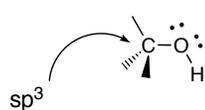
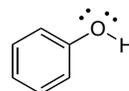


Chapter 17: Alcohols and Phenols



alcohol

pKa~ 16-18

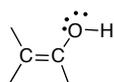


phenol
(aromatic alcohol)

pKa~ 10

Alcohols contain an OH group connected to a saturated carbon (sp^3)

Phenols contain an OH group connected to a carbon of a benzene ring



enol



keto

chemistry dominated
by the keto form

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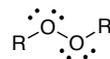
water



alcohol



ether



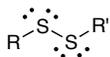
peroxide



thiols



thioether



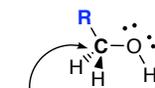
disulfides

Alcohols are classified as primary (1°), secondary (2°) or tertiary (3°), which refers to the carbon bearing the hydroxy group

methanol

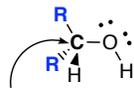


primary



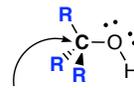
1° carbon

secondary



2° carbon

tertiary

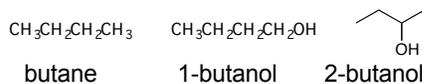


3° carbon

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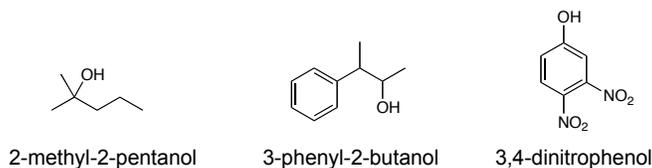
17.1: Nomenclature:

1. In general, alcohols are named in the same manner as alkanes; replace the -ane suffix for alkanes with an -ol for alcohols

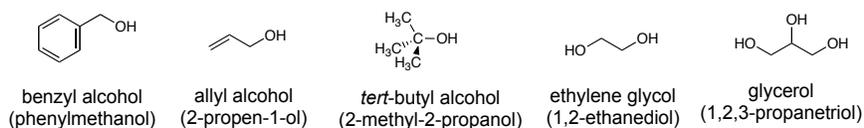


2. Number the carbon chain so that the hydroxyl group gets the lowest number
3. Number the substituents and write the name listing the substituents in alphabetical order.
4. For phenols, follow benzene nomenclature and use phenol as the parent name. The carbon bearing the -OH group gets number 1.

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Many alcohols are named using non-systematic nomenclature



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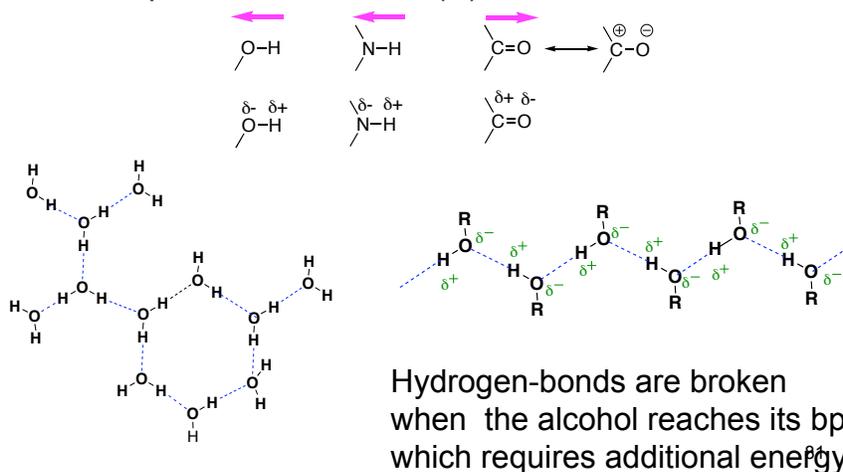
17.2: Properties of alcohols and phenols: Hydrogen bonding:
The structure around the oxygen atom of an alcohol or phenol is similar to that in water and is sp^3 hybridized

Alcohols and phenols have much higher boiling points than similar alkanes and alkyl halides

H₂O MW=18 bp= 100° C	CH₃CH₂CH₂CH₃ MW=58 bp= -0° C	CH₃CH₂CH₂CH₂Cl MW=92.5 bp= 77° C	CH₃CH₂CH₂OH MW=74 bp= 116° C
C₆H₆ MW=78 bp= 80° C	C₆H₆OH MW=94 bp= 182° C	C₆H₆CH₃ MW=92 bp= 110° C	C₆H₆CH₂OH MW=108 bp= 203° C

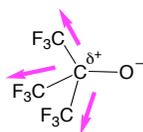
80

Alcohols and phenols, like water, can form *hydrogen bonds*:
non covalent interaction between a hydrogen atom (δ^+)
involved in a polar covalent bond, with the lone pair
of a heteroatom (usually O or N), which is also involved
in a polar covalent bond (δ^-)



Electronic factors that influence acidity:
inductive and resonance effect

	$\text{CH}_3\text{CH}_2\text{OH}$	$\text{FCH}_2\text{CH}_2\text{OH}$	$\text{F}_2\text{CHCH}_2\text{OH}$	$\text{F}_3\text{CCH}_2\text{OH}$	$(\text{F}_3\text{C})_3\text{CCH}_2\text{OH}$
$\text{pK}_a \sim$	16.0	14.4	13.3	12.4	5.4



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

$\text{X}-\text{C}_6\text{H}_4-\text{OH}$	$\text{X} = -\text{H}$	$-\text{Cl}$	$-\text{Br}$	$-\text{NO}_2$	$-\text{CH}_3$	$-\text{OCH}_3$	$-\text{NH}_2$
$\text{pK}_a \sim$	9.9	9.38	9.35	7.15	10.16	10.21	10.46

$\sim \text{pK}_a$	$\text{X} = -\text{Cl}$	9.38	8.85
	$-\text{NO}_2$	7.15	8.28
	$-\text{OCH}_3$	10.21	9.65
	$-\text{CH}_3$	10.17	10.16

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Phenols are much more acidic than aliphatic alcohols:
a benzene ring is generally considered electron withdrawing (inductive effect)
the benzene ring stabilizes the negative charge of the phenoxide ion through resonance

(Fig. 17.3, p. 595)

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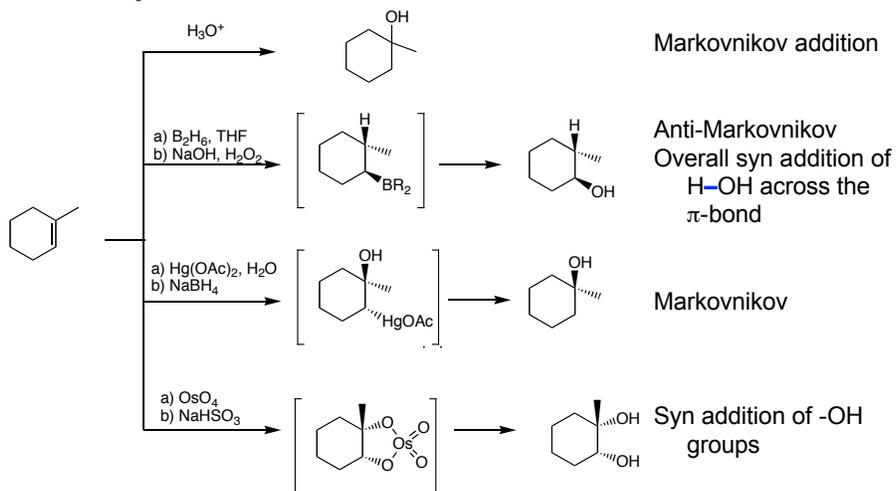
Electron-withdrawing substituents make a phenol more acidic by stabilizing the phenoxide ion through delocalization of the negative charge and through inductive effects

Electron-donating substituents make a phenol less acidic by destabilizing the phenoxide ion (resonance effect)

The location of the substituent relative to the phenol is important

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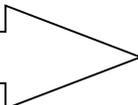
17.4: Preparation of alcohols:

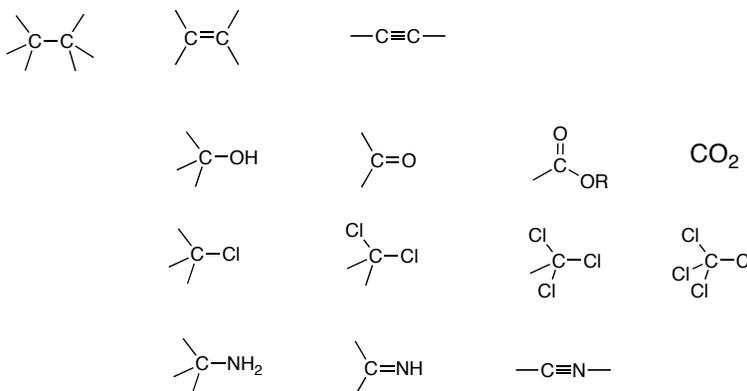


Hydration of alkenes (Ch. 7.4)
 Oxymercuration of alkenes (Ch. 7.4)
 Hydroboration of alkenes (Ch. 7.5)
 Di-hydroxylation of alkenes (Ch. 7.8)

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17.5: Alcohols from reduction of carbonyl compounds
 Figure 10.5 (Chapter 10.10)

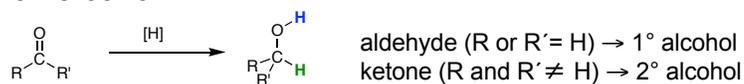
Increasing oxidation state 



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17.5: Alcohols from reduction of carbonyl compounds

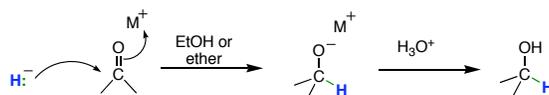
add the equivalent of H_2 across the π -bond of the carbonyl to give an alcohol



[H]: sodium borohydride: NaBH_4 , ethanol
 reduces aldehydes to 1° alcohols and ketones to 2° alcohols

lithium aluminum hydride (LAH): LiAlH_4 , ether
 reduces aldehydes, carboxylic acids, and esters to 1° alcohols and ketones to 2° alcohols

In general, NaBH_4 and LiAlH_4 will not reduce $\text{C}=\text{C}$.

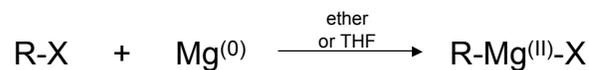


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17.6: Alcohols from reaction of carbonyl compounds with Grignard reagents

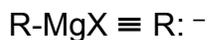
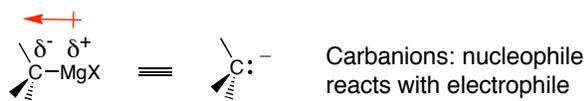
Alkyl halides will react with some metals (M^0) in ether or THF to form organometallic reagents

Grignard reagent- organomagnesium



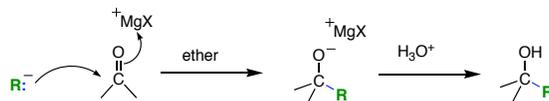
X= Cl, Br, or I

R can be a variety of groups: 1°-, 2°-, 3°-alkyl, aryl or vinyl

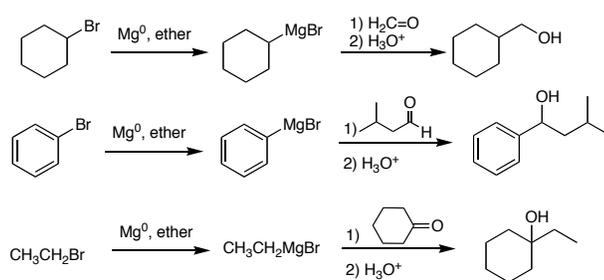


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Grignard reagents react with aldehydes or ketones to give alcohols

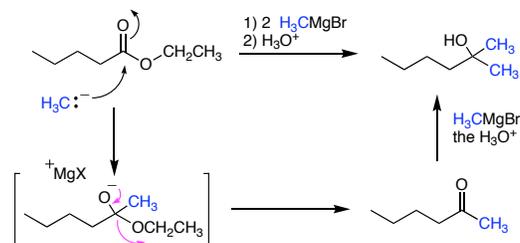


If, carbonyl = $H_2C=O$ \rightarrow 1° alcohol
 = aldehyde \rightarrow 2° alcohol
 = ketone \rightarrow 3° alcohol

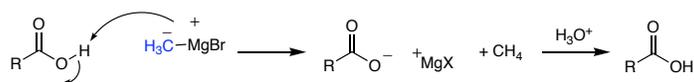


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Grignard reagents react with esters to give 3° alcohols



Some functional groups are incompatible with Grignard reagents
Grignard reagents are very strong bases as well as highly reactive nucleophiles



Carboxylic acids are simply deprotonated by Grignard reagents and do not give addition products

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Grignard reagents will deprotonate alcohols



Other incompatible groups:

-CO₂H, -OH, -SH, NH₂, CONHR (amides)

Reactive functional groups:

aldehydes, ketones, esters, amides, halides,
-NO₂, -SO₂R, nitriles

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17.7 Some reactions of alcohols

A. Reactions involving the C-O bond

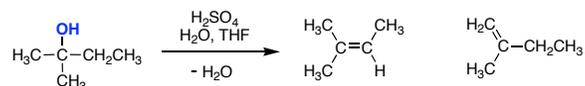
Dehydration to alkenes:

E1 mechanism (reactivity: $3^\circ > 2^\circ \gg 1^\circ$)

requires strong acid catalyst (H_2SO_4)

water is a much better leaving group than HO^-

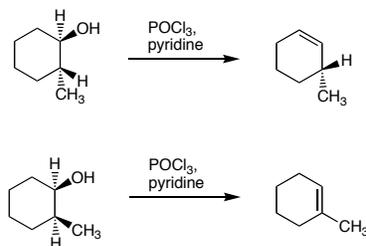
usually follows Zaitzev's rule



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Dehydration to alkenes with POCl_3

E2 mechanism- requires an anti-periplanar conformation between leaving group and the hydrogen that is being lost
mild conditions, requires a base (pyridine)



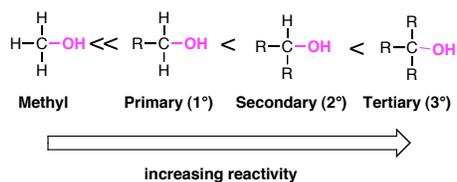
95

Conversion of an alcohol to an alkyl halide (R-OH → R-X)
(Chapter 10.7)

1. Substitution reaction of alcohols with HX



Works better with more substituted alcohols



S_N1 mechanism involving a carbocation intermediate:
rearrangements, stereochemistry (racemization)

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2. Preparation of alkyl chlorides by the treatment of alcohols
with thionyl chloride (SOCl₂)

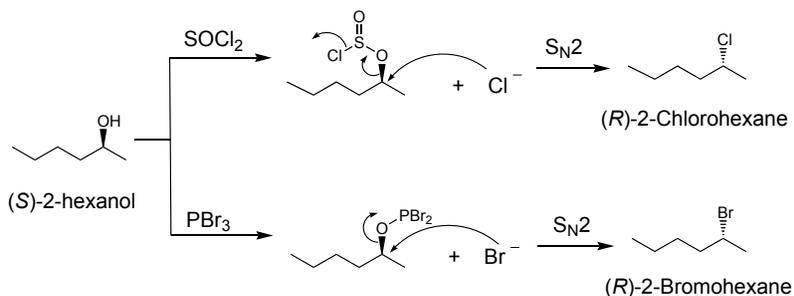


3. Preparation of alkyl bromides by the treatment of alcohols
with phosphorous tribromide (PBr₃)



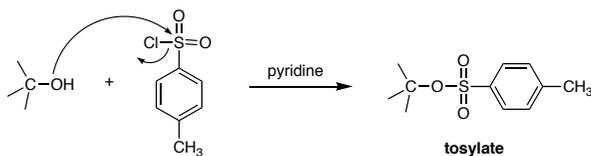
S_N2 mechanism: works best with 1° and 2° alcohols,
but not with 3° alcohols.
stereochemistry: inversion

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B. Reaction involving the O-H bond
Conversion of an alcohol to a tosylate (ROTs)

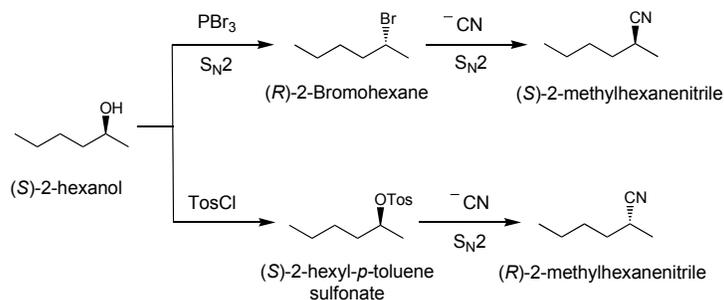
Reaction of an alcohol with with *p*-toluenesulfonyl chloride (tosyl chloride, *p*-TosCl) in pyridine gives a tosylates



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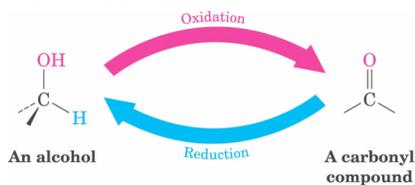
Formation of the tosylate does not involve the C–O bond so the stereochemistry of the carbon attached to the alcohol is not affected

Tosylates are good leaving groups and their reactivity is similar to alkyl halides

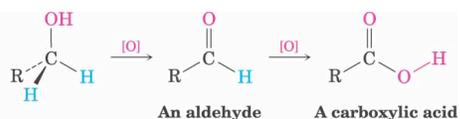


99

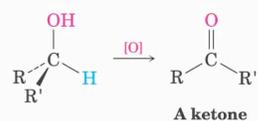
17.8 Oxidation of Alcohols



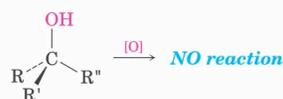
Primary alcohol



Secondary alcohol



Tertiary alcohol

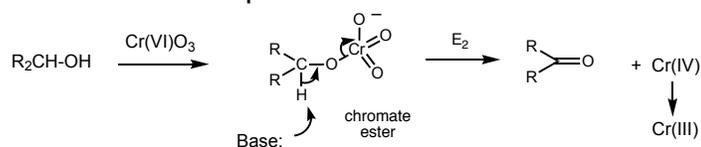


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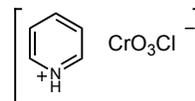
100

Oxidation of primary alcohols with Cr(VI)

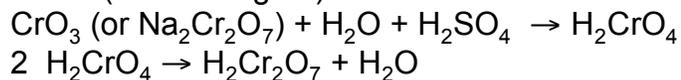
exact structure of the chromium reagent depends on solvent and pH



pyridinium chlorochromate (PCC)- oxidizes 1° alcohols to aldehydes; and 2° alcohols to ketones. Solvent: CH₂Cl₂

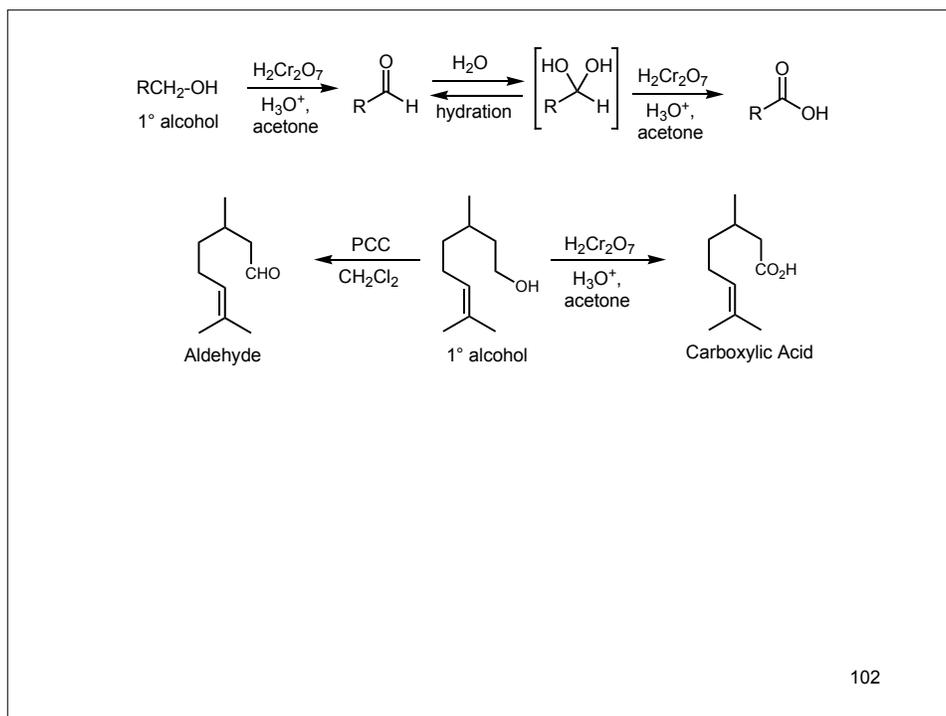


chromic acid (Jones reagent):



oxidizes 1° alcohols to carboxylic acids; and 2° alcohols to ketones. Solvent: H₃O⁺ and acetone

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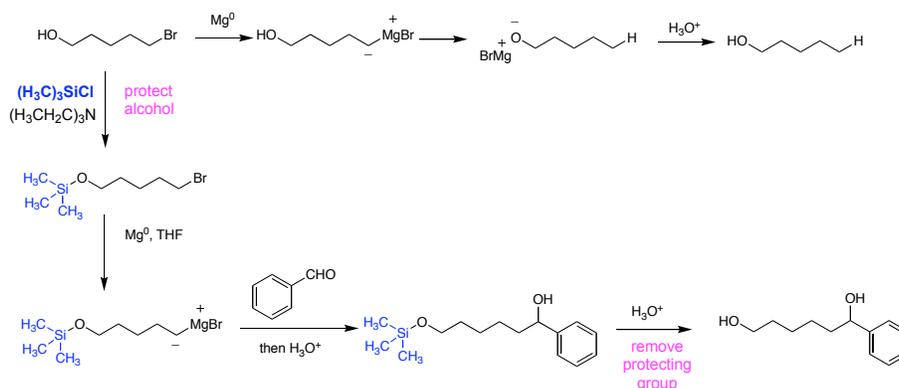
17.9 Protection of Alcohols

Hydroxyl groups are weak protic acids and can transfer a proton to a basic reagent, which may prevent a desired reaction.

Protecting group: Temporarily convert a functional group that is incompatible with a set of reaction conditions into a new functional group (with the protecting group) that is compatible with the reaction. The protecting group is then removed giving the original functional group (deprotection).

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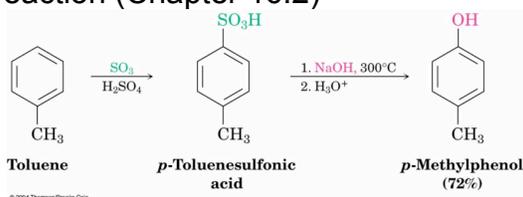
Trimethylsilyl ethers as a protecting group for alcohols



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17.10 Preparation of phenols

alkali fusion reaction (Chapter 16.2)



Chapter 24.8: anilines (Ar-NH₂) → phenols (Ar-OH)

17.11 Reactions of Phenols:

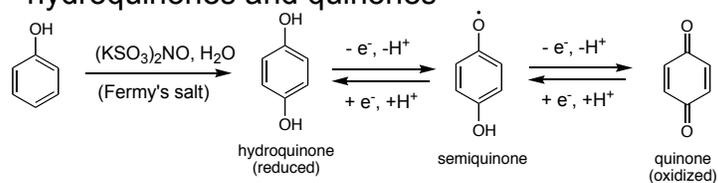
electrophilic aromatic substitution (Chapter 16.5-16.7)

phenols are highly activated toward electrophilic aromatic substitution and are *o*,*p*-directors

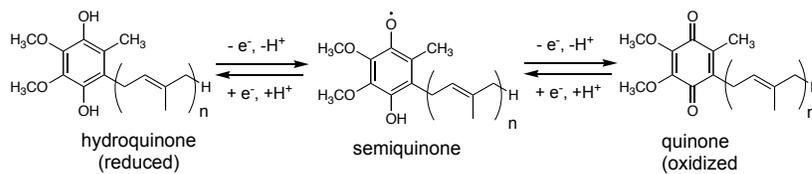
105

Oxidation of phenols to quinones (please read)

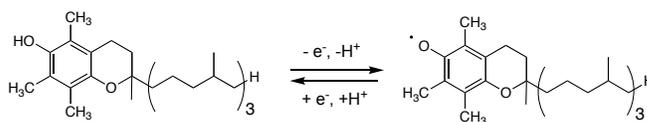
phenols can be oxidized by strong oxidants to give hydroquinones and quinones



Ubiquinones (n= 1-10): Coenzyme Q



α -tocopherol (vitamin E)



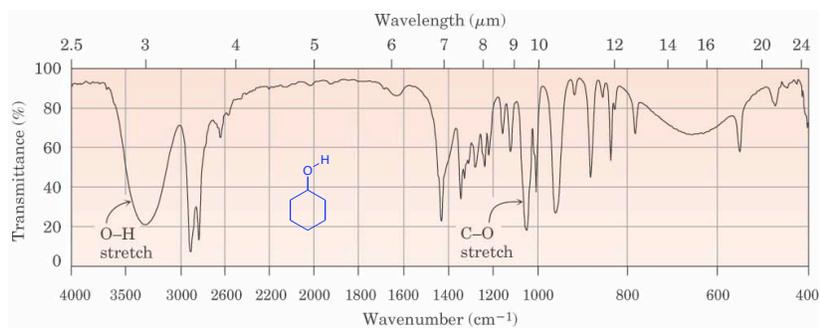
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17.12 Spectroscopy of Alcohols and Phenols:

Infrared (IR): Characteristic O–H stretching absorption at 3300 to 3600 cm^{-1}

Sharp absorption near 3600 cm^{-1} except if H-bonded:
then broad absorption 3300 to 3400 cm^{-1} range

Strong C–O stretching absorption near 1050 cm^{-1}

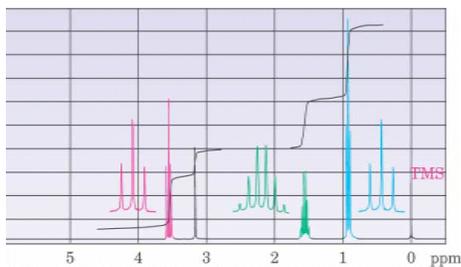
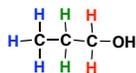


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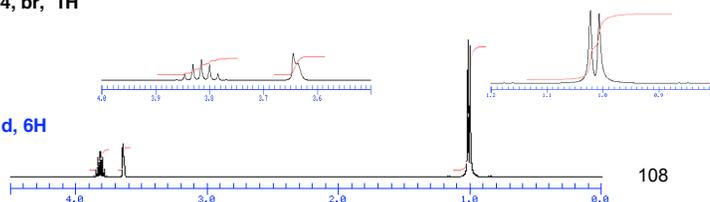
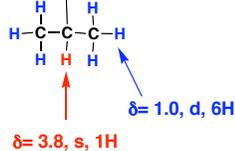
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^1H NMR:

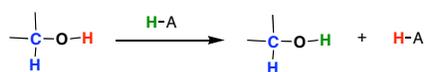
protons attached to the carbon bearing the hydroxyl group are deshielded by the electron-withdrawing nature of the oxygen, δ 3.5 to 4.0



OH \leftarrow $\delta=3.64$, br, 1H



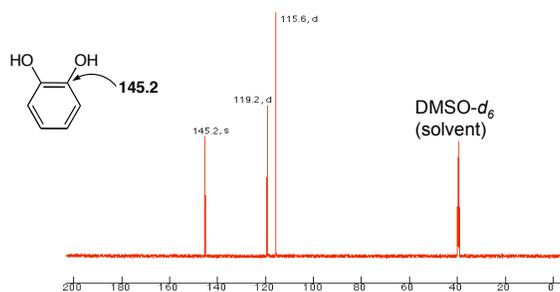
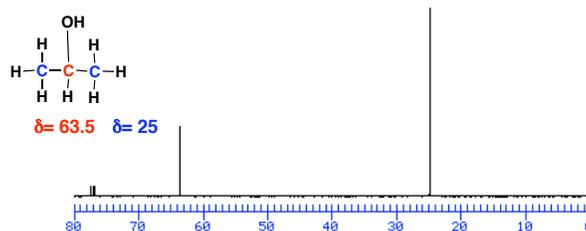
Usually no spin-spin coupling between the O-H proton and neighboring protons on carbon due to exchange reaction



The chemical shift of the -OH proton occurs over a large range (2.0 - 5.5 ppm). This proton usually appears as a broad singlet. It is not uncommon for this proton not to be observed.

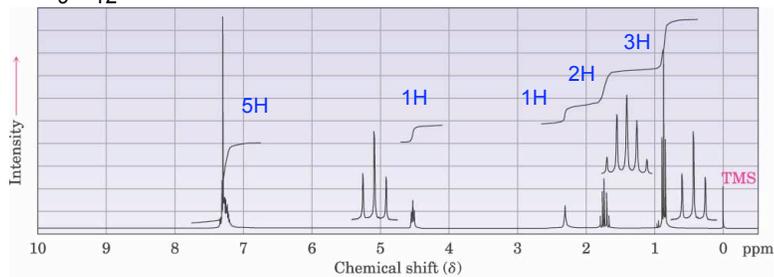
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^{13}C NMR: The oxygen of an alcohol will deshield the carbon it is attached to. The chemical shift range is 50-80 ppm



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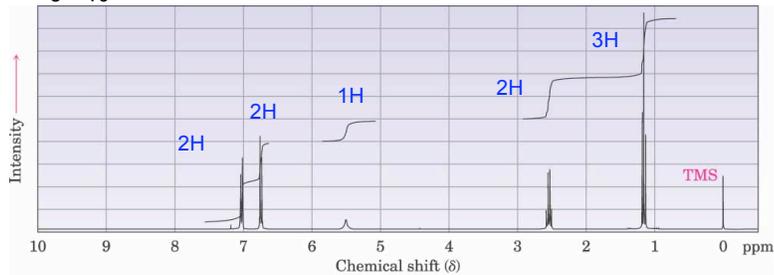
$\text{C}_9\text{H}_{12}\text{O}$



^{13}C : 138.6
129.0
128.0
126.1
79.0
31.8
7.5

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$\text{C}_8\text{H}_{10}\text{O}$



^{13}C : 153.7
132.1
129.2
115.8
32.4
14.6

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