ARENES AND AROMATICITY

By

Dr. Harpreet Kaur
Asst. Prof.
PGGCG-11
Arenes and Aromaticity

- Benzene has four degrees of unsaturation, making it a highly unsaturated hydrocarbon.
- Whereas unsaturated hydrocarbons such as alkenes, alkynes and dienes readily undergo addition reactions, benzene does not.
• Benzene does react with bromine, but only in the presence of \( \text{FeBr}_3 \) (a Lewis acid), and the reaction is a substitution, not an addition.

\[
\begin{align*}
\text{C}_6\text{H}_6 & \xrightarrow{\text{Br}_2/\text{FeBr}_3} \text{C}_6\text{H}_5\text{Br} \\
\text{substitution} & \text{Br replaces H}
\end{align*}
\]

• Proposed structures of benzene must account for its high degree of unsaturation and its lack of reactivity towards electrophilic addition.

• **August Kekulé** proposed that benzene was a rapidly equilibrating mixture of two compounds, each containing a six-membered ring with three alternating \( \pi \) bonds.

• In the Kekulé description, the bond between any two carbon atoms is sometimes a single bond and sometimes a double bond.
• These structures are known as Kekulé structures.

• Although benzene is still drawn as a six-membered ring with alternating $\pi$ bonds, in reality there is no equilibrium between the two different kinds of benzene molecules.

• Current descriptions of benzene are based on resonance and electron delocalization due to orbital overlap.

• In the nineteenth century, many other compounds having properties similar to those of benzene were isolated from natural sources. Since these compounds possessed strong and characteristic odors, they were called aromatic compounds. It should be noted, however, that it is their chemical properties, and not their odor, that make them special.
Any structure for benzene must account for the following facts:

1. It contains a six-membered ring and three additional degrees of unsaturation.
2. It is planar.
3. All C—C bond lengths are equal.

The Kekulé structures satisfy the first two criteria but not the third, because having three alternating \( \pi \) bonds means that benzene should have three short double bonds alternating with three longer single bonds.
• The resonance description of benzene consists of two equivalent Lewis structures, each with three double bonds that alternate with three single bonds.
• The true structure of benzene is a resonance hybrid of the two Lewis structures, with the dashed lines of the hybrid indicating the position of the $\pi$ bonds.
• We will use one of the two Lewis structures and not the hybrid in drawing benzene. This will make it easier to keep track of the electron pairs in the $\pi$ bonds (the $\pi$ electrons).
• Because each $\pi$ bond has two electrons, benzene has six $\pi$ electrons.

Some texts draw benzene as a hexagon with an inner circle:

The circle represents the $\textbf{six } \pi \textbf{ electrons}$, distributed over the six atoms of the ring.
In benzene, the actual bond length (1.39 Å) is intermediate between the carbon—carbon single bond (1.53 Å) and the carbon—carbon double bond (1.34 Å).

The C–C bonds in benzene are equal and intermediate in length.

Benzene—A planar molecule with $sp^2$ hybridization and $p$ orbitals.
• A benzene substituent is called a **phenyl group**, and it can be abbreviated in a structure as “**Ph-**”.

![Ph-](image)

**phenyl group**

\[ C_6H_5^- \]

• A phenyl group \((C_6H_5^-)\) is formed by removing one hydrogen from benzene \((C_6H_6)\).

• Therefore, benzene can be represented as **PhH**, and phenol would be **PhOH**.

![Chemical structures](image)

benzene  \(=\)  PhH  \(=\)  phenol  \(=\)  PhOH
• The **benzyl group**, another common substituent that contains a benzene ring, differs from a phenyl group.

\[
\text{benzyl group} \quad \text{C}_6\text{H}_5\text{CH}_2^-
\]

\[
\text{phenyl group} \quad \text{C}_6\text{H}_5^-
\]

• Substituents derived from other substituted aromatic rings are collectively known as **aryl groups**.

\[
\text{Examples of aryl groups}
\]

\[
\text{CH}_3
\]

\[
\text{CH}_3\text{Br}
\]
[3] A molecule must be completely conjugated. Aromatic compounds must have a \( p \) orbital on every atom.

\[
\begin{align*}
\text{A completely conjugated ring} & \quad \text{These rings are not completely conjugated.} \\
\text{benzene} & \quad \text{1,3-cyclohexadiene} \\
a \( p \) orbital on every \( C \) aromatic & \quad \text{not aromatic} \\
\end{align*}
\]

\[
\begin{align*}
\text{no } p \text{ orbitals} & \quad \text{no } p \text{ orbital} \\
\text{not aromatic} & \quad \text{not aromatic}
\end{align*}
\]
A molecule must satisfy Hückel’s rule, and contain a particular number of \( \pi \) electrons.

**Hückel's rule:**

- An aromatic compound must contain \( 4n + 2 \) \( \pi \) electrons (\( n = 0, 1, 2, \) and so forth).
- Cyclic, planar, and completely conjugated compounds that contain \( 4n \) \( \pi \) electrons are especially unstable, and are said to be antiaromatic.

Benzene is aromatic and especially stable because it contains 6 \( \pi \) electrons. Cyclobutadiene is antiaromatic and especially unstable because it contains 4 \( \pi \) electrons.
Note that Hückel’s rule refers to the number of $\pi$ electrons, not the number of atoms in a particular ring.

<table>
<thead>
<tr>
<th>$n$</th>
<th>$4n + 2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>4, etc.</td>
<td>18</td>
</tr>
</tbody>
</table>
Considering aromaticity, a compound can be classified in one of three ways:

1. Aromatic—A cyclic, planar, completely conjugated compound with $4n + 2\pi$ electrons.
2. Antiaromatic—A cyclic, planar, completely conjugated compound with $4n\pi$ electrons.
3. Not aromatic (nonaromatic)—A compound that lacks one (or more) of the following requirements for aromaticity: being cyclic, planar, and completely conjugated.
Note the relationship between each compound type and a similar open-chained molecule having the same number of $\pi$ electrons.

- An aromatic compound is *more* stable than a similar acyclic compound having the same number of $\pi$ electrons. Benzene is more stable than 1,3,5-hexatriene.

- An antiaromatic compound is *less* stable than an acyclic compound having the same number of $\pi$ electrons. Cyclobutadiene is less stable than 1,3-butadiene.

- A compound that is not aromatic is *similar* in stability to an acyclic compound having the same number of $\pi$ electrons. 1,3-Cyclohexadiene is similar in stability to cis,cis-2,4-hexadiene, so it is not aromatic.
Examples of Aromatic Rings

• Completely conjugated rings larger than benzene are also aromatic if they are planar and have $4n + 2 \pi$ electrons.

• Hydrocarbons containing a single ring with alternating double and single bonds are called annulenes.

• To name an annulene, indicate the number of atoms in the ring in brackets and add the word annulene.

\[ [14]-\text{annulene} \quad 4n + 2 = 4(3) + 2 = 14 \ \pi \text{ electrons} \quad \text{aromatic} \]

\[ [18]-\text{annulene} \quad 4n + 2 = 4(4) + 2 = 18 \ \pi \text{ electrons} \quad \text{aromatic} \]
• **[10]-Annulene** has 10 $\pi$ electrons, which satisfies Hückel's rule, but a planar molecule would place the two H atoms inside the ring too close to each other. Thus, the ring puckers to relieve this strain.

• Since [10]-annulene is not planar, the 10 $\pi$ electrons can’t delocalize over the entire ring and it is not aromatic.
Electrophilic Aromatic Substitution

Ar-H = aromatic compound

1. Nitration

\[
\text{Ar-H} + \text{HNO}_3, \text{H}_2\text{SO}_4 \rightarrow \text{Ar-NO}_2 + \text{H}_2\text{O}
\]

2. Sulfonation

\[
\text{Ar-H} + \text{H}_2\text{SO}_4, \text{SO}_3 \rightarrow \text{Ar-SO}_3\text{H} + \text{H}_2\text{O}
\]

3. Halogenation

\[
\text{Ar-H} + \text{X}_2, \text{Fe} \rightarrow \text{Ar-X} + \text{HX}
\]

4. Friedel-Crafts alkylation

\[
\text{Ar-H} + \text{R-X}, \text{AlCl}_3 \rightarrow \text{Ar-R} + \text{HX}
\]
Friedel-Crafts alkylation (variations)

a) $\text{Ar-H} + \text{R-X, AlCl}_3 \rightarrow \text{Ar-R} + \text{HX}$

b) $\text{Ar-H} + \text{R-OH, H}^+ \rightarrow \text{Ar-R} + \text{H}_2\text{O}$

c) $\text{Ar-H} + \text{Alkene, H}^+ \rightarrow \text{Ar-R}$
toluene

faster than the same reactions with benzene
nitrobenzene

slower than the same reactions with benzene
Substituent groups on a benzene ring affect electrophilic aromatic substitution reactions in two ways:

1) **reactivity**
   
   activate (faster than benzene)
   
   or deactivate (slower than benzene)

2) **orientation**

   *ortho* - + *para* - direction
   
   or *meta* - direction
-CH$_3$

activates the benzene ring towards EAS
directs substitution to the ortho- & para- positions

-NO$_2$

deaactivates the benzene ring towards EAS
directs substitution to the meta- position
Common substituent groups and their effect on EAS:

- $\text{NH}_2$, $\text{-NHR}$, $\text{-NR}_2$
- $\text{OH}$
- $\text{OR}$
- $\text{NHCOCCH}_3$
- $\text{C}_6\text{H}_5$
- $\text{R}$
- $\text{H}$
- $\text{X}$

$\text{CHO}$, $\text{-COR}$
$\text{-SO}_3\text{H}$
$\text{-COOH}$, $\text{-COOR}$
$\text{-CN}$
$\text{-NR}_3^+$
$\text{-NO}_2$

$\text{ortho/para directors}$

$\text{meta directors}$
If there is more than one group on the benzene ring:

1. The group that is more activating (higher on “the list”) will direct the next substitution.

2. You will get little or no substitution between groups that are *meta*- to each other.
CH₃
OH

Br₂, Fe

CH₃
OH

NHCOCH₃

HNO₃, H₂SO₄

CH₃

NHCOCH₃

CHO

OCH₃

Cl₂, Fe

CHO
OCH₃

Cl

CHO
OCH₃

CHO
OCH₃

CHO
OCH₃
**Orientation and synthesis.** Order is important!

synthesis of \( m \)-bromonitrobenzene from benzene:

\[
\text{H}_2\text{SO}_4 \quad \text{HNO}_3 \quad \text{Br}_2, \text{Fe} \quad \text{NO}_2
\]

synthesis of \( p \)-bromonitrobenzene from benzene:

\[
\text{Br}_2, \text{Fe} \quad \text{Br} \quad \text{HNO}_3 \quad \text{H}_2\text{SO}_4 \quad \text{Br} \quad + \quad \text{Br} \quad \text{NO}_2
\]

You may assume that you can separate a pure \textit{para}-isomer from an \textit{ortho-}/\textit{para}- mixture.
note: the assumption that you can separate a pure para isomer from an ortho/para mixture does not apply to any other mixtures.

synthesis of 1,4-dibromo-2-nitrobenzene from benzene

separate pure para isomer from ortho/para mixture

cannot assume that these can be separated!
synthesis of benzoic acids by oxidation of –CH₃
nitration

\[
\begin{align*}
\text{HO-NO}_2 & \quad + \quad \text{H}_2\text{SO}_4 \quad \Leftrightarrow \quad \text{H}_2\text{O-NO}_2 \quad + \quad \text{HSO}_4^- \\
\text{H}_2\text{O-NO}_2 & \quad \Leftrightarrow \quad \text{H}_2\text{O} \quad + \quad \text{NO}_2 \\
\text{H}_2\text{SO}_4 & \quad + \quad \text{H}_2\text{O} \quad \Leftrightarrow \quad \text{HSO}_4^- \quad + \quad \text{H}_3\text{O}^+ \\
\text{HNO}_3 & \quad + \quad 2 \quad \text{H}_2\text{SO}_4 \quad \Leftrightarrow \quad \text{H}_3\text{O}^+ \quad + \quad 2 \quad \text{HSO}_4^- \quad + \quad \text{NO}_2^+ 
\end{align*}
\]
nitration:

1) \[ \text{HONO}_2 + 2 \text{H}_2\text{SO}_4 \rightleftharpoons \text{H}_3\text{O}^+ + 2 \text{HSO}_4^- + \text{NO}_2^+ \]

2) \[ \text{R} + \text{NO}_2^+ \xrightarrow{\text{RDS}} \text{RNO}_2 \]

electrophile
resonance

[Chemical structure diagram]

34
Mechanism for nitration:

1) \[ \text{HONO}_2 + 2 \text{H}_2\text{SO}_4 \xleftrightarrow{} \text{H}_3\text{O}^+ + 2 \text{HSO}_4^- + \text{NO}_2^+ \]

2) \[
\begin{array}{c}
\text{C}_{6}\text{H}_5^+ \\
\text{H}
\end{array}
+ \text{NO}_2^+ \xrightarrow{\text{RDS}}
\begin{array}{c}
\text{C}_{6}\text{H}_5^+ \\
\text{NO}_2 \text{H}
\end{array}
\]

3) \[
\begin{array}{c}
\text{C}_{6}\text{H}_5^+ \\
\text{H}
\end{array}
+ \text{H}_2\text{SO}_4 \xrightarrow{}\]
\[
\begin{array}{c}
\text{C}_{6}\text{H}_5^+ \\
\text{NO}_2 \\
\text{H}
\end{array}
\]

\[+ \text{H}^+ \]
Mechanism for sulfonation:

1) \[ 2 \text{H}_2\text{SO}_4 \rightleftharpoons \text{H}_3\text{O}^+ + \text{HSO}_4^- + \text{SO}_3 \]

2) \[
\begin{array}{c}
\text{C}_6\text{H}_5^+ + \text{SO}_3^- \\
\xrightarrow{\text{RDS}} \\
\text{C}_6\text{H}_5\text{SO}_3^- \\
\end{array}
\]

3) \[
\begin{array}{c}
\text{C}_6\text{H}_5^+ + \text{SO}_3^- \\
\xrightarrow{} \\
\text{C}_6\text{H}_5\text{SO}_3^- + \text{H}^+ \\
\end{array}
\]

4) \[
\begin{array}{c}
\text{C}_6\text{H}_5\text{SO}_3^- + \text{H}_3\text{O}^+ \\
\xleftarrow{} \\
\text{C}_6\text{H}_5\text{SO}_3\text{H} + \text{H}_2\text{O} \\
\end{array}
\]
Mechanism for halogenation:

1) \( \text{Cl}_2 + \text{AlCl}_3 \rightleftharpoons \text{Cl-Cl-AlCl}_3 \)

2) \( \text{C}_{6}\text{H}_{5} + \text{Cl-Cl-AlCl}_3 \xrightarrow{\text{RDS}} \text{C}_{6}\text{H}_{4}^{+} \text{Cl}^{-} + \text{AlCl}_4^{-} \)

3) \( \text{C}_{6}\text{H}_{4}^{+} \text{Cl}^{-} + \text{AlCl}_4^{-} \rightarrow \text{C}_{6}\text{H}_{5} \text{Cl} + \text{HCl} + \text{AlCl}_3 \)
Mechanism for Friedel-Crafts alkylation:

1) \[ R-X + FeX_3 \rightleftharpoons R^+ + FeX_4^- \]

2) \[
\begin{array}{c}
\text{苯} + R^+ \xrightleftharpoons[\text{RDS}]{ \text{苯} R^+} \text{苯} R^+ \text{H} \\
\end{array}
\]

3) \[
\begin{array}{c}
\text{苯} R^+ \text{H} + FeX_4^- \rightarrow \text{苯} R + HX + FeX_3 \\
\end{array}
\]
Mechanism for Friedel-Crafts with an alcohol & acid

1) \[ R-\text{OH} + H^+ \rightleftharpoons ROH_2^+ \]

2) \[ ROH_2^+ \rightleftharpoons R^+ + H_2O \]

3) [Diagram of reaction]

4) [Diagram of reaction]
Mechanism for Friedel-Crafts with alkene & acid:

1) \[ \text{C}=\text{C}^- + \text{H}^+ \rightarrow \text{R}^+ \]

2) \[ \text{R} + \text{R}^+ \rightarrow \text{R}^+ \text{R} \]

3) \[ \text{R}^+ \text{R} \rightarrow \text{R}^- + \text{H}^+ \]

electrophile in Friedel-Crafts alkylation = carbocation
Electrophilic Aromatic Substitution mechanism:

1) \[ \text{Ar} + Y^+Z^- \xrightarrow{\text{RDS}} \text{Ar}Y^+ + Z^- \]

2) \[ \text{Ar}Y^+ + Z^- \xrightarrow{} \text{Ar}Y + HZ \]
Substituent groups on a benzene ring affect the reactivity and orientation in the way they do?

→ electronic effects, “pushing” or “pulling” electrons by the substituent.

Electrons can be donated (“pushed”) or withdrawn (“pulled”) by atoms or groups of atoms via:

**Induction** – due to differences in electronegativities

**Resonance** – delocalization via resonance
unshared pair of electrons on the nitrogen resonance **donating groups**
(weaker inductive withdrawal)

strong **inductive withdrawal**
(no unshared pair of electrons on the nitrogen & no resonance possible)
resonance donation
(weaker inductive withdrawal)

resonance donation
(weaker inductive withdrawal)

resonance donation
(weaker inductive withdrawal)
resonance donation

inductive donation
sp3 sp2 ring carbon

inductive withdrawal
resonance withdrawal and inductive withdrawal
resonance and inductive withdrawal

resonance and inductive withdrawal
Common substituent groups and their effect on reactivity in EAS:

- NH$_2$, -NHR, -NR$_2$
- OH
- OR
- NHCOCH$_3$
- C$_6$H$_5$
- R
- H
- X
- CHO, -COR
- SO$_3$H
- COOH, -COOR
- CN
- NR$_3^+$
- NO$_2$
Electron donating groups activate the benzene ring to electrophilic aromatic substitution.

1. electron donating groups increase the electron density in the ring and make it more reactive with electrophiles.

2. electron donation stabilizes the intermediate carbocation, lowers the E\text{act} and increases the rate.
Electron withdrawing groups deactivate the benzene ring to electrophilic aromatic substitution.

1. Electron withdrawing groups decrease the electron density in the ring and make it less reactive with electrophiles.

2. Electron withdrawal destabilizes the intermediate carbocation, raising the $E_{act}$ and slowing the rate.
electron withdrawing = deactivating & \emph{meta}-director

electron withdrawing = deactivating & \emph{meta}-director

electron donating = activating & \emph{ortho-}/\emph{para}-director
\[
\begin{align*}
\text{Cyclohexane} & \xrightarrow{\text{Br}_2, \text{Fe}} \text{Cyclohexane-Br} + \text{ortho-} \\
\text{Cyclohexane-NO}_2 & \xrightarrow{\text{Br}_2, \text{Fe}} \text{Cyclohexane-NO}_2 + \text{ortho-} \\
\text{Cyclohexane-\text{COO}} & \xrightarrow{\text{Br}_2, \text{Fe}} \text{Cyclohexane-\text{COO}} + \text{ortho-}
\end{align*}
\]
ortho-attack

meta-attack

para-attack
If G is an electron donating group, these structures are especially stable.
ortho-attack

meta-attack

para-attack
Electron donating groups stabilize the intermediate carbocations for ortho- and para- in EAS more than for meta-. The Eact’s for ortho-/para- are lower and the rates are faster.

**Electron donating groups direct ortho-/para- in EAS**
If G is an electron withdrawing group, these structures are especially unstable.
Electron withdrawing groups destabilize the intermediate carbocations for ortho- and para- in EAS more than for meta-. The Eact’s for ortho-/para- are higher and the rates are slower.

Electron withdrawing groups direct meta- in EAS
Halogens are electron withdrawing but are ortho/para directing in EAS.

The halogen atom is unusual in that it is highly electronegative but also has unshared pairs of electrons that can be resonance donated to the carbocation.
halogens are deactivating in EAS but direct ortho and para
Common substituent groups and their effect on EAS:

- NH₂, -NHR, -NR₂
- OH
- OR
- NHCOCCH₃
- C₆H₅
- R
- H
- X

ortho/para directors

CHO, COR
SO₃H
COOH, COOR
CN
NR₃⁺
NO₂

meta directors
**Arenes:**

compounds containing both aliphatic and aromatic parts.

Alkylbenzenes

Alkenylbenzenes

Alkynylbenzenes

Etc.

Emphasis on the effect that one part has on the chemistry of the other half.

**Reactivity & orientation**
Example: ethylbenzene

EAS in the aromatic part

-CH₂CH₃ activates and directs ortho- & para-

Free radical halogenation in the side chain

-C₆H₅ activates and directs benzyl
Alkylbenzenes, nomenclature:

Special names

toluene  
o-xylene  
m-xylene  
p-xylene
others named as “alkylbenzenes”:

- Isopropylbenzene
- n-Propylbenzene
- Isobutylbenzene
- o-Diethylbenzene
- n-Butylbenzene
Use of phenyl

$C_6H_5^- = \text{“phenyl”}$

2-methyl-3-phenylheptane

1,2-diphenylethane

do not confuse phenyl ($C_6H_5^-$) with benzyl ($C_6H_5CH_2^-$)
Alkenylbenzenes, nomenclature:

Special name

![Chemical structure of styrene]

Rest are named as substituted alkenes

![Chemical structures of 3-phenylpropene and (Z)-1-phenyl-1-butene]

3-phenylpropene (allylbenzene)  (Z)-1-phenyl-1-butene
Alkynylbenzenes, nomenclature:

phenylacetylene
phenylethyne

5-phenyl-2-hexyne
Alcohols, etc., nomenclature:

\[
\begin{align*}
\text{H}_3\text{C} \cdot \text{CH} \cdot \text{OH} & & \text{benzyl alcohol} \\
1\text{-phenylethanol} & & \text{benzyl alcohol} \\
\alpha \text{– phenylethyl alcohol} & & \\
\text{CH}_2\text{CH}_2\text{Cl} & & \text{cyclohexylbenzene} \\
1\text{-chloro-2-phenylethane} & & \text{phenylcyclohexane} \\
\beta \text{– phenylethyl chloride} & & \\
\end{align*}
\]
Alkylbenzenes, syntheses:

1. Friedel-Crafts alkylation

2. Modification of a side chain:
   a) addition of hydrogen to an alkene
   b) reduction of an alkylhalide
      i) hydrolysis of Grignard reagent
      ii) active metal and acid
   c) Corey-House synthesis
Modification of side chain:

\[
\text{Br} + \text{H}_2, \text{Ni} \quad \text{Br} + \text{Sn, HCl} \quad \text{Br} + \text{Mg; then H}_2\text{O}
\]

\rightarrow \text{ethylbenzene}
Friedel-Crafts:

\[
\text{Ar-H} + \text{R-X, AlCl}_3 \rightarrow \text{Ar-R} + \text{HX}
\]

\[
\text{Ar-H} + \text{R-OH, H}^+ \rightarrow \text{Ar-R} + \text{H}_2\text{O}
\]

\[
\text{Ar-H} + \text{alkene, H}^+ \rightarrow \text{Ar-R}
\]
\[
\text{C}_6\text{H}_6 + \text{CH}_2=\text{CHCH}_3, \text{H}^+ \rightarrow \text{C}_6\text{H}_5\text{CH}_3 \quad \text{isopropylbenzene}
\]

\[
\text{C}_6\text{H}_6 + \text{CH}_3\text{CH}_2\text{OH}, \text{H}^+ \rightarrow \text{C}_6\text{H}_5\text{CH}_2\text{CH}_3 \quad \text{ethylbenzene}
\]

\[
\text{CH}_3 \quad + \quad \text{CH}_3\text{C}-\text{C}-\text{CH}_3 \quad \text{Br} \quad \text{AlCl}_3 \quad \rightarrow \quad \text{C}_6\text{H}_5\text{CH}_3 \quad \text{H}_3\text{C}-\text{C}-\text{CH}_3 \quad \text{p-tert-butyltoluene}
\]
Cyclohexane + 1-Cyclohexene $\xrightarrow{H^+} \text{cyclohexylbenzene}$

H$_3$C + 1-CH$_2$Cl $\xrightarrow{\text{AlCl}_3} \text{p-benzyltoluene}$

2 Benzene + CH$_2$Cl$_2$, AlCl$_3$ $\xrightarrow{} \text{diphenylmethane}$
Friedel-Crafts limitations:

a) Polyalkylation

b) Possible rearrangement

c) R-X cannot be Ar-X

d) NR when the benzene ring is less reactive than bromobenzene

e) NR with -NH$_2$, -NHR, -NR$_2$ groups
The alkyl group activates the ring making the products more reactive that the reactants leading to polyalkylation. Use of excess aromatic compound minimizes polyalkylation in the lab.
The electrophile in Friedel Crafts alkylation is a carbocation:

\[
R-X + AlX_3 \rightarrow R^+
\]

\[
R-OH + H^+ \rightarrow R^+
\]

\[
\text{— C = C —} + H^+ \rightarrow R^+
\]

Carbocations can rearrange! 😞
rearrangement

\[
\begin{align*}
\text{C}_6\text{H}_6 & + \text{CH}_3\text{CH}_2\text{CH}_2\text{-Br, AlCl}_3 \\
& \rightarrow \text{isopropylbenzene}
\end{align*}
\]

\[
\begin{align*}
\text{C}_6\text{H}_6 & + \text{CH}_3\text{CHCH}_2\text{-Br, AlCl}_3 \\
& \rightarrow \text{tert-butylbenzene}
\end{align*}
\]

\[
\begin{align*}
\text{C}_6\text{H}_6 & + \text{CH}_3\text{CCH}_2\text{-OH} \quad \text{H}^+ \\
& \rightarrow \text{2-methyl-2-phenylbutane}
\end{align*}
\]

carbocation rearrangements are possible!
$n$-alkylbenzenes cannot be made by Friedel-Crafts alkylation due to carbocation rearrangements
R-X cannot be Ar-X

The Ar-X bond is strong and does not break like the R-X bond!
NR with rings less reactive than bromobenzene

\[
\text{Br} + \text{CH}_3\text{CH}_2\text{-Br, AlCl}_3 \rightarrow \text{Br} + \text{CH}_2\text{CH}_3
\]

\[
\text{COOH} + \text{CH}_3\text{-Br, AlCl}_3 \rightarrow \text{NR} -\text{CHO, -COR}
\]

\[
\text{NO}_2 + \text{CH}_3\text{CH}_2\text{-OH, H}^+ \rightarrow \text{NR} -\text{SO}_3\text{H}
\]

\[
\text{NO}_2 + \text{CH}_3\text{CH}_2\text{-OH, H}^+ \rightarrow \text{NR} -\text{COOH, -COOR}
\]

\[
\text{NO}_2 + \text{CH}_3\text{CH}_2\text{-OH, H}^+ \rightarrow \text{NR} -\text{CN}
\]

\[
\text{NO}_2 + \text{CH}_3\text{CH}_2\text{-OH, H}^+ \rightarrow \text{NR}_3^+ -\text{NO}_2
\]
NR with $-\text{NH}_2$, $-\text{NHR}$, $-\text{NR}_2$

\[
\text{NH}_2 + \text{CH}_3\text{CH}_2\text{-Cl, AlCl}_3 \rightarrow \text{NR}
\]

\[
\text{NH}_2 + \text{AlCl}_3 \rightarrow \text{AlCl}_3\text{NH}_2^+
\]

Lewis base  Lewis acid  deactivated to EAS
Friedel-Crafts limitations:

a) Polyalkylation

b) Possible rearrangement

c) R-X cannot be Ar-X

d) NR when the benzene ring is less reactive than bromobenzene

e) NR with -NH₂, -NHR, -NR₂ groups

In syntheses it is often best to do Friedel-Crafts alkylation in the first step!
Alkylbenzenes, reactions:

1. Reduction

2. Oxidation

3. EAS
   a) nitration
   b) sulfonation
   c) halogenation
   d) Friedel-Crafts alkylation

4. Side chain
   free radical halogenation
Alkylbenezenes, reduction:

\[
\begin{array}{ccc}
\text{CH}_3\text{CH}_3 & \text{NR} & \text{NR} \\
\text{NR} & \text{NR} & \text{NR} \\
\text{NR} & \text{NR} & \text{NR} \\
\end{array}
\]

\(\text{H}_2, \text{Ni}\)

\(300^{\circ}\text{C}, 100 \text{ atm.}\)
**Alkylbenezenes, oxidation:**

<table>
<thead>
<tr>
<th></th>
<th>CH$_3$CH$_3$</th>
<th>O</th>
<th>benzyl</th>
<th>COOH</th>
</tr>
</thead>
<tbody>
<tr>
<td>KMnO$_4$</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>KMnO$_4$</td>
<td>NR</td>
<td>NR</td>
<td></td>
<td>COOH</td>
</tr>
<tr>
<td>heat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
\[ \text{phenylpropane} + \text{KMnO}_4, \text{heat} \rightarrow \text{product} \]

\[ \text{phenylbutane} + \text{KMnO}_4, \text{heat} \rightarrow \text{product} + 2 \text{CO}_2 \]
Oxidation of alkylbenzenes.

1) Syn

2) identification

C₈H₁₀:

- BP 136°C
- BP 144°C
- BP 139°C
- BP 138°C

C₈H₁₀ COOH

- MP 122°C
- MP 231°C
- MP 348°C
- MP 300°C
Alkylbenzenes, EAS

-R is electron releasing.
Activates to EAS and directs ortho/para
Alkylbenzenes, free radical halogenation in side chain:

benzyl free radical

\[
\text{C}_6\text{H}_5\text{C}_2\text{H}_3 + \text{Cl}_2, \text{heat} \rightarrow \text{C}_6\text{H}_5\text{CHCH}_3 + \text{C}_6\text{H}_5\text{C}_2\text{CH}_2\text{Cl} \quad 91\%
\]

\[
\text{C}_6\text{H}_5\text{C}_2\text{H}_3 + \text{Br}_2, \text{heat} \rightarrow \text{C}_6\text{H}_5\text{CHCH}_3 + \quad \text{only}
\]
$X_2 \rightarrow 2 X \cdot$

$\text{-CH}_2\text{CH}_3 + X \cdot \rightarrow \text{-CHCH}_3$

benzyl free radical $> 3^o > 2^o > 1^o > \text{CH}_3$
Alkenylbenzenes, syntheses:

1. Modification of side chain:
   a) dehydrohalogenation of alkyl halide
   b) dehydration of alcohol
   c) dehalogenation of vicinal dihalide
   d) reduction of alkyne

(2. Friedel-Crafts alkylation)
Alkenylbenzenes, synthesis modification of side chain

\[
\begin{align*}
& \text{KOH(alc)} \\
& \text{H}^+, \text{heat} \\
& \text{Zn} \\
& \text{H}_2, \text{Pd-C}
\end{align*}
\]
Alkenylbenzenes, synthesis Friedel-Crafts alkylation

not normally used for alkenylbenzenes.

an exception:

\[ \text{Alkenylbenzene} + \text{CH}_2=\text{CH-Br, AlCl}_3 \rightarrow \text{NR} \]

\[ \text{Alkenylbenzene} + \text{CH}_2=\text{CHCH}_2-\text{Br, AlCl}_3 \rightarrow \text{Allylbenzene} \]
Bromine (Br) reacts with KOH (alcohol) to produce a conjugated compound with the ring.

Additionally, an alkene reacts with KOH in the presence of heat to form a conjugated compound with the ring.
Alkenylbenzenes, reactions:

1. Reduction
2. Oxidation
3. EAS
4. Side chain
   a) add’n of H$_2$
   b) add’n of X$_2$
   c) add’n of HX
   d) add’n of H$_2$SO$_4$
   e) add’n of H$_2$O
   f) add’n of X$_2$ & H$_2$O
   g) dimerization
   h) alkylation
   i) dimerization
   j) oxymercurcation
   k) hydroboration
   l) addition of free rad.
   m) add’n of carbenes
   n) epoxidation
   o) hydroxylation
   p) allylic halogenation
   q) ozonolysis
   r) vigorous oxidation
Alkenylbenzenes, reactions: reduction

\[
\text{C}_8\text{H}_8\text{C}=\text{C}_2\text{H}_2 + \text{H}_2, \text{Ni} \rightarrow \text{C}_8\text{H}_{10}\text{CH}_2\text{CH}_3
\]

\[
\text{C}_8\text{H}_8\text{C}=\text{C}_2\text{H}_2 + \text{H}_2, \text{Ni, 250}^\circ\text{C, 1,500 psi} \rightarrow \text{CH}_2\text{CH}_3\text{C}_8\text{H}_8\text{CH}_2\text{H}
\]
Alkenylbenzenes, reactions oxidation

\[
\text{CH} = \text{CH}_2 \quad \xrightarrow{\text{KMnO}_4} \quad \text{CHCH}_2\text{OH} \quad \text{OH} \quad \text{O} \\ \text{CH} = \text{CH}_2 \quad \xrightarrow{\text{KMnO}_4 \text{, heat}} \quad \text{COOH} \quad + \quad \text{CO}_2 \\ \text{CH} = \text{CH}_2 \quad \xrightarrow{1. \text{O}_3} \quad \xrightarrow{2. \text{Zn, H}_2\text{O}} \quad \text{CH}=\text{O} \quad + \quad \text{O}=\text{CH}_2
\]
Alkenylbenzenes, reactions EAS?

**Electrophilic addition**

\[ \text{C}_8\text{H}_8\text{CH} = \text{CH}_2 \]

**Electrophilic aromatic substitution**

Alkenes are more reactive with electrophiles than aromatic rings!

\[ \text{C}_8\text{H}_8\text{CH} = \text{CH}_2 + \text{Br}_2, \text{Fe} \rightarrow \text{C}_8\text{H}_8\text{CHCH}_2\text{Br} \text{ Br} \]
In syntheses of alkenylbenzenes, the carbon-carbon double bond must be synthesized after any EAS reactions.
Alkenylbenzenes, reactions Side chain:

\[
\begin{align*}
\text{CH} & \equiv \text{CHCH}_3 & \text{H}_2, \text{Ni} & \rightarrow & \text{CH}_2\text{CH}_2\text{CH}_3 \\
\text{Br}_2, \text{CCl}_4 & \rightarrow & \text{CHCHCH}_3 & \text{Br} \\
\text{HBr} & \rightarrow & \text{CHCH}_2\text{CH}_3 & \text{Br} \\
\text{H}_2\text{SO}_4 & \rightarrow & \text{CHCH}_2\text{CH}_3 & \text{OSO}_3\text{H}
\end{align*}
\]
Benzyl carbocation

\[
\text{benzene} - \text{CH}=\text{CHCH}_3 + \text{H}^+ \rightarrow \text{benzene}^+\text{CHCH}_2\text{CH}_3
\]

resonance stabilization of benzyl carbocation \( > 3^\circ > 2^\circ > 1^\circ \)
C\(\text{H}_2\text{CHCH}_3\) \(\xrightarrow{\text{HBr, perox.}}\) C\(\text{H}_2\text{CHCH}_3\) \(\text{Br}\)

C\(\text{H}=\text{CH}_2\) \(\xrightarrow{\text{polymer.}}\) \((\text{CHCH}_2)^n\) \text{polystyrene}

C\(\text{H}=\text{CHCH}_3\) \(\xrightarrow{\text{CH}_2\text{N}_2, \text{hv}}\) C\(\text{H}\text{CHC}\text{H}_3\)

C\(\text{H}=\text{CHCH}_3\) \(\xrightarrow{\text{PBA}}\) C\(\text{H}\text{CHC}\text{H}_2\text{O}\)

105
100 syn-oxidation; make a model!
Alkynylbenzenes, syntheses:

Dehydrohalogenation of vicinal dihalides

1. KOH
2. NaNH₂
Alkynylbenzenes, reactions:

1. Reduction

2. Oxidation

3. EAS

4. Side chain

   a) reduction                     e) as acids
   b) add’n of \( \text{X}_2 \)       f) with \( \text{Ag}^+ \)
   c) add’n of \( \text{HX} \)             g) oxidation
   d) add’n of \( \text{H}_2\text{O}, \text{H}^+ \)
Alkynylbenzenes, reactions: reduction

\[
\begin{align*}
\text{C} & \equiv \text{C} - \text{CH}_3 \\
+ & \quad 2 \text{H}_2, \text{Ni} \quad \rightarrow \\
\text{C} & \equiv \text{C} - \text{CH}_3 \\
+ & \quad (\text{xs}) \text{H}_2, \text{Ni} \\
& \quad \text{heat & pressure} \quad \rightarrow \\
\text{C} & \equiv \text{C} - \text{CH}_3 \\
+ & \quad \text{Li, NH}_3 \quad \rightarrow \\
\text{C} & \equiv \text{C} - \text{CH}_3 \\
+ & \quad \text{H}_2, \text{Pd-C} \quad \rightarrow
\end{align*}
\]
Alkynylbenzenes, reactions: oxidation

O\textsubscript{3}; then Zn, H\textsubscript{2}O

KMnO\textsubscript{4}

KMnO\textsubscript{4}, heat

C≡C–CH\textsubscript{3} → COOH + HOOCCH\textsubscript{3}
Alkynylbenzenes, reactions EAS?

\[
\begin{align*}
\text{electrophilic addition} & \\
& \xrightarrow{\text{EAS}} \\
& \text{electrophilic aromatic substitution}
\end{align*}
\]

alkynes are more reactive with electrophiles than aromatic rings!

\[
\begin{align*}
\text{C} & + \text{Br}_2, \text{Fe} \\
\xrightarrow{\text{EAS}} \\
& \rightarrow \text{Br}
\end{align*}
\]
Alkynylbenzenes, reactions: side chain:

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

\[
\text{2 Br}_2 \quad \text{Br Br}
\]

\[
\text{HBr} \quad \text{Br}
\]

\[
\text{2 HBr} \quad \text{Br}
\]
$\text{C} = \text{CCH}_3$ → $\text{H}_2\text{O}, \text{H}^+$ → $\text{CCH}_3$

$\text{C} = \text{CCH}_3$ → $\text{Na}$ → $\text{C} = \text{C}^-\text{Na}^+$

$\text{C} = \text{CCH}_3$ → $\text{Ag}^+$ → $\text{C} = \text{C}^-\text{Ag}^+$

$\text{C} = \text{C}\text{CH}_3$ → $\text{Ag}^+$ → NR, not terminal
THANK YOU