Chapter 4: Aromatic Compounds
General Properties

Benzene:

– formula: \( \text{C}_6\text{H}_6 \)
– IHD: 4 (highly unsaturated)
– chemical reactivity: substitution, but only 1 product \( \therefore \) all H atoms must be equivalent
– structure: cyclic, planar, \( \text{sp}^2 \) hybridized
  
  • Benzene is cyclic, is planar,
  • has an interrupted cloud of \( \pi \) electrons,
  • and has three pairs of electrons in the \( \pi \) cloud.

\[ \text{Kekule structure} \quad \leftrightarrow \quad \text{Robinson structure} \]
Benzene:

- C-C bond length: 1.39 Å
  - Intermediate to C-C (1.54 Å) and C=C (1.34 Å)
  - All C-C bond lengths are the same ➔ resonance!
General Properties

Benzene:

Chemical reactivity: electrophilic substitution

as opposed to electrophilic addition
General Properties

Why the difference between benzene and an alkene?

Aromaticity: the extra stability associated with aromatic compounds.

Aromatic compounds are:
- Cyclic
- planar
- fully conjugated
- contain $4n + 2 \pi$ electrons ($n=1,2,3...$) (Huckel’s rule: equivalent to an odd number of $\pi$ electrons pairs in the ring system).
Naming Monosubstituted Benzenes

Some monosubstituted benzenes are named by adding the name of the substituent to “benzene.”

- bromobenzene
- chlorobenzene
- nitrobenzene
- ethylbenzene
Some monosubstituted benzenes have names that incorporate the substituent.
Alkyl-Substituted Benzenes

Name as an **alkyl-substituted benzene** when the alkyl group has a name.

Otherwise, name as a **phenyl-substituted alkane**.

**Toluene** (methyl substituent on benzene) is an exception.
When two substituents are present, three isomeric structures are possible.

Specific examples are:

- **ortho-dichlorobenzene**
- **meta-dichlorobenzene**
- **para-dichlorobenzene**
- **para-xylene**
- **para-chlorobenzene-sulfonic acid**
o-bromochlorobenzene
(mine alphabetical order)

m-nitrotoluene

p-chlorostyrene

m-chlorophenol

o-ethylaniline

1,2,4-trimethylbenzene

3,5-dichlorotoluene

2,4,6-trinitrotoluene (TNT)
Phenyl and Benzyl Substituents

- phenyl group
- benzyl group

- 2-phenylpentane (or 2-pentylbenzene)
- phenylcyclopropane (or cyclopropylbenzene)
- 1,3,5-triphenylbenzene
- biphenyl
- benzyl chloride
- m-nitrobenzyl alcohol
The resonance energy is a measure of the extra stability of the cyclic conjugated system compared to the corresponding number of isolated double bonds, i.e.

\[
E = 3 \times 120 = 360 \text{ kJ/mol}
\]

hypothetical molecule with no resonance, cyclohexatriene

Resonance Energy 152 kJ/mol
Resonance Energy

The large resonance stabilization energy seen in aromatic compounds results in two effects on their chemical reactivity:

1) Since the resonance stabilization energy is lost when an electrophile adds to the ring you need to use much stronger electrophiles than for alkenes/alkynes, generally this means using a catalyst.

2) The resonance energy can be regained if the intermediate carbocation loses a $\text{H}^+$, this results in a substitution rather than the addition seen in alkenes/alkynes. The $\text{H}^+$ is lost to a base, even weak ones suffice here.
Mechanism of Electrophilic Aromatic Substitution (EArS)

In general all EArS reactions proceed by the same mechanism:

- **E**\(\rightarrow\) \(\text{benzenonium ion} \ (a \ carbocation)\) \(\rightarrow\) \(E\)

Benzenonium resonance structures:

- **ortho**
- **para**
- **ortho**
Mechanism of Electrophilic Aromatic Substitution (EArS)

As with allenes and alkynes, the carbocation generated by the addition of the electrophilic is a stable intermediate, i.e.

The formation of the carbocation is the rate determining step as it takes energy to break the aromaticity.
Cl₂ and Br₂ are weak electrophiles on their own so need to be “activated” by using a Lewis acid catalyst.

Commonly the corresponding iron trihalide is used, FeCl₃ or FeBr₃.
EArS - Halogenation

The rate determining step is:

\[
\text{Product} + \text{Base} \rightarrow \text{Product}
\]

This carbon is \(sp^3\)-hybridized; it is bonded to four other atoms, and has no double bond to it.

The base in this case is the chloride ion:

\[
\text{Product} + \text{Base} \rightarrow \text{Product} + \text{Base}
\]
EArS - Nitration

In the case of nitration, sulfuric acid is used to generate a more reactivity electrophile, a nitronium ion.

\[
\begin{align*}
\text{H} &= \text{O} \longrightarrow \text{N} \longrightarrow \text{O} \longrightarrow \text{H} \\
\text{nitric acid} & \quad \xleftrightarrow{\text{H}^+} \quad \text{H} \longrightarrow \text{O} \longrightarrow \text{N} \longrightarrow \text{O} \longrightarrow \text{H} \quad \xleftrightarrow{\text{H}^+} \quad \text{N}^+ \\
\text{protonated} & \quad \text{nitric acid} \quad \xleftrightarrow{\text{H}^+} \quad \text{nitronium} \quad \text{ion} \\
& + \text{H}_2\text{O}
\end{align*}
\]
The product of the reaction is nitrobenzene, i.e.
Sulfonation will generate a benzenesulfonic acid. The electrophile used is sulfur trioxide, which is a strong electrophile, i.e.
While benzenesulfonic acids are useful in their own right, they are also convenient as they can be modified to a phenol easily, i.e.
Alkylation will add an alkane group to benzene. In this case we need a carbocation as the electrophile. There are two ways to do this:

1) Friedel-Crafts alkylation
2) Alkylation using an alkene and acid
Friedel-Crafts Alkylation

This process uses an alkyl halide (Cl or Br usually) and a Lewis acid catalyst similar to a halogenation reaction. In this case we use the corresponding aluminum trihalide as the Lewis acid catalyst.
Friedel-Crafts Alkylation

The product is an alkylbenzene, i.e.

Note: there are limitations to Friedel-Crafts reactions, they can not be done on a nitrobenzene or benzenesulfonic acid as these group complex with the aluminum chloride catalyst deactivation it.
Alkylation from Alkenes

Alkylation can also be achieved by using an alkene and an acid (sulfuric as the conjugate base is a poor nucleophile), i.e.

\[
\begin{align*}
\text{H}_2\text{C=CH}_2 + \text{H}_2\text{SO}_4 &\rightarrow \text{H}_3\text{C}\text{CH}_2\text{H}_3^+ + \text{SO}_4^{2-} \\
\text{Note: this will generate the Markovnikov carbocation!}
\end{align*}
\]
Friedel-Crafts Acylation

This process is identical to an alkylation except we use an acyl chloride, i.e.

\[
\text{Cl-Al-Cl} + \text{O-C-R} \rightarrow \text{Cl-Al-Cl} + \text{R-C^+}=O
\]
Friedel-Crafts Acylation

The product is a phenyl ketone, i.e.

\[
\text{benzene} + \text{CH}_3\text{C}^+\text{O} \rightleftharpoons \text{benzyl cation} \xrightarrow{-\text{H}^+} \text{acetophenone}
\]

Note: the same limitations for nitro and sulfonic acid groups apply.
Reaction Rates

Experimentally you can observe the following relative rates of reaction:

- Phenol: 1000
- Toluene: 24.5
- Benzene: 1
- Chlorobenzene: 0.033
- Nitrobenzene: 0.0000001

What is causing these differences?
Reaction Rates

The reaction depends on the attack of an electrophile on the benzene ring, this means the charge density in the ring will be very important. Groups that increase the charge density will speed up the reaction while those that decrease charge density slow it down.
Reaction Rates

This can also be seen in the electron density of these molecules, i.e.
Directing Effects

A second experimental observation is:

\[
\text{CH}_3 \quad \text{Br}_2 \quad \text{FeBr}_3 \quad \text{CH}_3
\]

per cent yield 63% 3% 34%

\[
\text{CF}_3 \quad \text{Br}_2 \quad \text{FeBr}_3 \quad \text{CF}_3
\]

per cent yield 6% 91% 3%
Directing Effects

The directing effects are caused by the same processes that control the rate of the reaction. The table right groups substituents as o,p-directing or m-directing.

These are relative to an H atom.

Electron donating groups (EDG) activate the ring and are o,p-directing.

Electron withdrawing groups (EWG) deactivate the ring and are m-directing.

Why?

<table>
<thead>
<tr>
<th>Substituent group</th>
<th>Name of group</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{NH}_2$, $\text{NHR}$, $\text{NR}_2$</td>
<td>amino</td>
</tr>
<tr>
<td>$\text{OH}$, $\text{OCH}_3$, $\text{OR}$</td>
<td>hydroxy, alkoxy</td>
</tr>
<tr>
<td>$\text{O}$</td>
<td>acylamino</td>
</tr>
<tr>
<td>$\text{NH}-\text{R}$</td>
<td></td>
</tr>
<tr>
<td>$\text{CH}_3$, $\text{CH}_2\text{CH}_3$, $\text{R}$</td>
<td>alkyl</td>
</tr>
<tr>
<td>$\text{F}$, $\text{Cl}$, $\text{Br}$, $\text{I}$</td>
<td>halo</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Substituent group</th>
<th>Name of group</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{O}$</td>
<td>acyl, carboxy</td>
</tr>
<tr>
<td>$\text{C}=\text{R}$</td>
<td></td>
</tr>
<tr>
<td>$\text{C}=\text{OH}$</td>
<td></td>
</tr>
<tr>
<td>$\text{C}=\text{NH}_2$</td>
<td>carboxamido, carboalkoxy</td>
</tr>
<tr>
<td>$\text{C}=\text{OR}$</td>
<td></td>
</tr>
<tr>
<td>$\text{S}=\text{OH}$</td>
<td>sulfonic acid</td>
</tr>
<tr>
<td>$\text{O}$</td>
<td></td>
</tr>
<tr>
<td>$\text{C}=\text{N}$</td>
<td>cyano</td>
</tr>
<tr>
<td>$\text{N}^+$</td>
<td>nitro</td>
</tr>
</tbody>
</table>
Directing Effects

Two effects can account for these observations:

1) **Inductive effects**: this is the donation or withdrawal of electron density through the bond due to the EN of the atom.

- Alkyl groups are weakly EDG so activating
- Halides are more EN so weakly EWG and deactivating, but o,p-directing because of the lone pair electrons
- Any group where the atom attached to the ring has a formal or partial positive charge and no lone pair electrons, this includes nitro, cyano, carbonyl and alkyl halides.
2) **Resonance effects**: this is the donation or withdrawal of electrons in the $\pi$ system by resonance.

- Any group where the atom attached to the ring has a lone pair of electrons such as N and O. These are activating.
- Halides are more EN so weakly EWG and deactivating, but o,p-directing because of the lone pair electrons.
- Any group where the atom attached to the ring has a formal or partial positive charge and no lone pair electrons but attached to a more EN atom by multiple bonds, this includes nitro, cyano, sulfonyl and carbonyl groups.
Directing Effects

Examples of resonance effects:

Electron withdrawal:

Electron donation:
Directing Effects

So how does this effect a reaction?
Activating o,p-directing group, i.e. CH₃

Ortho,para attack

Meta attack
Directing Effects

So how does this effect a reaction? Activating o,p-directing group, i.e. OH
Directing Effects

So how does this effect a reaction?
Deactivating m-directing group, i.e. NO₂
Directing Effects

Besides electronic effects the size of the substituent can effect the location of a subsequent reaction. These are *steric effects*, i.e.

<table>
<thead>
<tr>
<th>Substituent</th>
<th>% ortho</th>
<th>% meta</th>
<th>% para</th>
</tr>
</thead>
<tbody>
<tr>
<td>-CH₃</td>
<td>58</td>
<td>4</td>
<td>37</td>
</tr>
<tr>
<td>-CH₂CH₃</td>
<td>49</td>
<td>6</td>
<td>49</td>
</tr>
<tr>
<td>-CH(CH₃)₂</td>
<td>30</td>
<td>8</td>
<td>62</td>
</tr>
<tr>
<td>-C(CH₃)₃</td>
<td>16</td>
<td>11</td>
<td>73</td>
</tr>
</tbody>
</table>

per cent yield for -R
Benzylic Reactions

The benzylic position has an enhanced reactivity similar to an allylic position, i.e.

As a result both benzylic cations and radicals form easily.
Benzylic Reactions

Common reactions for benzylic sites:

Radical halogenation:

\[
\text{Ph-CH}_2-\text{R} + \text{Cl}_2 \xrightarrow{\text{light or heat}} \text{Ph-CHCl-RI}
\]

Oxidation:

\[
\text{Ph-CH}_2-\text{R} + \text{KMnO}_4 \xrightarrow{\text{H}_3\text{O}^+} \text{Ph-COOH} + \text{R}(-1)\text{CO}_2\text{H}
\]
Other Functional Group Modifications

Reduction of carbonyls

\[
\text{RCO}_\text{R} \xrightarrow{\text{Zn(Hg)}} \text{R}_\text{CH}_2
\]

Reduction of nitro to amines

\[
\text{RNO}_2 \xrightarrow{\text{Sn(Hg)}} \text{RNH}_2
\]
Other Functional Group Modifications

Addition to alkenes (Markovnikov addition product)

Diazonium salts allows for a Nucleophilic attack!
Examples of Using Diazonium Salts

Controlled synthesis!

1. 

\[
\text{Br} \quad \text{NH}_2
\]

\[
\xrightarrow{\text{NaNO}_2 \quad \text{H}_2\text{SO}_4}
\]

\[
\text{Br} \quad \text{N}^+\text{N}^-
\]

\[
\xrightarrow{\text{Cu}_2\text{Br}_2}
\]

\[
\text{Br}
\]

2. 

\[
\text{Br} \quad \text{NH}_2
\]

\[
\xrightarrow{\text{NaNO}_2 \quad \text{H}_2\text{SO}_4}
\]

\[
\text{Br} \quad \text{N}^+\text{N}^-
\]

\[
\xrightarrow{\text{Cu}_2(\text{CN})_2}
\]

\[
\text{CN}
\]

3. 

\[
\text{NH}_2
\]

\[
\xrightarrow{\text{NaNO}_2 \quad \text{H}_2\text{SO}_4}
\]

\[
\text{N}^+\text{N}^-
\]

\[
\xrightarrow{\text{H}_3\text{O}^+}
\]

\[
\text{OH}
\]

4. 

\[
\text{Br} \quad \text{NH}_2
\]

\[
\xrightarrow{\text{NaNO}_2 \quad \text{H}_2\text{SO}_4}
\]

\[
\text{Br} \quad \text{N}^+\text{N}^-
\]

\[
\xrightarrow{\text{H}_3\text{PO}_2}
\]

\[
\text{H}
\]
Synthesis of Aromatic Compounds

You know what you want to make so the idea is to work backwards from the product, using well know reactions, to the starting material.

This process is known as Retrosynthesis.

This means you need to how the reactions and their directing effects, i.e.
Synthesis of Aromatic Compounds

“Direct” introduction of groups:

\[
\begin{align*}
\text{Br} & \quad \text{NO}_2 \\
\end{align*}
\]

desired product

\[
\begin{align*}
& \quad \text{Br} \\
\text{FeBr}_3 \\
\text{H}_2\text{SO}_4
\end{align*}
\]

\[
\begin{align*}
& \quad \text{NO}_2 \\
\text{Br}_2
\end{align*}
\]

\[
\begin{align*}
& \quad \text{Br} \\
\text{FeBr}_3 \\
\text{H}_2\text{SO}_4
\end{align*}
\]

\[
\begin{align*}
& \quad \text{Br} \\
\text{HNO}_3
\end{align*}
\]

\[
\begin{align*}
& \quad \text{NO}_2 \\
\text{Br}_2
\end{align*}
\]

\[
\begin{align*}
& \quad \text{Br} \\
\text{FeBr}_3
\end{align*}
\]

\[
\begin{align*}
& \quad \text{Br} \\
\text{H}_2\text{SO}_4
\end{align*}
\]
Synthesis of Aromatic Compounds

“Indirect” introduction of groups:

![Chemical reactions and structures](image)
Synthesis of Aromatic Compounds

Unusual substitution patterns:

\[
\begin{align*}
\text{desired product from} & \quad \text{desired product from} \\
\end{align*}
\]
Synthesis of Aromatic Compounds

Unusual substitution patterns:

desired product from

\[
\text{Br}
\]

\[
\text{O}
\]

\[
\text{Cl}
\]

\[
\text{O}
\]

\[
\text{Br}
\]

\[
\text{O}
\]

\[
\text{Br}
\]

desired product from

\[
\text{AlCl}_3
\]

\[
\text{FeBr}_3
\]

\[
\text{Zn} / \text{Hg}
\]

\[
\text{HCl}
\]
Polycyclic Aromatic Hydrocarbons

A number of polycyclic (multiple fused rings) hydrocarbons exist. They still obey Hückel’s rule, alternating single & double bonds etc. They also exhibit a reduced reactivity to addition / substitutions and react by EArS.

naphthalene  anthracene  phenanthrene  pyrene
Polycyclic Aromatic Hydrocarbons

Two other cases of polycyclic hydrocarbons exist, fullerenes and carbon nanotubes. These compounds have interesting properties of electrical conductance and very high strength.
Heterocyclic Aromatic Compounds

Aromatic compounds with a non-carbon (hetero) atom in the ring are possible. In many cases that atom provides a lone pair of electrons as part of the $4n + 2 \pi$ electrons in the system. Examples include:

- Furan
- Pyrrole
- Thiophene
- Pyrimidine
- Pyridine
- Imidazole
- Indole
- Purine
- Quinoline
Heterocyclic Aromatic Compounds

• The heteroatom has significant effects on the chemical reactivity.
• They are commonly used as polar aprotic (no acidic H atom) solvents.
• They are very common in biology.
• For more information see Chapter 13.