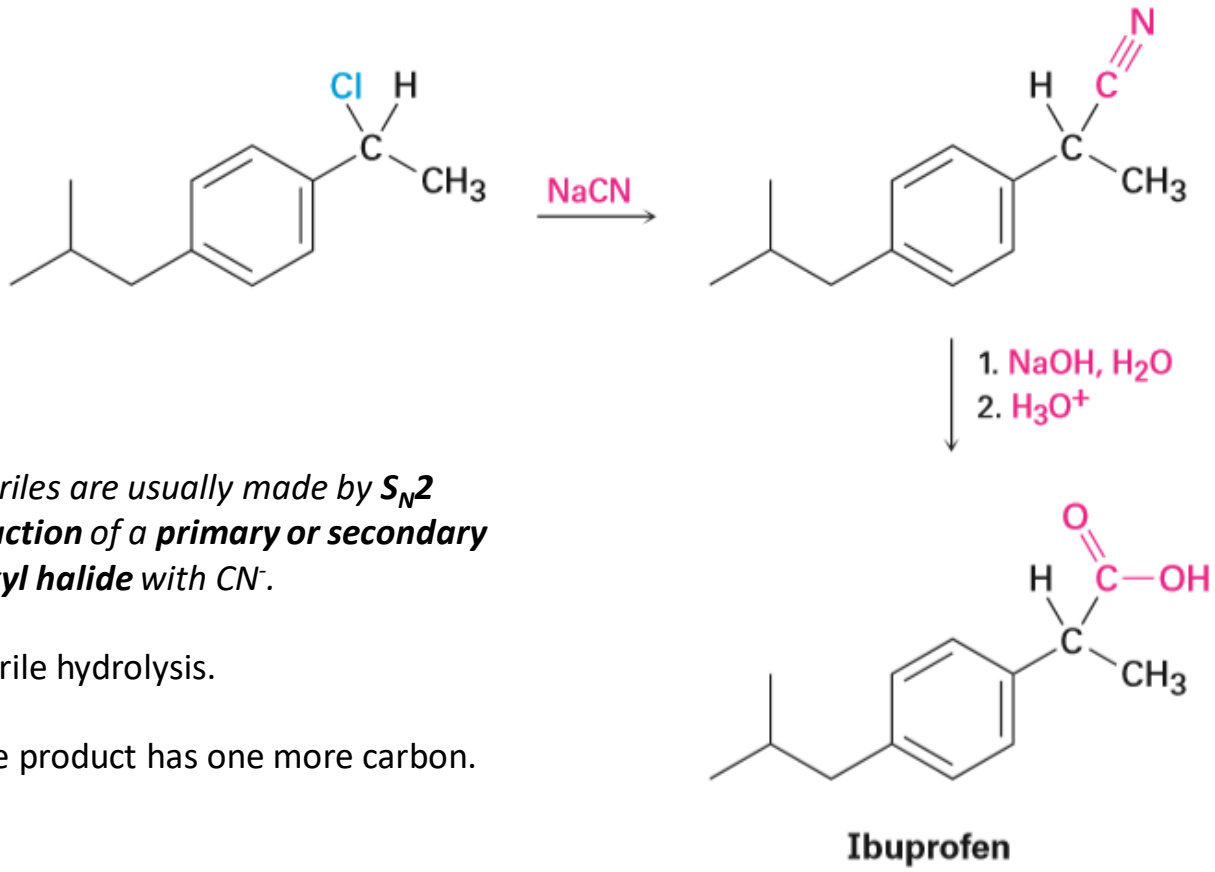
4-Methyl-1-pentanol **4-Methylpentanoic acid**



Hexanal **Hexanoic acid**

Oxidation of a primary alcohol or an aldehyde yields a carboxylic acid

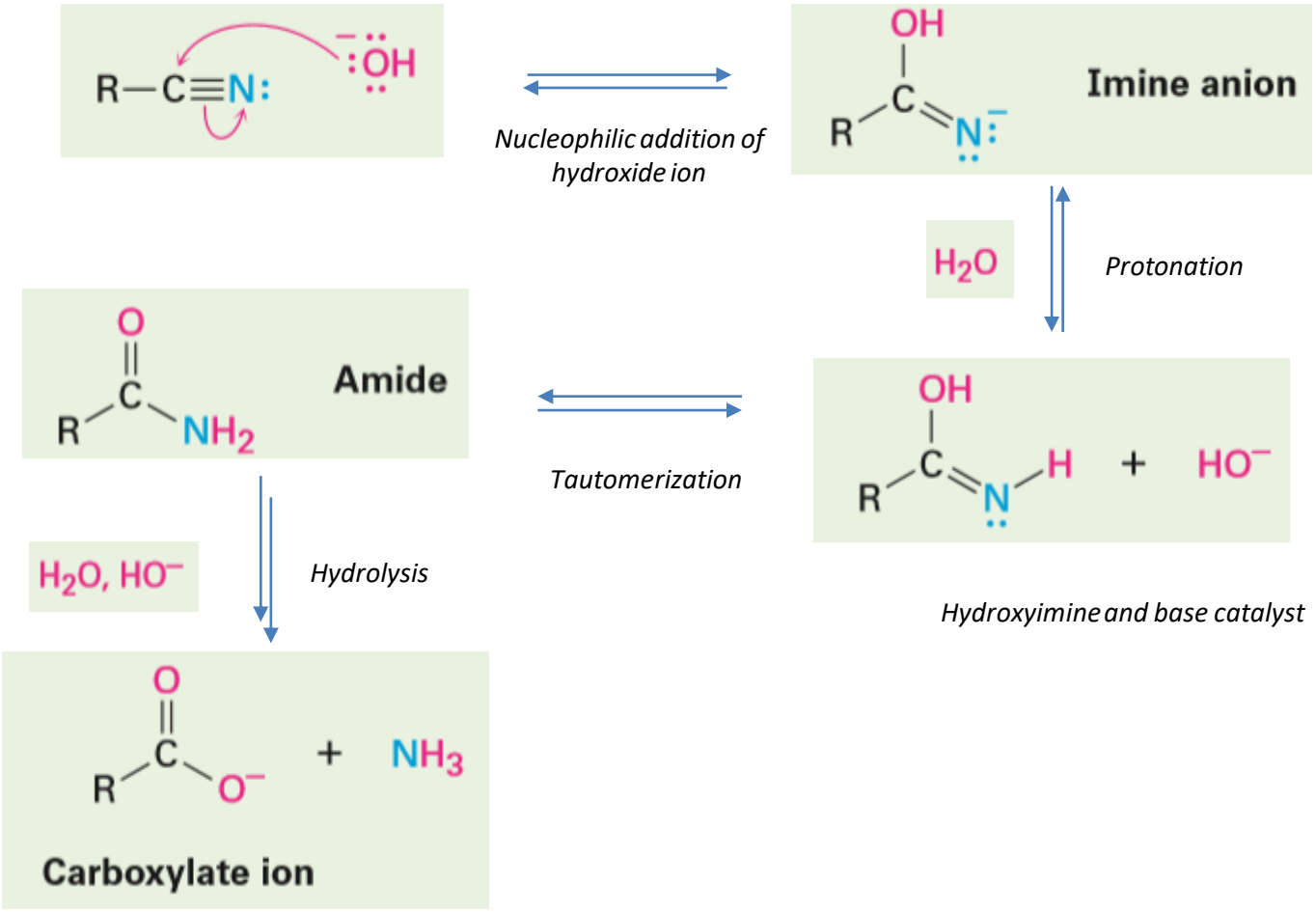
Hydrolysis of Nitriles



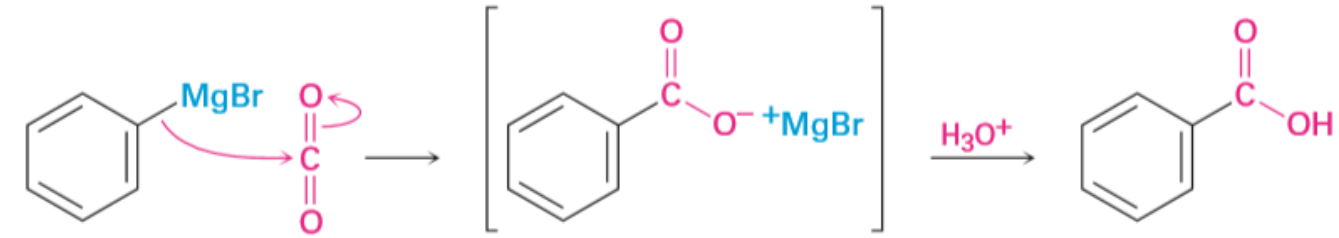
Ibuprofen

1. *Nitriles are usually made by* ***S_N2 reaction*** *of a* ***primary or secondary alkyl halide*** *with* CN^-.
2. Nitrile hydrolysis.
3. The product has one more carbon.

Mechanism of the basic hydrolysis of Nitriles



Carboxylation of Grignard Reagents



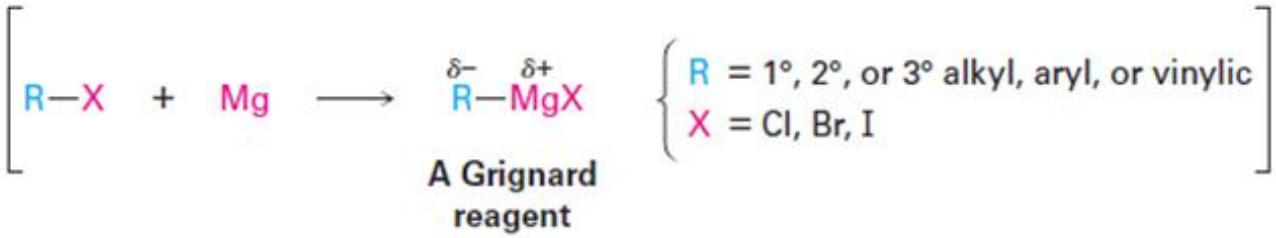
Phenylmagnesium bromide

Benzoic acid

Reaction of a Grignard reagent with CO_2 to yield a metal carboxylate

Protonation of the carboxylate

*The formation of the **Grignard reagent** from **organic halides that have no acidic hydrogens or reactive functional groups** elsewhere in the molecule.*



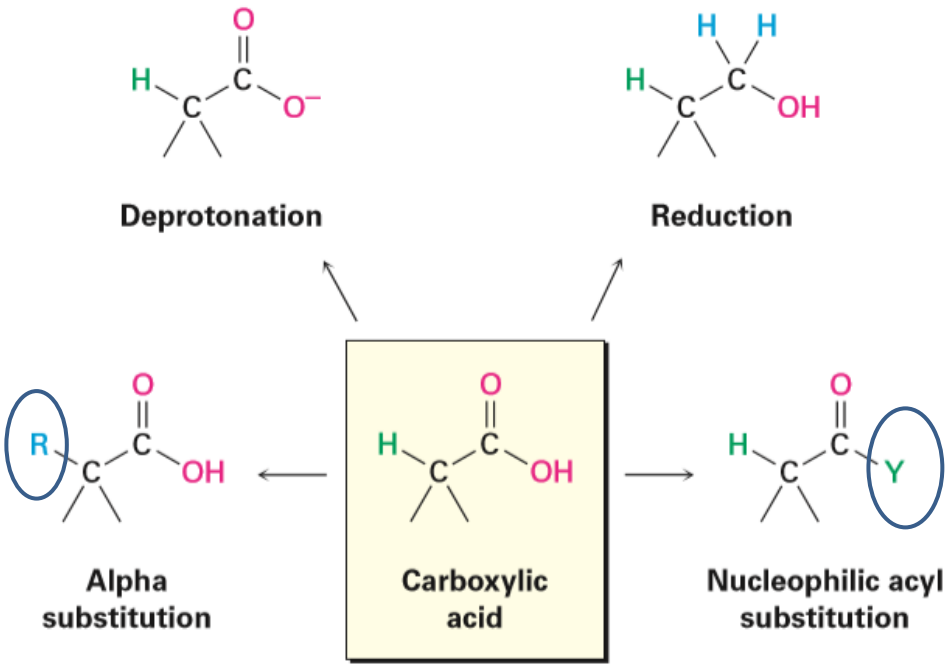
A Grignard reagent

Reactivity of Carboxylic Acids

An Overview

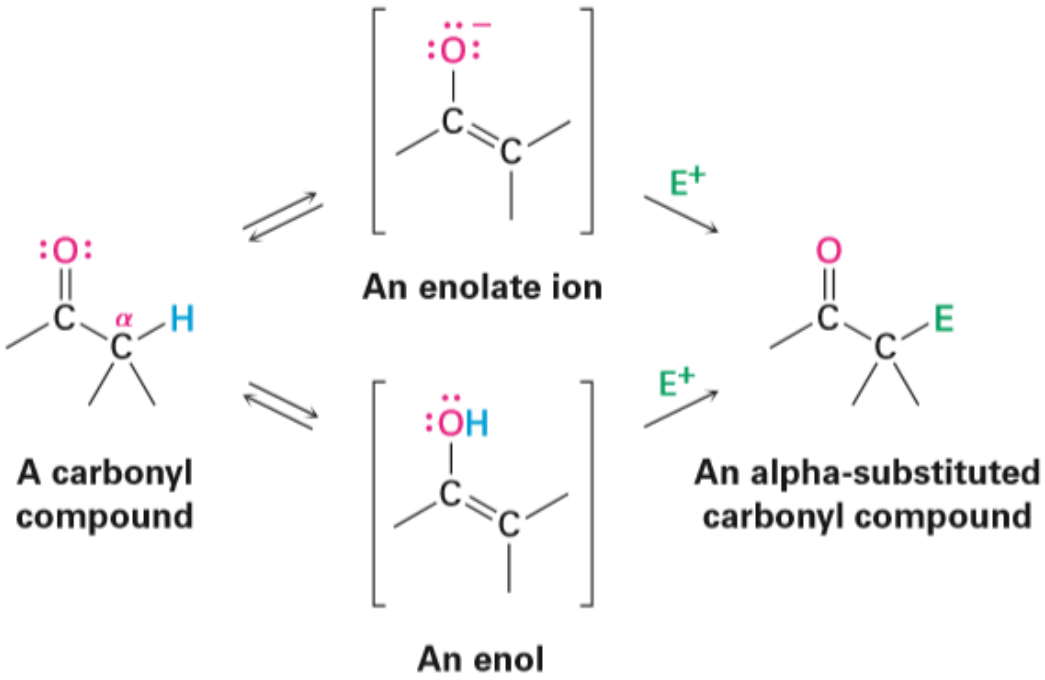
*Acidity of carboxylic acid (**pK_a**)*

*Treatment of the acid with **$LiAlH_4$** (Topic 8)*



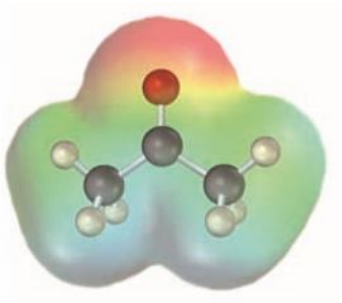
Some general reactions of carboxylic acids.

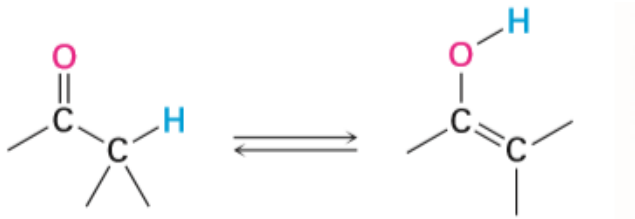
Alpha-Substitution Reactions



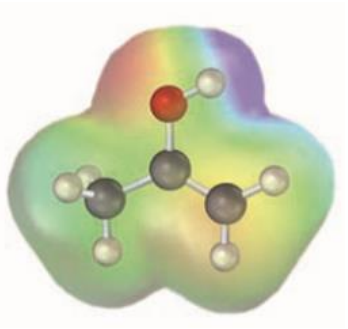
Substitution of an a hydrogen atom by an electrophile, E, through either an enol or enolate ion intermediate

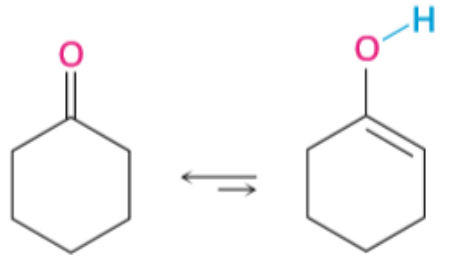
Keto-Enol Tautomerism





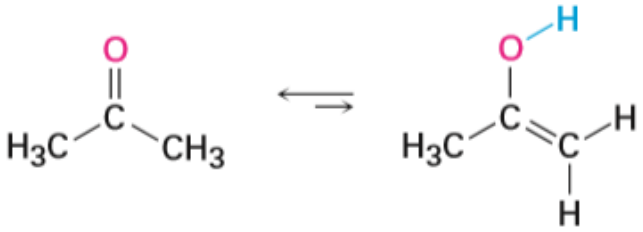
Keto tautomer **Enol tautomer**





99.999 9% 0.000 1%

Cyclohexanone

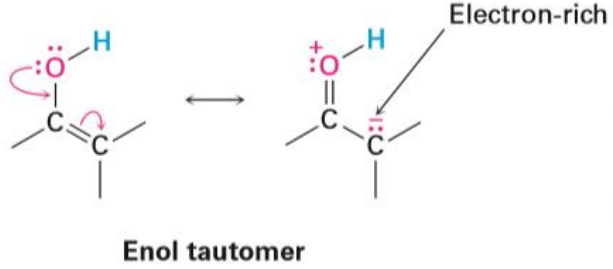


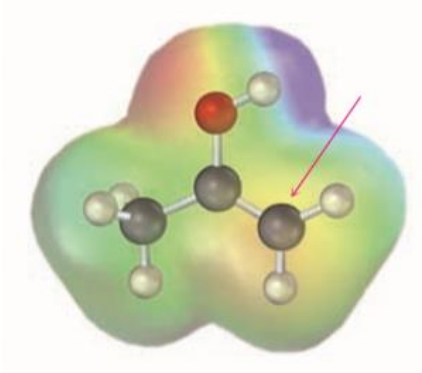
99.999 999 9% 0.000 000 1%

Acetone

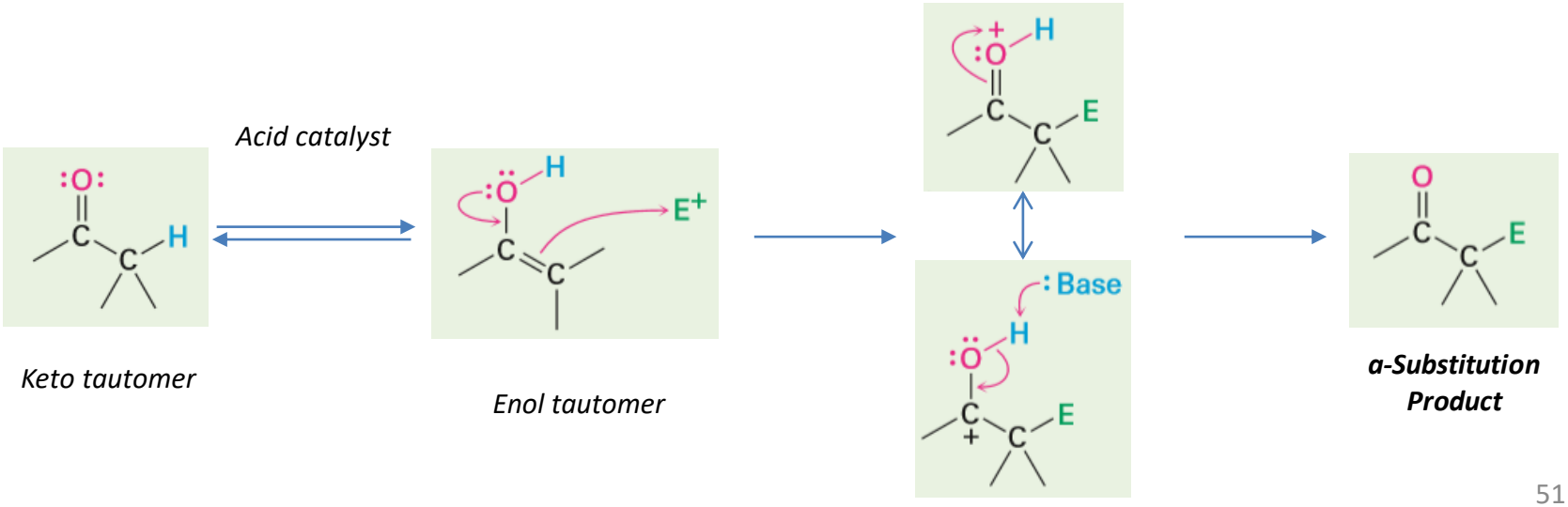
Reactivity of enols: Mechanism of alpha-Substitution Reactions

Enols are more electron-rich and correspondingly more reactive than alkenes



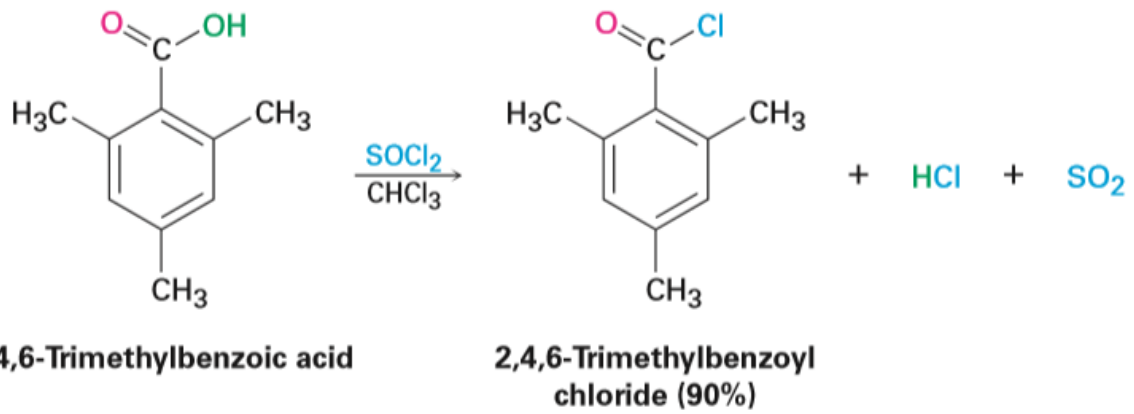


Mechanism



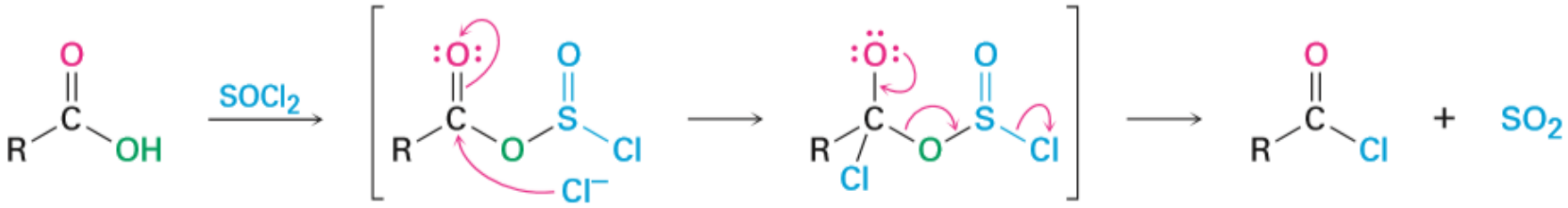
Nucleophilic Acyl Substitution

Conversion into
Acid Chloride



2,4,6-Trimethylbenzoic acid | **2,4,6-Trimethylbenzoyl chloride (90%)**

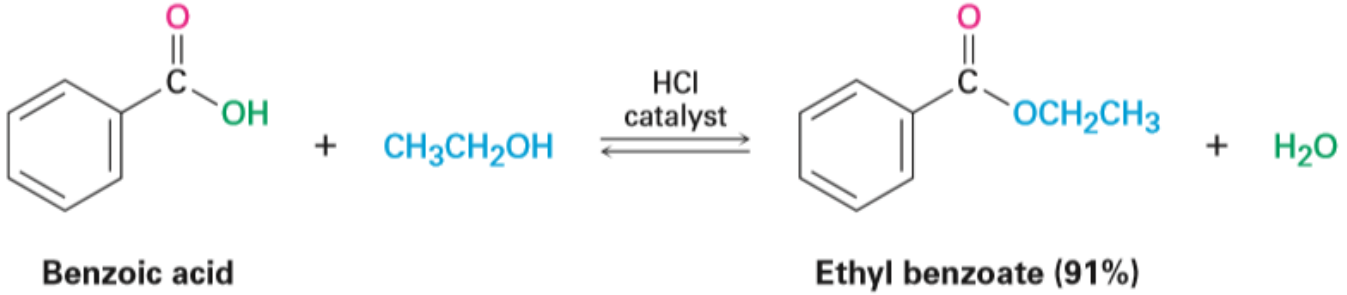
Mechanism



Carboxylic acid | **A chlorosulfite** | **Acid chloride**

Conversion into ***Esters***

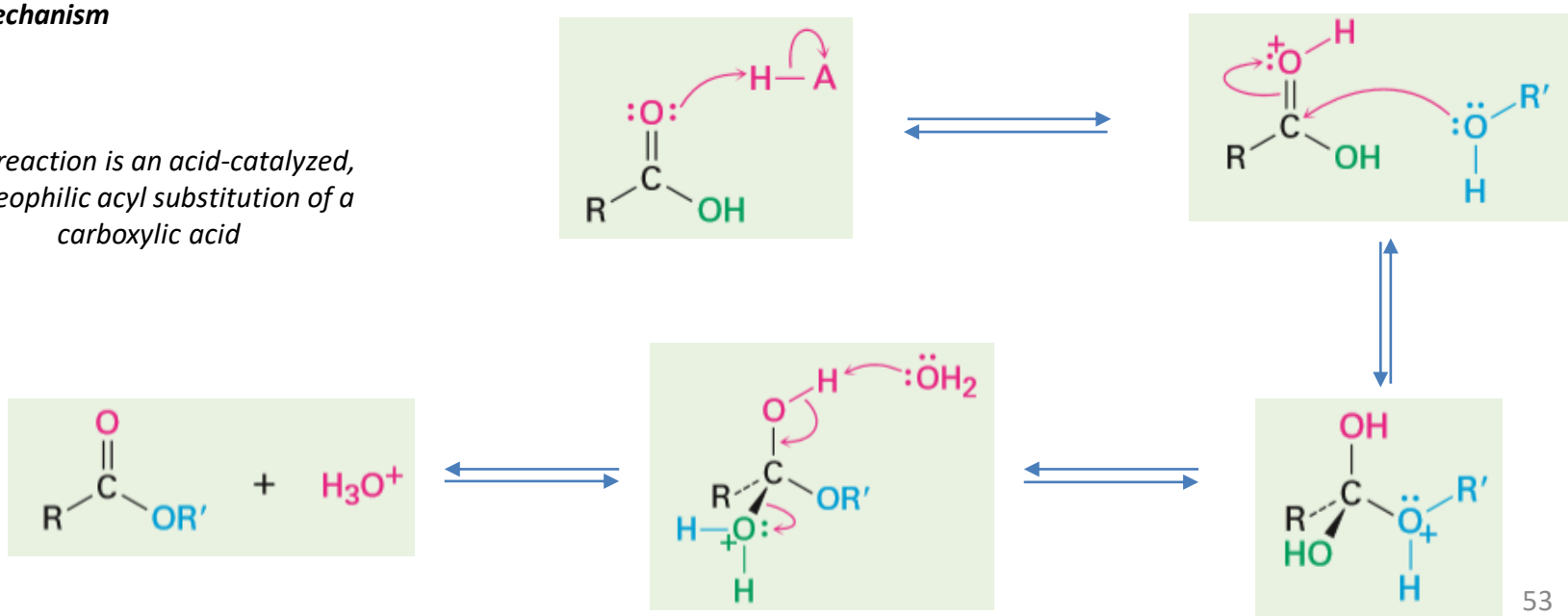
Fischer Esterification



Benzoic acid **Ethyl benzoate (91%)**

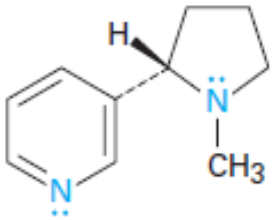
Mechanism

The reaction is an acid-catalyzed, nucleophilic acyl substitution of a carboxylic acid

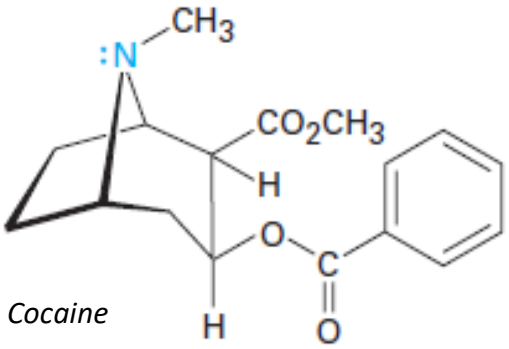


Introduction

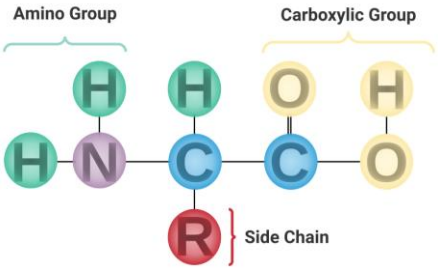
Amines *are derivatives of ammonia, in which one, two, or three of the hydrogens have been replaced by alkyl or aryl groups*



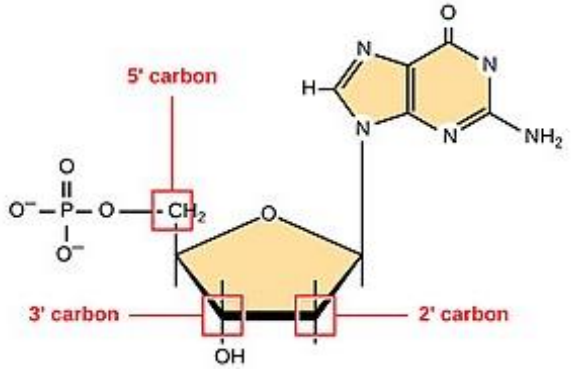
Nicotine



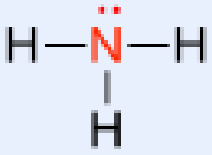
Cocaine



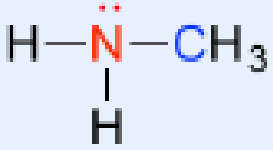
Amino acids form Proteins



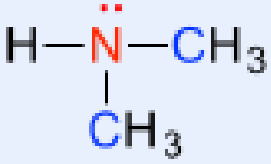
Nucleic Acids



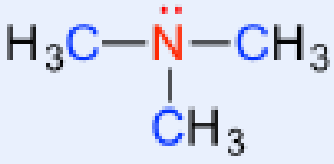
ammonia



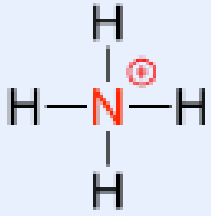
a primary amine



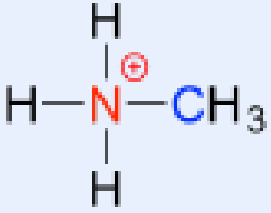
a secondary amine



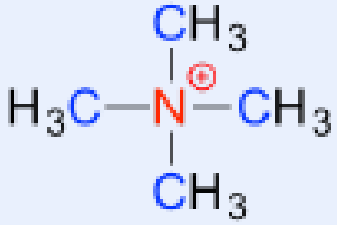
a tertiary amine



ammonium ion



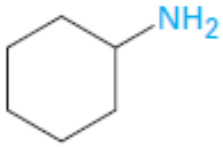
a primary ammonium ion



a quaternary ammonium ion

Naming Amines

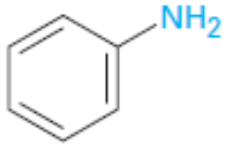
Primary Amines. The suffix –amine is added to the name of the alkyl substituent.



Cyclohexylamine

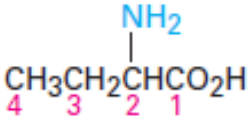
$H_2NCH_2CH_2CH_2CH_2NH_2$

1,4-Butanediamine

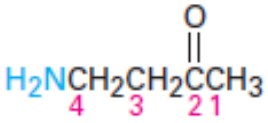


Aniline

Amines with more than one functional group

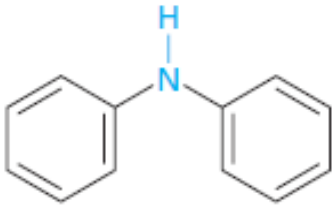


2-aminobutanoic acid

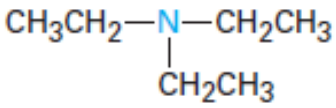


4-amino-2-butanone

Symmetrical Amines. Prefix di- or tri- to the alkyl group.

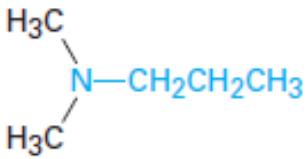


Diphenylamine

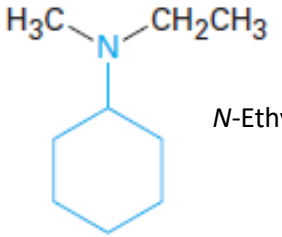


Triethylamine

Unsymmetrically substituted Amines. The largest alkyl group is considered the parent name and the other are considered N-substituents.

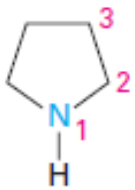


N,N-Dimethylpropylamine

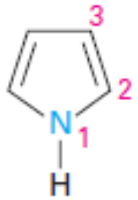


N-Ethyl-*N*-methylcyclohexylamine

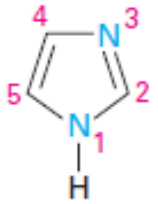
Heterocyclic Amines. The heterocyclic nitrogen atom is numbered as position 1.



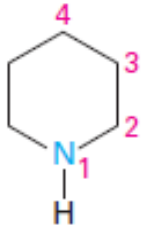
Pyrrolidine



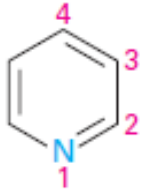
Pyrrole



Imidazole



Piperidine



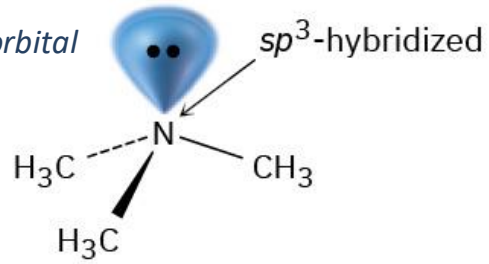
Pyridine

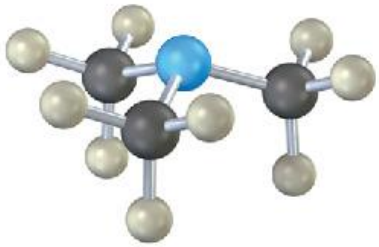
Pyrimidine

Structure

Lone electron pair in sp^3 hybrid orbital

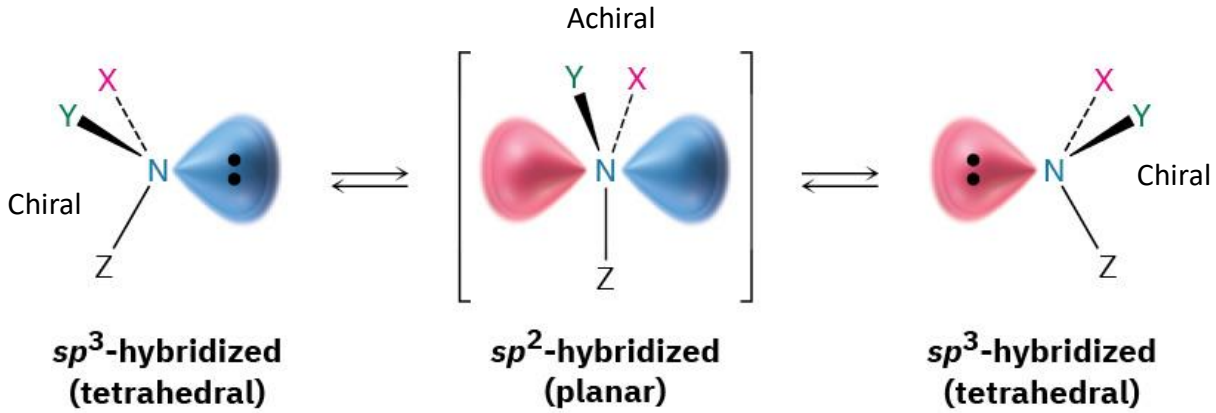
Structure of Trimethylamine





Inversion of Chiral Amines

Transition state of Inversion

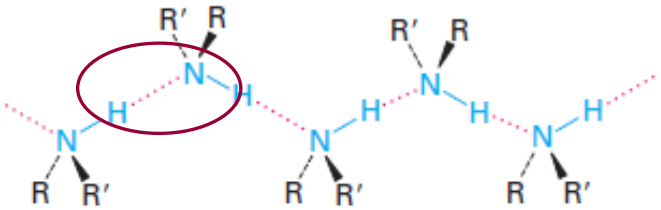


Rehybridization of nitrogen atom

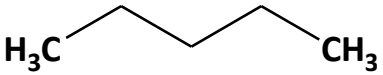
Physical and Chemical Properties

Polarity and boiling points

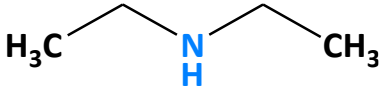
Hydrogen Bond



✓ Higher boiling point than alkanes of similar molecular weight.

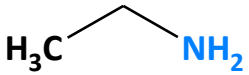


Pentane (36.1°)

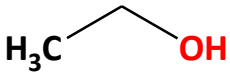


Diethylamine (56.3°)

✓ *Electronegativity of Nitrogen:* N is less electronegative than oxygen; amines form weaker hydrogen bonds than alcohols.

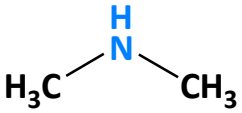


Ethylamine (16.6°)

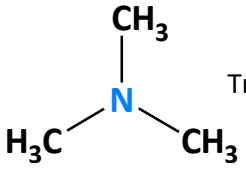


Ethanol (78.5°)

✓ Tertiary amines do not form hydrogen bond, so they have lower boiling points than primary and secondary amines.

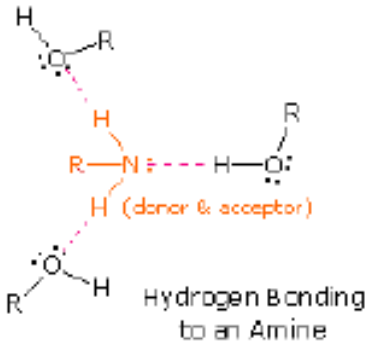


Dimethylamine (6.8°)



Trimethylamine (2.9°)

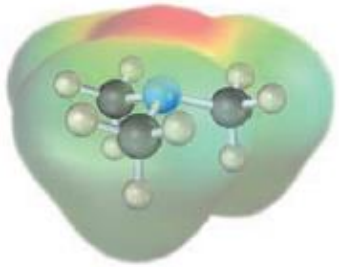
Solubility



✓ Amines are water soluble.

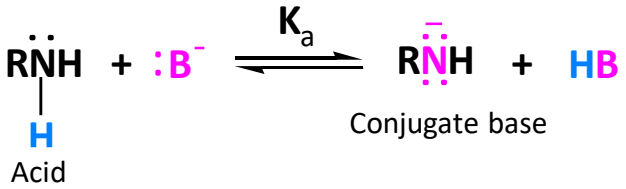
✓ If the hydrophobic part of an amine exceeds six carbons, the solubility decreases.

Basicity of Amines

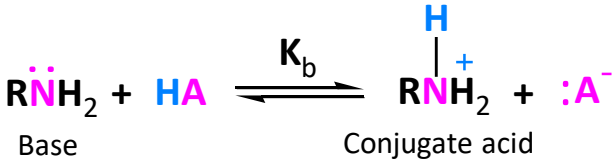


Basic and nucleophilic

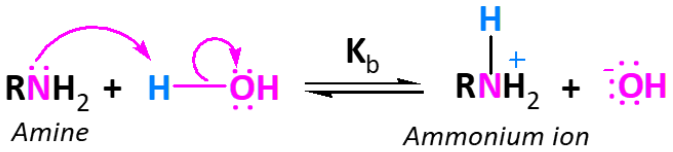
Amine acting as an acid:



Amine acting as a base:



Basicity of Amines



Basicity of an amine → acidity of their conjugate acids:

$$K_a = \frac{[R\dot{N}H_2][H_2\dot{\overset{+}{O}}H]}{[R\overset{+}{N}H_2\overset{|}{H}]} \approx 10^{-10}$$

Weaker base ⇒ Smaller pK_a for ammonium ion

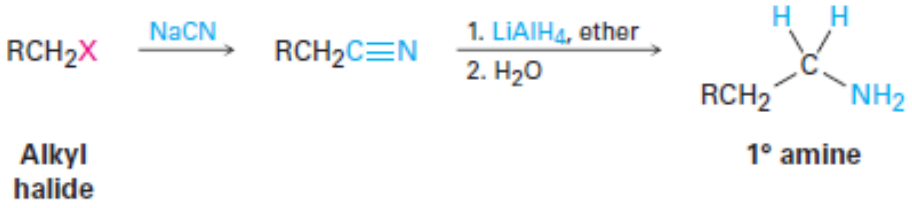
Stronger base ⇒ Larger pK_a for ammonium ion

- *Alkylamines are stronger bases than ammonia.*
- *Increasing the number of alkyl groups decreases solvation of ion so decrease basicity.*
- *Arylamines are less basic than alkylamines.*
- *Electron-withdrawing substituents (Cl, NO_2, CN) decrease arylamine basicity.*

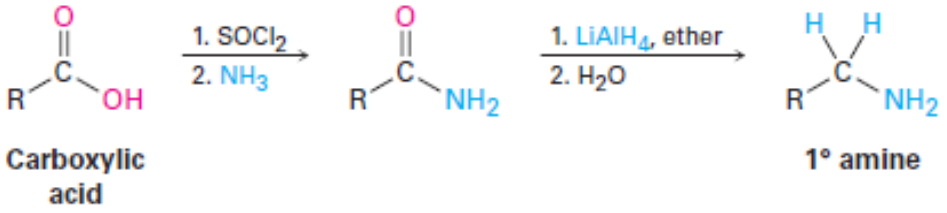
Synthesis of amines

Reduction of N compounds

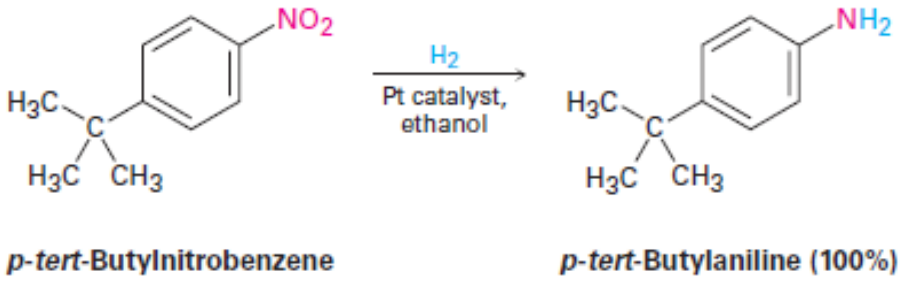
Reduction of Nitrile



Reduction of amide



Reduction of nitro group

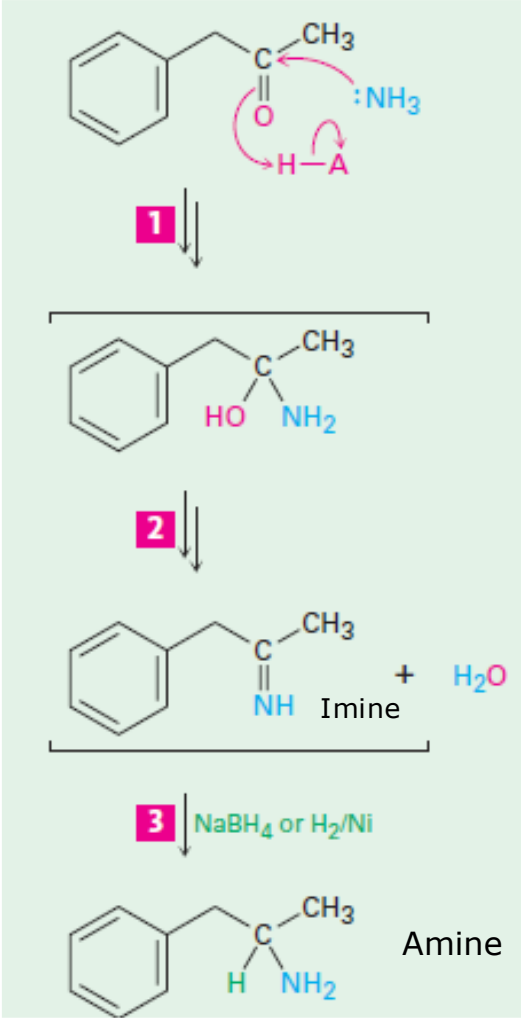


Reductive Amination

Step 1: Nucleophilic addition of ammonia

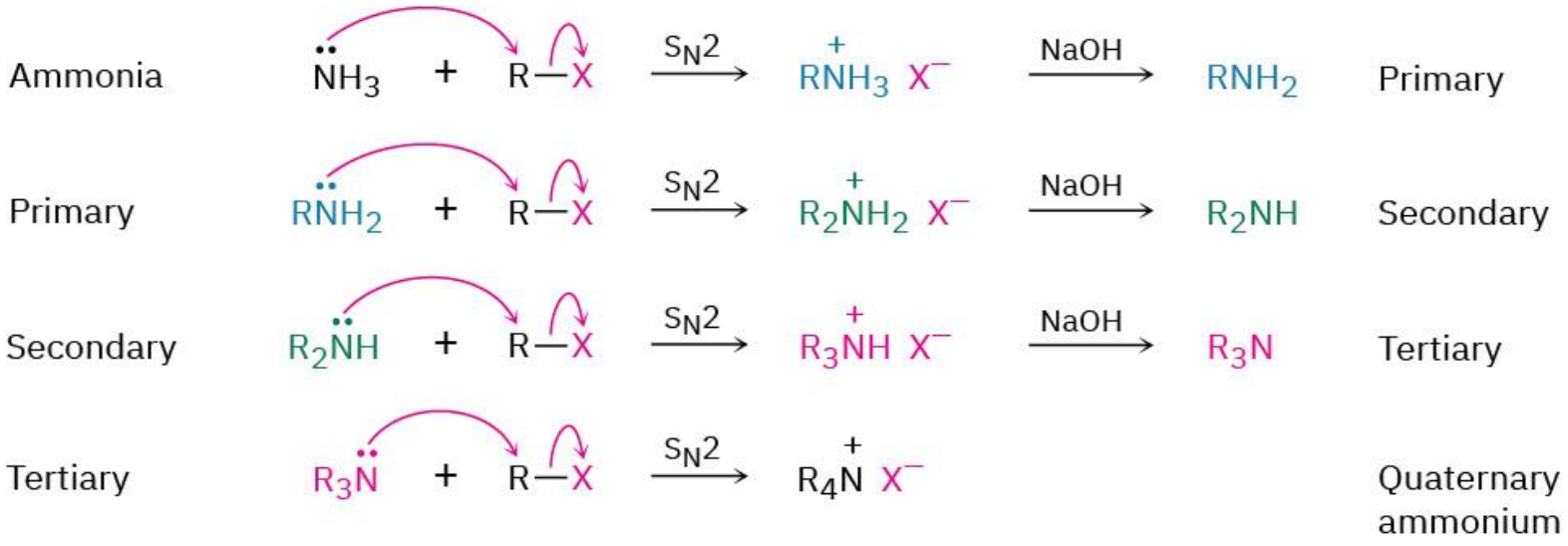
Step 2: Lose of water to give an imine

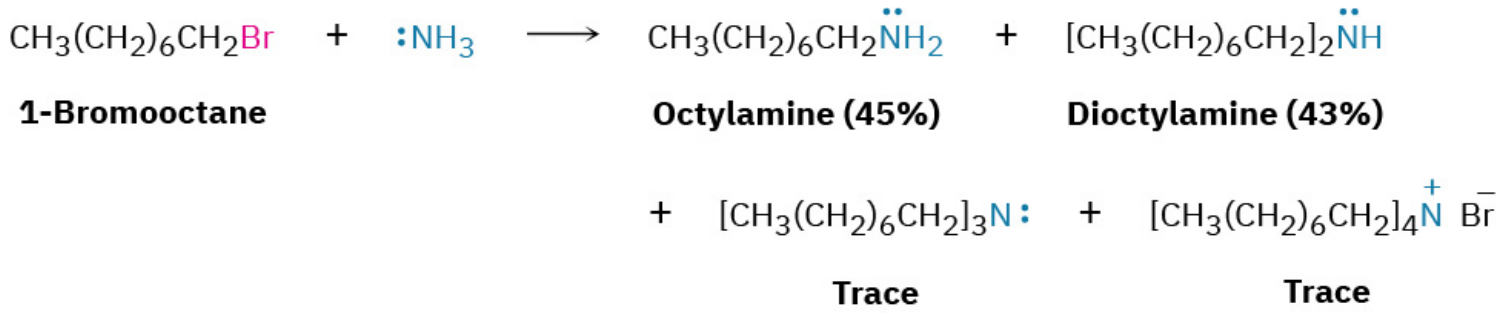
Step 3: The imine is reduced



Reactions of Alkylamines

Alkylation

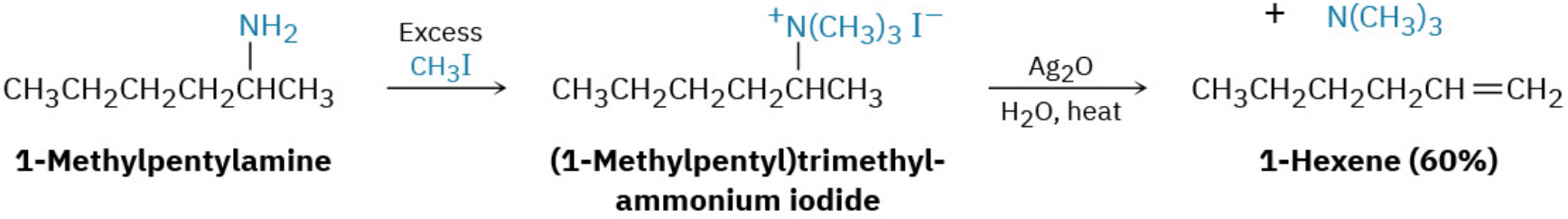




Hofmann Elimination: Mechanism

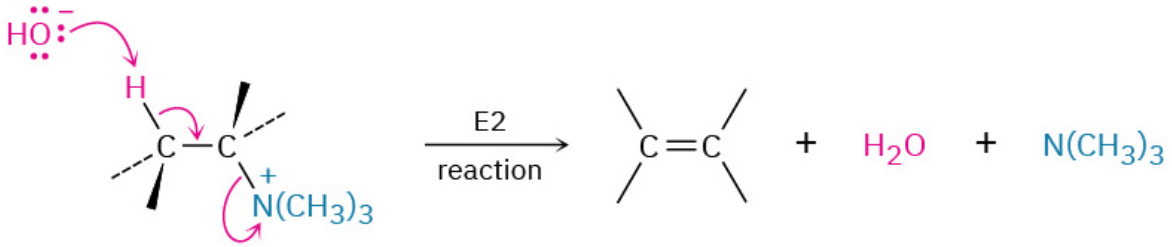
Elimination is *non-Zaitsev*
↓
Less highly substituted alkene
↓
Steric reason

Step 1: Amine is methylated with iodomethane



1-Methylpentylamine | **(1-Methylpentyl)trimethyl-ammonium iodide** | **1-Hexene (60%)**

Step 2: E2 elimination, with Ag_2O and heat, to give and alkene

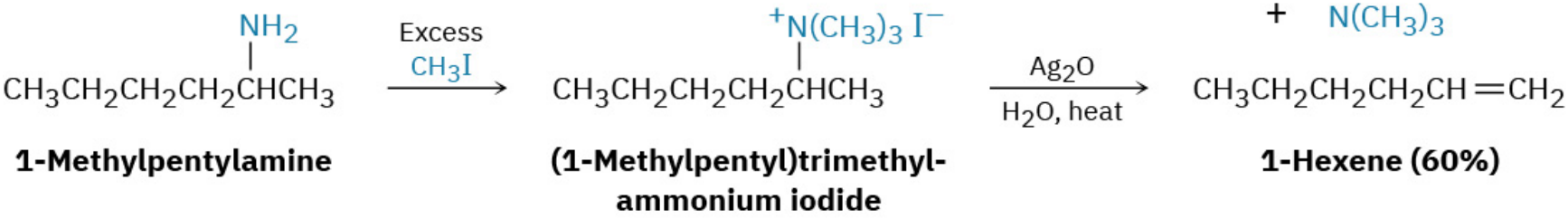


Quaternary ammonium salt | **Alkene**

Hofmann Elimination: Mechanism

Elimination is *non-Zaitsev*
↓
Less highly substituted alkene
↓
Steric reason

Step 1: Amine is methylated with iodomethane



1-Methylpentylamine | **(1-Methylpentyl)trimethyl-ammonium iodide** | **1-Hexene (60%)**

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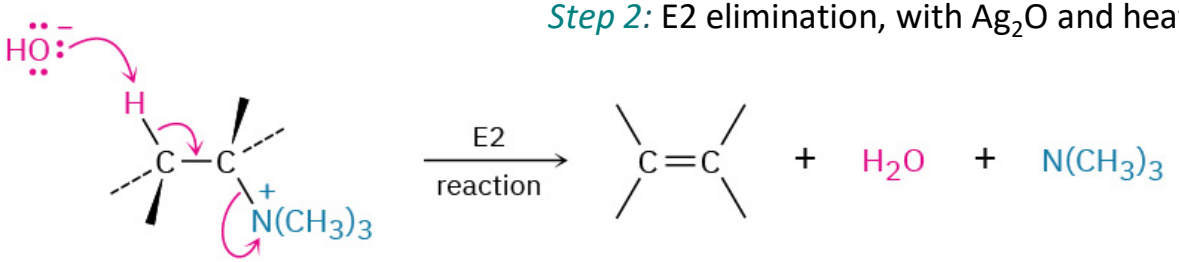
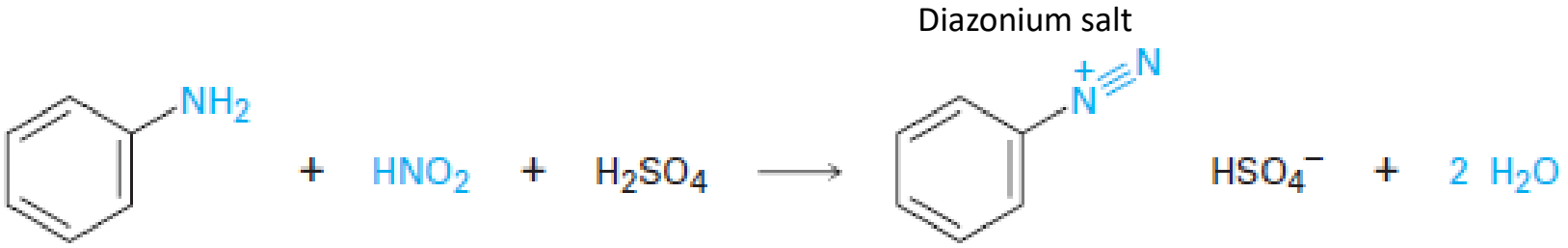


Quaternary ammonium salt | **Alkene**

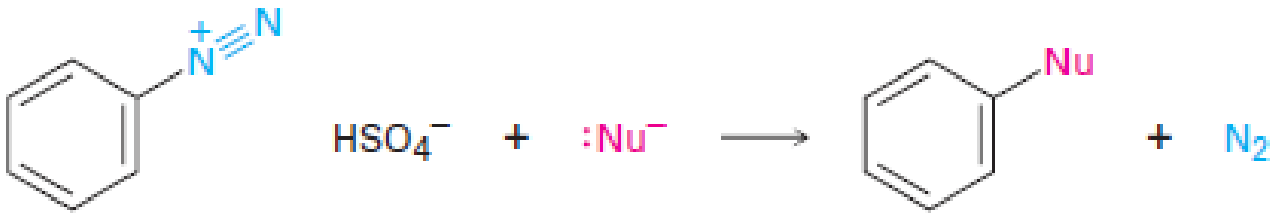
Reactions of Arylamines

Reaction through Diazonium Salts

Step 1: Diazotization reaction



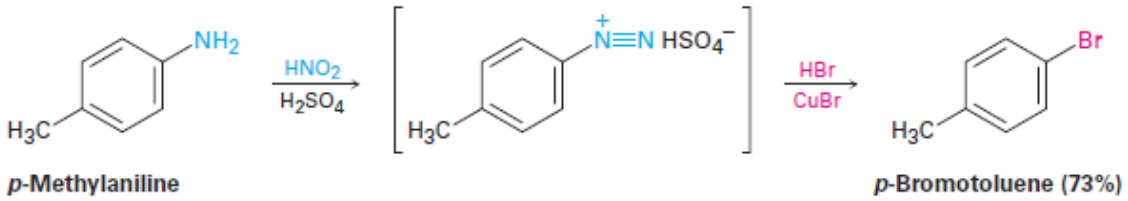
Step 2: Nucleophilic substitution



Examples:

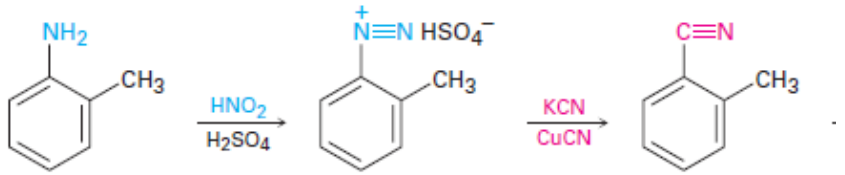
Sandmeyer Reaction:

Formation of aryl chlorides and bromides

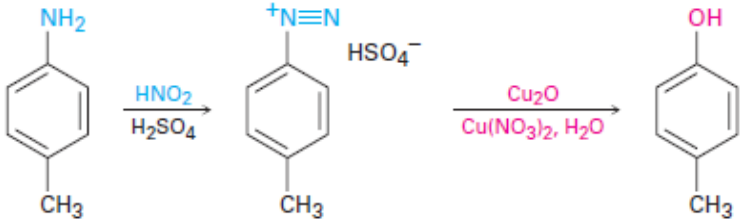


***p*-Methylaniline** **p-Bromotoluene (73%)**

Substitution by a nitrile group



***o*-Methylaniline** ***o*-Methylbenzene-diazonium bisulfate** ***o*-Methylbenzonitrile**



***p*-Methylaniline (*p*-Toluidine)** ***p*-Cresol (93%)**

Substitution by a hydroxyl group

Image Credits

Slide 3:

- Ethanol 3D structure: Herman Bergwerf, CC0 1.0, https://ndla.no/image/50769.
- Wine and grapes: Rawpixel, CC0 1.0, https://www.rawpixel.com/search/white%20wine%20grape?page=1&path=_topics&sort=curated.
- Phenol 3D structure: Jynto, CC0 1.0, https://commons.wikimedia.org/wiki/File:Cyclohexanol_3D_ball.png.

Slides 3 (alcohol, phenol, and enol structures), 4-19, 21-29, 31-37, 39-53, 54 (nicotine and cocaine structures), 56-58, 59 (hydrogen bonding), 60 (potential map of amine), 62-67 :

- Organic Chemistry. A tenth Edition. John McMurry, Cornell University (Emeritus), CC BY-SA 4.0, https://openstax.org/details/books/organic-chemistry.

Slides 12 (mechanism), 55, 60 (solubility of amines):

- Chem 12A: Organic Chemistry Fall 2022. Andy Wells, Chabot College, Open Education Resource (OER) LibreTexts Project, https://chem.libretexts.org/Courses/Chabot_College/Chem_12A:_Organic_Chemistry_Fall_2022.

Slide 20:

- Et*her* 3D structure: Jynto, CC0 1.0, https://commons.wikimedia.org/wiki/File:Dimethyl_ether_3D_ball.png.
- Bottle of ethyl ether: Fabexplosive, CC BY-SA 3.0, https://commons.wikimedia.org/wiki/File:Diethyl_ether_bottle.jpg.
- Anaesthesic: Wellcome Library, London, CC BY 4.0, https://commons.wikimedia.org/wiki/File:Portable_anaesthetic_kit,_Germany,_1914-1918_Wellcome_L0059539.jpg.

Slides 29 (electrophilic and nucleophilic character), 40 (electrophilic and nucleophilic character), 59, 60 (amines acting as an acid and as a base), 61:

- Images made by the authors.

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- Carboxy group 3D structure: Bin im Garten, CC BY-SA 3.0, https://commons.wikimedia.org/wiki/File:Functional_group_with_oxygen_carboxylic_acid_8299.JPG.
- Carboxy group kekulé structure: Rhadamante, CC BY-SA 3.0, https://commons.wikimedia.org/wiki/File:Acide_carboxylique.gif.
- Acetic acid 3D structure: Claudio Pistilli, CC0 1.0, https://eo.wikipedia.org/wiki/Dosiero:Acetic_acid_3D.png.
- Vinegar: Willis Lam, CC BY-SA 2.0, https://www.flickr.com/photos/85567416@N03/30720256055.
- Palmitic acid 3D structure: Alejandro Porto, CC BY-SA 3.0, https://commons.wikimedia.org/wiki/File:Palmitic-acid.jpg.
- Palm: Bigul Malayi, CC0, https://wordpress.org/photos/photo/28264b2cf9/.

Slide 54:

- Amino acid structure: Scott Henry Maxwell, CC BY-SA 4.0, https://commons.wikimedia.org/wiki/File:Unionized_Alpha_Amino_Acid_Structure.svg.
- Nucleic acid structure: CNX OpenStax, CC BY 4.0, https://commons.wikimedia.org/wiki/File:Figure_03_05_01.jpg.