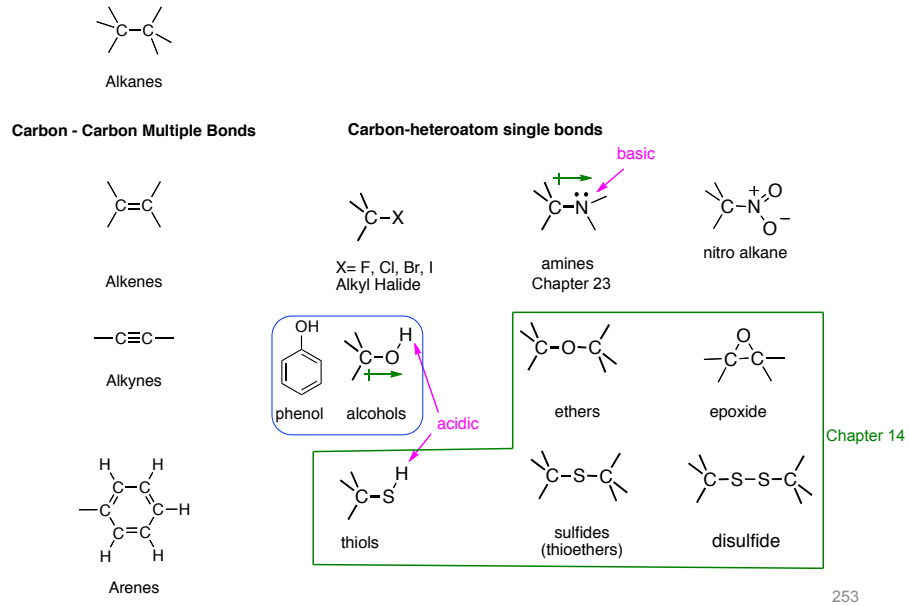
Chapter 13: Alcohols and Phenols

13.1 Structure and Properties of Alcohols



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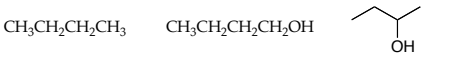
Nomenclature of alcohols

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

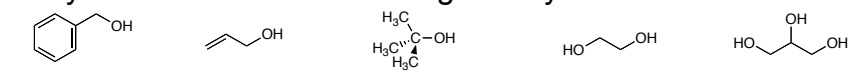


butane | 1-butanol, butan-1-ol | 2-butanol, butan-2-ol

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.

Many alcohols are named using non-systematic nomenclature



benzyl alcohol (phenylmethanol) | allyl alcohol (2-propen-1-ol) | *tert*-butyl alcohol (2-methyl-2-propanol) | ethylene glycol (1,2-ethanediol) | glycerol (1,2,3-propanetriol)

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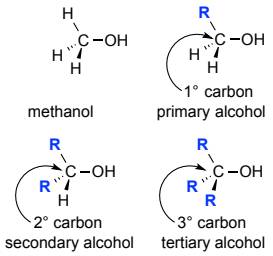
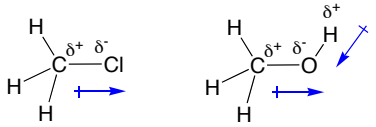
Alcohols are classified according to the degree of substitution of the carbon bearing the -OH group

primary (1°) : one alkyl substituent
secondary (2°) : two alkyl substituents
tertiary (3°) : three alkyl substituents



Physical properties of alcohols – the C-OH bond of alcohols has a significant dipole moment.



μ = 1.9 μ = 1.7

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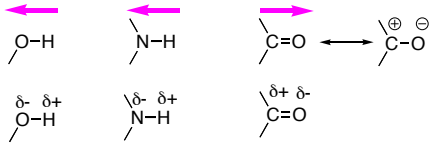
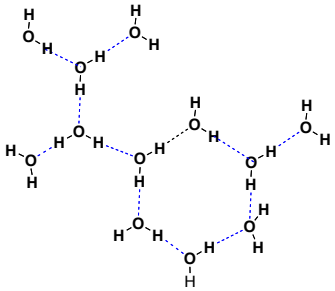
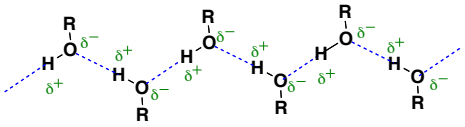
Like water, alcohols can form *hydrogen bonds*: a non-covalent interaction between a hydrogen atom (δ^+) involved in a polar covalent bond, with the lone pair of a heteroatom (usually O or N), which is also involved in a polar covalent bond (δ^-)







Hydrogen-bonds are broken when the alcohol reaches its bp, which requires additional energy

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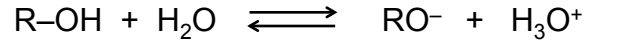
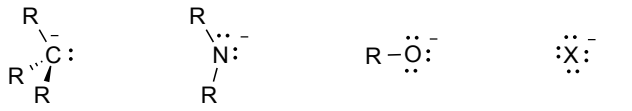
H_2O	$CH_3CH_2CH_2CH_3$	$CH_3CH_2CH_2CH_2Cl$	$CH_3CH_2CH_2CH_2OH$
MW=18	MW=58	MW=92.5	MW=74
bp= 100° C	bp= 0° C	bp= 77° C	bp= 116° C
	CH_3CH_3	CH_3CH_2Cl	CH_3CH_2OH
	MW= 30.1	MW= 64.5	MW=60
	bp = -89° C	bp= 12° C	bp= 78° C

13.2 Acidity of Alcohols and Phenols



Increasing stability of the conjugate base



pK_a =	50 – 60	35 – 40	15 – 18	-10 – 3

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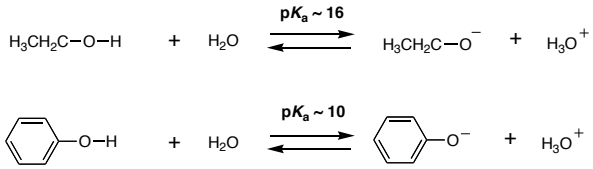
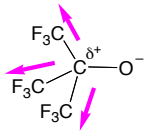
Factors affecting the acidity of alcohols and phenols



Inductive effects – an atom's (or group of atoms) ability to polarize a bond through electronegativity differences (σ-bonds)

	CH_3CH_2OH	FCH_2CH_2OH	F_2CHCH_2OH	F_3CCH_2OH	$(F_3C)_3COH$
pK_a ~	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)

A benzene ring is generally considered electron withdrawing and stabilizes the negative charge through inductive effects

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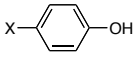
Resonance effect: the benzene ring stabilizes the the phenoxide ion by resonance delocalization of the negative charge

Substituents on the phenol can effect acidity – Electron-donating substituents make a phenol less acidic by destabilizing the phenoxide ion (resonance effect). Electron-withdrawing substituents make a phenol more acidic by stabilizing the phenoxide ion through delocalization of the negative charge and through inductive effects.



X=	**-NO_2**	**-Br**	**-Cl**	**-H**	**-CH_3**	**-OCH_3**	**-NH_2**
pK_a ~	7.2	9.3	9.4	10	10.3	10.2	10.5

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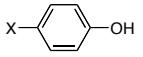
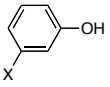
The influence of a substituent on phenol acidity is also dependent on its position relative to the -OH





pK_a	X=		
	-Cl	9.4	9.1
	-NO_2	7.2	8.4
	-OCH_3	10.2	9.6
	-CH_3	10.3	10.1

Reagents for deprotonating an alcohol – alcohols and phenols are deprotonated to alkoxides with a strong base such as sodium hydride (NaH).

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13.3 Preparation of Alcohols via Substitution or Addition

Substitution Reactions (Chapter 7)

Addition Reactions (Chapter 9)

Hydration of alkenes (Chapter 6)

1. Acid-catalyzed hydration (Chapter 9.4)
2. Oxymercuration – demercuration (Chapter 9.5)
3. Hydroboration – oxidation (Chapter 9.6)

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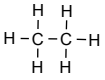
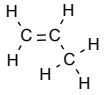
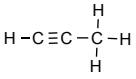
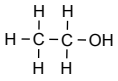
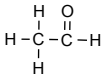
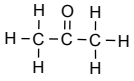
13.4 Preparation of Alcohols via Reduction

Oxidation State of Carbon (-4 – +4): C is a group IV element

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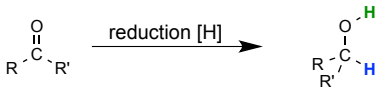
Reduction of ketone and aldehydes to alcohols – adds the equivalent of H_2 across the π-bond of the carbonyl (C=O) to yield an alcohol.



aldehyde (R or R´= H) → 1° alcohol
ketone (R and R´≠ H) → 2° alcohol

Catalytic hydrogenation is not typically used for the reduction of ketones or aldehydes to alcohols.

Metal hydride reagents: equivalent to $H:^-$ (hydride)

	sodium borohydride ($NaBH_4$)	lithium aluminium hydride ($LiAlH_4$)
	Na^+ $H-\underset{H}{\overset{H}{B}}-H^-$	Li^+ $H-\underset{H}{\overset{H}{Al}}-H^-$
	B–H	Al—H
electronegativity	2.0 2.1	1.5 2.1

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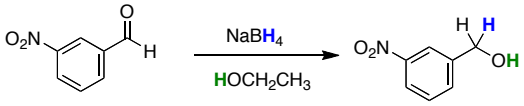
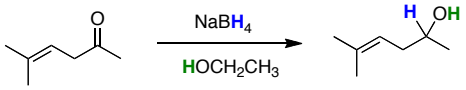
$NaBH_4$ reduces aldehydes to primary alcohols

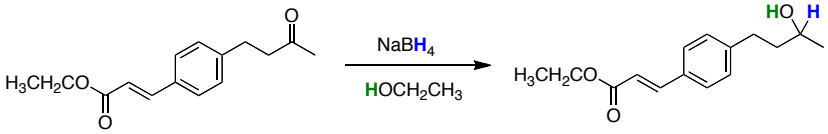


$NaBH_4$ reduces ketones to secondary alcohols



ketones 2° alcohols

$NaBH_4$ does not react with esters or carboxylic acids



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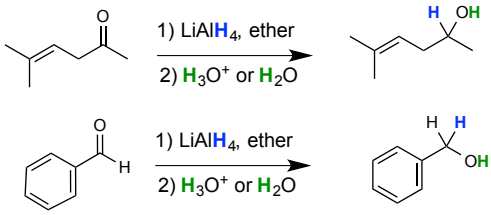
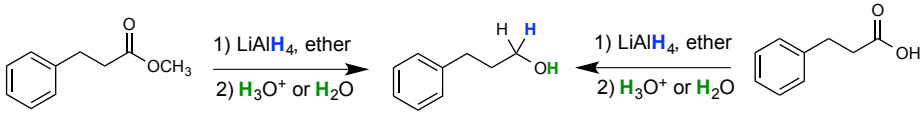
Lithium Aluminium Hydride ($LiAlH_4$, LAH) - much more reactive than $NaBH_4$. Incompatible with protic solvents (alcohols, H_2O).

$LiAlH_4$ (in ether) reduces aldehydes, carboxylic acids, and esters to 1° alcohols and ketones to 2° alcohols.



Carboxylic Acids and esters are reduced to 1° alcohols by $LiAlH_4$ (but not $NaBH_4$ or catalytic hydrogenation).



ester | 1° alcohol | carboxylic acid

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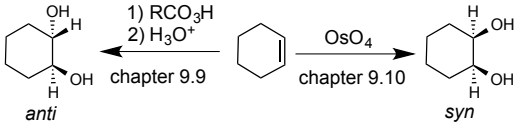
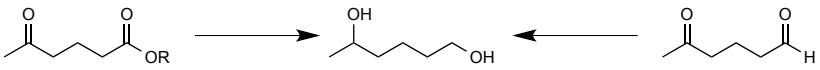
13.5 Preparation of Diols (Chapters 9.9 & 9.10) – Vicinal diols have hydroxyl groups on adjacent carbons (1,2-diols, *vic*-diols, glycols).

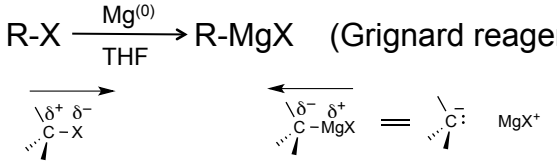


anti *syn*

other diols



13.6 Preparation of Alcohols via Grignard Reagents



alkyl halide = electrophile

carbanion = nucleophile reacts with electrophiles

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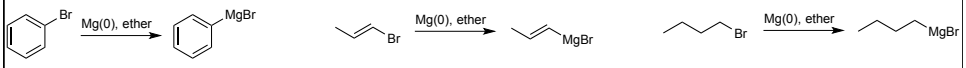
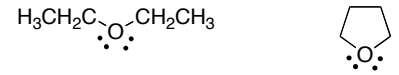
R-X can be an alkyl, vinyl, or aryl halide (chloride, bromide, or iodide)



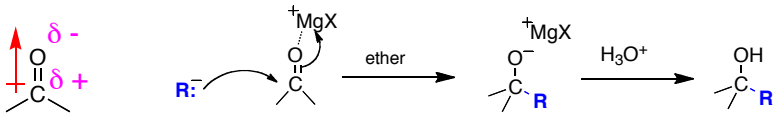
Solvent: diethyl ether (Et_2O) or tetrahydrofuran (THF)



diethyl ether (Et_2O)

tetrahydrofuran (THF)

Grignard reagents react with aldehydes, ketones, and esters to afford alcohols



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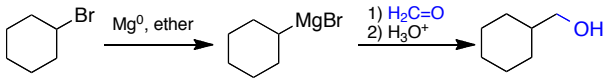
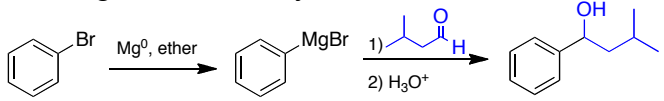
Grignard reagents react with . . .

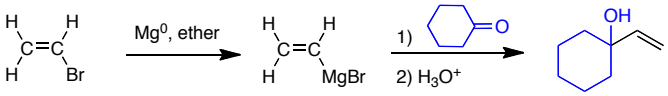
formaldehyde ($H_2C{=}O$) to give primary alcohols



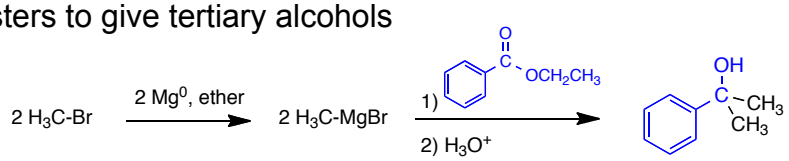
aldehydes to give secondary alcohols



ketones to give tertiary alcohols



esters to give tertiary alcohols



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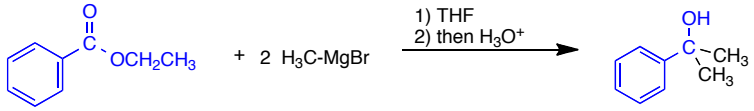
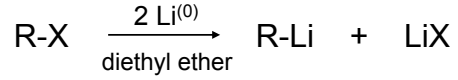
Tertiary alcohols from esters and Grignard reagents - mechanism:



Organolithium Reagents – can generally be used interchangeably with Grignard reagents



very strong bases
very strong nucleophiles

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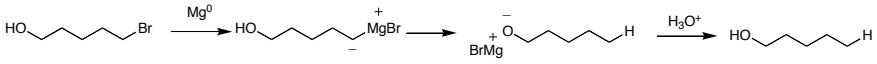
13.7 Protection of Alcohols – Grignard Reagents are highly basic; therefore the solvent or reactant can not contain functional groups that are acidic or electrophilic. These are incompatible with the formation and/or reactivity of the Grignard reagent.



Other incompatible groups:
$-CO_2H$, -OH, -SH, NH_2, CONHR (amides)

Reactive functional groups:
aldehydes, ketones, esters, amides, halides,
$-NO_2$, $-SO_2R$, nitriles

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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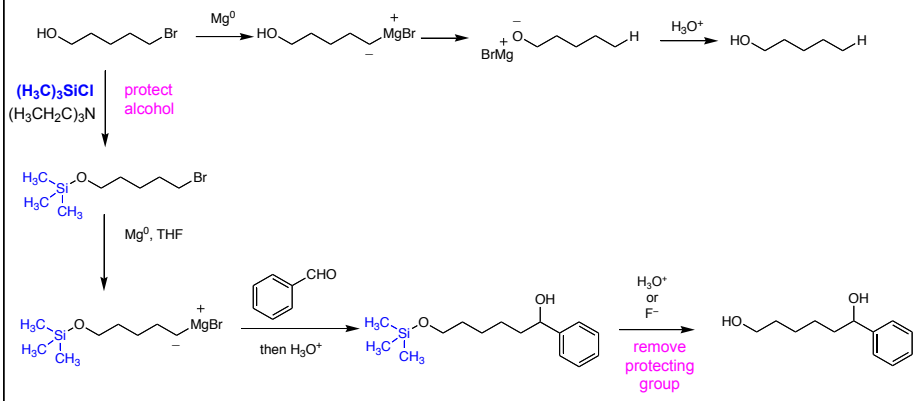
Trimethylsilyl ethers as a protecting group for alcohols



13.8 Preparation of Phenols (please read)

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13.9 Reaction of Alcohols: Substitution and Elimination

Substitution reaction of alcohols with HX – works well for 3° alcohols

$$R\text{–}OH + H\text{–}X \longrightarrow R\text{–}X + H_2O$$

1° and 2° alcohols react with *thionyl chloride* ($SOCl_2$) or *phosphorous tribromide* (PBr_3) to afford 1° and 2° alkyl chlorides and bromides, respectively

$$R\text{–}OH + SOCl_2 + \text{base} \longrightarrow R\text{–}Cl + SO_2 + HCl$$

$$R\text{–}OH + PBr_3 \longrightarrow R\text{-}Br + P(OH)_3$$

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Elimination reaction of alcohols (Chapter 8.9)
E1 mechanism – 3° alcohol undergo E1 elimination under strongly acidic conditions (H_2SO_4, Δ)

E2 mechanism - 1° and 2° alcohols must be converted to a better leaving group (halide or sulfonate) to be reactive toward E2 elimination.

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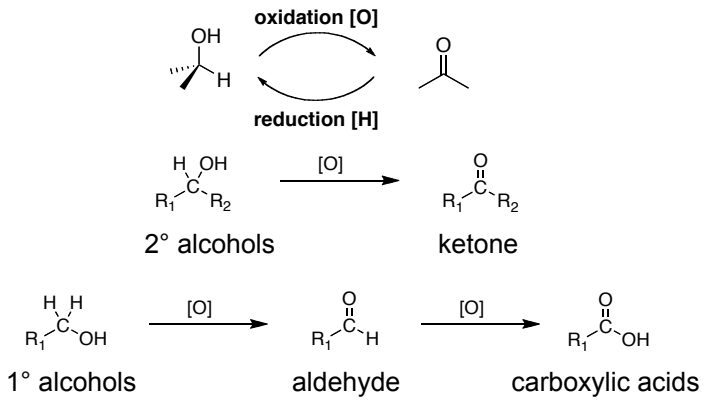
13.10 Reactions of Alcohols: Oxidations



Chromic acid ($Na_2Cr_2O_7$, H_3O^+) oxidize secondary alcohols to ketones, and primary alcohols to carboxylic acids.

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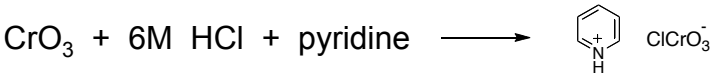
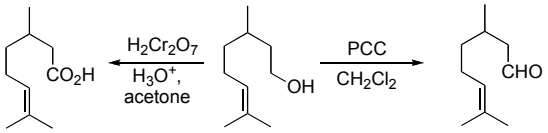
Oxidation of primary alcohols to aldehydes

Pyridinium Chlorochromate (PCC)



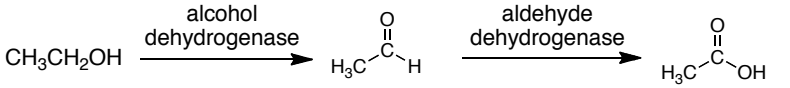
PCC is soluble in *anhydrous* organic solvent such as CH_2Cl_2. The oxidation of primary alcohols with PCC in anhydrous CH_2Cl_2 stops at the aldehyde.



Carboxylic Acid **1° alcohol** **Aldehyde**

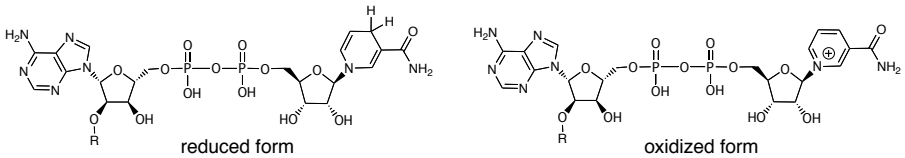
13.11: Biological Redox Reactions (please read)

Ethanol metabolism:



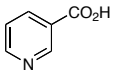
ethanol **acetaldehyde** **acetic acid**

Nicotinamide Adenine Dinucleotide (NAD)

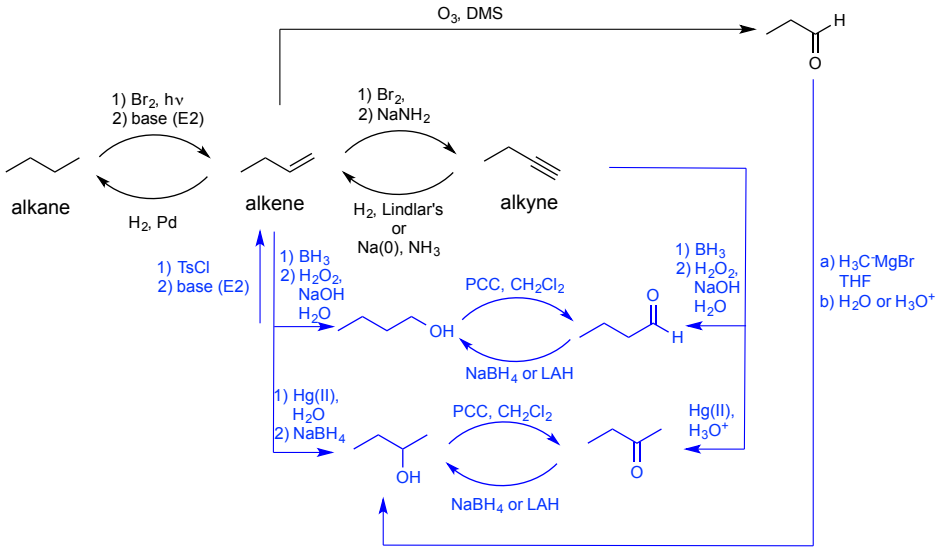


reduced form oxidized form

R= H NADH, NAD+
R= PO_3^{2-} NADPH, NADP+

Vitamin B_3, nicotinic acid, niacin 

13.12 Oxidation of Phenols (please read)
13.13 Synthetic Strategies



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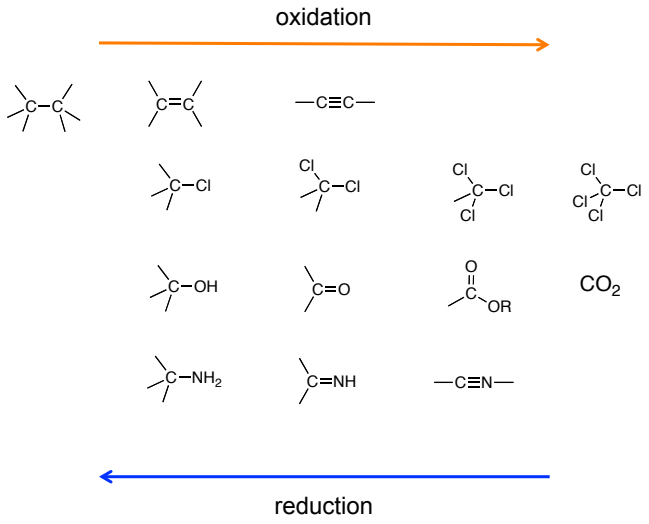
Oxidation states of functional groups



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