Electrophilic Aromatic Substitution: Nitration and Sulfonation

How can we replace a hydrogen (H^+) with a nitro group (NO_2^+)?

How can we replace a hydrogen (H^+) with a sulfonic acid group (SO_3H^+)?

Reading: Section 16.4

Electrophilic Aromatic Substitution: Alkylation

How can we replace a hydrogen (H^+) with an alkyl group (R^+, a carbocation)? This reaction is known as *Friedel-Crafts Alkylation.*

What are the significant problems with Friedel-Crafts alkylation*?*

Reading: Section 16.4

Electrophilic Aromatic Substitution: Acylation

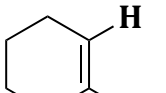
How can we replace a hydrogen (H^+) with an acyl group (a ketone)?
This reaction is known as *Friedel-Crafts Acylation.*

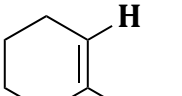
How can use *acylation* to avoid some of the problems of alkylation?

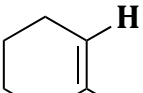
Reading: Section 16.4

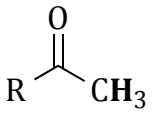
Electron Donating & Withdrawing Groups

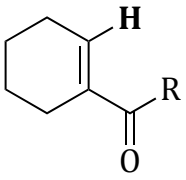
Match the chemical shifts with the highlighted protons in the compounds shown. *Why* are these trends observed?











Reading: Section 16.5

Inductive vs. Resonance Effects

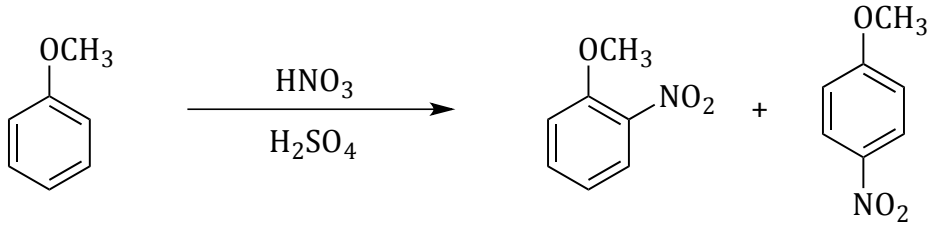
Complete the following table, indicating the relative magnitude of the various effects.

Functional Group	Inductive Effect	Resonance Effect
$-NMe_2$		
$-OH$		
$-CH_3$		
$-Cl$		
$-C(=O)OEt$		
$-CN$		
$-N^+Me_3$		
$-NO_2$		

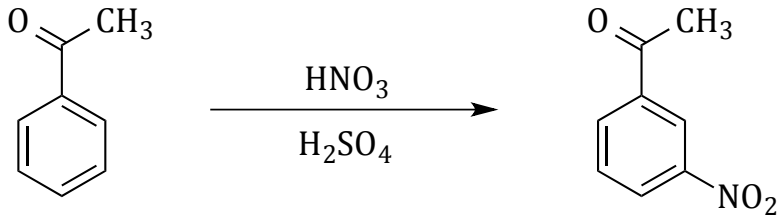
Reading: Section 16.5

Electrophilic Aromatic Substitution: Directing Effects ("Regioselectivity")

When anisole is nitrated, the *ortho* and *para* products predominate. Why?



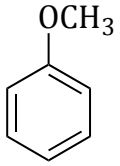
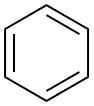
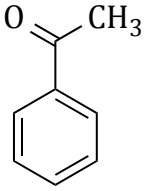
When acetophenone is nitrated, the *meta* product predominates. Why?



Reading: Section 16.5

Electrophilic Aromatic Substitution: Activating Effects

Explain the observed trend in the *rate* of nitration of the following compounds:

			
Relative rate of reaction with HNO_3/H_2SO_4:	*fast*	*normal*	*slow*

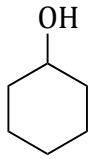
In general, *ortho/para*-directing groups are *activating*, while *meta*-directing groups are *deactivating*. Why?

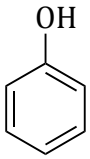
However, *halogen* substituents are *deactivating*, but are *o/p*-directors. Why?

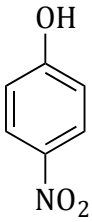
Reading: Section 16.5

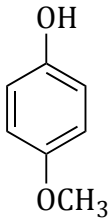
Application of Substituent Effects: The Acidity of Phenols

Explain the observed trends in the pK_a values of the following compounds:





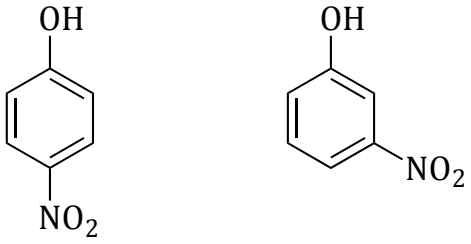




Reading: Section 18.6

Application of Substituent Effects: The Acidity of Phenols, cont.

Explain the observed trends in the pK_a values of the following compounds:



Reading: Section 18.6

Reactivity of Vinylic Halides

Draw an example of a vinylic halide.

Why does that halide *not* usually exhibit S_N2 reactivity?

Why does that halide *not* usually exhibit S_N1 or E1 reactivity?

What product would be formed from an E2 reaction of that halide?

Reading: Section 18.1-18.3

Reactivity of Aryl Halides

Draw an example of an *aryl* halide; how is it different from a *benzylic* halide?

Why are S_N2 reactions of aryl halides *impossible*?

Why are S_N1 reactions of aryl halides (very nearly) *impossible*?

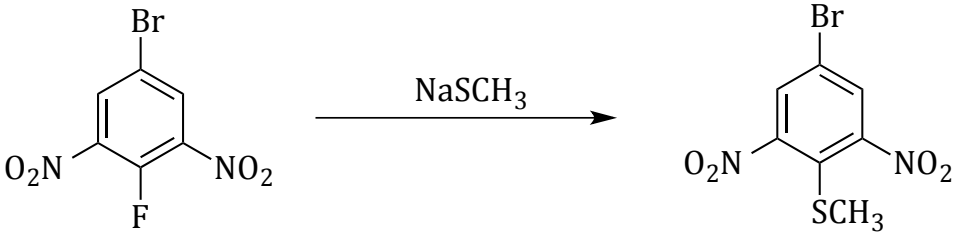
Are there *any* leaving groups that can provide S_N1 reactivity by forming an aryl cation?

Reading: Section 18.1-18.3

Nucleophilic Aromatic Substitution: Addition-Elimination

When an *aryl halide* has *nitro groups* in *o/p* positions, then nucleophilic substitution can take place **IF** you have a good nucleophile. This reaction is referred to as "*Nucleophilic aromatic substitution* (S_NAr) *by the addition-elimination mechanism*."

Consider the following reaction:



Provide a complete curved-arrow mechanism for this transformation.

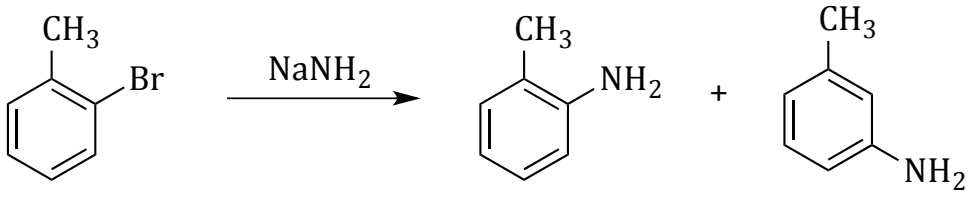
Why does substitution replace the fluoride, but not the bromide?

Reading: Section 18.4

Nucleophilic Aromatic Substitution: Elimination-Addition ("The Benzyne Mechanism")

When an *aryl halide* does **not** have EWGs in *o/p* positions, and it is treated with a ***very*** strong base, then nucleophilic substitution can take place via an intermediate known as a *benzyne*. Substitution by this mechanism is referred to as "*Nucleophilic aromatic substitution* (S_NAr) *by the elimination-addition mechanism*."

Provide a curved-arrow mechanism for the following reaction; this mechanism *must* account for why a *mixture* of products is formed!

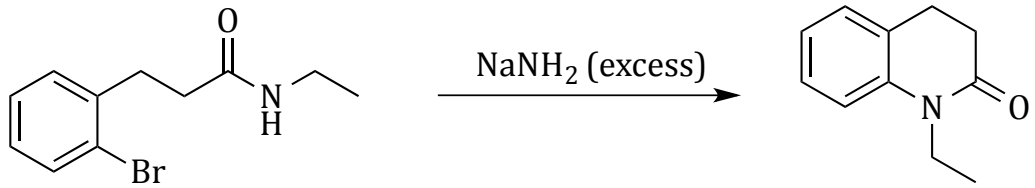


Reading: Section 18.5

Structure and Reactivity of Benzyne

Benzyne is a very unstable species. How can we think about bonding in benzynes?

Provide a complete curved-arrow mechanism for the following transformation:



Reading: Section 18.5

Electrophilic π-Bonds: Carbonyl Chemistry

What functional groups contain a carbonyl group?

What distinguishes some carbonyl-containing compounds from others?

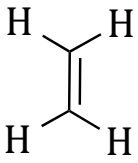
Reading: Section 19.1 & 19.4

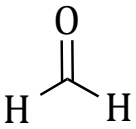
Oxidation Levels in Organic Chemistry

# of bonds to e^--neg atoms	Oxidation "level"	Examples
4	*carbon dioxide*	
3	*carboxylic acid*	
2	*ketone*	
1	*alcohol*	
0	*alkane*	

Molecular Orbitals of Aldehydes & Ketones

Draw molecular orbital diagrams for the following molecules and identify the HOMO and LUMO of each. In what ways are they similar; in what ways are they different?

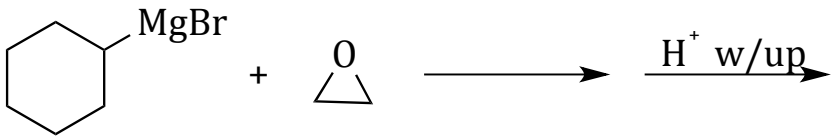


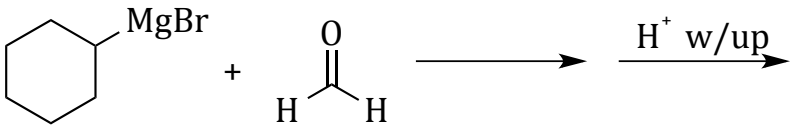


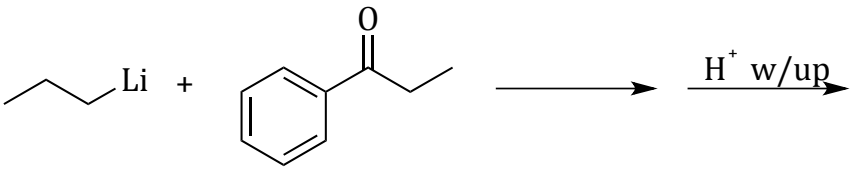
Reading: Section 19.1 & 19.4

Irreversible Addition to Aldehydes & Ketones: Organometallic Reagents

Provide a curved-arrow mechanism and predict the product of the following reactions:



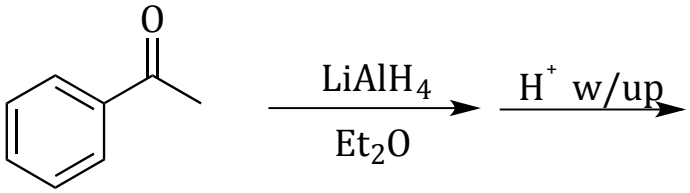


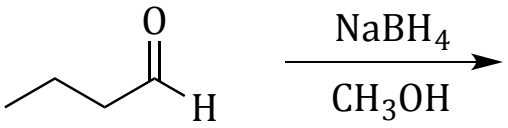


Reading: Section 19.9

Irreversible Addition to Aldehydes & Ketones: Hydride Reducing Reagents

Provide a curved-arrow mechanism and predict the product of the following reactions:





Why is acid work-up required for reduction with $LiAlH_4$,
but not for reduction with $NaBH_4$?

Reading: Section 19.8

Putting it Together: Synthesis

Starting from *benzene*, provide a synthesis of the following compound: