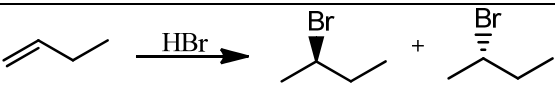
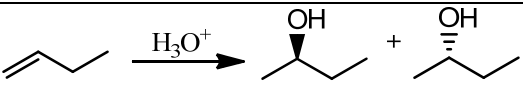
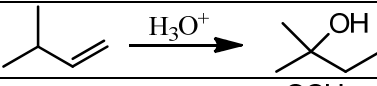
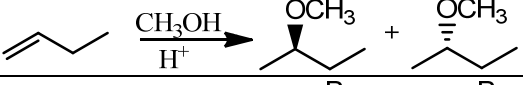
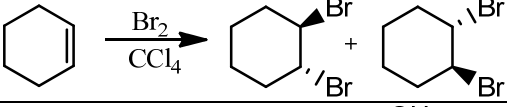
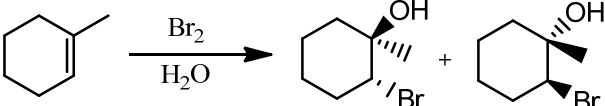
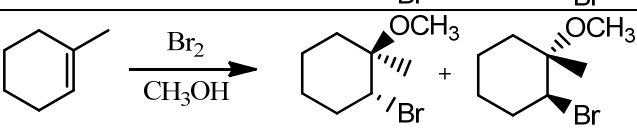
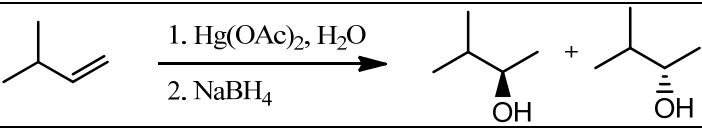
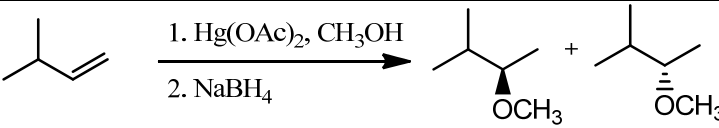
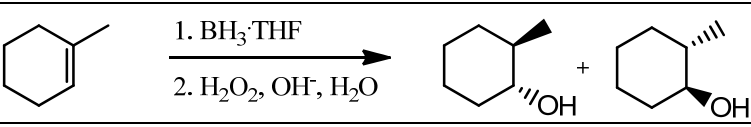
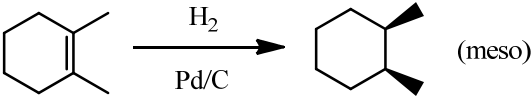
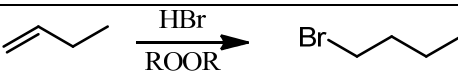
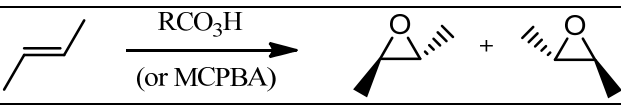
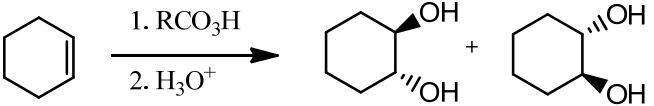
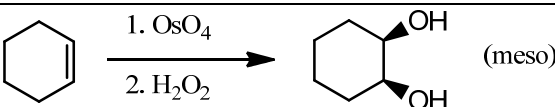
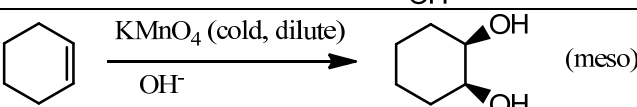
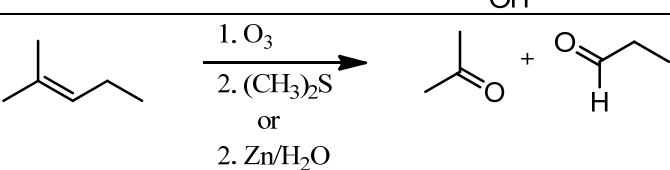


Alkene Rxns

Hydrohalogenation	
Hydration	
Hydration (with rearrangement)	
Addition of Alcohol	
Bromination	
Bromination in H2O	
Bromination in Alcohol	
Oxymercuration-Demercuration	
Alkoxymercuration-Demercuration	
Hydroboration-Oxidation	
Catalytic Hydrogenation (Catalytic Reduction)	
Hydrobromination with Peroxide	
Epoxidation	
Anti-Hydroxylation	
Syn-Hydroxylation	
Syn-Hydroxylation	
Ozonolysis under Reducing Conditions	

Ozonolysis under Oxidizing Conditions	<chem>CC(C)=CC >> CC(=O)C + CC(=O)O</chem>
Oxidative Cleavage	<chem>CC(C)=CC >> CC(=O)C + CC(=O)O</chem>

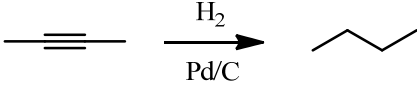
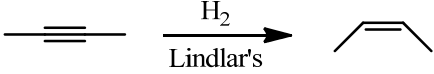
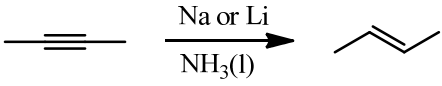
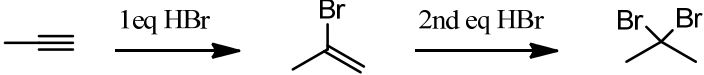
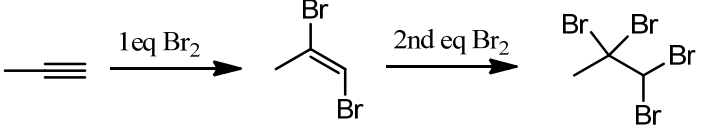
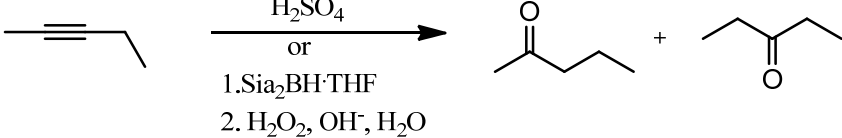
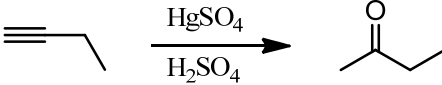
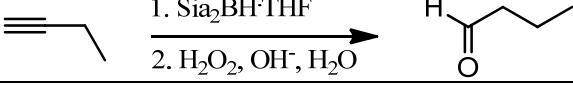
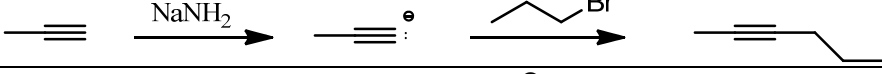
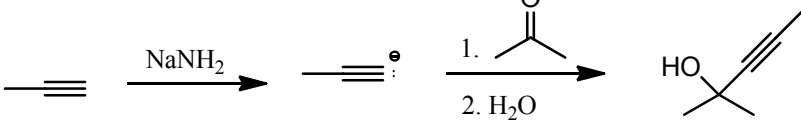
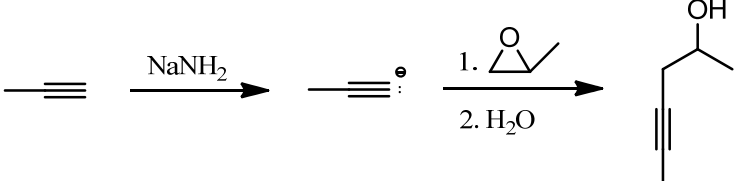
Free Radical Halogenation

Free Radical Bromination (high selectivity)	<chem>CC1CCCCC1 >> CC1(Br)CCCCC1</chem>
Free Radical Chlorination (low selectivity)	<chem>CCC >> CCCl + CC(C)Cl</chem>
Allylic/Benzylic Bromination	<chem>C=CC >> C=CCBr</chem> <chem>CCc1ccccc1 >> CC(Br)c1ccccc1</chem>

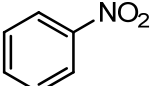
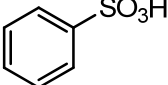
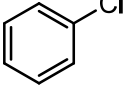
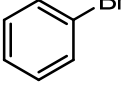
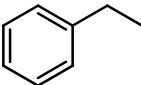
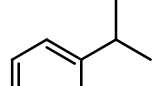
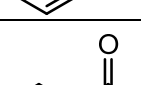
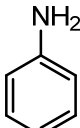
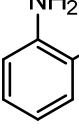
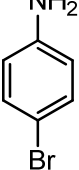
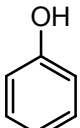
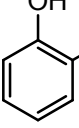
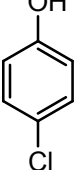
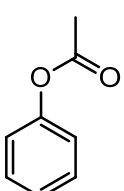
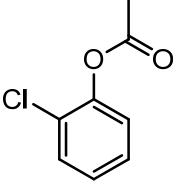
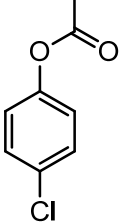
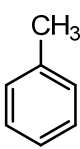
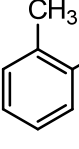
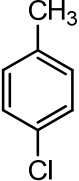
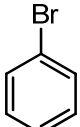
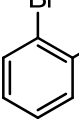
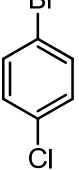
Grignard Rxns

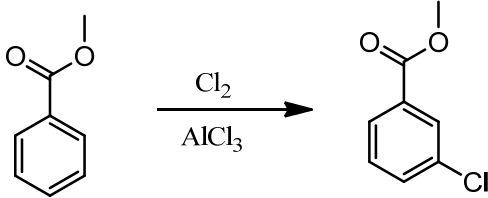
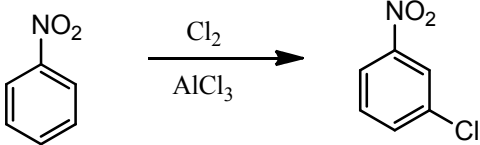
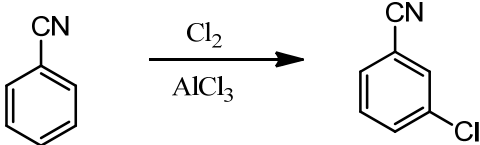
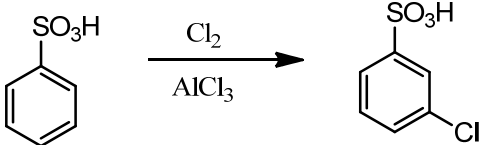
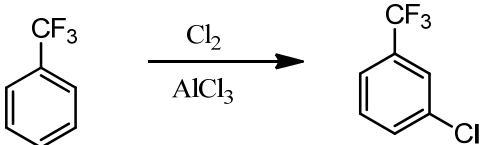
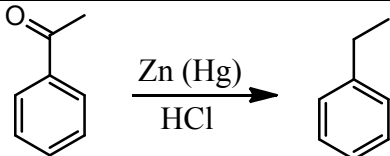
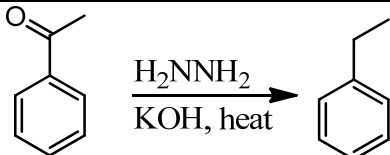
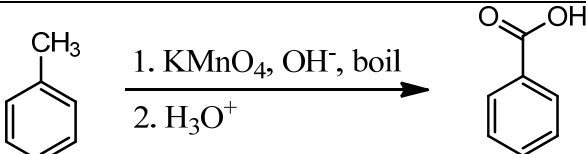
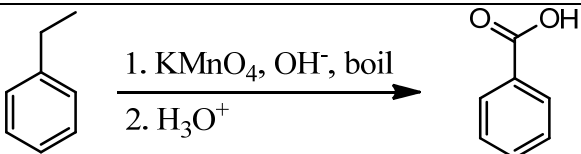
Nucleophilic Addition of a Grignard Reagent to a Ketone	<chem>c1ccccc1Br >> CC(O)(CC)c1ccccc1</chem>
Nucleophilic Addition of a Grignard Reagent to an Epoxide (attacks less substituted side)	<chem>c1ccccc1Br >> CC(O)Cc1ccccc1</chem>
Nucleophilic Addition of a Grignard Reagent to CO ₂	<chem>c1ccccc1Br >> OC(=O)c1ccccc1</chem>
Protonation of a Grignard Reagent (Grignards are protonated in protic solutions)	<chem>c1ccccc1Br >> c1ccccc1</chem>

Alkyne Rxns

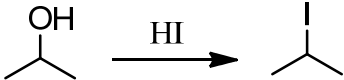
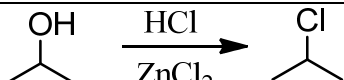
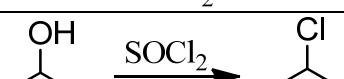
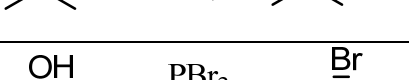
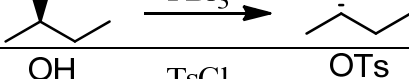
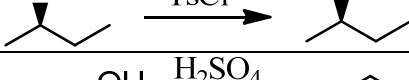
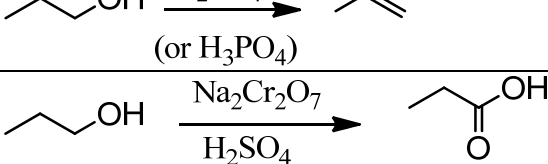
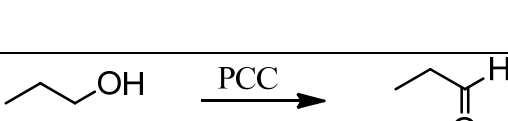
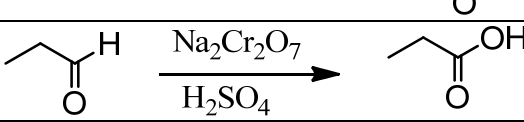
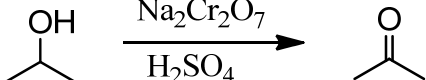
Catalytic Hydrogenation (Catalytic Reduction)	
Reduction to cis-alkene	
Reduction to trans-alkene	
Hydrohalogenation	
	
Hydration of an Internal Alkyne	
Hydration (Markovnikov)	
Hydration (Anti-Markovnikov)	
S _N 2 Addition of an Acetylide Ion	
Addition of an Acetylide Ion to a Ketone	
Addition of an Acetylide Ion to an Epoxide	

Benzene Rxns

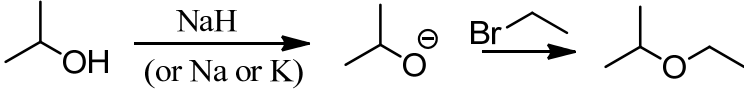
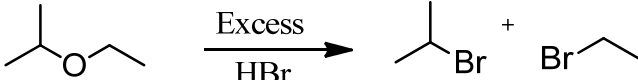
Nitration (EAS)	 $\xrightarrow[\text{H}_2\text{SO}_4]{\text{HNO}_3}$ 
Sulfonation (EAS)	 $\xrightarrow[\text{H}_2\text{SO}_4]{\text{SO}_3}$ 
Chlorination (EAS)	 $\xrightarrow[\text{AlCl}_3]{\text{Cl}_2}$ 
Bromination (EAS)	 $\xrightarrow[\text{FeBr}_3]{\text{Br}_2}$ 
Friedel-Crafts Alkylation (EAS)	 $\xrightarrow[\text{AlCl}_3]{\text{Cl}-\text{CH}_2\text{CH}_3}$ 
Friedel-Crafts Alkylation (EAS) (with rearrangement)	 $\xrightarrow[\text{AlCl}_3]{\text{Cl}-\text{CH}_2\text{CH}_2\text{CH}_3}$ 
Friedel-Crafts Acylation (EAS)	 $\xrightarrow[\text{AlCl}_3]{\text{Cl}-\text{C}(=\text{O})\text{CH}_3}$ 
Bromination (EAS) -NH ₂ is an ortho/para director and doesn't require a catalyst like FeBr ₃	 $\xrightarrow{\text{Br}_2}$  + 
Chlorination (EAS) -OH is an ortho/para director	 $\xrightarrow[\text{AlCl}_3]{\text{Cl}_2}$  + 
Chlorination (EAS) -OR is an ortho/para director	 $\xrightarrow[\text{AlCl}_3]{\text{Cl}_2}$  + 
Chlorination (EAS) -CH ₃ is an ortho/para director	 $\xrightarrow[\text{AlCl}_3]{\text{Cl}_2}$  + 
Chlorination (EAS) -Br is an ortho/para director	 $\xrightarrow[\text{AlCl}_3]{\text{Cl}_2}$  + 

Chlorination (EAS) Carbonyl is a meta director	
Chlorination (EAS) -NO ₂ is a meta director	
Chlorination (EAS) -CN is a meta director	
Chlorination (EAS) -SO ₃ H is a meta director	
Chlorination (EAS) -CF ₃ is a meta director	
Clemmensen Reduction	
Wolff-Kishner Reduction	
Side-chain Oxidation (Benzylic Oxidation)	
Side-chain Oxidation (Benzylic Oxidation)	

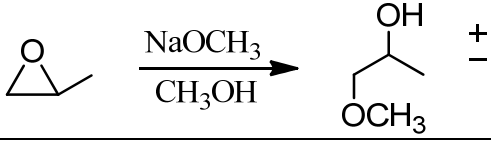
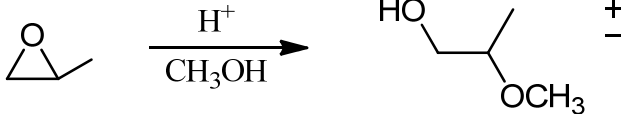
Alcohol Rxns

Conversion to an alkyl iodide	
Conversion to an alkyl bromide	
Conversion to an alkyl chloride	
Conversion to an alkyl chloride with thionyl chloride (only for 1° and 2°)	
Conversion to an alkyl bromide (only for 1° and 2°)	
Conversion to a tosylate ester	
Acid-catalyzed Dehydration	
Chromic Acid Oxidation of a 1° Alcohol (Chromic Acid can also be written as H ₂ CrO ₄ or CrO ₃ /H ₂ SO ₄)	
PCC Oxidation of a 1° Alcohol	
Chromic Acid Oxidation of an Aldehyde	
Chromic Acid Oxidation of a 2° Alcohol	
PCC Oxidation of a 2° Alcohol	

Ether Rxns

Williamson Ether Synthesis (2 nd step is S _N 2)	
Acid-Catalyzed cleavage of Ethers (also works with HI and HCl)	

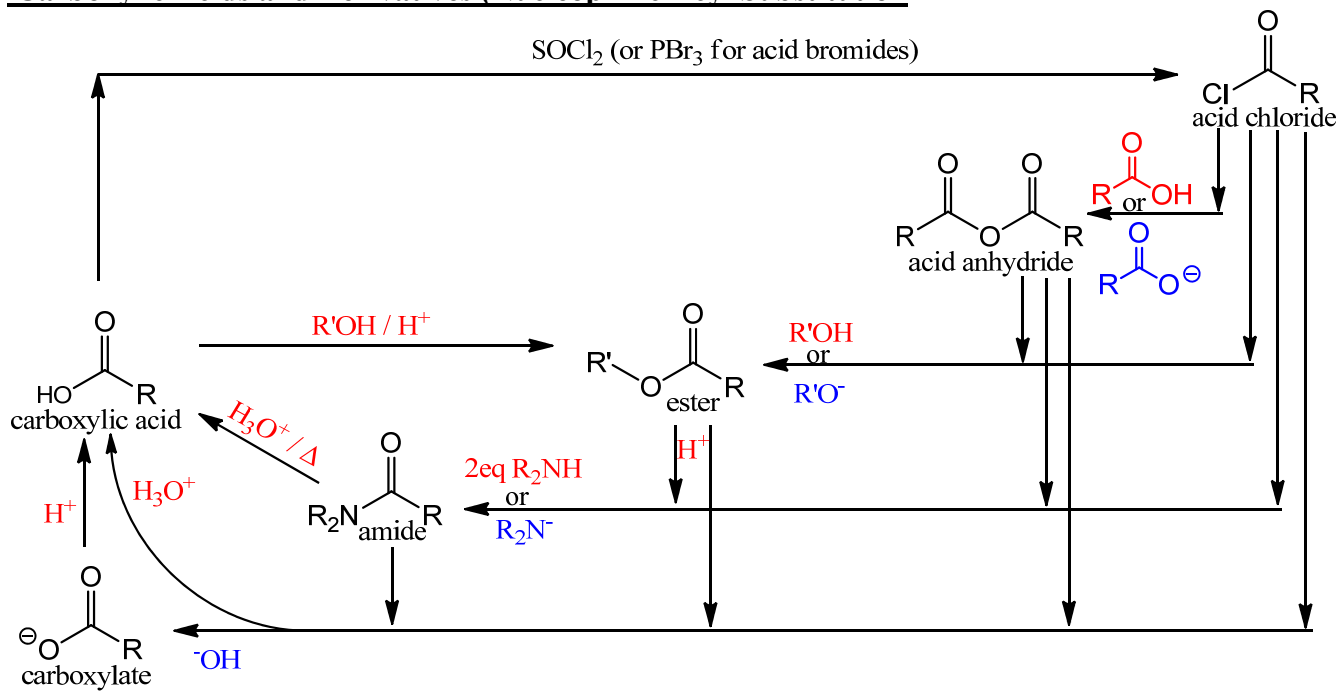
Epoxide Rxns

Base-Catalyzed Ring Opening of an Epoxide (Attacks less-substituted side)	
Acid-Catalyzed Ring Opening of an Epoxide (Attacks more-substituted side)	

Hydride Reduction Rxns

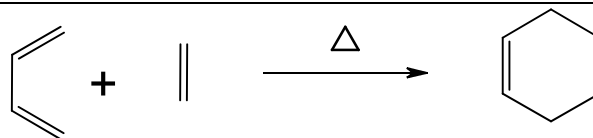
Reduction of a ketone to a 2° alcohol	$\xrightarrow[\text{EtOH}]{\text{NaBH}_4}$ $\xrightarrow[2. \text{H}_3\text{O}^+]{1. \text{LiAlH}_4}$
Reduction of an aldehyde to a 1° alcohol	$\xrightarrow[\text{EtOH}]{\text{NaBH}_4}$ $\xrightarrow[2. \text{H}_3\text{O}^+]{1. \text{LiAlH}_4}$
Reduction of an acid chloride to a 1° alcohol	$\xrightarrow[\text{EtOH}]{\text{NaBH}_4}$ $\xrightarrow[2. \text{H}_3\text{O}^+]{1. \text{LiAlH}_4}$
Reduction of an ester to two alcohols	$\xrightarrow[2. \text{H}_3\text{O}^+]{1. \text{LiAlH}_4}$ +
Reduction of a carboxylic acid to a 1° alcohol	$\xrightarrow[2. \text{H}_3\text{O}^+]{1. \text{LiAlH}_4}$
Reduction of an amide to an amine	$\xrightarrow[2. \text{H}_3\text{O}^+]{1. \text{LiAlH}_4}$
Reduction of an ester to an aldehyde using DIBALH (also called DIBALH) DIBALH is diisobutylaluminum hydride (shown below)	$\xrightarrow[2. \text{H}_2\text{O}]{1. \text{DIBALH } -78^\circ\text{C}}$
Reduction of an acid chloride to an aldehyde using tri- <i>t</i> -butoxyaluminum hydride	$\xrightarrow[-78^\circ\text{C}]{\text{LiAl}[\text{OC}(\text{CH}_3)_3]_3\text{H}}$
Hoffman Rearrangement Converts an amide to an amine with the loss of a carbon (note the difference with reduction of an amide with LiAlH_4 where there is no loss of carbon)	$\xrightarrow[\text{OH}^-]{\text{Br}_2}$

Carboxylic Acids and Derivatives (Nucleophilic Acyl Substitution)



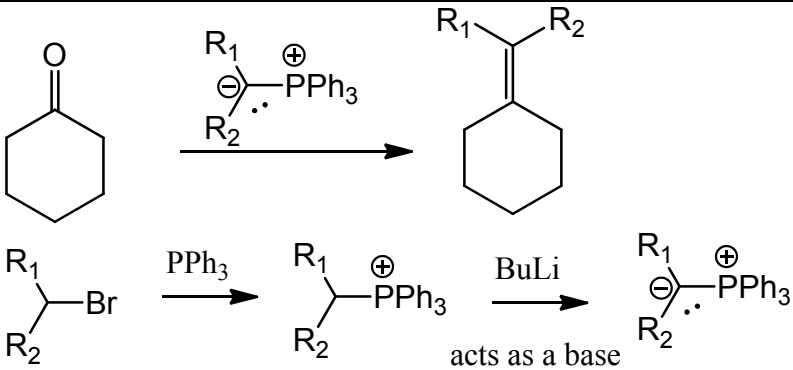
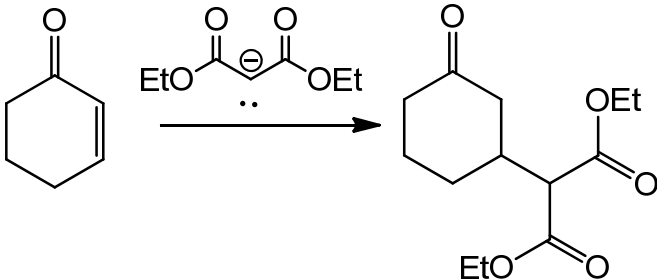
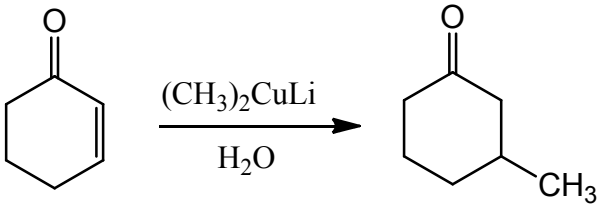
Diels-Alder Rxns

Basic Diels-Alder Rxn (a 4+2 cycloaddition rxn)



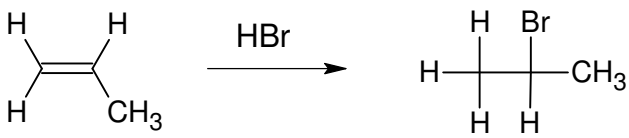
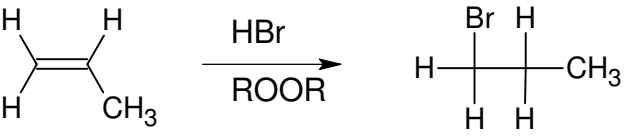
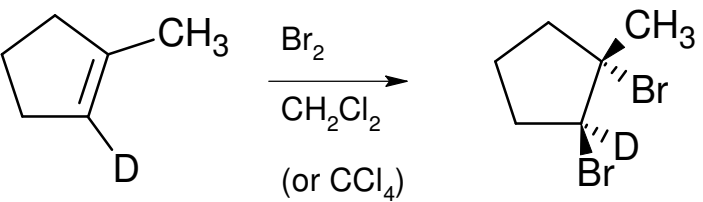
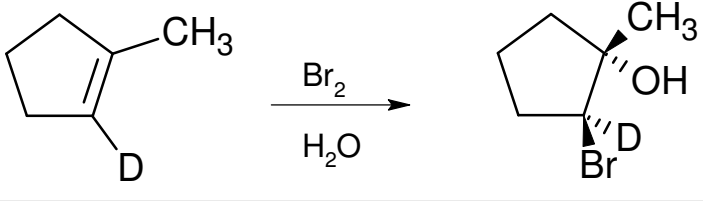
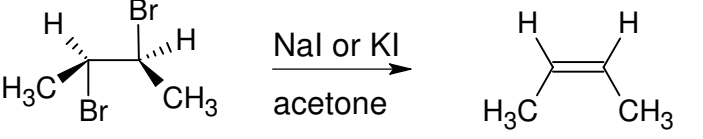
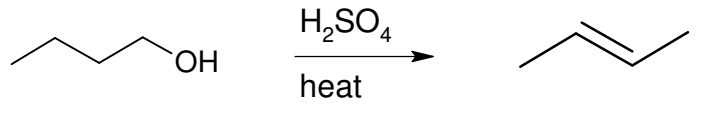
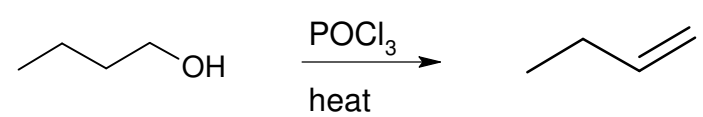
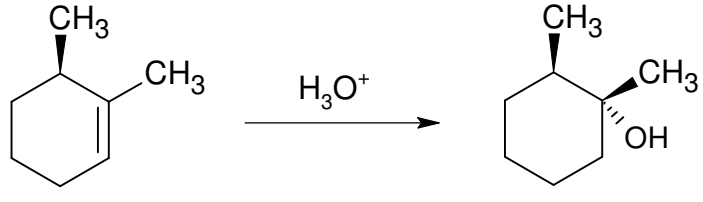
Nucleophilic Addition to Ketones and Aldehydes

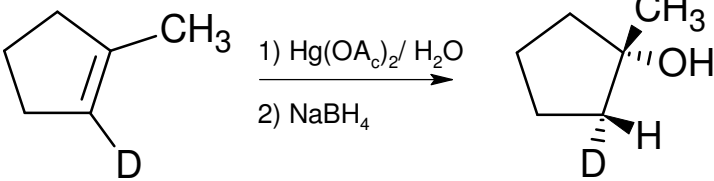
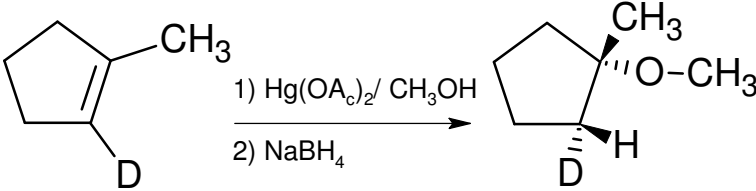
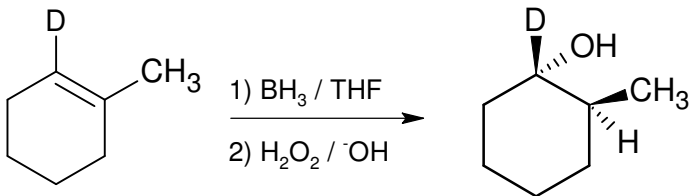
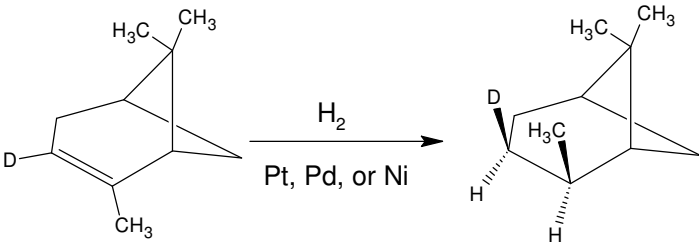
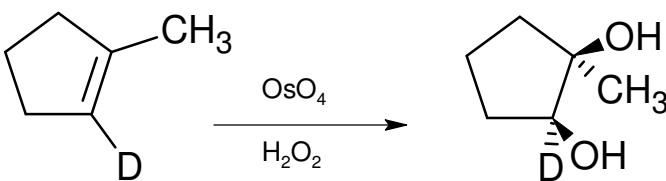
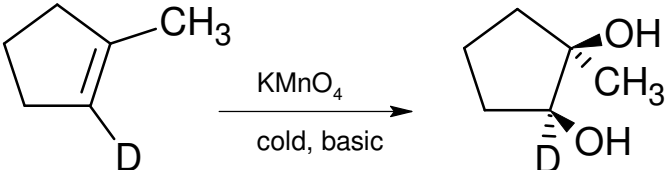
Addition of water to form a hydrate	
Addition of an alcohol under basic conditions to form a hemi-ketal	
Addition of 1eq of an alcohol in acid to form a hemi-ketal and then a 2 nd eq to form a ketal	
Addition of ethylene glycol to form a cyclic ketal which functions as a protecting group for ketones and aldehydes H_3O^+ is used to de-protect	
Addition of a 1° amine to form an imine (can be reversed with H_3O^+)	
Addition of a 2° amine to form an enamine Forms on less substituted side if there's a difference (can be reversed with H_3O^+)	

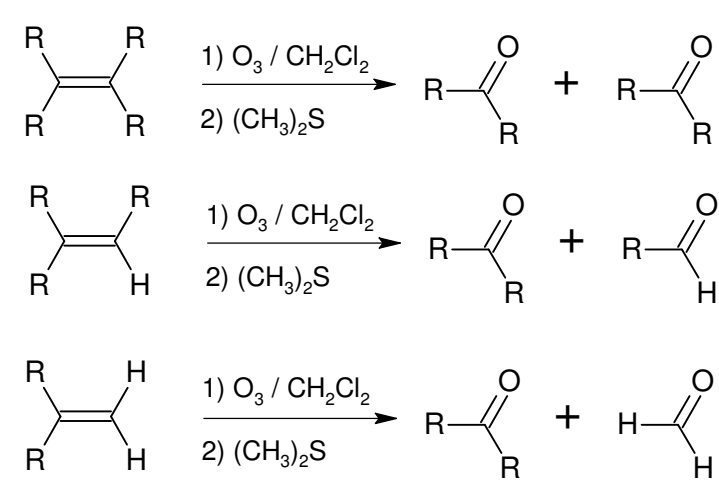
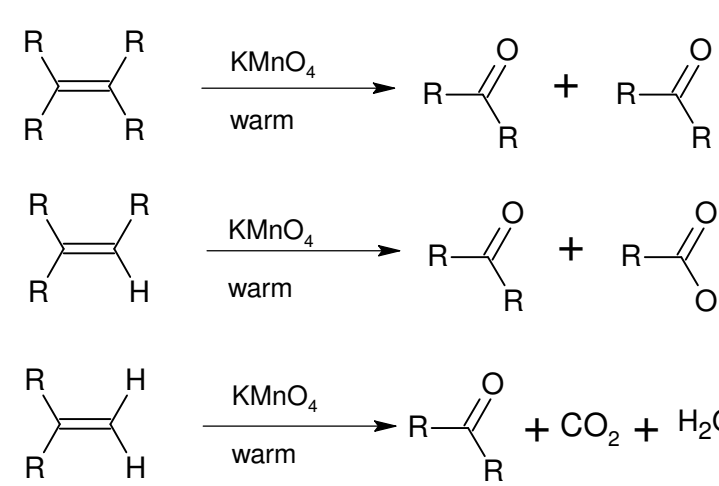
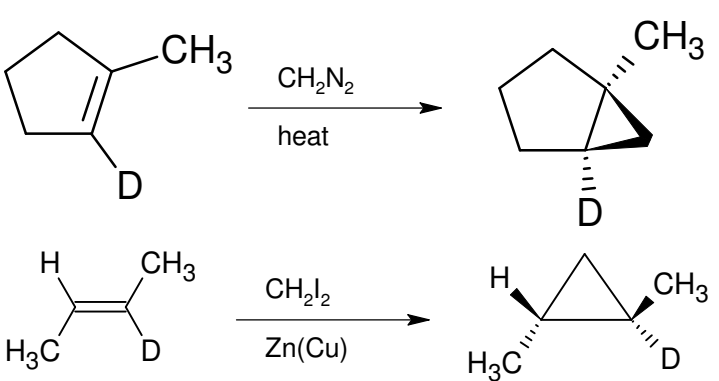
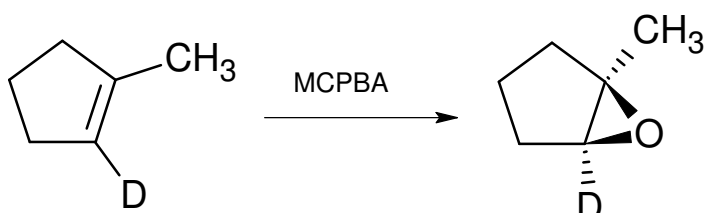
Wittig Rxn Addition of a phosphylide to form an alkene	
Michael Addition (also called β-addition or conjugate addition)	
Michael Addition with a lithium dialkylcuprate	

Alpha Addition Rxns

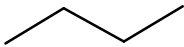
Self Aldol Condensation	$2 \text{ CH}_3\text{COCH}_3 \xrightarrow{\text{OH}^-} \text{CH}_3\text{CH(OH)CH}_2\text{CH}_3 \xrightarrow{\Delta} \text{CH}_3\text{CH=CHCH}_3$
Mixed Aldol Condensation	$\text{C}_6\text{H}_5\text{CHO} + \text{CH}_3\text{COCH}_3 \xrightarrow{\text{OH}^-} \text{C}_6\text{H}_5\text{CH(OH)CH}_2\text{COCH}_3 \xrightarrow{\Delta} \text{C}_6\text{H}_5\text{CH=CHCOCH}_3$
Self Claisen Condensation	$2 \text{ CH}_3\text{CH}_2\text{CO}_2\text{Et} \xrightarrow[2. \text{H}_2\text{O}]{1. \text{NaOEt}} \text{CH}_3\text{CH}_2\text{COCH(CH}_3\text{)CO}_2\text{Et}$
Mixed Claisen Condensation	$\text{Cyclohexanone} \xrightarrow[3. \text{H}_2\text{O}]{1. \text{LDA}, 2. \text{CH}_3\text{CH}_2\text{CO}_2\text{Et}} \text{Cyclohexanone-CH}_2\text{CH}_2\text{COCH}_3$
Malonic Ester Synthesis	$\text{EtO}_2\text{CCH}_2\text{CO}_2\text{Et} \xrightarrow[4. \text{C}_6\text{H}_5\text{CH}_2\text{Br}]{1. \text{NaOEt}, 2. \text{CH}_3\text{CH}_2\text{Br}, 3. \text{NaOEt}} \text{EtO}_2\text{CCH(C}_6\text{H}_5\text{)CH}_2\text{CO}_2\text{Et} \xrightarrow[\Delta]{\text{H}_3\text{O}^+} \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CO}_2\text{H} + \text{CO}_2$
Acetoacetic Ester Synthesis	$\text{EtO}_2\text{CCH}_2\text{COCH}_3 \xrightarrow[4. \text{C}_6\text{H}_5\text{CH}_2\text{Br}]{1. \text{NaOEt}, 2. \text{CH}_3\text{CH}_2\text{Br}, 3. \text{NaOEt}} \text{EtO}_2\text{CCH(C}_6\text{H}_5\text{)CH}_2\text{COCH}_3 \xrightarrow[\Delta]{\text{H}_3\text{O}^+} \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{COCH}_3 + \text{CO}_2$

Task	Reaction	Notes
Addition of HX (Mark)		*Adds a halide to more substituted carbon.
Addition of HX (Anti-Mark)		*Adds a halide to least substituted carbon.
Add two Br's anti to alkene		*Anti and co planar
Adding a Br and OH (Mark w/ Br as H and anti-planar)		*Anti and co planar
Forming alkene from vicinal dihalide		*Wedges with wedges and dashes with dashes *E2 Like!
Dehydration to alkene		*E1 like and it cannot give terminal alkene
		*SPECIAL REACTION: dehydrates to form terminal alkene.
Addition of OH (direct and mark)		*CANNOT CONTROL STEREOCHEM! *Low yield! *C+ formation!

Task	Reaction	Notes
Oxymercuration/ demercuration (Add OH from alkene mark and antiplanar)		*Complex mechanism *Mark and antiplanar
SPECIAL: Adds alcohol instead to form ethers!		*Complex mechanism *Mark and antiplanar *WILL BE SEEING THIS MORE IN ORGO II
Hydroboration (Add OH anti-mark and syn planar)		*Anti-mark *Notice Peroxide
Catalytic Hydrogenation (Alkenes -> Alkane, Syn Addition of H)		*Steric factors must be payed attention to *Can use D ₂ instead
Formation of Vicinal Diols (Syn)		*expensive *toxic *great yield
		*cheaper *safer *poor yield

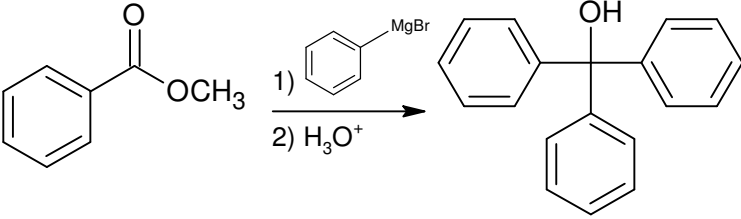
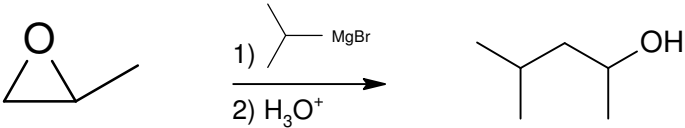
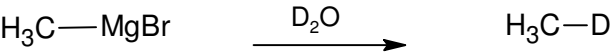
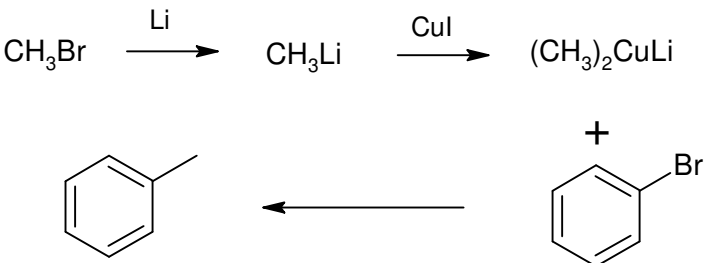
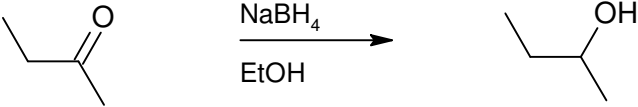
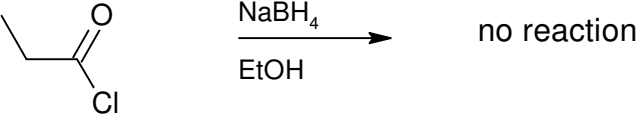
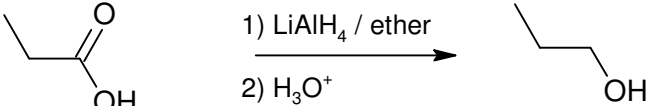
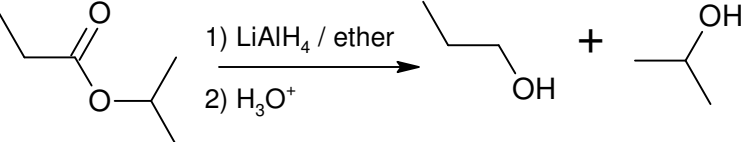
Task	Reaction	Notes
Ozonolysis (double bond cleavage)		*Can use Zn/acetic acid instead of $(\text{CH}_3)_2\text{S}$ *Can isolate the formaldehyde.
Warm KMnO_4 cleavage		*further oxidizes to form carboxylic acids *cannot isolate the formaldehyde
Carbene / Carbenoid addition (formation of cyclopropane)		*syn *stereochem is preserved *Second reaction uses the Simmons-Smith reagent
Formation of epoxides from alkenes		*useful for synthesis (ESPECIALLY IN ORGO II)

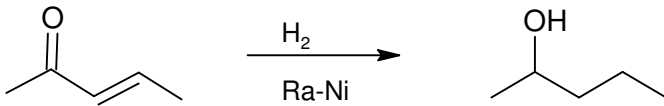
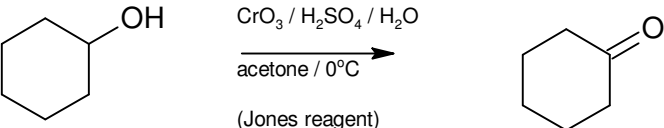
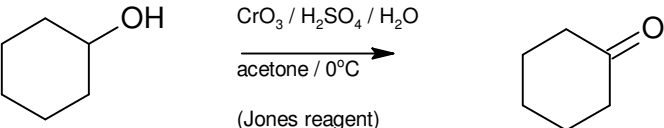
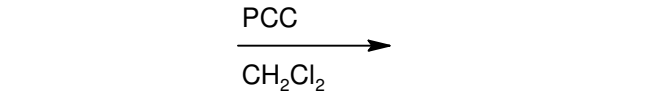
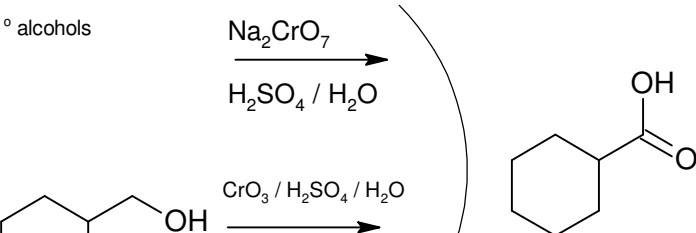
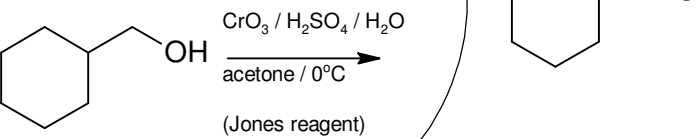
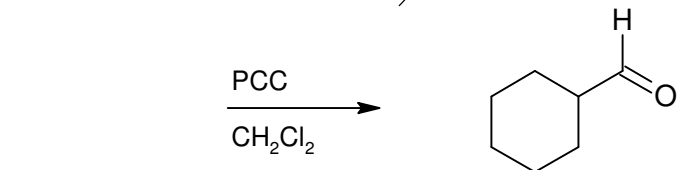
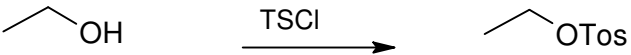
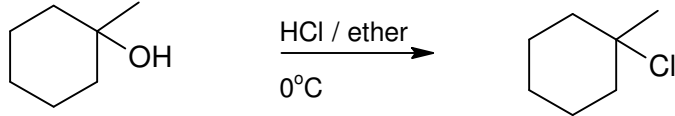
Task	Reaction	Notes
Opening of Epoxides NOTE: Can use RO^- to form ethers. You will see this in Orgo II.		*acidic conditions opens from more substituted side. *Basic are like $\text{S}_{\text{N}}2$ (least substituted side) *Please look up mechanism.
Formation of Dibromocarbenes and Dichlorocarbenes		*please look up the mechanism so you can see how the carbene is formed
Formation of the acetylide anion	$\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{H} \xrightarrow{\text{NaNH}_2} \text{H}_3\text{C}-\text{C}\equiv\text{C}^-$	*forms the nucleophile that is handy when connecting carbons!
Uses of the acetylide anion	with methyl or 1° halides $\text{H}_3\text{C}-\text{C}\equiv\text{C}^- \xrightarrow{\text{CH}_3\text{Br}} \text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{CH}_3$	*$\text{S}_{\text{N}}2$ because of the exception we learned from before!!!!
	with 2° or 3° halides $\text{H}_3\text{C}-\text{C}\equiv\text{C}^- \xrightarrow{\text{H}_3\text{C}-\overset{\text{Br}}{\underset{ }{\text{CH}}}-\text{CH}_3} \text{H}_3\text{C}-\text{CH}=\text{CH}_2$	*E2 remember from last test!!!
	with carbonyl groups (ketones, aldehydes, and formaldehydes)	*acetylide anion attacks partially positive carbon *DO NOT FORGET then H_3O^+

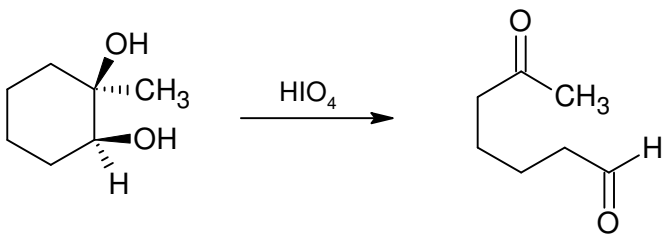
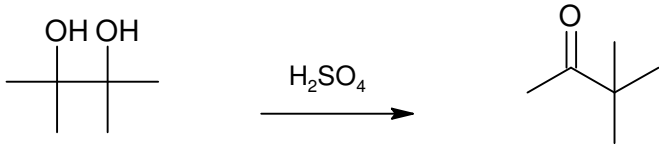
Task	Reaction	Notes
Synthesis of Alkynes	$\begin{array}{c} \text{Br} \quad \text{Br} \\ \quad \\ \text{H}_3\text{C}-\text{CH}-\text{CH}-\text{CH}_3 \end{array}$ $\begin{array}{c} \text{Br} \quad \text{Br} \\ \quad \\ \text{CH}_2-\text{CH}-\text{CH}_2-\text{CH}_3 \end{array}$ $\begin{array}{c} \text{Br} \\ \\ \text{H}_3\text{C}-\text{C}-\text{CH}_2-\text{CH}_3 \\ \\ \text{Br} \end{array}$ $\begin{array}{c} \text{Br} \\ \\ \text{HC}-\text{CH}_2-\text{CH}_2-\text{CH}_3 \\ \\ \text{Br} \end{array}$ $\xrightarrow[2) \text{H}_3\text{O}^+]{1) \text{NaNH}_2 / 100^\circ\text{C}}$ $\text{HC}\equiv\text{C}\cdot\text{CH}_2\cdot\text{CH}_3$ $\begin{array}{c} \text{Br} \\ \\ \text{H}_3\text{C}-\text{C}-\text{CH}_2-\text{CH}_3 \\ \\ \text{Br} \end{array}$ $\begin{array}{c} \text{Br} \\ \\ \text{HC}-\text{CH}_2-\text{CH}_2-\text{CH}_3 \\ \\ \text{Br} \end{array}$ $\xrightarrow[200^\circ\text{C}]{\text{KOH}}$ $\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{CH}_3$	*Need either geminal or vicinal dihalides *Look up mechanism *NaNH₂ gives terminal *KOH gives internal
Halogenation of alkynes	Br₂ and alkyne $\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{H} \xrightarrow[(1 \text{ eq})]{\text{Br}_2}$ $\begin{array}{c} \text{H}_3\text{C} \quad \text{H} \\ \diagdown \quad \diagup \\ \text{C}=\text{C} \\ \diagup \quad \diagdown \\ \text{Br} \quad \text{Br} \end{array}$ + $\begin{array}{c} \text{Br} \quad \text{H} \\ \diagdown \quad \diagup \\ \text{C}=\text{C} \\ \diagup \quad \diagdown \\ \text{H}_3\text{C} \quad \text{Br} \end{array}$	*Stereochem cannot be controlled
	HBr and alkyne $\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{H} \xrightarrow[(1 \text{ eq})]{\text{HBr}}$ $\begin{array}{c} \text{Br} \quad \text{H} \\ \diagdown \quad \diagup \\ \text{C}=\text{C} \\ \diagup \quad \diagdown \\ \text{H}_3\text{C} \quad \text{H} \end{array}$ + $\begin{array}{c} \text{Br} \\ \\ \text{---} \text{C} \text{---} \\ \\ \text{Br} \end{array}$ $\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{H} \xrightarrow[(2 \text{ eq})]{\text{HBr}}$	*Mark *syn addition
	HBr and alkyne $\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{H} \xrightarrow[\text{ROOR}]{\text{HBr}}$ $\begin{array}{c} \text{H} \quad \text{Br} \\ \diagdown \quad \diagup \\ \text{C}=\text{C} \\ \diagup \quad \diagdown \\ \text{H}_3\text{C} \quad \text{H} \end{array}$	*Anti mark *syn addition
Catalytic reduction with reactive catalyst	$\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{CH}_3 \xrightarrow[\text{Pt, Pd, or Ni}]{\text{H}_2}$ 	*Takes it all the way back to alkane *generally bad yield

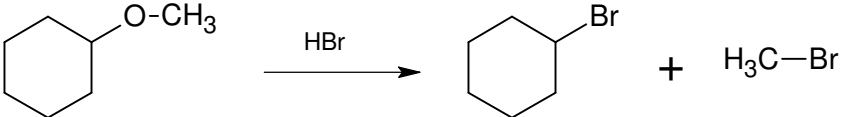
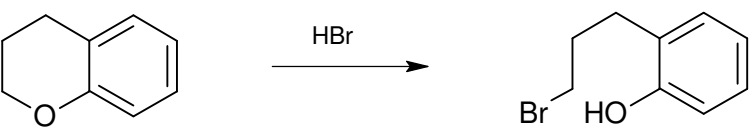
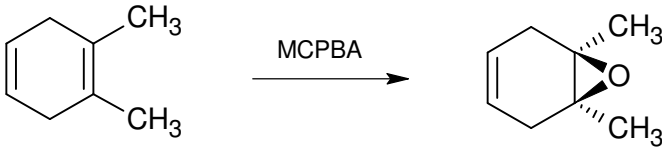
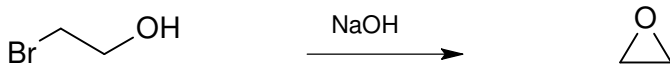
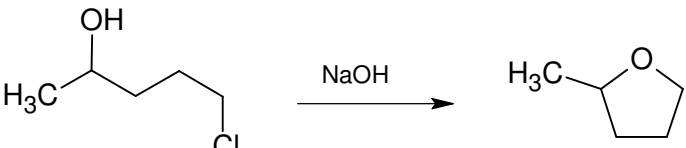
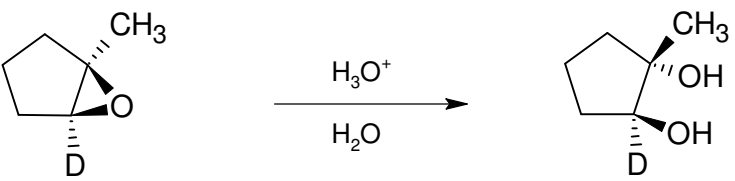
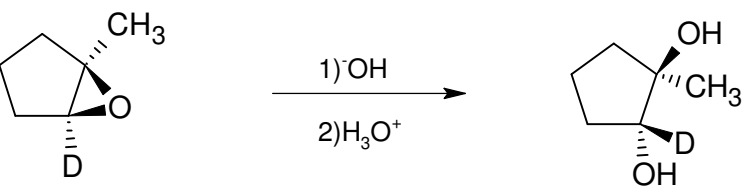
Task	Reaction	Notes
Alkyne to Alkene: TRIPLE to DOUBLE	Lindlar's catalyst $\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{CH}_3 \xrightarrow[\text{quinoline}]{\text{H}_2 / \text{Pd}(\text{BaSO}_4)} \begin{array}{c} \text{H} \quad \text{H} \\ \diagdown \quad \diagup \\ \text{C}=\text{C} \\ \diagup \quad \diagdown \\ \text{H}_3\text{C} \quad \text{CH}_3 \end{array}$	*isolates an alkene with a SYN addition of H
	Dissolving metal $\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{CH}_3 \xrightarrow{\text{NaNH}_3} \begin{array}{c} \text{H} \quad \text{CH}_3 \\ \diagdown \quad \diagup \\ \text{C}=\text{C} \\ \diagup \quad \diagdown \\ \text{H}_3\text{C} \quad \text{H} \end{array}$	*isolates an alkene with an ANTI addition of H
Addition of H-OH to alkynes	Mercuric Ion $\text{H}_3\text{C}-\text{CH}_2-\text{C}\equiv\text{C}-\text{H} \xrightarrow[\text{H}_2\text{SO}_4]{\text{HgSO}_4 / \text{H}_2\text{O}} \begin{array}{c} \text{O} \\ \parallel \\ \text{H}_3\text{C}-\text{CH}_2-\text{C}-\text{CH}_3 \end{array}$ $\text{H}_3\text{C}-\text{CH}_2-\text{C}\equiv\text{C}-\text{CH}_3 \xrightarrow[\text{H}_2\text{SO}_4]{\text{HgSO}_4 / \text{H}_2\text{O}} \begin{array}{c} \text{O} \\ \parallel \\ \text{H}_3\text{C}-\text{CH}_2-\text{C}-\text{CH}_2-\text{CH}_3 \end{array} + \begin{array}{c} \text{O} \\ \parallel \\ \text{H}_3\text{C}-\text{CH}_2-\text{CH}_2-\text{C}-\text{CH}_3 \end{array}$	*Mark addition *If not terminal, you will get a mixture. *Formation of ketone
	Hydroboration $\text{H}_3\text{C}-\text{CH}_2-\text{C}\equiv\text{C}-\text{H} \xrightarrow[2) \text{H}_2\text{O}_2 / ^-\text{OH}]{1) \text{Si}_2\text{BH}} \begin{array}{c} \text{O} \\ \parallel \\ \text{H}_3\text{C}-\text{CH}_2-\text{CH}_2-\text{C}-\text{H} \end{array}$	*Antimark addition *will get a mixture if not terminal *Formation of aldehyde
Oxidation of alkynes (mild conditions)	$\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{CH}_3 \xrightarrow[\text{neutral / cold}]{\text{KMnO}_4 / \text{H}_2\text{O}} \begin{array}{c} \text{O} \quad \text{O} \\ \parallel \quad \parallel \\ \text{CH}_3-\text{C}-\text{C}-\text{CH}_3 \end{array}$ $\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{H} \xrightarrow[\text{neutral / cold}]{\text{KMnO}_4 / \text{H}_2\text{O}} \begin{array}{c} \text{O} \quad \text{O} \\ \parallel \quad \parallel \\ \text{CH}_3-\text{C}-\text{C}-\text{OH} \end{array}$	*Forms vicinal carbonyls *further oxidizes terminal alkynes to form carboxylic acid.

Task	Reaction	Notes
Cleavage of Alkynes:	Oxidation of alkyne (strong) $\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{CDH}_2 \xrightarrow[2) ^-\text{OH} / \text{heat}]{1) \text{KMnO}_4 / \text{H}_2\text{O}} \begin{array}{c} \text{H}_3\text{C}-\text{C}(=\text{O})\text{OH} \\ + \\ \text{HO}-\text{C}(=\text{O})\text{CDH}_2 \end{array}$ $\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{H} \xrightarrow[2) ^-\text{OH} / \text{heat}]{1) \text{KMnO}_4 / \text{H}_2\text{O}} \text{H}_3\text{C}-\text{C}(=\text{O})\text{OH} + \text{H}_2\text{O} + \text{CO}_2$	*Forms H ₂ O and CO ₂ if terminal.
	Ozonolysis $\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{CDH}_2 \xrightarrow[2) \text{H}_2\text{O}]{1) \text{O}_3} \text{H}_3\text{C}-\text{C}(=\text{O})\text{OH} + \text{HO}-\text{C}(=\text{O})\text{CDH}_2$ $\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{H} \xrightarrow[2) \text{H}_2\text{O}]{1) \text{O}_3} \text{H}_3\text{C}-\text{C}(=\text{O})\text{OH} + \text{H}_2\text{O} + \text{CO}_2$	*Same products as previous
The Grignard Reagent	$\text{H}_3\text{C}-\text{CH}=\text{C} \begin{array}{l} \text{H} \\ \text{Br} \end{array} \xrightarrow[\text{ether}]{\text{Mg}} \text{H}_3\text{C}-\text{CH}=\text{C} \begin{array}{l} \text{H} \\ \text{MgBr} \end{array}$	*Forms from 1°, 2°, 3°, allyl, vinyl, and aryl carbons.
The Organolithium Reagent	$\text{H}_3\text{C}-\text{CH}_2-\text{Br} \xrightarrow[\text{pentane or hexane}]{\text{Li}} \text{H}_3\text{C}-\text{CH}_2-\text{Li}$	*This reagent acts like grignard but is stronger.
Formation of alcohols from Grignard	1° alcohols. (Grignard and formaldehyde) $\text{CH}_3\text{CH}_2\text{CH}_2\text{MgBr} \xrightarrow[2) \text{H}_3\text{O}^+]{1) \text{H}-\text{C}(=\text{O})\text{H}} \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$	*Know this mechanism! *Carbon attachment
	2° alcohols. (Grignard and aldehyde) $\text{CH}_3\text{CH}_2\text{CH}_2\text{MgBr} \xrightarrow[2) \text{H}_3\text{O}^+]{1) \text{H}-\text{C}(=\text{O})\text{CH}_2\text{CH}_3} \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{CH}_3$	*Know this mechanism! *Carbon attachment
	3° alcohols. (Grignard and ketone) $\text{CH}_3\text{CH}_2\text{CH}_2\text{MgBr} \xrightarrow[2) \text{H}_3\text{O}^+]{1) \text{CH}_3\text{C}(=\text{O})\text{CH}_2\text{CH}_3} \text{CH}_3\text{CH}_2\text{CH}_2\text{C}(\text{OH})(\text{CH}_3)\text{CH}_2\text{CH}_3$	*Know this mechanism! *Carbon attachment

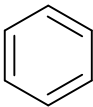
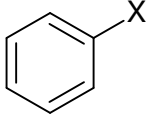
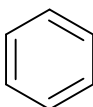
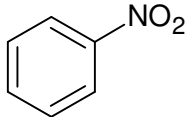
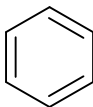
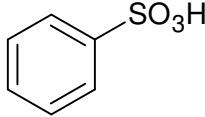
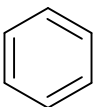
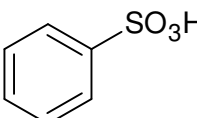
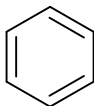
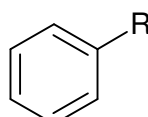
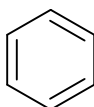
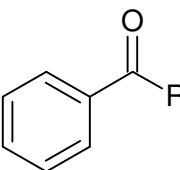
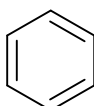
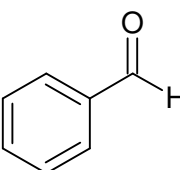
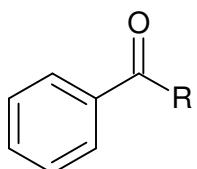
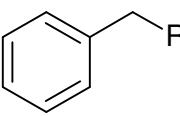
Task	Reaction	Notes
Grignard and esters or acid halides		*Reaction goes until completion *Know this mechanism!
Grignard and Epoxides (opening of epoxides)		*SN2 like (attacks least substituted side) *Know this mechanism!
Attaching Deuterium to carbons		*This is just good to know.
Corey-House Reaction		*not well understood (do not need to know mechanism) *another way to attach carbons.
Hydride reduction of carbonyls	mild conditions (NaBH ₄ as reagent)  	*reduces only aldehydes and ketones . *use alcohols as a solvent.
	strong conditions (LiAlH ₄ as reagent)  	*reduces aldehydes , ketones , esters , acid halides , carboxylic acids . *Use ethers solvents *Two step process

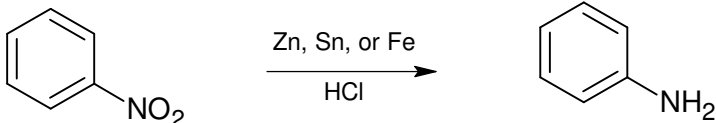
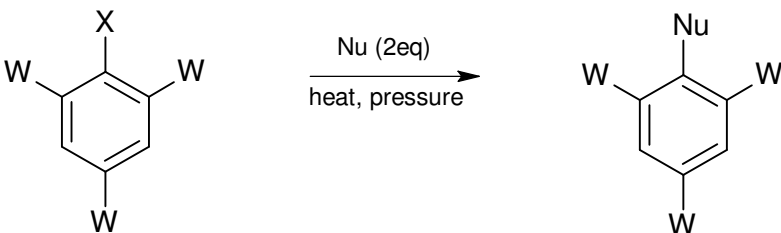
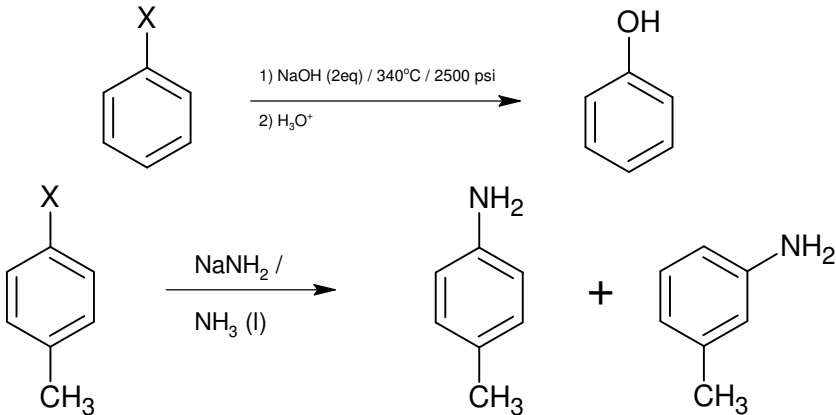
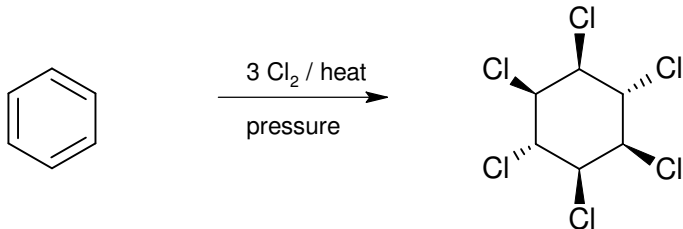
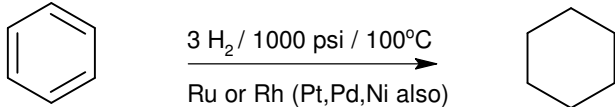
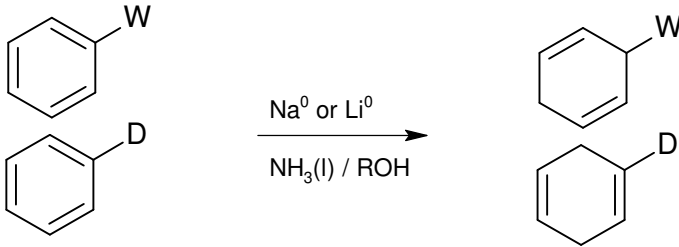
Task	Reaction	Notes
Raney Nickel	 <chem>CC(=O)C=CC + H2 >> CC(O)CCC</chem>	*Reduces both carbonyl and alkene.
Oxidation of alcohols	2° alcohols  <chem>C1CCCCC1O + Na2CrO7 + H2SO4 + H2O >> C1CCCCC1=O</chem>  <chem>C1CCCCC1O + CrO3 + H2SO4 + H2O >> C1CCCCC1=O</chem> (Jones reagent)  <chem>C1CCCCC1O + PCC >> C1CCCCC1=O</chem> CH₂Cl₂	*any [ox] can be used *KMnO₄ and NO₃ can be used but they are harsh.
	1° alcohols  <chem>C1CCCCC1CO + Na2CrO7 + H2SO4 + H2O >> C1CCCCC1C(=O)O</chem>  <chem>C1CCCCC1CO + CrO3 + H2SO4 + H2O >> C1CCCCC1C(=O)O</chem> (Jones reagent)  <chem>C1CCCCC1CO + PCC >> C1CCCCC1C=O</chem> CH₂Cl₂	*PCC is the only one that can isolate the formaldehyde.
Formation of the Tosylate Ester	 <chem>CCO + TsCl >> CCOS(=O)(=O)c1ccc(C)cc1</chem>	* RETENTION from where alcohol was originally (SN2 purposes)
Formation of alkyl halide from 3° alcohols	 <chem>CC1(O)CCCCC1 + HCl >> CC1(Cl)CCCCC1</chem> ether, 0°C	

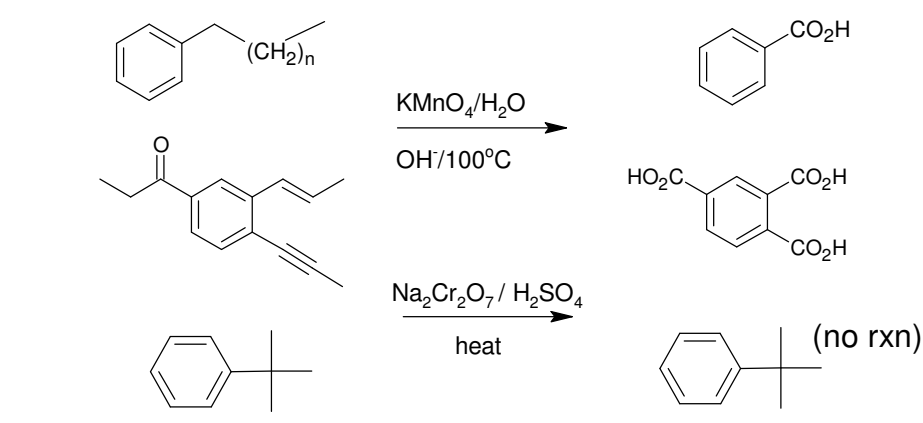
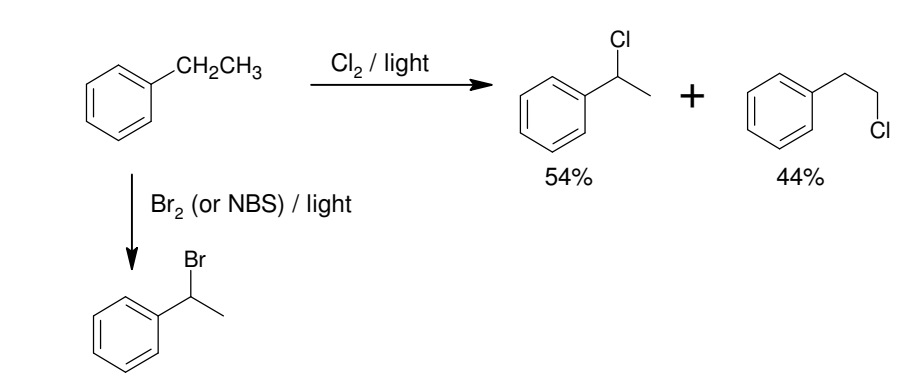
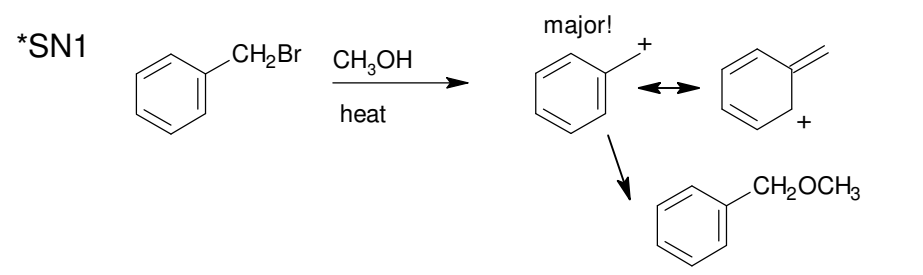
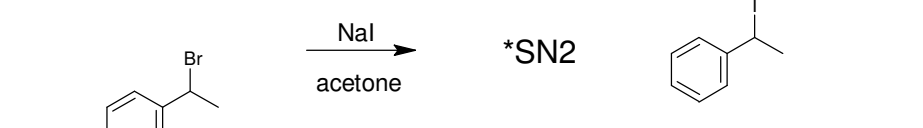
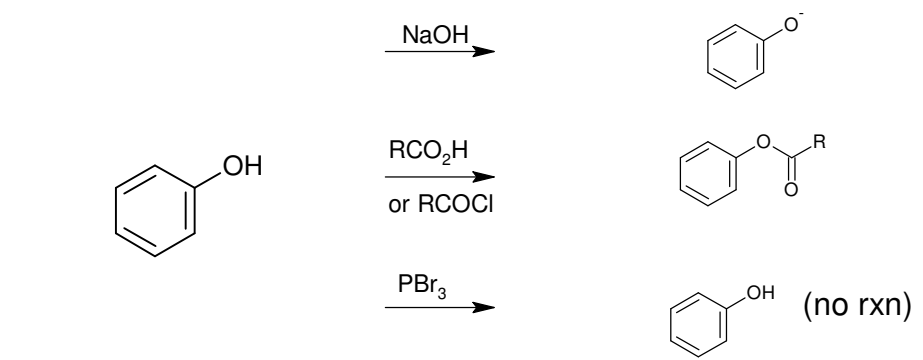
Task	Reaction	Notes
Formation of 1°/2° alkyl halides from 1°/2° alcohols	$\begin{array}{ccc} & \xrightarrow[\text{CH}_2\text{Cl}_2]{\text{PBr}_3} & \text{Br}-\text{CH}_3 \\ \text{H}_3\text{C}-\text{OH} & & \\ & \xrightarrow[\text{CH}_2\text{Cl}_2]{\text{PCl}_3} & \text{Cl}-\text{CH}_3 \\ & \xrightarrow[\text{CH}_2\text{Cl}_2]{\text{P} / \text{I}_2} & \text{I}-\text{CH}_3 \end{array}$	*Basically an SN2 reaction. (Inversion from original alcohol) *Can also use SOCl₂ for Cl, but it undergoes a special mechanism!
Unique cleavage with HIO ₄		*Vicinal diols must be syn
Formation of Alkoxide Anion	$\begin{array}{ccc} \text{1° or 2° alcohols} & \xrightarrow{\text{Na}^\circ} & \text{alkoxide}^- \\ \text{2° or 3° alcohols} & \xrightarrow{\text{K}^\circ} & \text{alkoxide}^- \end{array}$	
Williamson ether synthesis	$\text{H}_3\text{C}-\text{Br} \xrightarrow{\text{alkoxide}^-} \text{ether}$	*Basically that SN2 exception we learned in test 2
Ethers from intermolecular dehydration	$2 \times \text{CH}_3\text{CH}_2-\text{OH} \xrightarrow[140^\circ\text{C}]{\text{H}_2\text{SO}_4} \text{CH}_3\text{CH}_2-\text{O}-\text{CH}_2\text{CH}_3$	* Must be identical alcohols or else you will get a mixture!!!
Pinacol - Pinacolone Rearrangement		*Need vicinal diols *Know mechanism (methyl shift!)
Fischer Esterification	$\text{H}_3\text{C}-\text{CH}_2-\text{OH} + \text{HO}-\text{C}(=\text{O})-\text{CH}_3 \xrightleftharpoons{\text{H}^+} \text{H}_3\text{C}-\text{CH}_2-\text{O}-\text{C}(=\text{O})-\text{CH}_3$	* CAN USE ACID HALIDE instead of carboxylic acid!!!

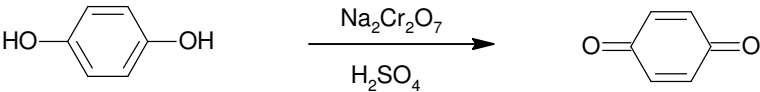
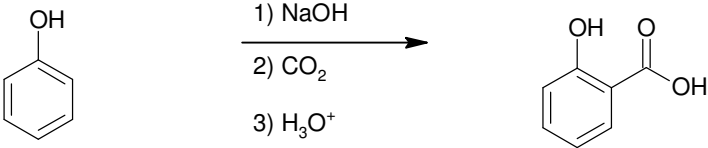
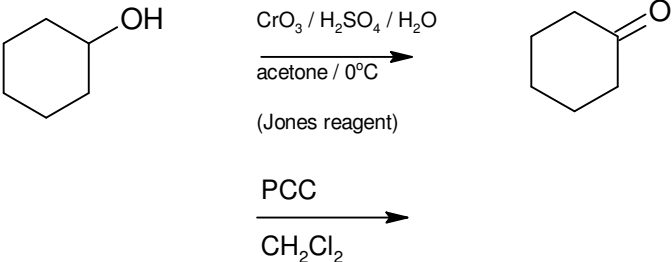
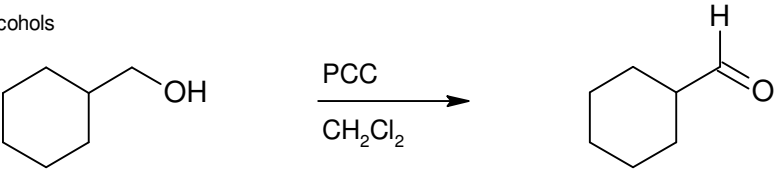
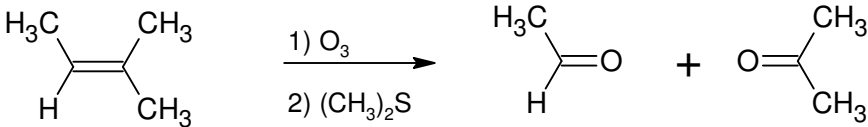
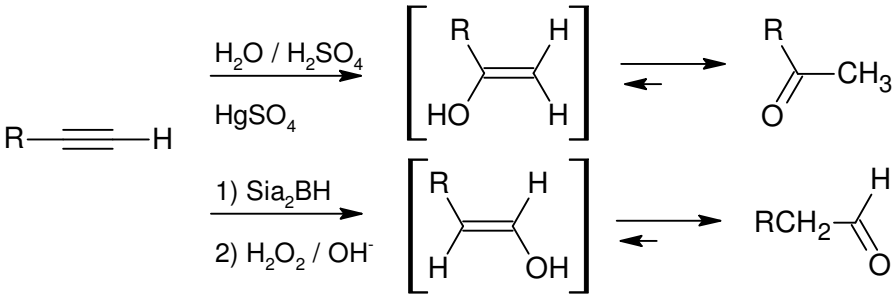
Task	Reaction	Notes
Symmetrical ethers through dehydration of 1° alcohols	$ \begin{array}{ccc} \text{R-OH} & \xrightarrow[140^{\circ}\text{C}]{\text{H}_2\text{SO}_4} & \text{R-O-R} \\ \text{x 2} & & \end{array} $	*cannot be unsymmetrical (you will get mixtures!)
Cleavage of ethers by strong acids	 	*can also use HI, HCl, etc *vinyl or aryl do not get cleaved (NO SN2 ON SP2)
Autoxidation	$ \begin{array}{ccc} \text{R-O}-\text{C}(\text{R})_2\text{H} & \xrightarrow[\text{slow}]{\text{O}_2 (\text{xs})} & \text{R-O}-\text{C}(\text{R})_2\text{O-OH} + \text{R-O-O}-\text{C}(\text{R})_2\text{H} \end{array} $	*basically forms peroxides.... which EXPLODE!
MCPBA		*epoxide will form along the more substituted alkene
Intramolecular Williamson	 	*SN2 like *forms O⁻ that attacks halogenated C
Opening of Epoxides		*activate the O first *weak Nu are good *more substituted side attacked
		*SN2 like (least subs) so strong Nu and base *Grignard reagent and acetylide anion can work too

Task	Reaction	Notes
Free Radical Halogenation Expanded	transition state	*Low T: more stable TS *High T: more stable compound
Conjugated Systems	*in this example we will examine the case of HBr transition state	*Low T: more stable TS *High T: more stable compound *NOTE: If more than one conjugated system possibly exists, examine the transition states of each one and do the reactions with the more stable transition states!
Diels-Alder Reaction	D = donating group W = withdraw group	*1,2 or 1,4 adduct *know endo rule *Diene and Dienophile *Know Stereochem *PRACTICE THIS!!!

NOTE: FROM HERE, YOU HAVE TO KNOW YOUR META, ORTHO, AND PARA DIRECTORS		
Task	Reaction	Notes
Halogenation of Benzene	 $\xrightarrow[\text{(I}_2 / \text{CuCl}_2\text{)}]{\text{X}_2, \text{FeX}_3 \text{ or}}$ 	*X = Cl or Br
Nitration of Benzene	 $\xrightarrow[\text{H}_2\text{SO}_4 \text{ heat}]{\text{HNO}_3}$ 	*H ₂ SO ₄ acts as a catalyst
Sulfonation (fuming sulfuric)	 $\xrightarrow[\text{heat}]{\text{SO}_3 / \text{H}_2\text{SO}_4}$   + H ₂ SO ₄ $\rightleftharpoons$  + H ₂ O	*REVERSIBLE DUE TO ENTROPY
Friedel-Crafts Alkylation	 $\xrightarrow[\text{AlCl}_3]{\text{RCl}}$ 	*watch rearrangement! *no strong deactivators (no strong W grps) *no amino groups *watch for polyalkylation
Friedel-Crafts Acetylation	 $\xrightarrow[\text{AlCl}_3]{\text{Cl}-\text{C}(=\text{O})-\text{R}}$ 	*no strong deactivators (no strong W grps) *no amino groups
Gatterman-Koch Formation (forming benzaldehyde)	 $\xrightarrow[\text{AlCl}_3 / \text{CuCl}]{\text{CO} / \text{HCl}}$ 	*no strong deactivators (no strong W grps) *no amino groups
Clemmensen Reduction	 $\xrightarrow[\text{HCl}]{\text{Zn(Hg)}}$ 	*avoid using this reactant in the presence of alkenes, alkynes, alcohols and amines.

Task	Reaction	Notes
Reduction of Nitro group into Amino Group		*Do not confuse with Clemmenson Red.
Nucleophilic Aromatic Substitution of Aryl Halides: Addition / Elimination	W = withdraw group X = leaving grp (halide) Nu = nucleophile 	*need Strong W groups ortho and/or para to leaving group. *Nu can be OH⁻, RO⁻, NH₃. *NOTE: If ⁻OCH₃ is the Nu, only need 1 eq
Nucleophilic Aromatic Substitution of Aryl Halides: Elimination / Addition		*occurs when Strong W group is not O/P *formation of benzyne in mechanism * Nu can be OH⁻, RO⁻, NH₃. *will get a mixture (like second example)
Chlorination of Benzene		*8 different stereochems actually occur *this particular molecule is the commercial compound Rid (lice killer)
Catalytic Hydrogenation		
Birch Reduction		*withdraw groups -> sp³ *donating groups -> sp²

Task	Reaction	Notes
Side Chain Rxn: Oxidation		*Can use either reagent *Does not work for bulky groups.
Halogenation of side chains		*If aromatic ring is activated, use NBS instead of Br₂ *Pay attention to Temp (if it's low or high) *WILL EXPLAIN THIS BETTER IN CLASS
Nucleophilic Subs of Benzylic Halides	*SN1  *SN2  *E2 	*SN1 or SN2 or E2? Depends on conditions! *Resonance form that does not disrupt the aromaticity is more stable
Rxns of phenols similar to alcohols		*2nd rxn is Fischer Esterification *3rd rxn is only one that is different!

Task	Reaction	Notes
Oxidation of Phenols to Quinones	 <chem>Oc1ccc(O)cc1 >> O=C1C=CC(=O)C=C1</chem>	*This reaction forms a D-A dienophile!
Formation of Salicylic Acid	 <chem>Oc1ccccc1 >> Oc1ccccc1C(=O)O</chem>	*Phenoxide anion can react with the weak electrophile because it is so strongly activated.
REVIEW: Oxidation of alcohols	2° alcohols  <chem>C1CCCCC1O >> C1CCCCC1=O</chem>	*any [ox] can be used *KMnO ₄ and NO ₃ can be used but they are harsh.
	1° alcohols  <chem>C1CCCCC1CO >> C1CCCCC1C=O</chem>	*Only use PCC because Jones reagent will yield carboxylic acid
REVIEW: Cleavage of Alkenes by Ozonolysis	 <chem>CC(C)=CC >> CC=O + CC=O</chem>	
REVIEW: Hydration of Alkynes	 <chem>R-C#C-H >> R-C(=O)-CH3</chem> <chem>R-C#C-R^1 >> R-C(=O)-R^1 + R^1-C(=O)-R</chem>	*Really know the mechanism now and how the enols tautomerize.

Task	Reaction	Notes
Dithiane Synthesis of Aldehydes and Ketones		*Dithiane will be given *BuLi = $\text{CH}_3(\text{CH}_2)_2\text{CH}_2\text{-Li}$ *Halide must be methyl or 1°
Ketones from Carboxylic Acids		*2 eq because first is used to make salt
Ketones from Nitriles		
Aldehydes from Acid Chlorides	*lithium aluminum tri(t-butoxy)hydride *Rosenmund Reduction	
Ketones from Acid Chlorides		*Make sure you know how to form Gilman Reagent (refer to Corey-House in previous rxn sheet)
Wittig Reaction: Ald and Ketones ONLY		*Know how to prep the phosphorous ylide! *trans is more stable because you want bulky groups to be furthest away from each other.

Task	Reaction	Notes
Aldehydes and Ketones: Formation of Cyanohydrins	 	*Aldehydes or <u>unhindered</u> ketones *will use this as a reagent in the future.
Aldehydes and Ketones: Addition of 1° Amines		*non AQ favors reactant *AQ favors product
Wolf-Kishner Reaction		*avoid halogens and other good LGs. (Use Clemmensen instead)
Aldehydes and Ketones: Addition of 2° Amines		
Acetal Formations "protected carbonyls"		
	*easier to just use	*aldehyde protected before ketone because it is more reactive

Substituent Effects in Aromatic Substitution

First group on the ring determines the reactivity of the ring toward further substitution relative to benzene itself, and also determines the where the second incoming group will go. These are two separate aspects to consider in further substitution on the ring.

An **activating group** makes the ring more reactive than benzene to further substitution. In some cases the activation is so great that polysubstitution occurs and cannot be controlled.

A **deactivating group** makes the ring less reactive than benzene to further substitution. In some cases the ring is deactivated sufficiently to prevent certain reactions from occurring.

With one group already on the ring, a second substituent can come on the ring in ortho, meta or para positions.

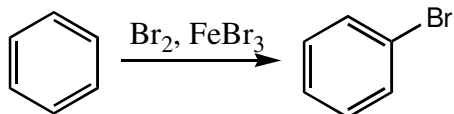
ORTHO, PARA DIRECTORS			META DIRECTORS	
-NH ₂ -NHR -NR ₂ -OH	-OCH ₃ -OR -NHCOCH ₃	Phenyl- -CH=CH ₂ Alkyl-	-F -Cl -Br -I	-CHO -COOH -COOR -COCl -CONH ₂ -SO ₃ H -CN
strong	moderate	weak	weak	strong very strong
ACTIVATORS			DEACTIVATORS	

Two effects are working here. One is **induction**, which is an effect that occurs through the sigma bond system. Electron withdrawing groups will "pull" electron density away from the ring making the electrons of the ring less available for attack by an electrophile. Electron donating groups do the opposite. Induction also plays a role in some of the directional effects.

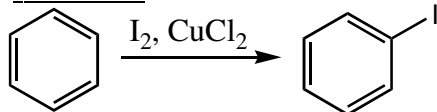
The other effect is **resonance**, which occurs through the pi system of bonds in the molecule. Resonance plays an important role in the stability of intermediates of the reactions.

Chapter 16 Overview:

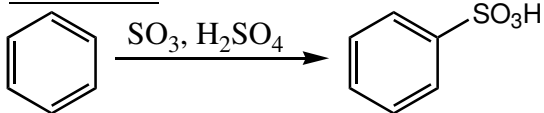
Bromination



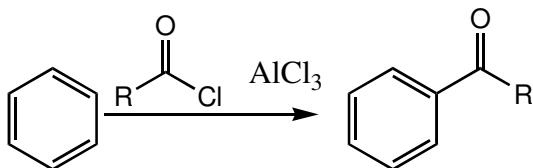
Iodination



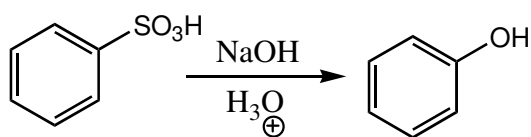
Sulfonation



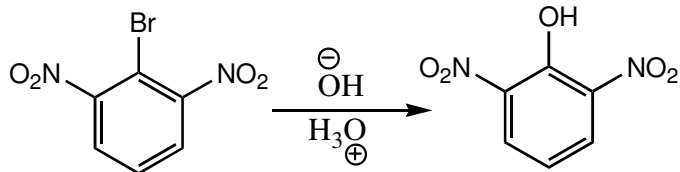
Friedel-Crafts Acylation



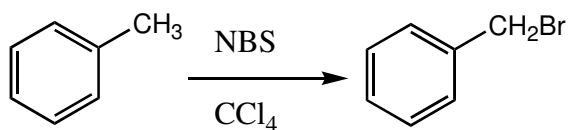
Alkali Fusion of Aromatic Sulfonates



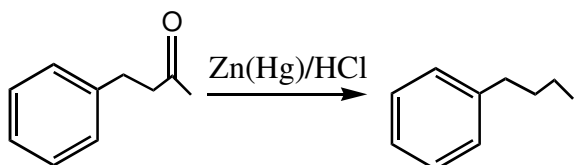
Addition/Elimination to an Activated Aryl Halide



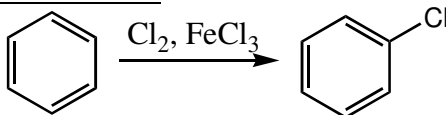
Benzylic Bromination of Alkylbenzenes with NBS



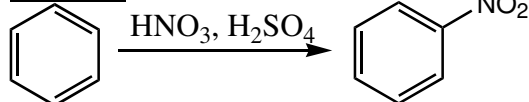
Clemeson Reduction of Dialkyl Ketones



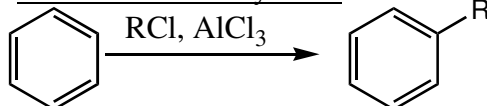
Chlorination



Nitration



Friedel-Crafts Alkylation

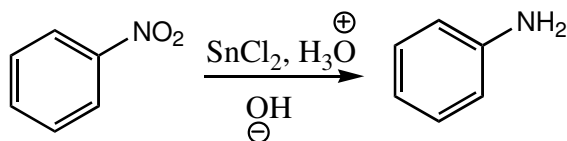


R group may rearrange

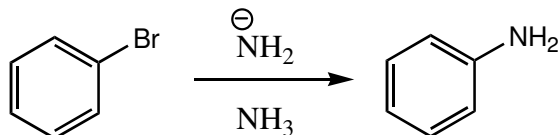
Substrate must be at least as reactive as a halobenzene

Deactivated rings don't react

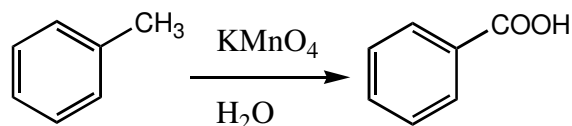
Nitro Reduction to an Amine



Benzyne Intermediate for Amination

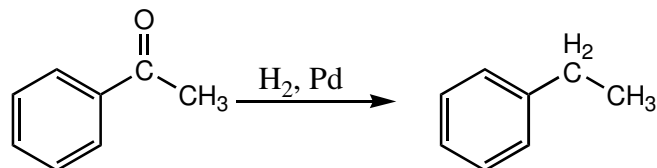


Oxidation of Alkylbenzene Side Chains



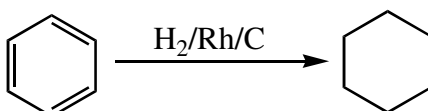
reaction doesn't work with tertiary alkanes

Reduction of Aryl Alkyl Ketones



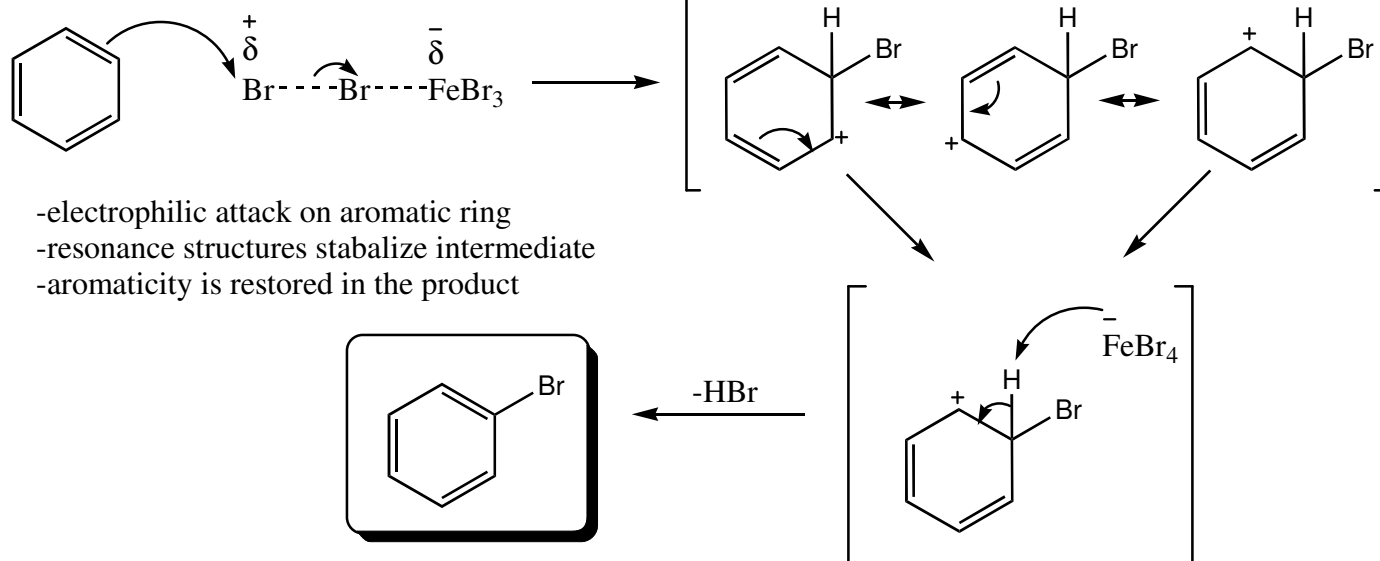
only works with benzylic ketones

Catalytic Hydrogenation



Electrophilic Aromatic Substitution

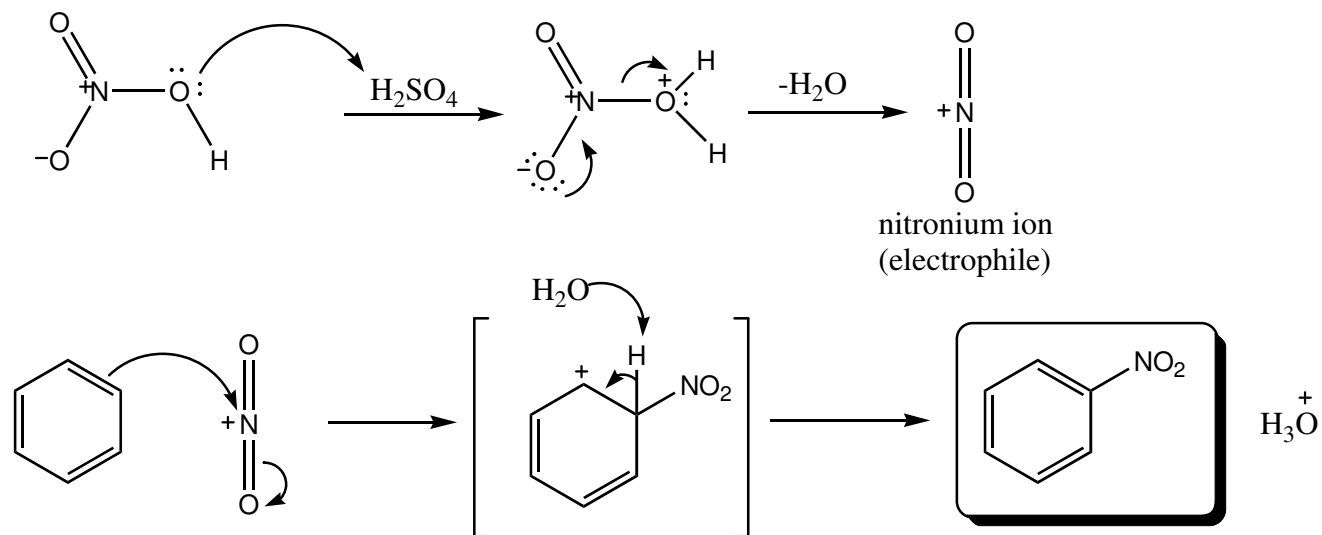
Bromination



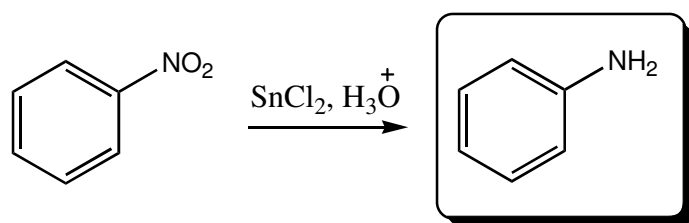
Aromatic chlorination and iodination happen in the same manner but use different lewis acid catalysts: FeCl_3 and CuCl_2 respectively.

Aromatic Nitration

begins with formation of the nitronium ion: $+\text{NO}_2$

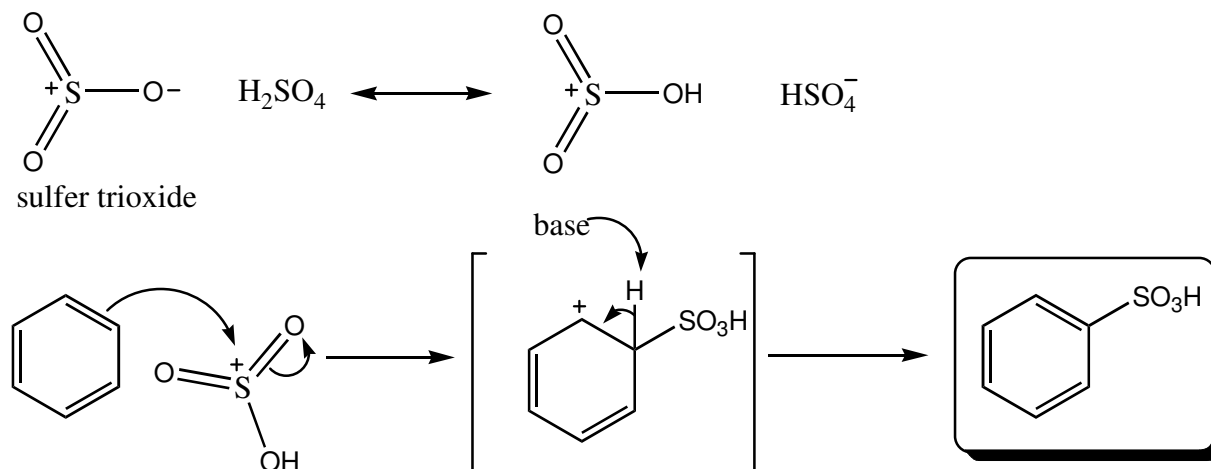


Remember: Reduction of a nitro group to form an amino group

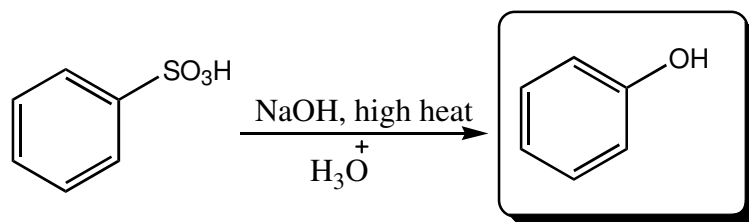


Aromatic Sulfonation

useful for sulfonation, protecting group and as an intermediate to phenols



Remember: alkali fusion to produce phenol

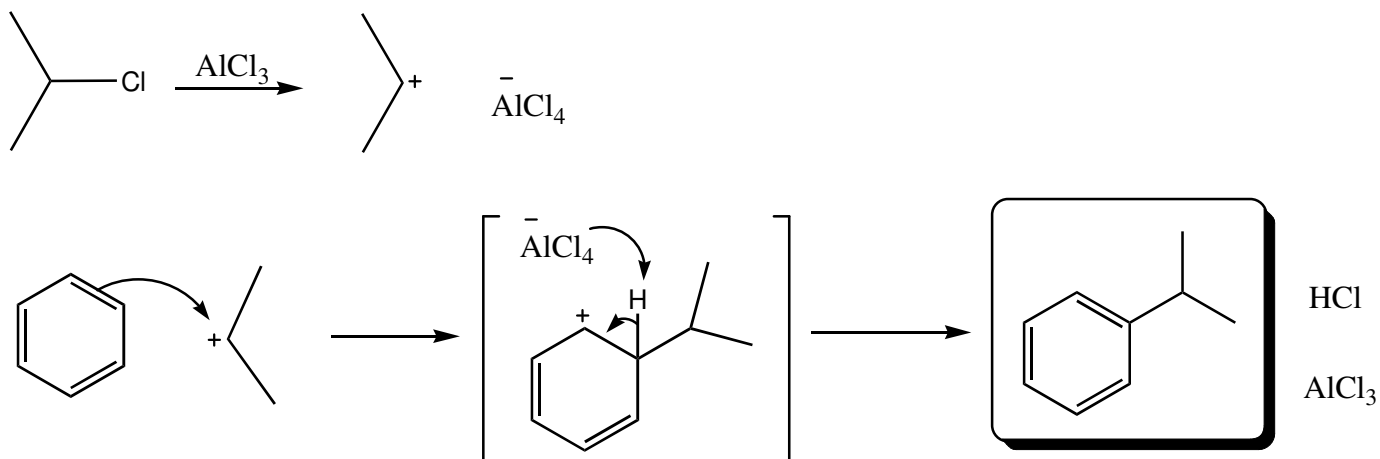


Note: the alkali fusion reaction requires harsh solvent free conditions, therefore it is typically only useful with alkyl groups present on the ring

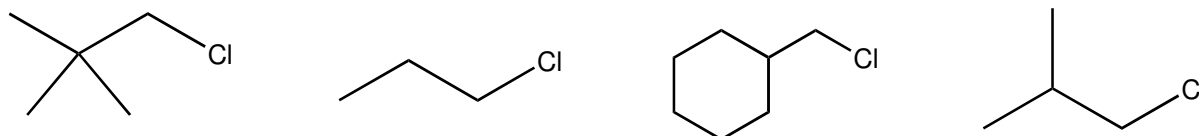
Friedel-Crafts Alkylation

problems/limitations

- prone to carbocation rearrangements
- will not work on an aromatic ring with electron withdrawing groups or amino groups
- poly-alkylation certain to occur

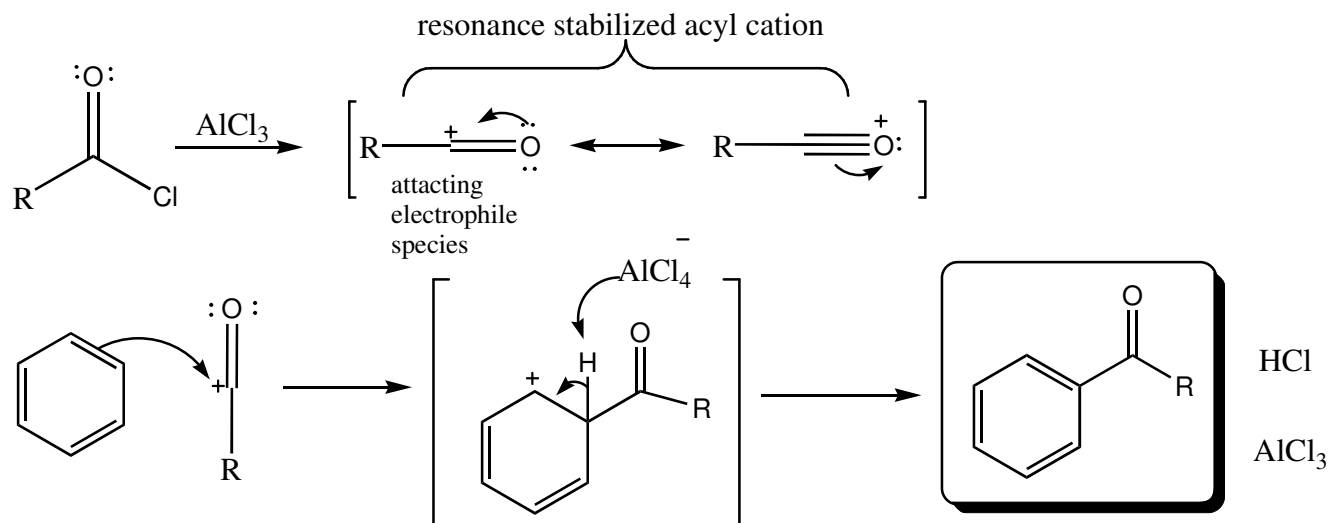


These are examples of alkyl halides that can rearrange:



Friedel-Crafts acylation reaction

Acid chloride can be made from a carboxylic acid and SOCl_2



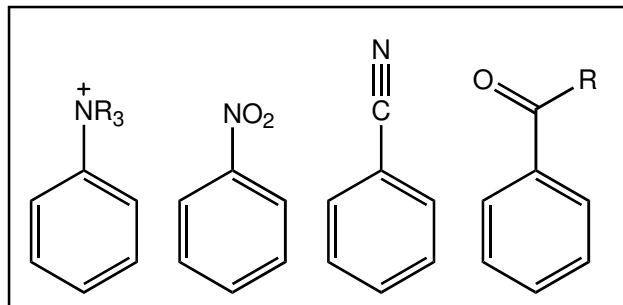
Acylation does not occur more than once since the acylated product is less reactive than the starting material, due to the electron withdrawing nature of the group.

Substituent Effects in Substituted Aromatic Rings

The substituents on an aromatic ring determine the reactivity of the aromatic substrate in subsequent reactions (either activating or deactivating). Examples:

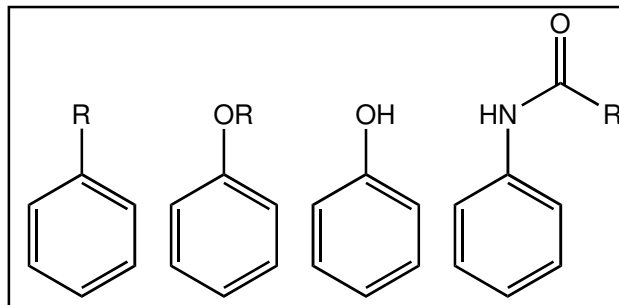
They will also direct the incoming reagent to a specific site on the ring (either ortho/para or meta).

Deactivators/Meta Directors: EWG



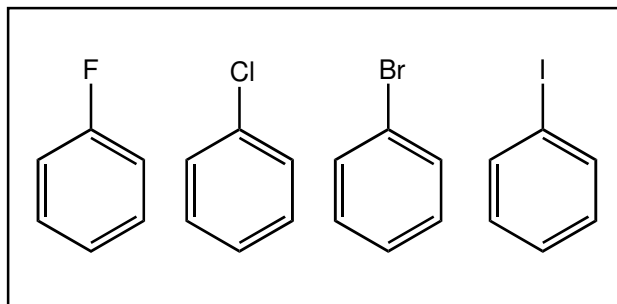
R=any alkyl group or H

Activators/Ortho-Para Directors: EDG



R=any alkyl group or H

Deactivators/Ortho-Para Directors: EWG



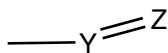
Reactivity and directing ability in electrophilic aromatic substitutions are controlled by inductive effects and resonance.

Inductive Effect-withdrawal or donation of electrons (electron density) through σ bonds. This is a result of a polarization in electronegativity.

Resonance Effect-withdrawal or donation of electrons through π bonds. Resonance structures can be drawn to explain the placement of electron density.

General Structures:

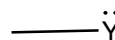
Electron-withdrawing groups(EWG):



Z is a more electronegative atom than Y

destabilize the intermediate carbocation
therefore the ring is less reactive

Electron-donating groups(EDG):



Y is an electronegative atom

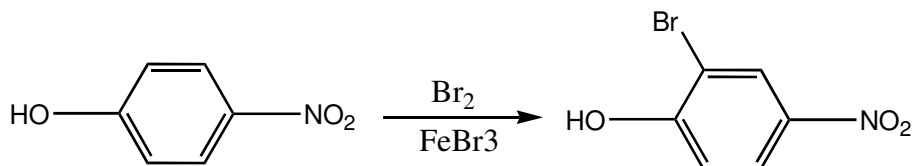
stabilize the intermediate carbocation
therefore the ring is more reactive

Halogens, despite the fact that they are electron-donating groups, deactivate the ring since they have stronger electron-withdrawing capabilities.

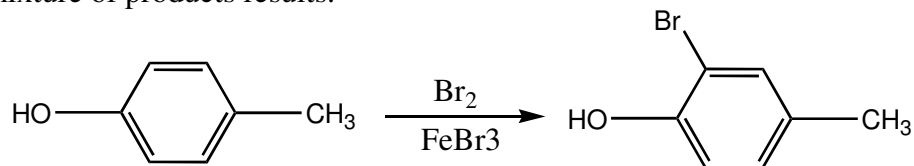
Resonance Structures for electron-donating groups show that the most stable electrophilic attacks take place in the ortho and para positions; electron-withdrawing groups show that the most stable electrophilic attacks take place in the meta position.

Trisubstituted Benzene: Considerations of Different Effects

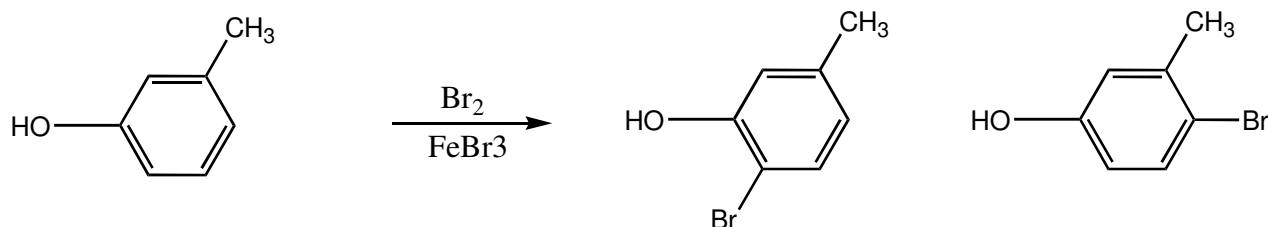
1. If two directing groups direct to the same place then the incoming reagent will react in this position.



2. If two groups oppose each other then the more powerful activating group has the major influence. Often a mixture of products results.



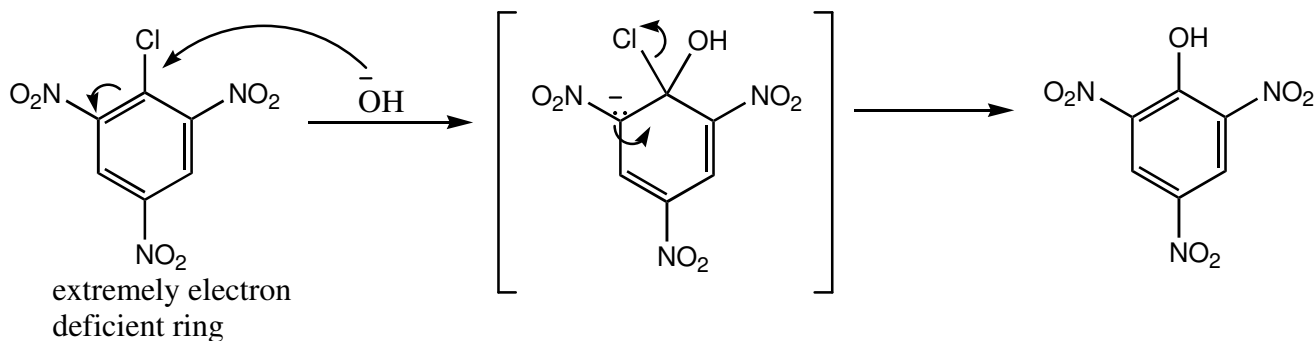
3. If two groups are meta to one another they are usually too bulky to allow attack between them. The incoming reagent will be directed to another site on the ring.



Nucleophilic Aromatic Substitution

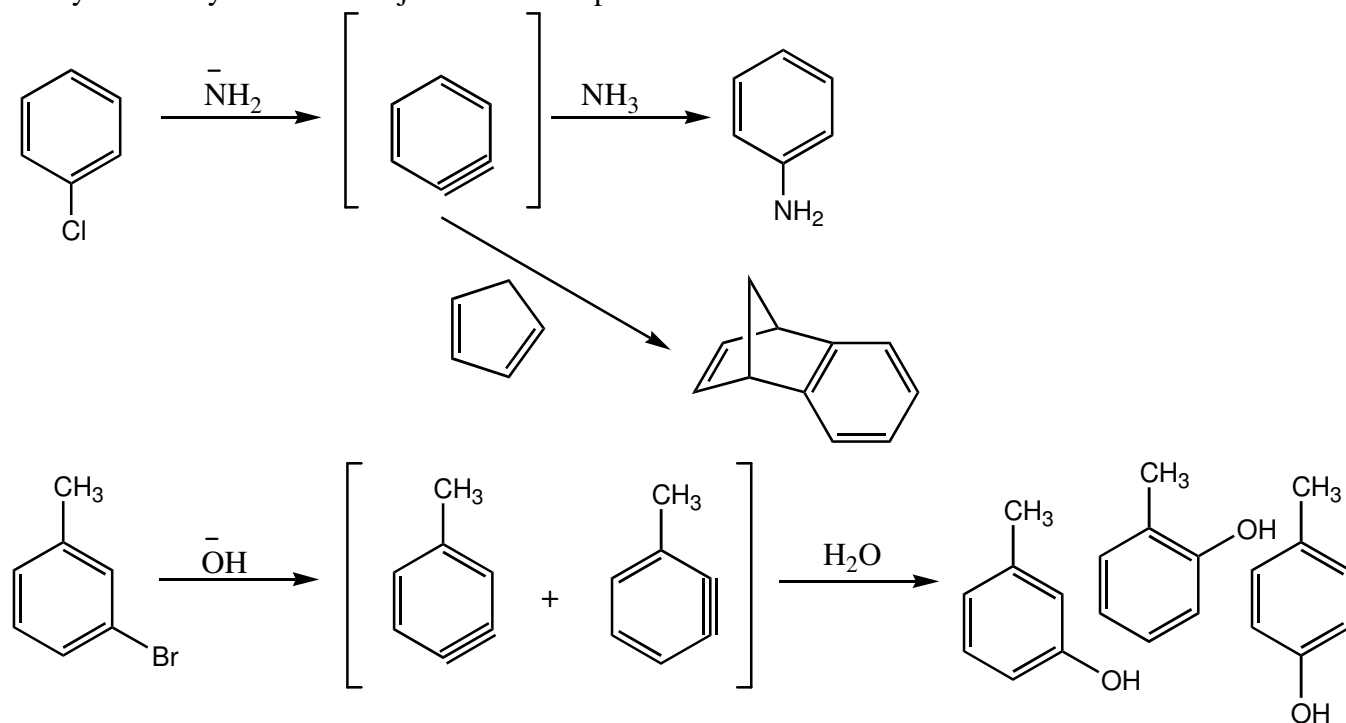
Only takes place on electron deficient rings! EWG must be present!

Proceed through an addition/elimination mechanism



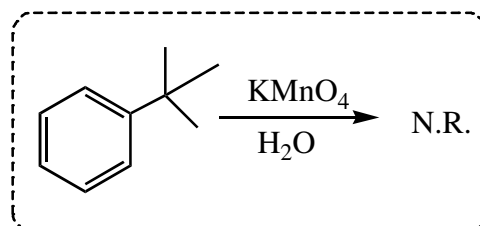
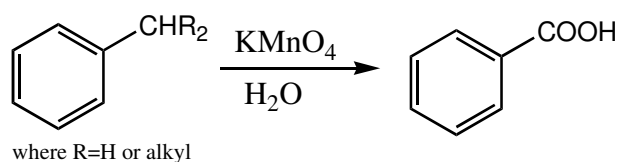
Benzyne: Triple bond in an aromatic ring.

Strong base (either OH or NH₂) eliminates HX (via an E2 mechanism) where X is Cl or Br producing benzyne. Benzyne is then subject to a nucleophilic attack as well as other reactions such as Diels-Alder



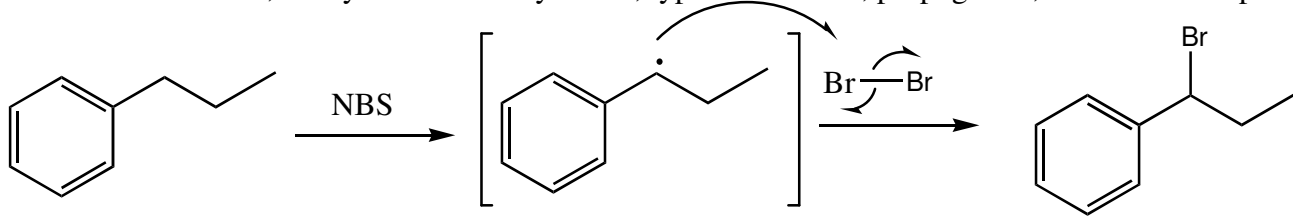
Oxidation of alkylbenzene side chains to carboxylic acids.

Must have a benzylic proton. Tert-butyl won't react!



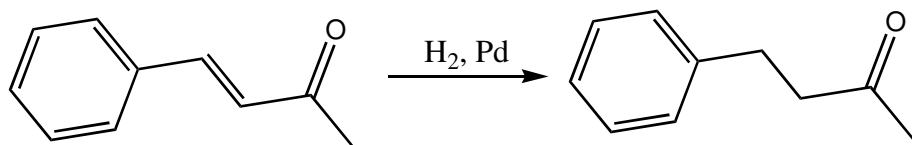
Bromination of Alkylbenzene Side Chains

Radical mechanism, benzylic radical very stable, typical initiation, propagation, termination steps.

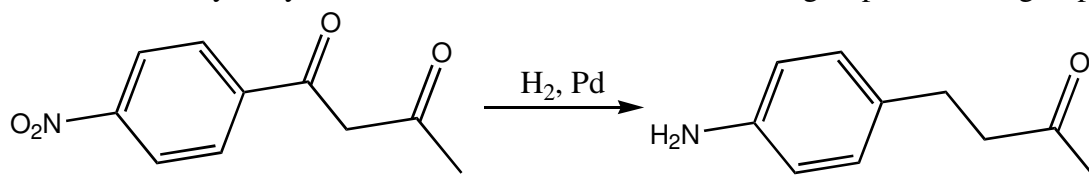


Reduction with aromatic rings

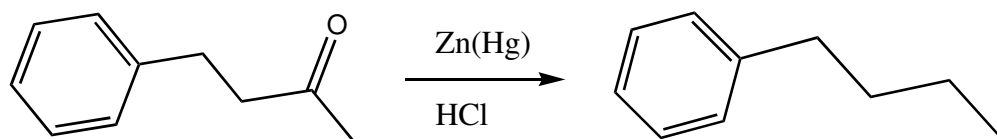
Hydrogen with Pd or Pt catalysts won't reduce aromatic rings or non-benzylic carbonyls.



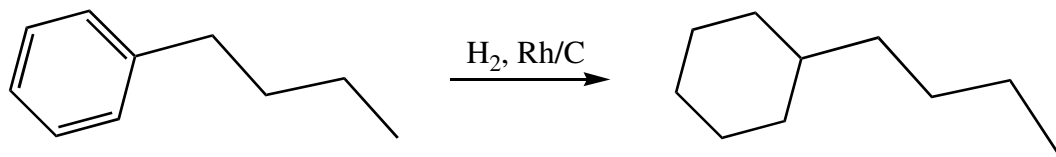
It will reduce aryl alkyl ketones to alkanes and aromatic nitro groups to amino groups



Clemmensen Reduction will reduce all carbonyls, it will also reduce aromatic nitro groups to amino groups

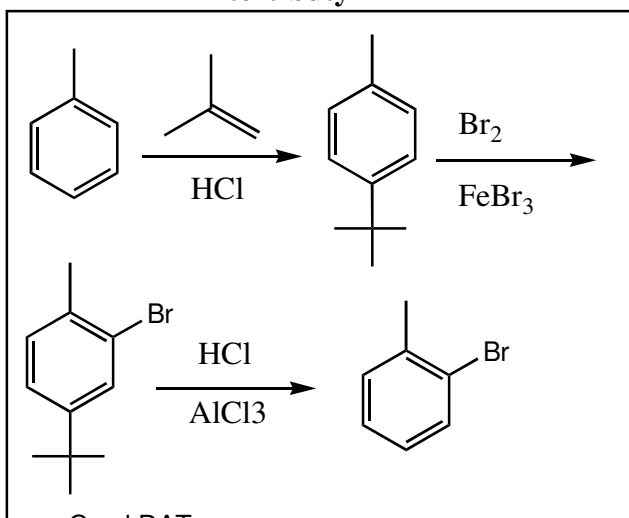


Hydrogen with Rhodium Catalyst will reduce the aromatic ring to cyclohexane

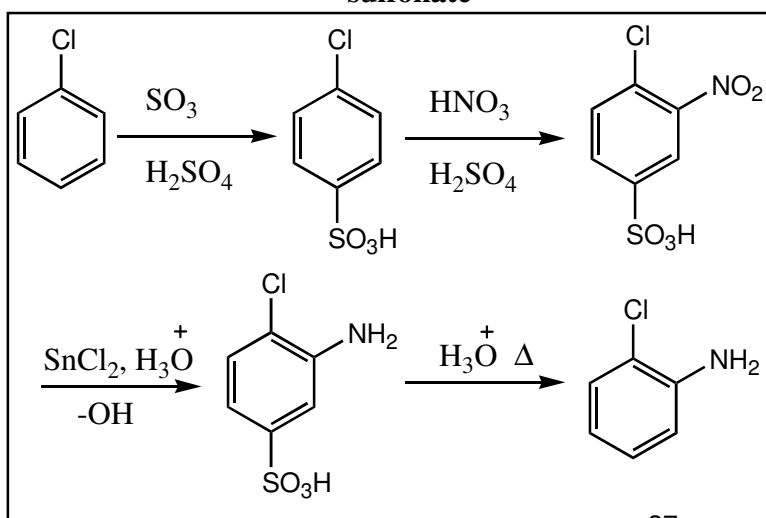


Protecting Groups for Synthesis: put in a place holder group so the position it occupies is not attacked.

tert-butyl



sulfonate



SUBSTRATE	REAGENT catalyst	REACTION	MECHANISM	MAJOR PRODUCT	BYPRODUCT	NOTE
ALKANES						
CH ₄	Cl ₂ or Br ₂	Radical Halogenation	S _R	CH ₃ Cl	HCl	
ALKENES						
CH ₂ =CH ₂	H ₂ (Pt, Ni, Pd)	Catalytic Hydrogenation (Reduction)	Cis A _E	CH ₃ -CH ₃		
CH ₂ =CH ₂	HX	Hydrohalogenation	Trans or anti A _E	CH ₃ CH ₂ X Organic monohalide		X on more substituted C; H on less substituted C
CH ₂ =CH ₂	X ₂	Halogenation	Trans or anti A _E	CH ₂ XCH ₂ X Vicinal dihalide		
CH ₂ =CH ₂	HOH H ₂ SO ₄	Hydration	Trans or anti A _E	CH ₃ CH ₂ OH Alcohols		
CH ₂ =CH ₂	Neutral or basic KMnO ₄ (aq.)	Hydroxylation	REDOX (Oxidation)	Diols		
CH ₂ =CH ₂	Acidic KMnO ₄	Oxidative Multiple Bond Cleavage	REDOX (Oxidation)	If terminal = CO ₂ + H ₂ O If internal = RCOOH		
CH ₂ =CH ₂	Peroxyacid	Epoxidation	REDOX (Oxidation)	Epoxide	RCOOH	
CH ₂ =CH ₂	X ₂ , H ₂ O	Halohydratation	Trans A _E	Halohydrins HO-C-C-X	HX	
ALKYNES						
HCCH	H ₂ (Lindlar's Catalyst)	Catalytic Hydrogenation (Reduction)	Cis A _E	CH ₂ =CH ₂		

HCCH	HOH H ₂ SO ₄ , HgSO ₄	Hydration	Trans or anti A _E	Enol H ₂ =CHOH Ketone R ₂ CO		Markovnikov's rule Keto-enol Tautomerism
HCCH	HX	Hydrohalogenation	Trans or anti A _E	CH ₂ =CHX		
HCCH	X ₂	Halogenation	Trans or anti A _E	CH ₂ X=CH ₂ X		
HCCH	Neutral or basic KMnO ₄ (aq.)	Hydroxylation	REDOX (Oxidation)	Diols		
HCCH	Acidic KMnO ₄ (aq.)	Oxidative Multiple Bond Cleavage	REDOX (Oxidation)	If terminal = CO ₂ + H ₂ O If internal = RCOOH		
HCCH	NaNH ₂	Acetylide Formation	Acid-base reaction (or S _N)	Acetylide	NH ₃	
AROMATIC COMPOUNDS						
Benzene	X ₂ FeX ₃ or AlX ₃	Halogenation	S _E	Halobenzene	HX	Note activators and deactivators
Benzene	Conc. HNO ₃ and Conc. H ₂ SO ₄	Nitration	S _E	Nitrobenzene	HOH	
Benzene	Fuming H ₂ SO ₄ (conc. H ₂ SO ₄ + SO ₃)	Sulfonation	S _E	Benzenesulfonic Acid	HOH	
Benzene	RCOX (Acid halide) AlX ₃	Friedel-Crafts Acylation	S _E	Aromatic ketone	HX	Cannot undergo friedel-craft if the ring contains a deactivator
Benzene	RX (Alkyl halide) AlX ₃	Friedel-Crafts Alkylation	S _E	Arenes	HX	
Benzene	Zn(Hg), conc. HCl heat	Clemmenson Reduction	S _E	Acyl to Alkyl		
Ethyl Benzene	KMnO ₄ , H ₂ O	REDOX (Oxidation)	S _E	If terminal = CO ₂ + H ₂ O If internal = RCOOH		

				(Benzoic Acid)		
ALKYL HALIDES						
R-X	Mg ⁰	Synthesis of Grignard Reagent	A _N	R-Mg-X Grignard reagent		Condensation Reaction (A _N E)
R-Mg-X	H ₂ O	Hydrolysis	E	R-H	Mg(OH)X Basic magnesium halide	
R-X	Strong or weak nucleophile; dependent on substrate; polar protic solvent		S _N 1	Racemization (enantiomeric products)		3° > 2° > 1°
R-X	Strong nucleophile; dependent on both substrate and nucleophile; polar aprotic or nonpolar solvent		S _N 2	Inversion prod.		1° > 2° > 3°
R-C-X	Nu ⁻ heat	elimination	E ₁	R=C	X ⁻	
R-C-X	Nu ⁻ (basic) heat	elimination	E ₂	R=C	X ⁻	Major product in more substituted C atom
ALCOHOLS AND PHENOLS						
R-OH	H-X Hydrogen halide ether	Hydrohalogenation	S _N 1	R-X	H ₂ O	Most reactive with 3° alcohols
R-OH	p-TosCl Toluenesulfonyl chloride pyridine		S _N 1 or S _N 2	ROTs	Pyridine HCl	
CH ₃ CH ₂ -OH	H ₃ O ⁺ , THF	dehydration	E ₁	CH ₂ =CH ₂ More substituted alkene product	Less substituted alkene product	Follows Zaitsev's rule
R-OH (1°) (2°)	KMnO ₄ /CrO ₃ / Na ₂ Cr ₂ O ₇	REDOX	oxidation	Aldehydes → Carboxylic acids Ketones		
R-OH (1°)	Dess-martin periodinane CH ₂ Cl ₂	REDOX	oxidation	RCHO		

Ar-OH phenol	$\text{Na}_2\text{Cr}_2\text{O}_7$ H_2O	REDOX	Oxidation	Benzoquinone		
Quinone	SnCl_2 H_2	REDOX	Reduction	Hydroquinone		
ETHERS						
ROR'	HBr or HI	Acidic Cleavage	$\text{S}_{\text{N}}2$: If 1° or 2° $\text{S}_{\text{N}}1$: If 3°	R'Br or R'Cl + ROH		Br or I will bond with the less sterically hindered R between 1° and 2° If there is a tertiary R, Br and I will automatically bond with it
EPOXIDES (AKA OXIRANES)						
ROH	Na° metal or NaH	Williamson Ether Synthesis		RONa^+ (Alkoxide Ion)	H_2	In short: $\text{ROH} + \text{NaH} \rightarrow \text{H}_2 + \text{RONa}$ a $\text{RONa} + \text{RX} \rightarrow \text{NaX} + \text{ROR}$
RONa	R-X		$\text{S}_{\text{N}}2$: If 1° or 2° $\text{S}_{\text{N}}1$: If 3°	ROR'	NaX	
EPOXIDE	HX, Ether	Ring Opening	$\text{S}_{\text{N}}2$ like: If 1° or 2° $\text{S}_{\text{N}}1$ like: If 3° is present $\text{S}_{\text{N}}2$ (accdg to Torres)	Halohydrin		X or the halogen will bond with the 1° (between 1° and 2°) X will bond with 3° if it is present
EPOXIDE	H^+ , HOH	Ring Opening	$\text{S}_{\text{N}}2$	1,2 diol (glycol)		
ALDEHYDES						
RCHO	$\text{KMnO}_4/\text{CrO}_3/$ $\text{Na}_2\text{Cr}_2\text{O}_7$	REDOX	Oxidation	RCOOH		
RCHO	H_2O (basic OH^-) or (acidic H^+)	Hydration	A_{N}	Hydrate (gem diol)		

RCHO	HCN	Cyanohydrin formation	A _N	nitriles		
RCHO	NaBH ₄ ; ethanol	REDOX	reduction	Primary alcohols		
RCHO	R-Mg-X	Addition of grignard reagent	A _N	Secondary alcohols		
RCHO	RNH ₂	Imine formation	A _N E	RCH-Imine		
RCHO	R ₂ NH	Enamine formation	A _N E	Enamine		
RCHO	H ₂ NNH ₂ KOH	Wolff-Kishner	A _N	RCH ₃	N ₂ + H ₂ O	
RCHO	ROH Acid catalyst	Acetal formation	A _N E	Hemiacetal → acetal	H ₂ O	
KETONES						
R ₂ CO	H ₂ O (basic OH ⁻) or (acidic H ⁺)	Hydration	A _N	Hydrate (gem diol)		
R ₂ CO	HCN	Cyanohydrin formation	A _N	Nitriles		
R ₂ CO	NaBH ₄ ; ethanol	REDOX	reduction	Secondary alcohols		
R ₂ CO	R-Mg-X	Addition of grignard reagent	A _N	Tertiary alcohols		
R ₂ CO	RNH ₂	Imine formation	A _N E	R ₂ C-Imine	H ₂ O	

R_2CO	R_2NH_2	Enamine formation	A_NE	Enamine	H_2O	
R_2CO	H_2NNH_2 KOH	Wolff-Kishner	A_N	R_2CH_2	$N_2 + H_2O$	
R_2CO	ROH Acid catalyst	Ketal formation	A_NE	Hemiketal $\rightarrow$ ketal	H_2O	
CARBOXYLIC ACIDS						
$RCOOH$	$SOCl_2$		S_NAcyl	$RCOCl$		
$RCOOH$	PBr_3 , Ether		S_NAcyl	$RCOBr$		
$RCOOH$ (2 moles acetic acid)	heating			Acetic anhydride	H_2O	Only acetic anhydride is prepared this way
$RCOOH$	ROH Acid catalyst	Fischer Esterification	S_NAcyl	Ester ($RCOOR'$)	H_2O	
$RCOOH$	$NH_3(alc.)$ DCC	ammonolysis	S_NAcyl	Amide ($RCONH_2$)	H_2O	
$RCOOH$	$RNH_2(alc.)$ DCC	aminolysis	S_NAcyl	Amide ($RCONHR'$)	H_2O	
$RCOOH$	1. $LiAlH_4$, ether 2. H_3O^+	REDOX	Reduction	Primary alcohol (RCH_2OH)		
ACID HALIDES (CARBOXYLIC ACID DERIVATIVE)						
$RCOX$	H_2O	Hydrolysis	S_NAcyl	$RCOOH$	HX	
$RCOX$	Carboxylate anion		S_NAcyl	Acid Anhydride (symmetrical or unsymmetrical)		
$RCOX$	ROH	Alcoholysis	S_NAcyl	Ester ($RCOOR'$)	HX	
$RCOX$	$R'-NH_2(alc)$	Aminolysis	S_NAcyl	Amides ($RCONHR'$)	HX	Trisubstituted amines can't be used
$RCOX$	$NH_3(alc)$	Ammonolysis	S_NAcyl	$RCONH_2$	HX	

RCOX	1. LiAlH ₄ , ether 2. H ₃ O ⁺	REDOX (reduction)	S _N Acyl	Primary alcohol (RCH ₂ OH)	HX	
RCOX	2 R-Mg-X (Grignard reagent)	Grignard	S _N Acyl	Tertiary alcohols		
RCOX	R ₂ CuLi Lithium diorganocopper (Gilman) reagent	Diorganocopper	S _N Acyl	Ketone (RCOR')	R'Cu	
ACID ANHYDRIDES (CARBOXYLIC ACID DERIVATIVE)						
(RC(O)) ₂ O	H ₂ O	Hydrolysis	S _N Acyl	RCOOH	RCOOH	
(RC(O)) ₂ O	ROH	Alcoholysis	S _N Acyl	Ester (RCOOR')	RCOOH	
(RC(O)) ₂ O	R'-NH ₂ (alc)	Aminolysis	S _N Acyl	Amide (RCONHR')	RCOOH	
(RC(O)) ₂ O	1. LiAlH ₄ , ether 2. H ₃ O ⁺	REDOX	reduction	2 Primary alcohol 2 (RCH ₂ OH)		
ESTERS (CARBOXYLIC ACID DERIVATIVE)						
RCOOR'	H ₂ O, NaOH H ₃ O ⁺	Hydrolysis saponification	S _N Acyl	RCOOH	R'OH	
RCOOR'	NH ₃ ether	Aminolysis	S _N Acyl	RCO-NH ₂	R'OH	
RCOOR'	1. ROH 2. H ₃ O ⁺ or base	Trans esterification	S _N Acyl	Ester (RCOOR')	R'OH Primary alcohol	Double bond O will become ester Ester must not have the same
RCOOR'	1. LiAlH ₄ , ether 2. H ₃ O ⁺	REDOX	reduction	RCOH Primary alcohol	R'OH Primary alcohol	
RCOOR'	R-Mg-X (Grignard reagent)	Grignard	S _N Acyl	Tertiary alcohol		
AMIDES (CARBOXYLIC ACID DERIVATIVE)						
RCONH ₂	H ₂ O, NaOH H ₃ O ⁺	Hydrolysis	S _N Acyl	RCOOH	NH ₃	
RCONH ₂	1. LiAlH ₄ , ether	REDOX	reduction	RCH ₂ NH ₂	H ₂ O	

	2. H_3O^+					
NITRILES						
$\text{RC}\equiv\text{N}$	H_2O	Hydration	A_N	amide RCONH_2		
$\text{RC}\equiv\text{N}$	H_2O , NaOH H_3O^+	Hydrolysis		RCOOH	NH_3	
$\text{RC}\equiv\text{N}$	LiAlH_4 , ether	REDOX	reduction	RNH_2 Primary amine		
$\text{RC}\equiv\text{N}$	R-Mg-X (Grignard reagent), H_2O			R_2CO	NH_3	