Chapter 16
The Chemistry of Benzene Derivatives

Marc Loudon

Eric J. Kantorowski
California Polytechnic State University
San Luis Obispo, CA
Chapter 16 Overview

• 16.1 Nomenclature of Benzene Derivatives
• 16.2 Physical Properties of Benzene Derivatives
• 16.3 Spectroscopy of Benzene Derivatives
• 16.4 Electrophilic Aromatic Substitution Reactions of Benzene
• 16.5 Electrophilic Aromatic Substitution Reactions of Substituted Benzenes
• 16.6 Hydrogenation of Benzene Derivatives
• 16.7 Source and Industrial Use of Aromatic Hydrocarbons
Nomenclature

• Substitutive nomenclature

\[
\begin{align*}
\text{chloro} & \text{benzene} & \text{nitro} & \text{benzene} & \text{ethyl} & \text{benzene} \\
\end{align*}
\]

• Note the resonance hybrids for the \(-\text{NO}_2\) group

\[
\begin{align*}
\text{R} & - \text{N} & \overset{\ddots}{\text{O}} & - & \overset{\ddots}{\text{O}} & - \\
\text{R} & - \text{N} & \overset{+}{\text{O}} & & & - \\
\end{align*}
\]

\[
\begin{align*}
\text{R} - \text{N} & \overset{\ddots}{\text{O}} & - & \overset{\ddots}{\text{O}} & = & \text{R} - \text{NO}_2 \\
\end{align*}
\]

16.1 Nomenclature of Benzene Derivatives
Nomenclature

• Common names

- toluene
- styrene
- phenol
- anisole

• Ortho, meta, and para prefixes

- o-dichlorobenzene
- 1,2-dichlorobenzene
- m-bromonitrobenzene
- 1-bromo-3-nitrobenzene
- p-fluoroiodobenzene
- 1-fluoro-4-iodobenzene
Nomenclature

• Principle groups

\[ \text{OH} \]
\[ \text{NO}_2 \]

\( m \)-nitrophenol (3-nitrophenol)
—OH group is the principal group

• Other common names

\[ \text{CH}_3 \]
\[ \text{OH} \]
\[ \text{CH}_3 \]

\( o \)-xylene

\[ \text{OH} \]
\[ \text{CH}_3 \]

\( m \)-cresol

\[ \text{HO} \]
\[ \text{OH} \]

catechol

\[ \text{HO} \]
\[ \text{OH} \]

resorcinol

\[ \text{HO} \]
\[ \text{OH} \]

hydroquinone

16.1 Nomenclature of Benzene Derivatives
Nomenclature

• Numbers are required when more than two substituents are present

alphabetical citation: bromodifluoro
numbering: 1,2,3
name: 1-bromo-2,3-difluorobenzene

2-ethoxy-5-nitrophenol

16.1 Nomenclature of Benzene Derivatives
Nomenclature

• The benzene ring may also be a substituent

\[
\text{diphenyl ether (phenoxybenzene)} \\
\text{three different ways to write the structure}
\]

• The **phenyl group** = \( C_6H_5^- = \text{Ph-} \)
• The **benzyl group** = \( C_6H_5CH_2^- \)

\[
\text{PhCH}_2^-\text{Cl} \\
\text{benzyl chloride or (chloromethyl)benzene}
\]
Physical Properties

• Benzene derivatives and hydrocarbons have similar boiling points

\[
\text{bp} \quad \text{mp} \\
\text{benzene} & \quad 80.1 ^\circ C \quad 5.5 ^\circ C \\
\text{cyclohexane} & \quad 80.7 ^\circ C \quad 6.6 ^\circ C \\
\text{toluene} & \quad 110.6 ^\circ C \quad -95 ^\circ C
\]

• Note how the melting points of the highly symmetrical compounds are unusually high
Physical Properties

• Para-disubstituted derivatives typically have mp’s higher than those of ortho and meta

Benzene and other aromatic hydrocarbon derivatives are insoluble in water

• If H-bonding is possible, then water solubility is improved (e.g., phenol, PhOH)
IR Spectroscopy

16.3 Spectroscopy of Benzene Derivatives
\(^1\)H NMR Spectroscopy

• Benzene: \(\delta\) 7.4
• Most benzene derivatives: \(\delta\) 7.0-8.0
• If an unknown compound has an unsaturation number of \(\geq 4\), immediately check this region

• Note: Vinyl protons of alkenes are at \(\delta\) 5.0-5.7
• Why do benzene derivatives appear more downfield?
Ring Current in NMR Spectroscopy

The induced field $B_i$ opposes $B_0$ in the center of the ring.

The induced field $B_i$ reinforces $B_0$ at the benzene protons.

Induced $\pi$-electron circulation (ring current).

$B_0$ (external applied field).

16.3 Spectroscopy of Benzene Derivatives
Ring Current in NMR Spectroscopy

- Ring current is believed to be the best *experimental evidence* of aromatic character.

- Outer protons: 9.28 ppm
- Inner protons: -2.99 ppm (!)
1H NMR Spectroscopy

• Benzylic protons also experience a downfield shift relative to ordinary alkyl absorptions

\[
\begin{align*}
\text{benzylic protons} & \quad (\delta 2.29) \\
\text{CH}_3 & \\
\text{ring protons} & \quad (\delta 7.1)
\end{align*}
\]

\[
\begin{align*}
\text{benzylic protons} & \quad (\delta 2.53, q) \\
\text{CH}_2-\text{CH}_3 & \\
\text{benzylic protons} & \quad (\delta 1.22(t))
\end{align*}
\]

• The \(-\text{OH}\) absorption in phenols is typically higher \((\delta 5-6)\) than that of alcohols \((\delta 2-3)\)
## Coupling Constants of Aromatic Protons

<table>
<thead>
<tr>
<th>Relationship of protons</th>
<th>Coupling constant</th>
</tr>
</thead>
<tbody>
<tr>
<td>ortho</td>
<td>$J_{ortho} = 6–10$ Hz</td>
</tr>
<tr>
<td>meta</td>
<td>$J_{meta} = 1–3$ Hz</td>
</tr>
<tr>
<td>para</td>
<td>$J_{para} = 0–1$ Hz</td>
</tr>
</tbody>
</table>

---

16.3 Spectroscopy of Benzene Derivatives
Para-Substituted Benzenes

• A pair of “leaning doublets” with a large ortho coupling is characteristic.
$^{13}$C NMR Spectroscopy

- Benzene: $\delta$ 128.5
- Most benzene derivatives: $\delta$ 110-160
- Benzylic carbons: $\delta$ 18-30

- Recall that carbons that do not bear Hs are considerably smaller in size
UV-Vis Spectroscopy

• Aromatic hydrocarbons typically have two bands: 210 nm (strong), 260 (weak)
• Substituents can alter both the $\lambda_{\text{max}}$ values and the intensities
• This is more pronounced when the substituent can extend conjugation of the ring
16.3 Spectroscopy of Benzene Derivatives
Electrophilic Aromatic Substitution

• A hydrogen of an aromatic ring is replaced by an electrophile

\[
\begin{array}{c}
\text{H} + \text{E} \rightarrow \text{E} + \text{H}
\end{array}
\]

• All electrophilic aromatic substitution reactions occur by similar mechanisms

16.4 Electrophilic Aromatic Substitution Reactions of Benzene
Halogenation of Benzene

\[
\text{benzene} + \text{Br}_2 \xrightarrow{\text{FeBr}_3 \text{ or Fe} \ (0.2 \text{ equiv.})} \text{bromobenzene} \\
\]

(50% yield)

• Compare with the *addition* product for that of an alkene

\[
\text{alkene} + \text{Br}_2 \rightarrow \text{alkene} + \text{Br}_2
\]
Mechanism of Halogenation

$$:\text{Br} \rightarrow :\text{Br} \xrightleftharpoons{\text{FeBr}_3} :\text{Br} \rightarrow :\text{Br} \rightarrow \text{FeBr}_3$$

- a better electron acceptor and better leaving group
- a weaker electron acceptor and poorer leaving group

Nuc: $$:\text{Br} \rightarrow :\text{Br} \rightarrow \text{FeBr}_3$$ (a nucleophile)

- a weaker base
- a stronger base

16.4 Electrophilic Aromatic Substitution Reactions of Benzene
Mechanism of Halogenation

16.4 Electrophilic Aromatic Substitution Reactions of Benzene
Three Mechanistic Steps in EAS

1. Generation of an electrophile

2. Nucleophilic reaction of the $\pi$ electrons of the aromatic ring with the electrophile

3. Loss of a proton from the carbocation to form a substituted aromatic compound

16.4 Electrophilic Aromatic Substitution Reactions of Benzene
Nitration of Benzene

• Mechanism:

\[
\begin{align*}
\text{benzene} + \text{HONO}_2 + \text{H}_2\text{SO}_4 & \rightarrow \text{nitrobenzene} \\
(81\% \text{ yield})
\end{align*}
\]
Nitration of Benzene

\[
\begin{align*}
&\text{Nitric acid} \quad \text{Benzene} \\
\rightarrow \\
&\text{Nitrobenzene} + \text{H}_2\text{SO}_4
\end{align*}
\]
Sulfonation of Benzene

**Mechanism:**

\[
\text{benzene} + \text{sulfur trioxide} \xrightarrow{\text{H}_2\text{SO}_4} \text{benzenesulfonic acid (52\% yield)}
\]
Friedel-Crafts Alkylation of Benzene

Mechanism:

\[
\begin{align*}
\text{benzene} \quad \text{(large excess)} & \quad + \quad \text{Cl}^{-}\text{CHCHCH}_{2}\text{CH}_{3} \quad \xrightarrow{\text{AlCl}_{3} \ (0.1 \text{ equiv.})} \quad \text{benzene} \quad \text{CHCHCH}_{2}\text{CH}_{3} + \text{HCl} \\
\text{sec-butyl chloride} & \quad \xrightarrow{\text{AlCl}_{3}} \quad \text{sec-butylbenzene} \quad \text{(71% yield)}
\end{align*}
\]

16.4 Electrophilic Aromatic Substitution Reactions of Benzene
Friedel-Crafts Alkylation of Benzene

• Compare the role of AlCl$_3$ with that of FeBr$_3$ in the bromination reaction
Rearrangements in Friedel-Crafts Alkylation

\[
\text{benzene} + \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl} \xrightarrow{\text{AlCl}_3, 0^\circ\text{C}} \text{HCl} + \text{butylbenzene} (27\% \text{ yield}) + \text{CH}_3 \text{CHCH}_2\text{CH}_3 \quad (49\% \text{ yield})
\]

- Stable carbocations do not rearrange

\[
\text{benzene} + (\text{CH}_3)_3\text{C}-\text{Cl} \xrightarrow{\text{AlCl}_3, (0.04 \text{ equiv.})} \text{C(CH}_3)_3 \text{C}_3 + (\text{CH}_3)_3\text{C}-\text{C(CH}_3)_3 + \text{HCl}
\]

16.4 Electrophilic Aromatic Substitution Reactions of Benzene
Overalkylation in Friedel-Crafts Alkylations

• The alkyl benzene products are typically *more reactive* than benzene itself

\[
\text{benzene} \quad \text{Cl} \quad \text{CH}_2\text{CH}_3 
\quad \xrightarrow{\text{AlCl}_3} 
\quad \text{ethylbenzene (83% yield)}
\]

• A large excess of benzene can minimize this problem

\[
\text{H} \quad \text{CH}_3\text{Cl} 
\quad \xrightarrow{\text{AlCl}_3} 
\quad \text{toluene, xylenes, trimethylbenzenes, etc. (equimolar amounts)}
\]
Friedel-Crafts Alkylations

- Alkenes and alcohols can also be used as alkylation reagents

![Reaction Diagram]

\[
\text{benzene} + \text{cyclohexene} \xrightarrow{\text{H}_2\text{SO}_4, 5-10\,^{\circ}\text{C}} \text{cyclohexylbenzene} (65-68\% \text{ yield})
\]
Friedel-Crafts Acylation of Benzene

The acyl group is typically derived from an acid chloride.

16.4 Electrophilic Aromatic Substitution Reactions of Benzene
Friedel-Crafts Acylation of Benzene

- **Mechanism:**

\[
\begin{align*}
R-C-Cl + AlCl_3 &\rightarrow [R-C^+ = O] \quad \text{(acylium ion)} \\
&\rightarrow R-C=O + AlCl_4^{-} \\
\end{align*}
\]

\[
\begin{align*}
Cl-AlCl_3 &\rightarrow R + HCl + AlCl_3
\end{align*}
\]
Friedel-Crafts Acylation of Benzene

- In contrast to the alkylation version, one equivalent of AlCl$_3$ is required
Intramolecular Friedel-Crafts Reactions

- Both the alkylation and acylations can occur intramolecularly.
- The reaction occurs at an ortho position and is best for five- and six-membered rings.

\[
\text{4-phenylbutanoyl chloride} \xrightarrow{1) \text{AlCl}_3 \ 2) \text{H}_2\text{O}} \text{α-tetralone} + \text{HCl}
\]

(74–91% yield)

16.4 Electrophilic Aromatic Substitution Reactions of Benzene
Directing Effects of Substituents

- Regioselectivity is observed in EAS reactions on monosubstituted benzene rings

- Ortho, para-directing:

  \[
  \text{bromobenzene} \xrightarrow{HNO_3 \text{ acetic acid}} \text{o-bromonitrobenzene (36\%)} + \text{p-bromonitrobenzene (62\%)} + \text{m-bromonitrobenzene (2\%)}
  \]

- Meta-directing:

  \[
  \text{nitrobenzene} \xrightarrow{\text{Br}_2, \text{FeBr}_3 \text{ heat}} \text{m-bromonitrobenzene (only product observed)}
  \]

16.5 Electrophilic Aromatic Substitution Reactions of Substituted Benzenes
## Directing and Activating Effects

(Groups are listed in decreasing order of activation.)

<table>
<thead>
<tr>
<th>Substituent group</th>
<th>Name of group</th>
<th>Directing effect</th>
<th>Activating or deactivating</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{NH}_2)</td>
<td>amino</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(\text{NH}_2)</td>
<td>amino</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(\text{OH})</td>
<td>hydroxy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(\text{OR})</td>
<td>alkoxy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(\text{NH} \rightarrow \text{C} \rightarrow \text{R})</td>
<td>acylamino</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(\text{R})</td>
<td>alkyl</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(\text{O} \rightarrow \text{C} \rightarrow \text{R})</td>
<td>acyloxy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(\text{phenyl})</td>
<td>phenyl</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(\text{F}, \text{Br}, \text{Cl}, \text{I})</td>
<td>halogens</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(\text{CO} \rightarrow \text{NH}_2 \rightarrow \text{C} \rightarrow \text{OH}, \text{CO} \rightarrow \text{OR})</td>
<td>carboxy, carboxamido, carboxalkoxy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(\text{acyl})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(-\text{SO}_3\text{H})</td>
<td>sulfonic acid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(-\text{CN})</td>
<td>cyano</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(-\text{NO}_2)</td>
<td>nitro</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Ortho, para directors

Activating substituents

Meta directors

Deactivating substituents

---

16.5 Electrophilic Aromatic Substitution Reactions of Substituted Benzenes
Ortho, Para-Directing Groups

- Alkyl groups
- Groups that have unshared electron pairs on atoms directly attached to the benzene ring

16.5 Electrophilic Aromatic Substitution Reactions of Substituted Benzenes
Ortho, Para-Directing Groups

- The charge on the meta-derived intermediate cannot be delocalized onto the -OCH₃ group
Ortho, Para-Directing Groups

16.5 Electrophilic Aromatic Substitution Reactions of Substituted Benzenes
Ortho, Para-Directing Groups

- Alkyl substituted benzene rings have a similar explanation

16.5 Electrophilic Aromatic Substitution Reactions of Substituted Benzenes
The Ortho, Para Ratio

- Rarely do $o,p$-directors provide twice as much ortho product as para product.
- Typically para predominates over ortho.
- Sometimes this is due to spatial demands, but many cases are less easily explained.
- Fortunately, ortho and para products have different physical properties and can be separated.

16.5 Electrophilic Aromatic Substitution Reactions of Substituted Benzenes
Meta-Directing Groups

• Groups that have positive charges adjacent to the benzene ring

• Groups that have bond dipoles with a partial positive charge adjacent to the benzene ring
Meta-Directing Groups

$\text{E}^+ \rightarrow \text{meta}$

16.5 Electrophilic Aromatic Substitution Reactions of Substituted Benzenes
Meta-Directing Groups

16.5 Electrophilic Aromatic Substitution Reactions of Substituted Benzenes
Activating and Deactivating Effects

• Activating group: A group that allows the derivative to react more rapidly than benzene
• Deactivating group: A group that causes the derivative to react more slowly than benzene

1. All meta-directors are deactivating
2. All ortho, para-directors are activating
3. Halogens are deactivating
Activating and Deactivating Effects

• Controlled by two *simultaneously operating* properties of substituents

• **Resonance effect:**

  ![Resonance Effect Diagram]

  (two of the four important resonance structures)

  the resonance effect of the methoxy group *stabilizes* the carbocation

• **Polar effect:**

  ![Polar Effect Diagram]

  the polar effect of the methoxy group *destabilizes* the carbocation

*16.5 Electrophilic Aromatic Substitution Reactions of Substituted Benzenes*
Activating and Deactivating Effects

16.5 Electrophilic Aromatic Substitution Reactions of Substituted Benzenes
Activating and Deactivating Effects

• Orbital overlap may also affect the degree to which the resonance effect operates

Overlap of carbon and oxygen 2p orbitals (a)

Overlap of carbon 2p and chlorine 3p orbitals (b)

16.5 Electrophilic Aromatic Substitution Reactions of Substituted Benzenes
Use of EAS in Organic Synthesis

- With two or more substituents, the activating and directing effects are roughly the sum of the effects of the individual substituents.
Use of EAS in Organic Synthesis

[Chemical equation]

\[
\text{phenol} + 3 \text{Br}_2 \xrightarrow{\text{H}_2\text{O}} \text{2,4,6-tribromophenol} \quad \text{quantitative; virtuallly instantaneous}
\]

[Chemical structures]

4-chlorotoluene

\[
\text{Cl} \quad \text{CH}_3
\]

4-chloro-3-nitrotoluene (42%)

\[
\text{Cl} \quad \text{CH}_3
\]

4-chloro-2-nitrotoluene (58%)

\[
\text{Cl} \quad \text{CH}_3
\]

16.5 Electrophilic Aromatic Substitution Reactions of Substituted Benzenes
Use of EAS in Organic Synthesis

• Some EAS reactions can be carried out under very mild conditions and without a catalyst

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{CH}_3 & + & \text{Br}_2 & \quad \overset{0-10^\circ\text{C}}{\text{CCl}_4} & \quad \rightarrow & & \text{H}_3\text{C} & \quad \text{Br} & \quad \text{CH}_3 & \quad + & \text{HBr} \\
& & & & & & & & & & & \text{(80% yield)}
\end{align*}
\]

\[
\begin{align*}
\text{H}_3\text{C} & \quad + & \text{H}_2\text{SO}_4 & \quad \rightarrow & & \text{H}_3\text{C} & \quad \text{SO}_3\text{H} & + & \text{H}_2\text{O} \\
& \text{toluene} & & & & & \text{p-toluenesulfonic acid}
\end{align*}
\]
Use of EAS in Organic Synthesis

Use of EAS in Organic Synthesis

16.5 Electrophilic Aromatic Substitution Reactions of Substituted Benzenes
Hydrogenation

- Aromatic rings are resistant to hydrogenation

\[
\text{stilbene (cis or trans)} \quad \text{Pd/C, 25°C} \quad \text{(2-phenylethyl)benzene (bibenzyl)} (95\% \text{ yield})
\]

- More extreme conditions are generally required (higher T and/or P)

\[
\text{ethylbenzene} \quad \text{Ni, 175°C, 180 atm} \quad \text{ethylcyclohexane (93\% yield)}
\]
Hydrogenation

• The reaction cannot be selectively stopped

\[
\text{C}_6\text{H}_5 + \text{H}_2 \rightarrow \text{C}_6\text{H}_{12} \quad \Delta H^\circ = +24.3 \text{ kJ mol}^{-1} (+5.8 \text{ kcal mol}^{-1})
\]

\[
\text{C}_6\text{H}_4 + \text{H}_2 \rightarrow \text{C}_6\text{H}_{14} \quad \Delta H^\circ = -111 \text{ kJ mol}^{-1} (-26.5 \text{ kcal mol}^{-1})
\]

\[
\text{C}_6\text{H}_3 + \text{H}_2 \rightarrow \text{C}_6\text{H}_{16} \quad \Delta H^\circ = -118 \text{ kJ mol}^{-1} (-28.2 \text{ kcal mol}^{-1})
\]

16.6 Hydrogenation of Benzene Derivatives
Aromatic Hydrocarbons

• The most common source of aromatic hydrocarbons is *petroleum*

• *Coal tar* is another potentially important, but currently minor source

• Benzene is the principle source of styrene, ethylbenzene, and cumene

\[
\text{propene} \quad \text{AlCl}_3/\text{HCl} \quad \text{or H}_2\text{SO}_4 \quad \text{cumene}
\]
Aromatic Hydrocarbons

• Xylenes are also obtained from petroleum
• Para-xylene is the most important of these
• Virtually the entire production of $p$-xylene is used for preparation of terephthalic acid
• Terephthalic acid is used in polyester synthesis

\[
\text{H}_3\text{C} - \text{CH}_3 + \text{O}_2 \xrightarrow{\text{Co–Mn catalyst, heat}} \text{HO}_2\text{C} - \text{CO}_2\text{H}
\]

$p$-xylene  \hspace{1cm} \xrightarrow{\text{reaction}} \hspace{1cm} \text{terephthalic acid}