

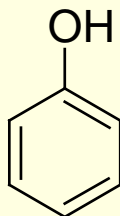


Chapter 17: Alcohols and Phenols

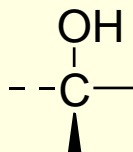


Alcohols and Phenols

- Alcohols contain an OH group connected to a saturated C (sp^3).
- They are important solvents and synthesis intermediates.
- Phenols contain an OH group connected to a carbon in a benzene ring.
- Methanol, CH_3OH , called methyl alcohol, is a common solvent, a fuel additive, produced in large quantities.
- Ethanol, CH_3CH_2OH , called ethyl alcohol, is a solvent, fuel, beverage.
- Phenol, C_6H_5OH ("phenyl alcohol") has diverse uses - it gives its name to the general class of compounds



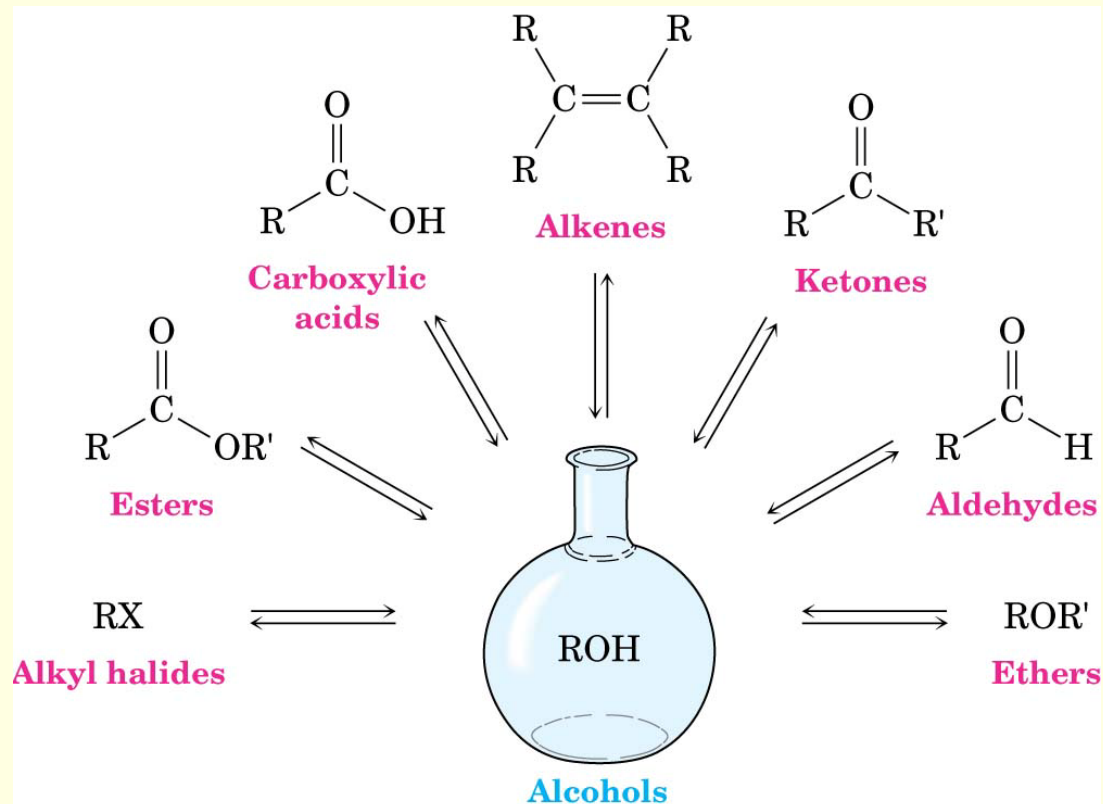
Phenol



Alcohol

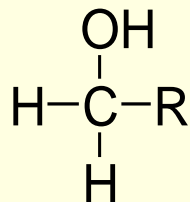
Preparation of Alcohols: an Overview

- Alcohols are derived from many types of compounds
- The alcohol hydroxyl can be converted to many other functional groups
- This makes alcohols useful in synthesis

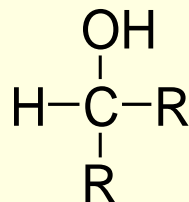


Naming Alcohols

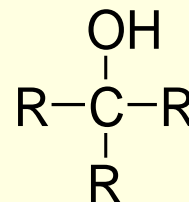
General classifications of alcohols based on substitution on C to which OH is attached.



Primary



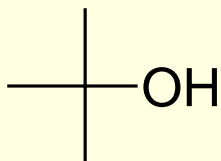
Secondary



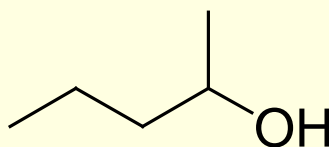
Tertiary

IUPAC Rules for Naming Alcohols

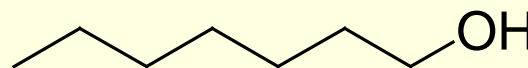
- Select the **longest carbon** chain containing the **hydroxyl group**.
- derive the parent name by replacing the **-e** ending of the corresponding alkane with **-ol**.
- Number the chain from the end nearer the hydroxyl group.
- Number substituents according to position on chain, listing the substituents in alphabetical order.



t-butanol



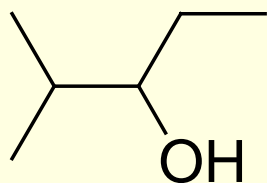
2-pentanol



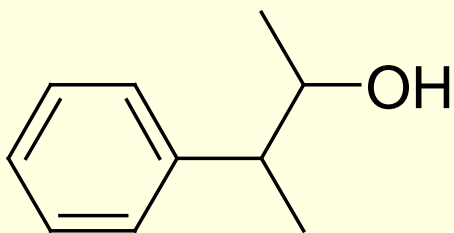
heptanol

Many Alcohols Have Common Names

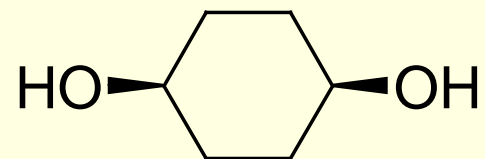
These are accepted by IUPAC



2-methyl-3-pentanol



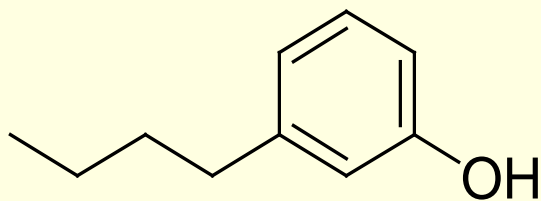
3-phenyl-2-butanol



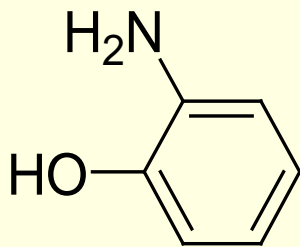
cis-1,4-cyclohexadiol

Naming Phenols

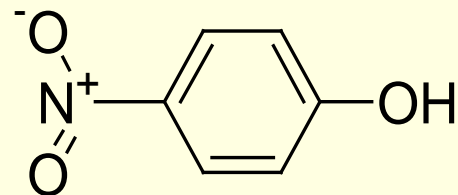
- Use “phene” (the French name for benzene) as the parent hydrocarbon name, not benzene.
- Name substituents on aromatic ring by their position from OH.



3-butylphenol



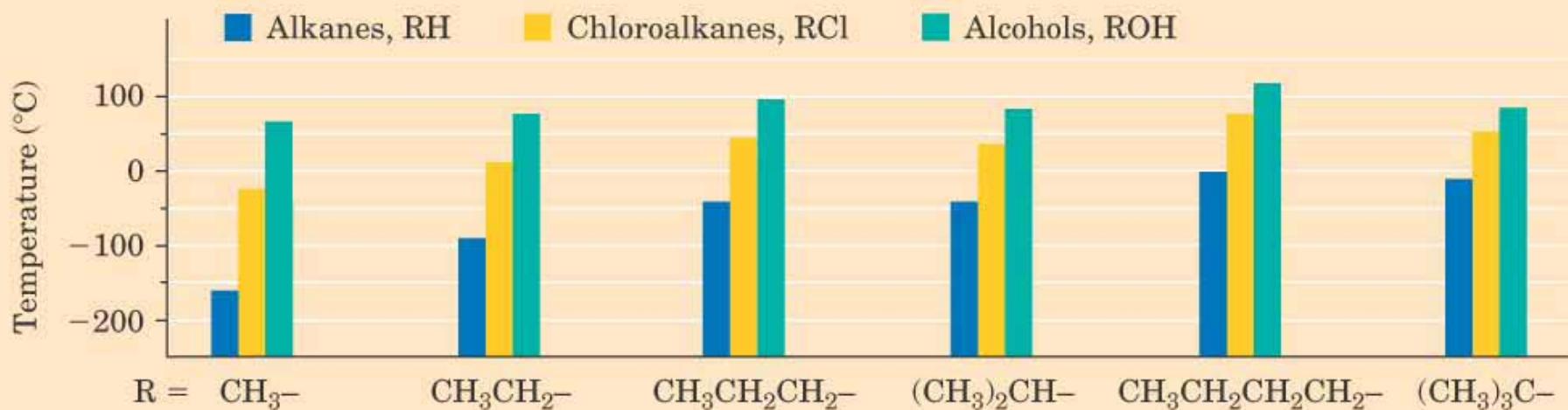
2-aminophenol



4-nitrophenol

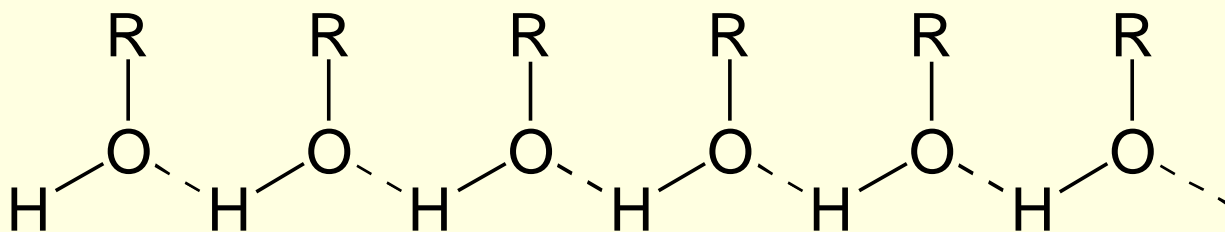
Properties of Alcohols and Phenols: Hydrogen Bonding

- The structure around O of the alcohol or phenol is similar to that in water, sp^3 hybridized
- Alcohols and phenols have much higher boiling points than similar alkanes and alkyl halides



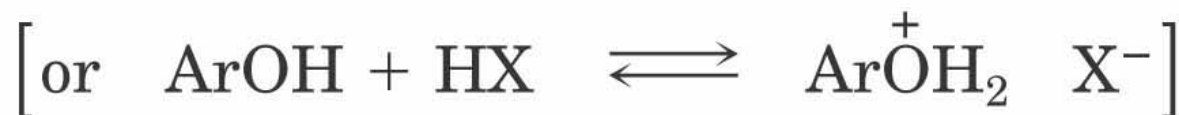
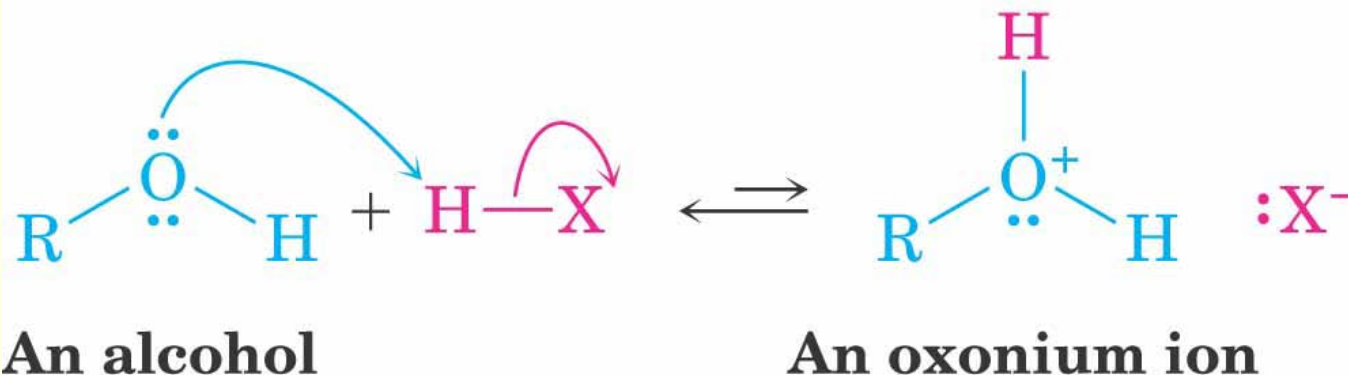
Alcohols Form Hydrogen Bonds

- A positively polarized —OH hydrogen atom from one molecule is attracted to a lone pair of electrons on a negatively polarized oxygen atom of another molecule
- This produces a force that holds the two molecules together
- These intermolecular attractions are present in solution but not in the gas phase, thus elevating the boiling point of the solution



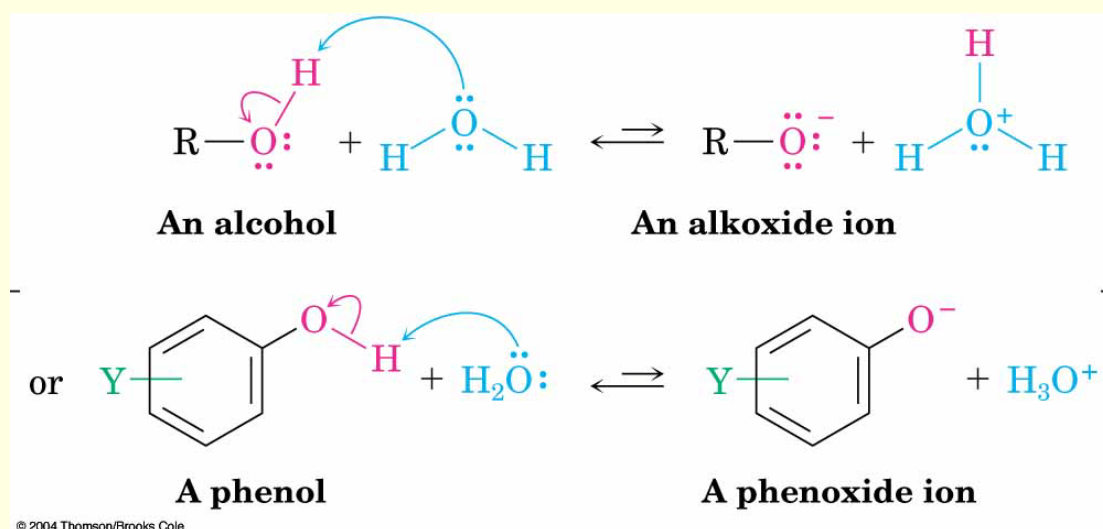
Properties of Alcohols and Phenols: Acidity and Basicity

- Weakly basic and weakly acidic
- Alcohols are weak Brønsted bases
- Protonated by strong acids to yield oxonium ions, ROH_2^+




Alcohols and Phenols are Weak Brønsted Acids

- Can transfer a proton to water to a very small extent
- Produces H_3O^+ and an **alkoxide ion**, RO^- , or a **phenoxide ion**, ArO^-



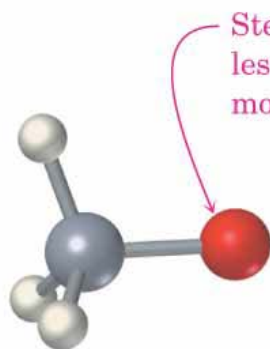
pK_a Values for Typical OH Compounds

TABLE 17.1 Acidity Constants of Some Alcohols and Phenols

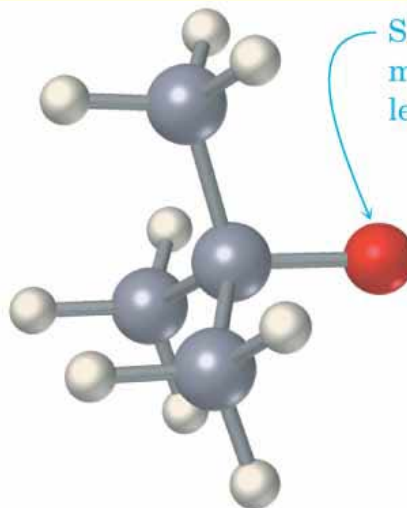
Alcohol or phenol	pK _a		
(CH ₃) ₃ COH	18.00	Weaker acid	
CH ₃ CH ₂ OH	16.00		
HOH (water)	(15.74)		
CH ₃ OH	15.54		
CF ₃ CH ₂ OH	12.43		
<i>p</i> -Aminophenol	10.46		
<i>p</i> -Methoxyphenol	10.21		
<i>p</i> -Methylphenol	10.17		
Phenol	9.89		
<i>p</i> -Chlorophenol	9.38		
<i>p</i> -Bromophenol	9.35		
<i>p</i> -Nitrophenol	7.15		
2,4,6-Trinitrophenol	0.60		Stronger acid

Relative Acidities of Alcohols

- Simple alcohols are about as acidic as water.
- Alkyl groups make an alcohol a weaker acid.
- Steric effects are important.



Methoxide ion, CH_3O^-
($\text{p}K_{\text{a}} = 15.54$)

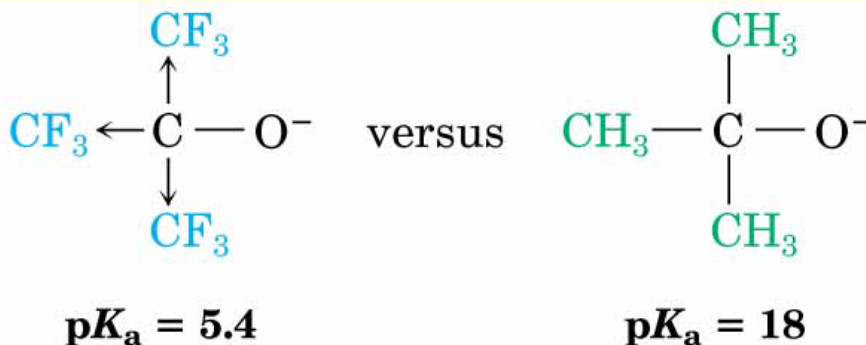


***tert*-Butoxide ion, $(\text{CH}_3)_3\text{CO}^-$**
($\text{p}K_{\text{a}} = 18.00$)

Inductive Effects

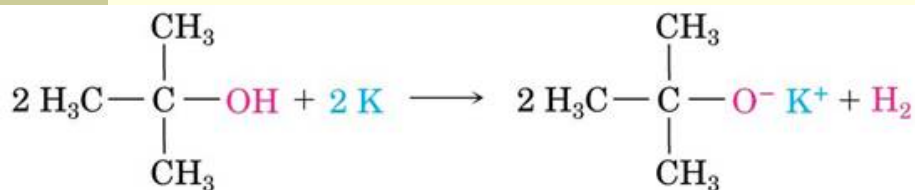
- Electron-withdrawing groups make an alcohol a stronger acid by stabilizing the conjugate base (alkoxide)

Electron-withdrawing groups stabilize alkoxide and lower pK_a



Generating Alkoxides from Alcohols

- Alcohols are weak acids – requires a strong base to form an alkoxide such as NaH, sodium amide NaNH_2 , and Grignard reagents (RMgX)
- Alkoxides are bases used as reagents in organic chemistry



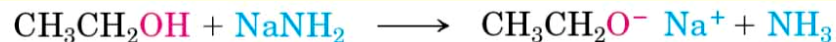
tert-Butyl alcohol

Potassium *tert*-butoxide



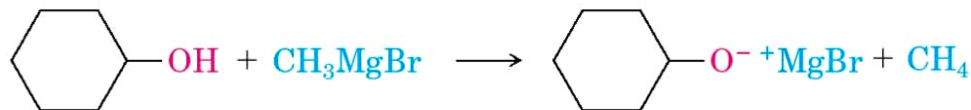
Methanol

Sodium methoxide



Ethanol

Sodium ethoxide



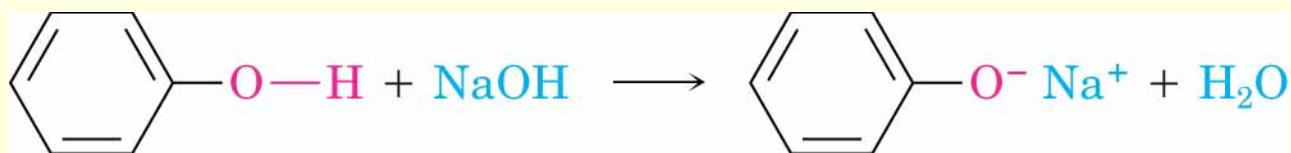
Cyclohexanol

Bromomagnesium cyclohexoxide

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Phenol Acidity

- Phenols ($\text{pK}_a \sim 10$) are much more acidic than alcohols ($\text{pK}_a \sim 16$) due to resonance stabilization of the phenoxide ion
- Phenols react with NaOH solutions (but alcohols do not), forming soluble salts that are soluble in dilute aqueous
- A phenolic component can be separated from an organic solution by extraction into basic aqueous solution and is isolated after acid is added to the solution

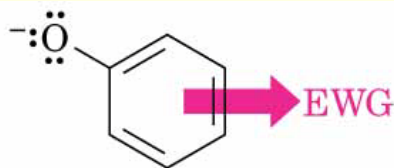


Phenol

Sodium phenoxide

Substituted Phenols

- Can be more or less acidic than phenol itself
- An electron-withdrawing substituent makes a phenol more acidic by delocalizing the negative charge
- Phenols with an electron-donating substituent are less acidic because these substituents concentrate the charge



Electron-withdrawing groups (EWG)
stabilize phenoxide anion, resulting
in increased phenol acidity

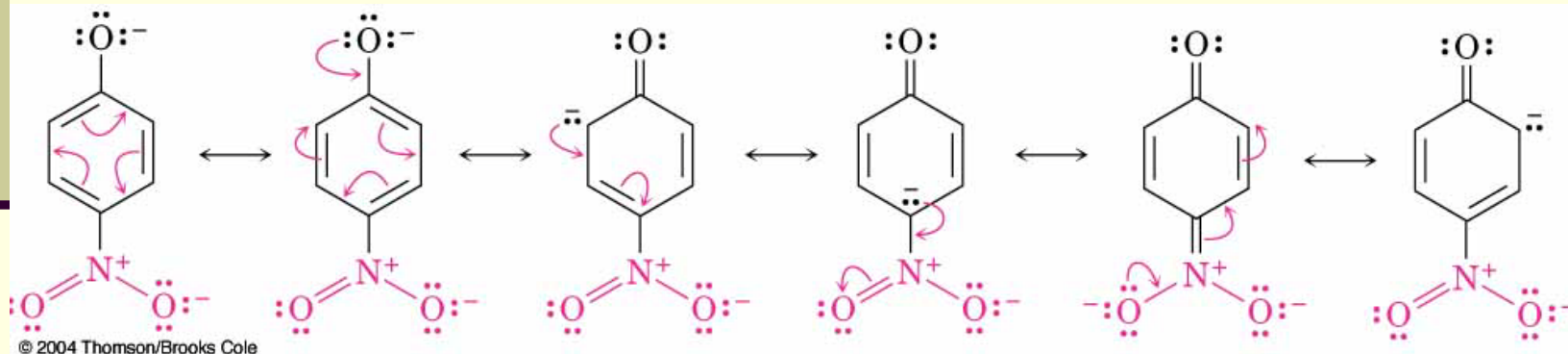
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Electron-donating groups (EDG)
destabilize phenoxide anion,
resulting in decreased phenol acidity

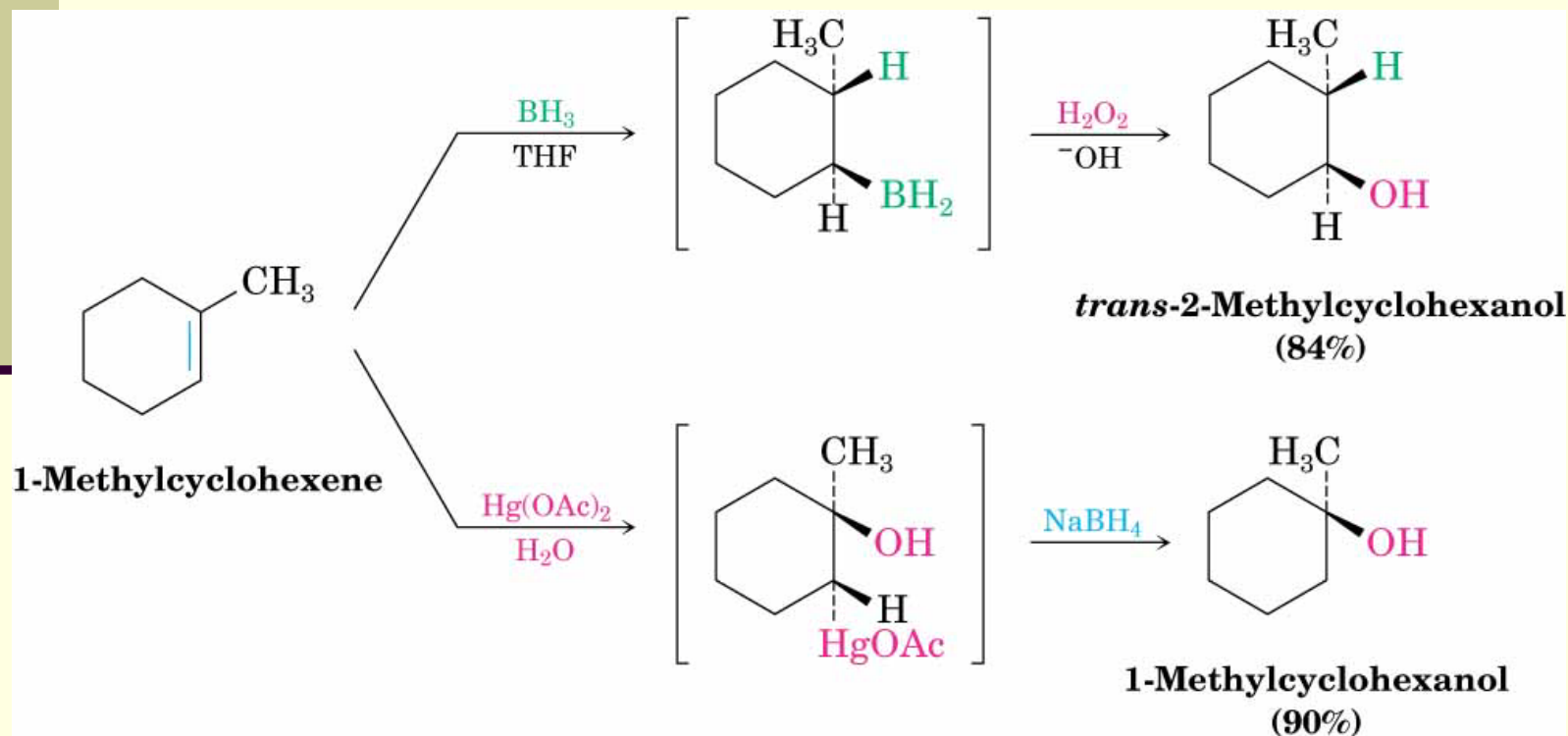
Nitro-Phenols

- Phenols with nitro groups at the ortho and para positions are much stronger acids
- The pKa of 2,4,6-trinitrophenol is 0.6, a very strong acid



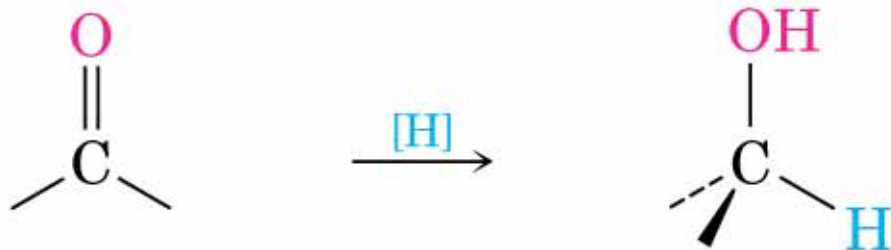
Review: Preparation of Alcohols by Regiospecific Hydration of Alkenes

- Hydroboration/oxidation: syn, non-Markovnikov hydration
- Oxymercuration/reduction: Markovnikov hydration



Alcohols from Reduction of Carbonyl Compounds

- Reduction of a carbonyl compound in general gives an alcohol
- Note that organic reduction reactions add the equivalent of H_2 to a molecule



where $[H]$ is a generalized reducing agent

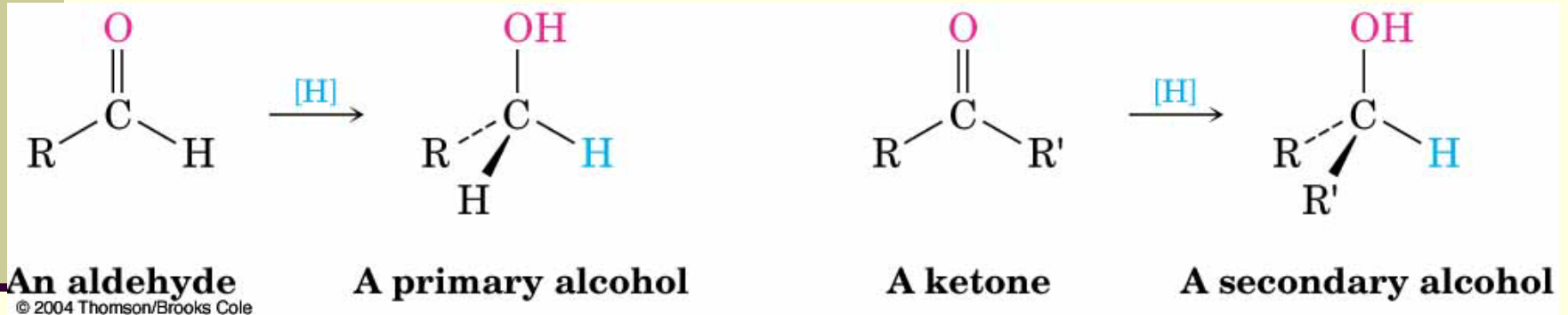
A carbonyl compound

An alcohol

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Reduction of Aldehydes and Ketones

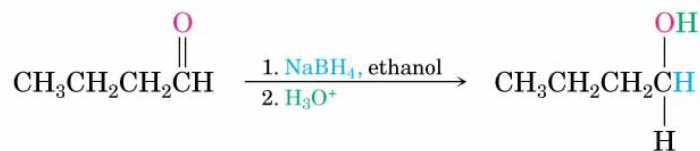
- Aldehydes gives primary alcohols
- Ketones gives secondary alcohols



Reduction Reagent: Sodium Borohydride

- NaBH_4 is not sensitive to moisture and it does not reduce other common functional groups
- Lithium aluminum hydride (LiAlH_4) is more powerful, less specific, and very reactive with water
- Both add the equivalent of "H⁻"

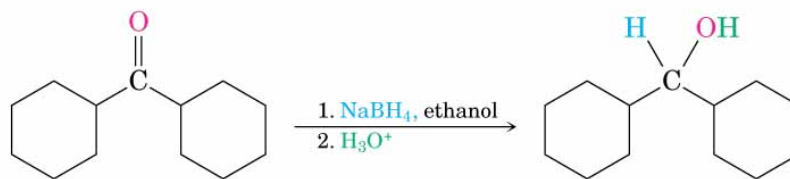
Aldehyde reduction



Butanal

1-Butanol (85%)
(a 1° alcohol)

Ketone reduction



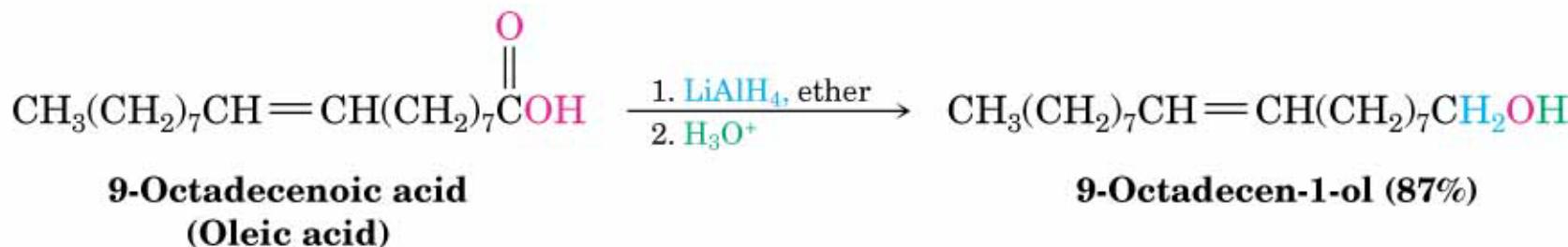
Dicyclohexyl ketone

Dicyclohexylmethanol (88%)
(a 2° alcohol)

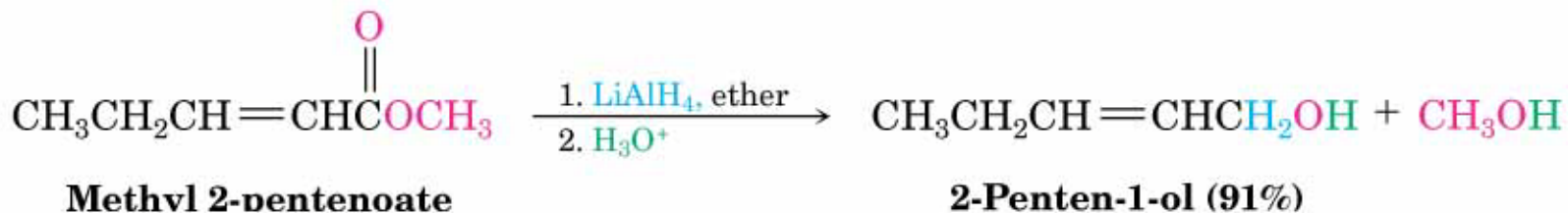
Reduction of Carboxylic Acids and Esters

- Carboxylic acids and esters are reduced to give primary alcohols
- LiAlH_4 is used because NaBH_4 is not effective

Carboxylic acid reduction



Ester reduction



Alcohols from Reaction of Carbonyl Compounds with Grignard Reagents

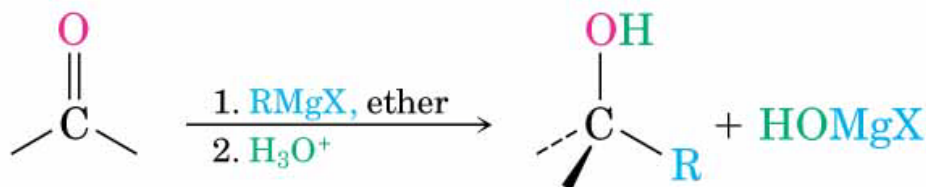
- Alkyl, aryl, and vinylic halides react with magnesium in ether or tetrahydrofuran to generate Grignard reagents, RMgX
- Grignard reagents react with carbonyl compounds to yield alcohols

Grignard formation



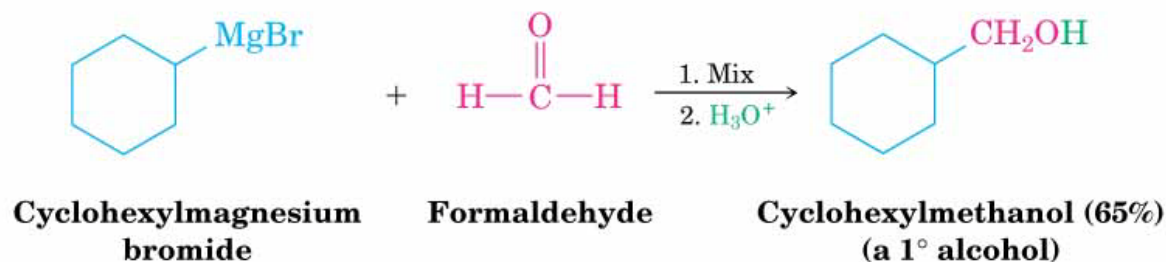
A Grignard reagent

$\text{R} = 1^\circ, 2^\circ, \text{ or } 3^\circ$ alkyl, aryl, or vinylic
 $\text{X} = \text{Cl}, \text{Br}, \text{ or } \text{I}$

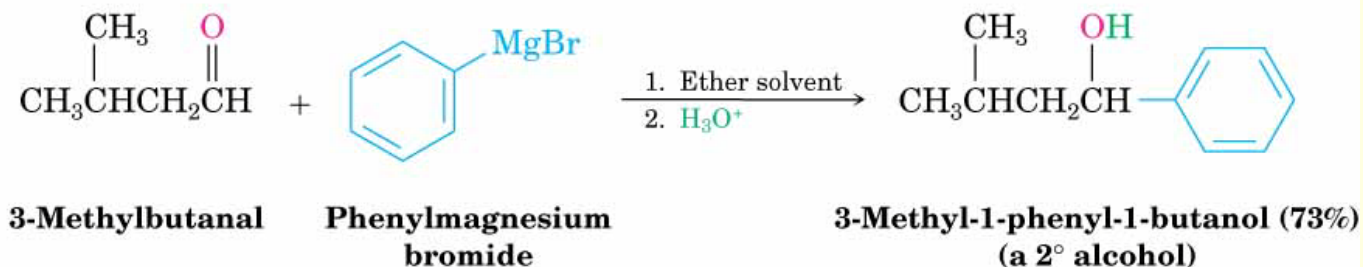


Examples of Reactions of Grignard Reagents with Carbonyl Compounds

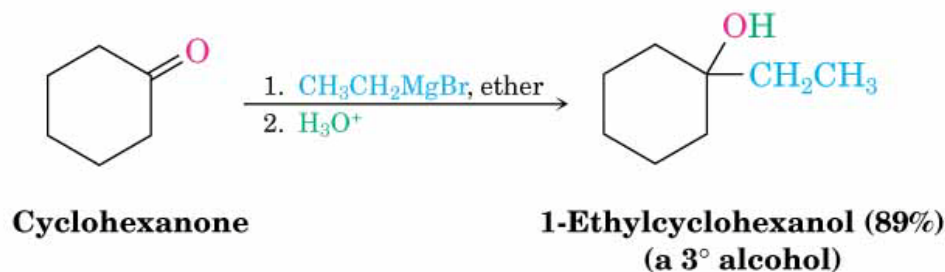
Formaldehyde reaction



Aldehyde reaction

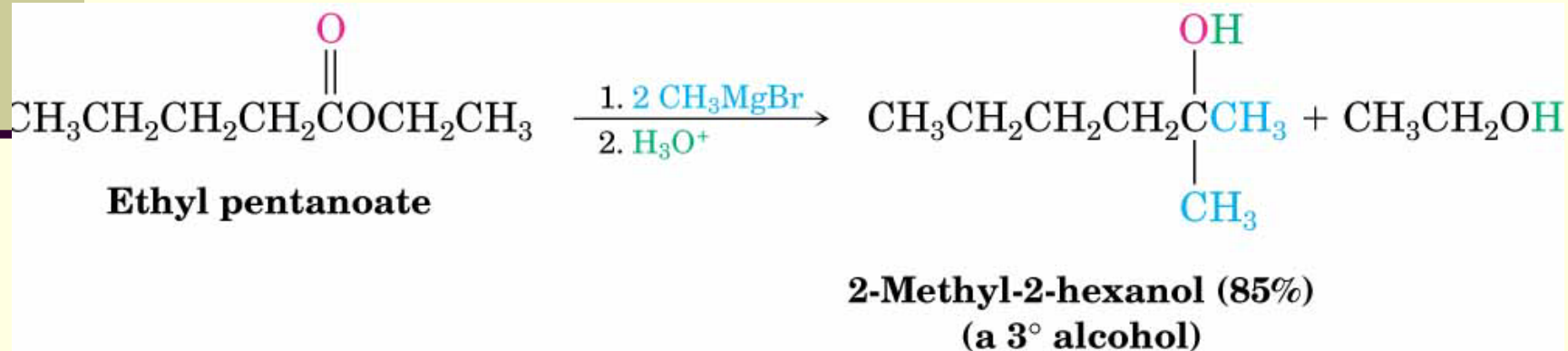


Ketone reaction



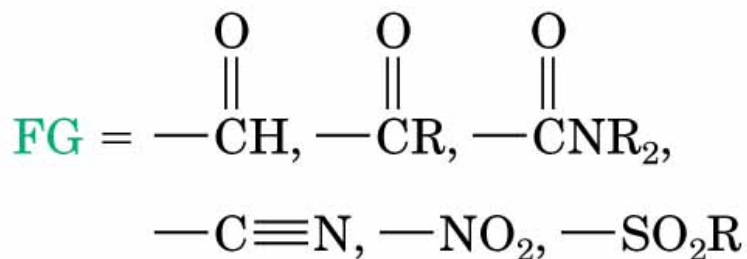
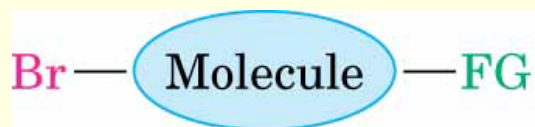
Reactions of Esters and Grignard Reagents

- Yields tertiary alcohols in which *two* of the substituents carbon come from the Grignard reagent
- Grignard reagents do not add to carboxylic acids – they undergo an acid-base reaction, generating the hydrocarbon of the Grignard reagent



Grignard Reagents and Other Functional Groups in the Same Molecule

- Can't be prepared if there are reactive functional groups in the same molecule, including proton donors.

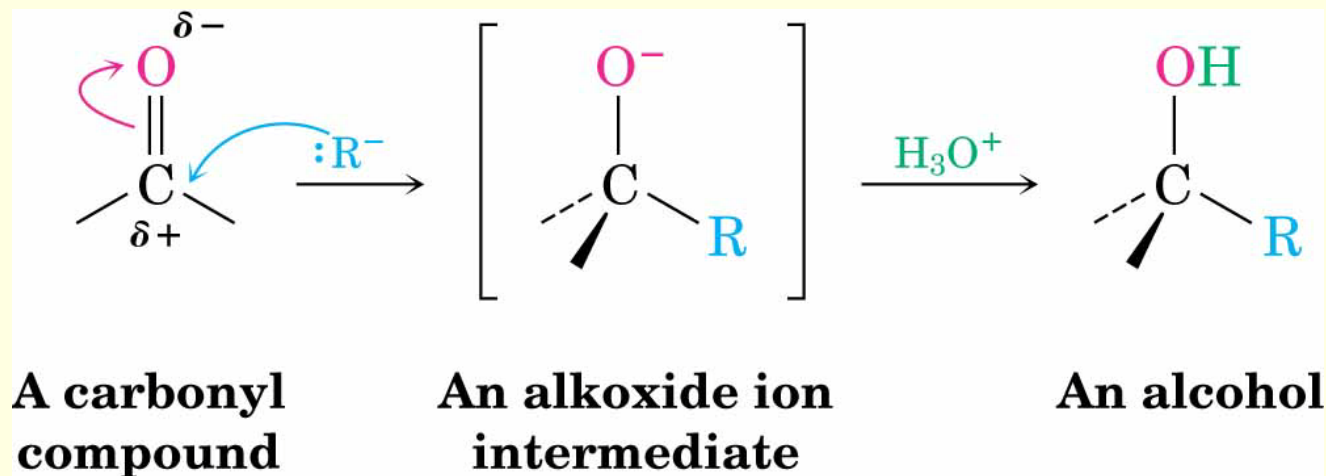


The Grignard reagent is protonated by these groups.

The Grignard reagent adds to these groups.

Mechanism of the Addition of a Grignard Reagent

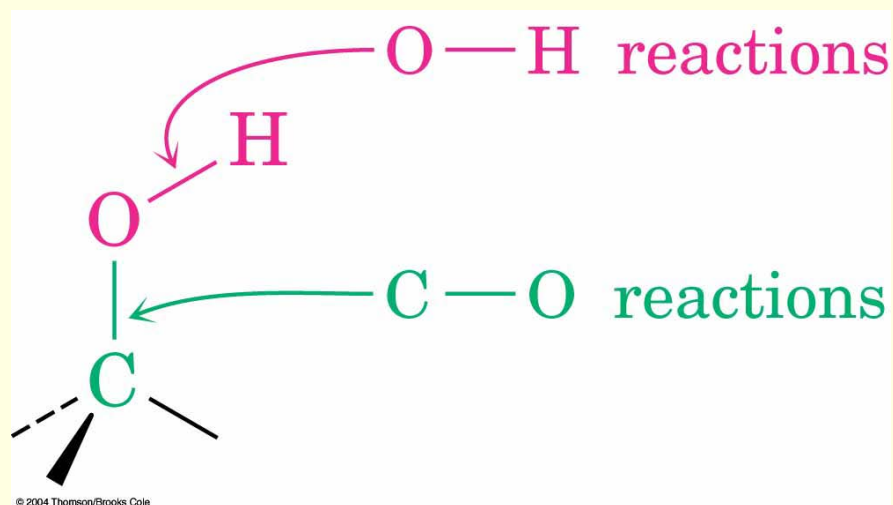
- Grignard reagents act as nucleophilic carbon anions (carbanions, :R^-) in adding to a carbonyl group.
- The intermediate alkoxide is then protonated to produce the alcohol.



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Some Reactions of Alcohols

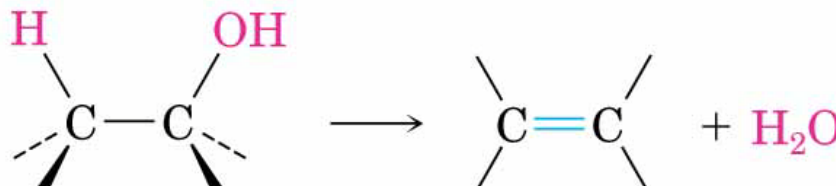
- Two general classes of reaction
 - At the carbon of the C–O bond
 - At the proton of the O–H bond



Dehydration of Alcohols to Yield Alkenes

- The general reaction: forming an alkene from an alcohol through loss of O-H and H (hence dehydration) of the neighboring C-H to give π bond
- Specific reagents are needed

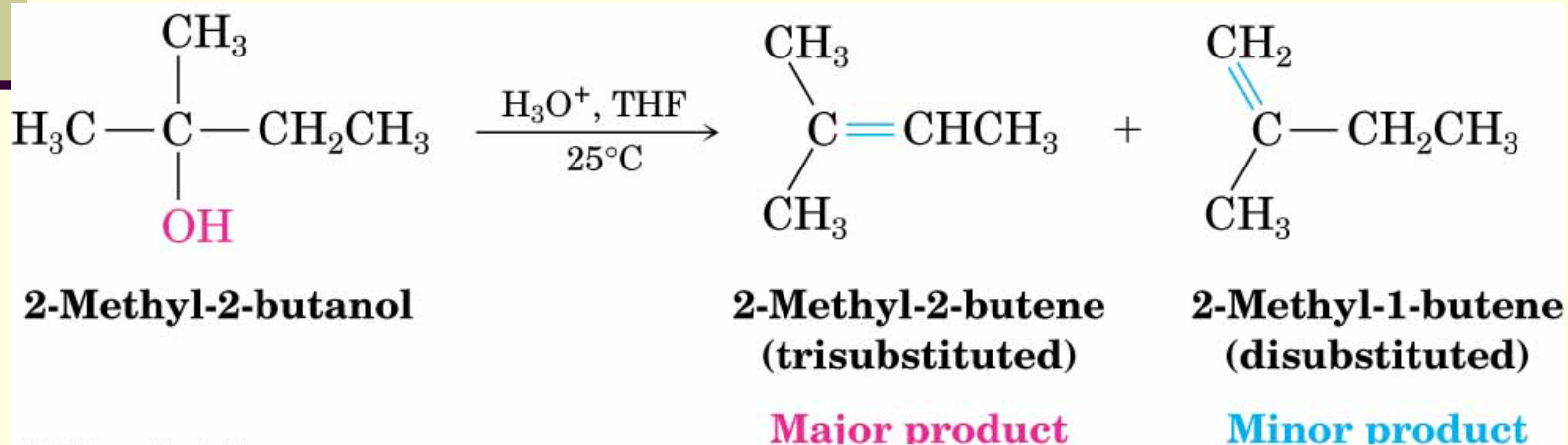
A dehydration reaction



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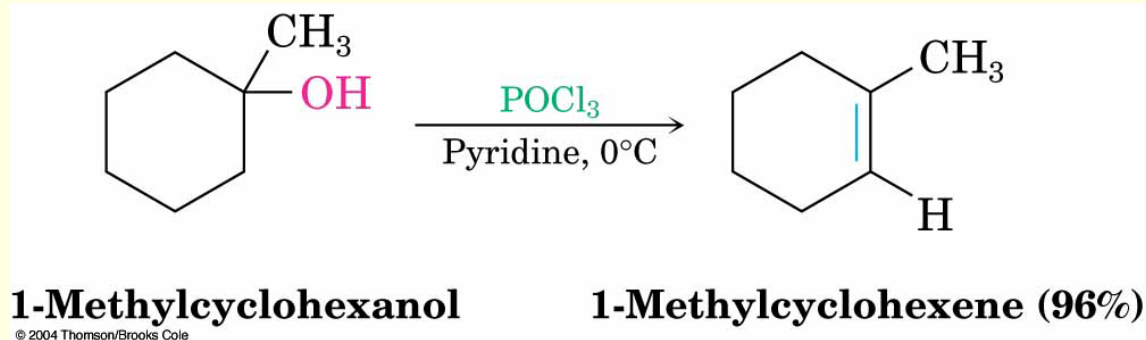
Acid- Catalyzed Dehydration

- Tertiary alcohols are readily dehydrated with acid
- Secondary alcohols require severe conditions (75% H₂SO₄, 100°C) - sensitive molecules don't survive
- Primary alcohols require very harsh conditions – impractical
- Reactivity is the result of the nature of the carbocation intermediate



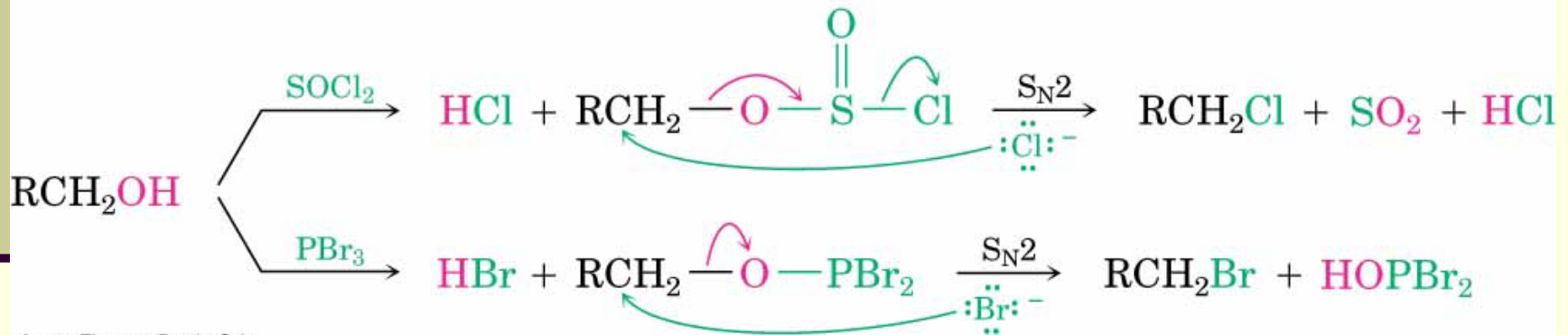
Dehydration with POCl_3

- Phosphorus oxychloride in the amine solvent pyridine can lead to dehydration of secondary and tertiary alcohols at low temperatures
- An E2 via an intermediate ester of POCl_2



Conversion of Alcohols into Alkyl Halides

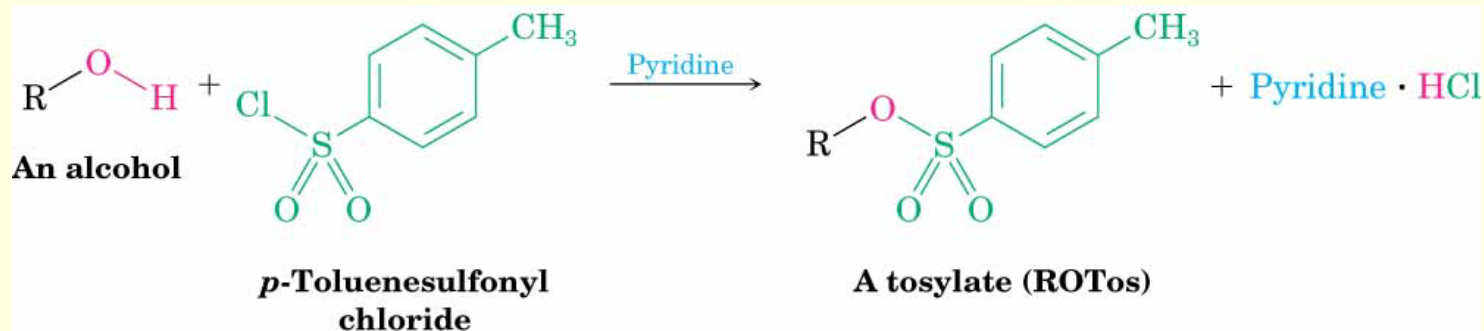
- 3° alcohols are converted by HCl or HBr at low temperature
- 1° and alcohols are resistant to acid – use SOCl₂ or PBr₃ by an S_N2 mechanism



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Conversion of Alcohols into Tosylates

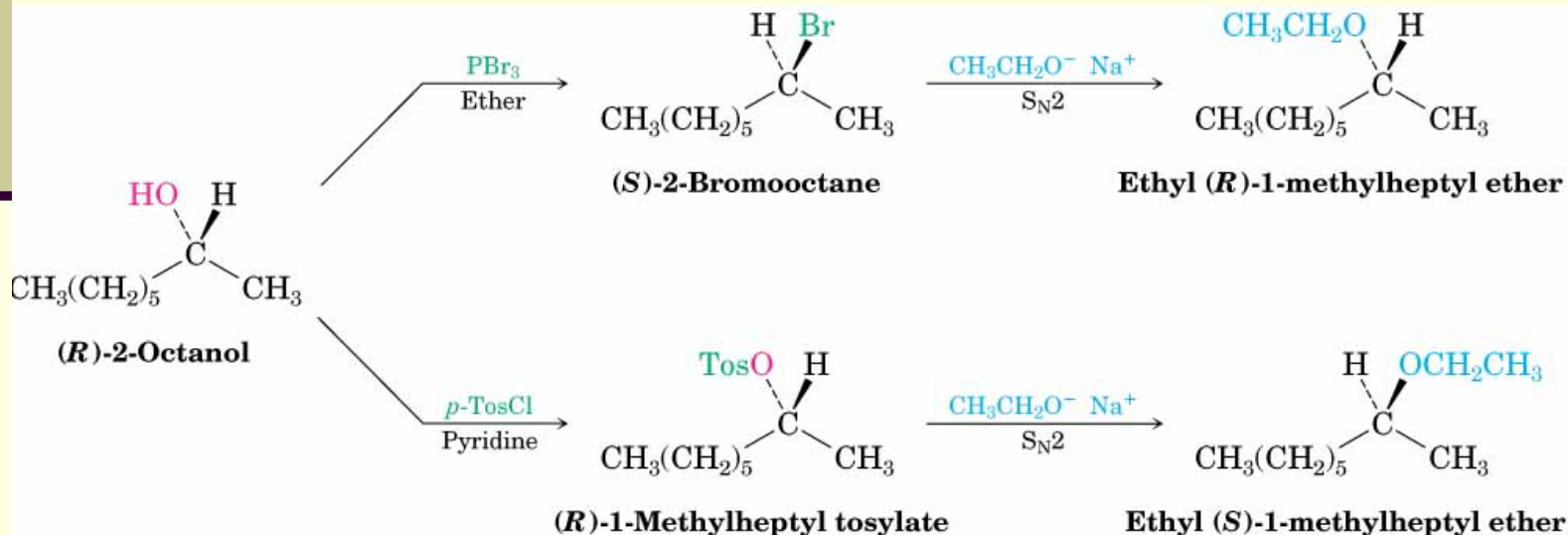
- Reaction with *p*-toluenesulfonyl chloride (tosyl chloride, *p*-TosCl) in pyridine yields alkyl tosylates, ROTos
- Formation of the tosylate does not involve the C–O bond so configuration at a chirality center is maintained
- Alkyl tosylates react like alkyl halides



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Stereochemical Uses of Tosylates

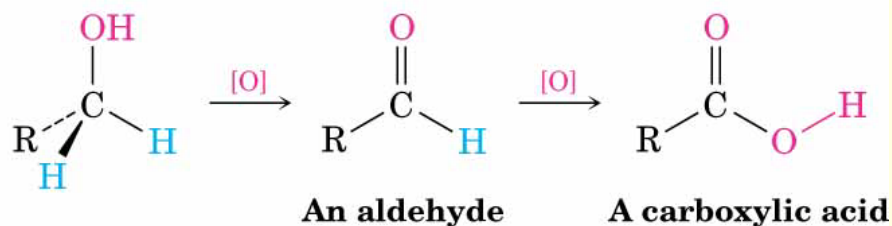
- The S_N2 reaction of an alcohol via a tosylate, produces inversion at the chirality center
- The S_N2 reaction of an alcohol via an alkyl halide proceeds with *two* inversions, giving product with same arrangement as starting alcohol



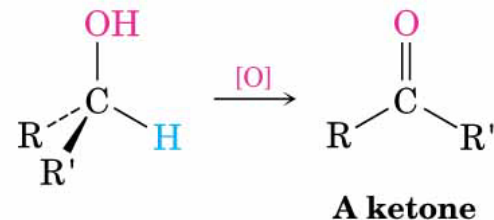
Oxidation of Alcohols

- Can be accomplished by inorganic reagents, such as KMnO_4 , CrO_3 , and $\text{Na}_2\text{Cr}_2\text{O}_7$ or by more selective, expensive reagents

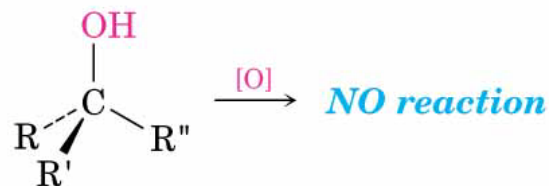
Primary alcohol



Secondary alcohol

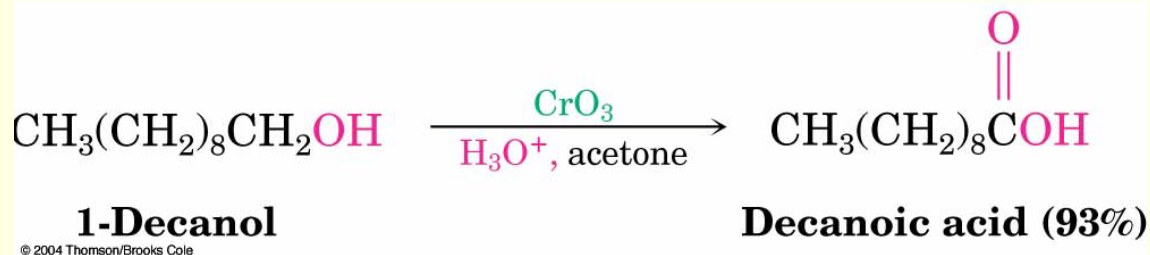
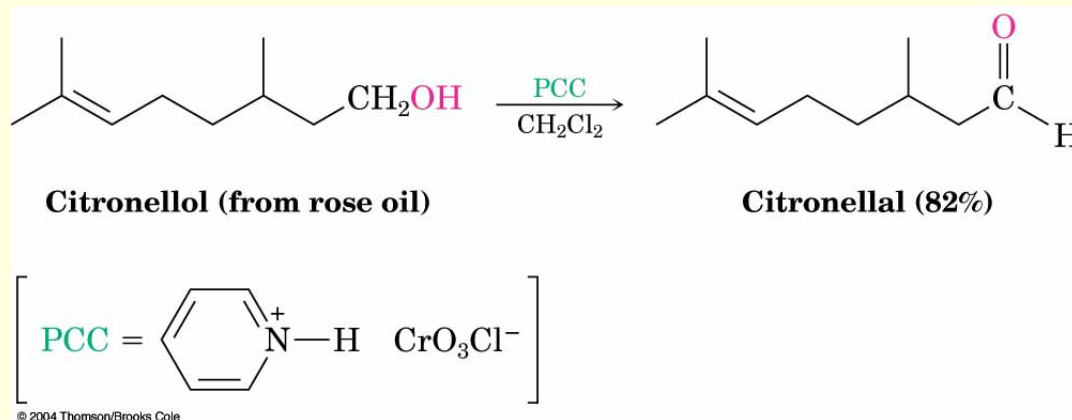


Tertiary alcohol



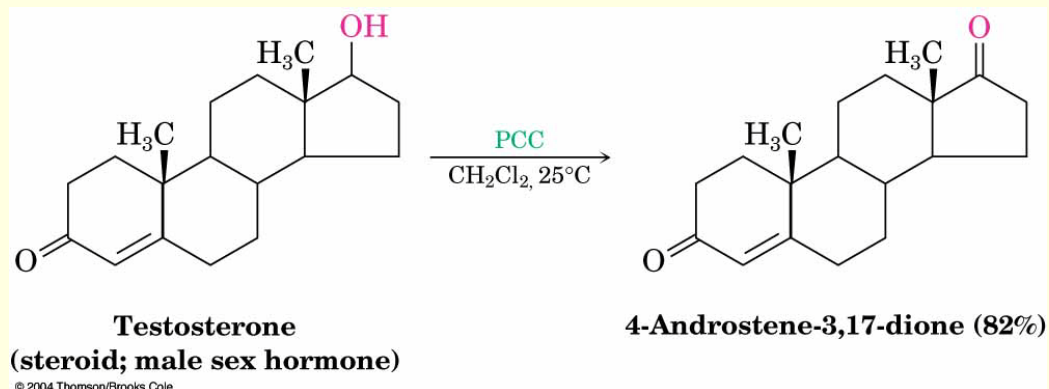
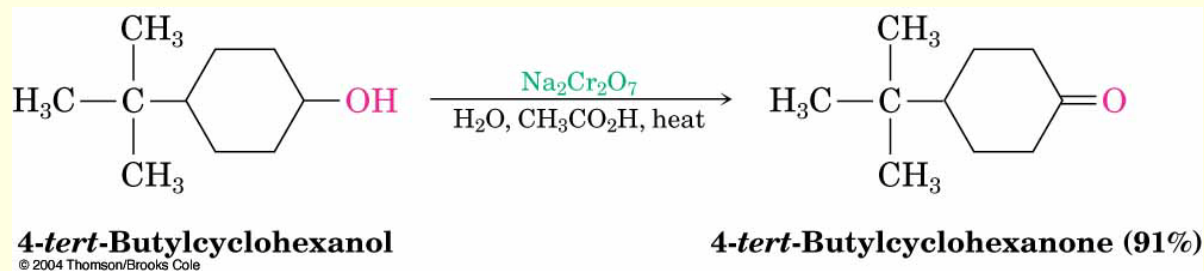
Oxidation of Primary Alcohols

- ~~To aldehyde: pyridinium chlorochromate (PCC, C₅H₆NCrO₃Cl)~~ in dichloromethane
- Other reagents produce carboxylic acids



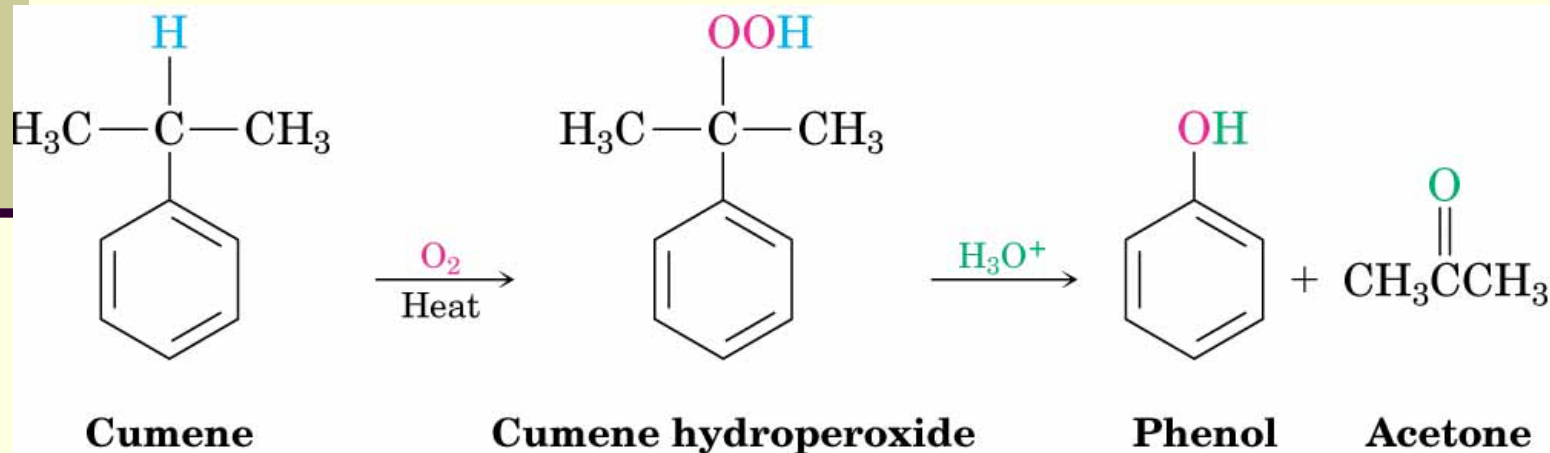
Oxidation of Secondary Alcohols

- Effective with inexpensive reagents such as $\text{Na}_2\text{Cr}_2\text{O}_7$ in acetic acid
- PCC is used for sensitive alcohols at lower temperatures



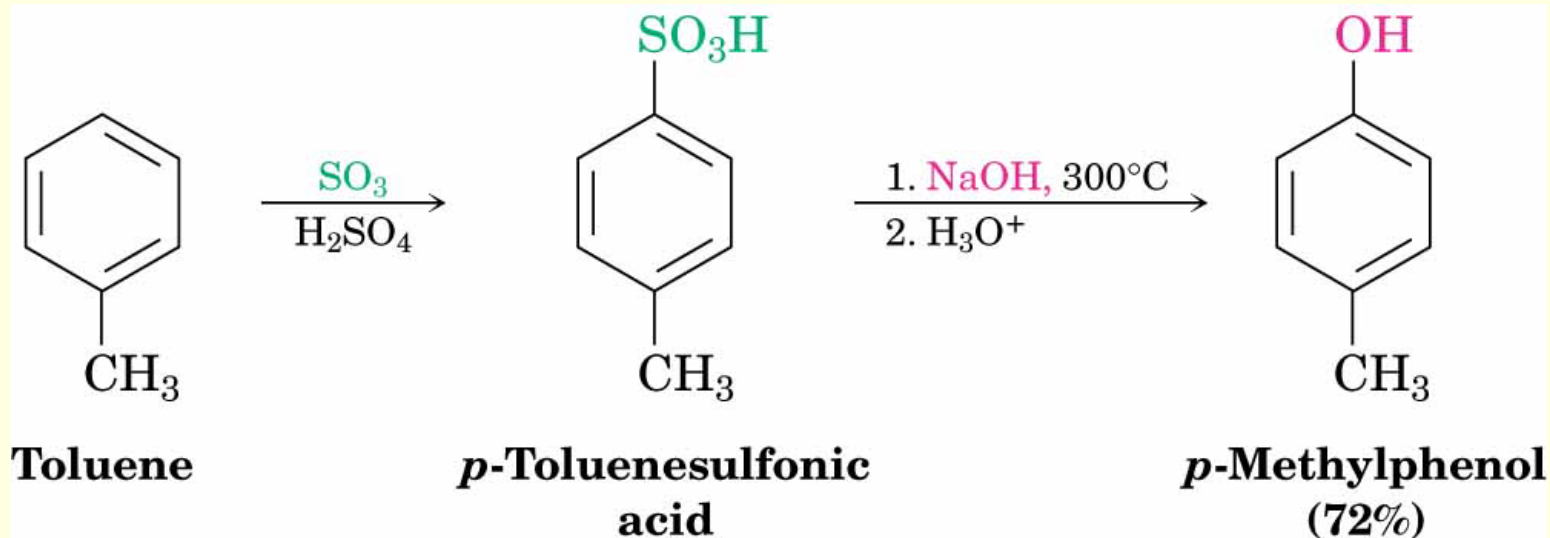
Preparation and Uses of Phenols

- Industrial process from readily available cumene.
- Forms cumene hydroperoxide with oxygen at high temperature.
- Converted into phenol and acetone by acid.



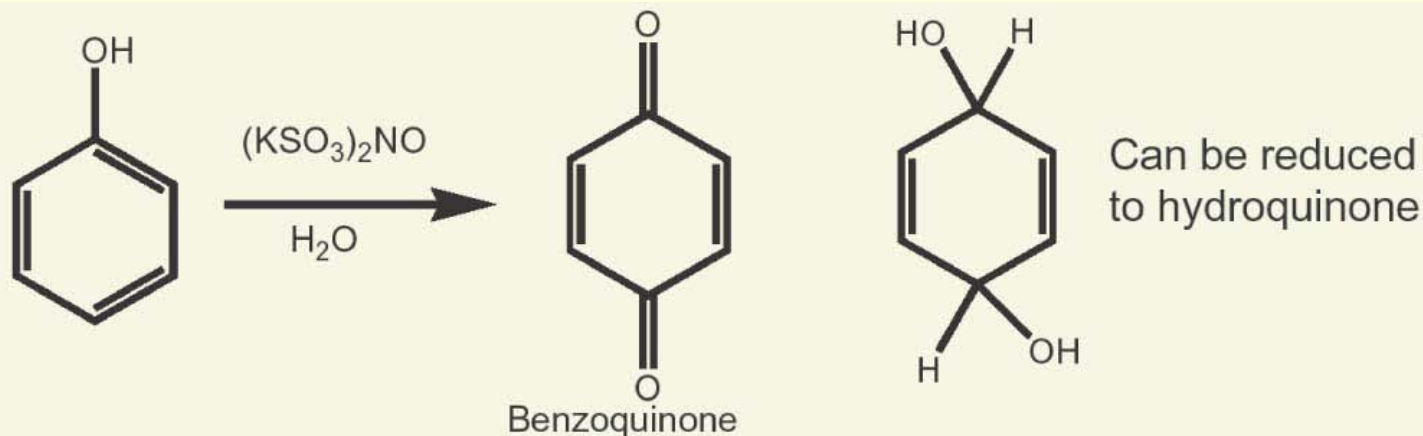
Laboratory Preparation of Phenols

- From aromatic sulfonic acids by melting with NaOH at high temperature.
- Limited to the preparation of alkyl-substituted phenols.



Reactions of Phenols

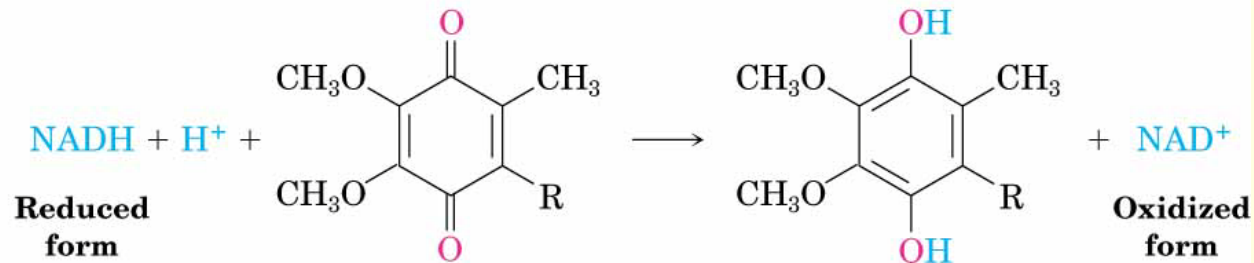
- The hydroxyl group is a strongly activating, making phenols substrates for electrophilic halogenation, nitration, sulfonation, and Friedel–Crafts reactions
- Reaction of a phenol with strong oxidizing agents yields a quinone
- Fremy's salt $[(\text{KSO}_3)_2\text{NO}]$ works under mild conditions through a radical mechanism



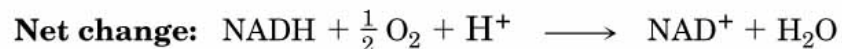
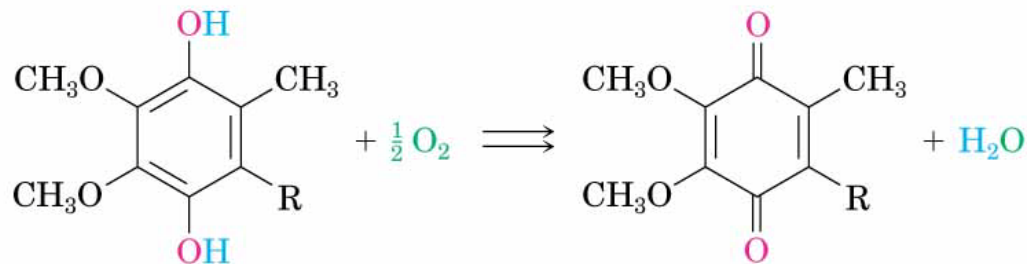
Quinones in Nature

- *Ubiquinones* mediate electron-transfer processes involved in energy production through their redox reactions

STEP 1



STEP 2



Summary - Alcohols

- Synthesis
 - Reduction of aldehydes and ketones
 - Addition of Grignard reagents to aldehydes and ketones
- Protection of OH as TMS) ether
- Reactions
 - Conversion to alkyl halides
 - Dehydration
 - Oxidation

Summary - Phenols

- Much more acidic ($pK_a \approx 10$) than alcohols
- Substitution of the aromatic ring by an electron-withdrawing group increases phenol acidity
- Substitution by an electron-donating group decreases acidity
- Oxidized to quinones
- Quinones are reduced to hydroquinones