1. Give the complete curved arrow mechanism for each reaction, including the generation of the electrophile.

a. \[ \text{Cl}_2, \text{FeCl}_3 \quad \text{aryl} \rightarrow \text{aryl-Cl} \]

b. \[ \text{aryl} \quad \text{HNO}_3, \text{H}_2\text{SO}_4 \rightarrow \text{aryl-NO}_2 \]

c. \[ \text{aryl} \quad \text{SO}_3, \text{H}_2\text{SO}_4 \rightarrow \text{aryl-SO}_3\text{H} \]

2. Use your mechanism for question 1a to briefly explain why FeCl$_3$ is a catalyst for the halogenation reaction.
   - It makes the reaction faster by lowering the activation barrier. Cl$_2$ is not as reactive as [Cl-Cl$^-$-Fe Cl$_3$].
   - It is not consumed by the reaction. FeCl$_3$ is used to make [Cl-Cl$^-$-Fe Cl$_3$], but is regenerated when FeCl$_4^-$ decomposes to FeCl$_3$ and Cl$^-$. 

Page 1
3. Which energy diagram represents this reaction?

\[
\text{Cationic “sigma complex”}
\]

\[
\text{MECHANISMS OF FRIEDEL CRAFTS ALKYLATION + ACYLATION}
\]

4. Give the curved arrow mechanism for each Friedel Crafts reaction.

a. \[
\text{CH}_3\text{CH}_2\text{Cl}^+ + \text{AlCl}_3 \rightarrow \text{CH}_3\text{CH}_2\text{Cl} \quad \text{AlCl}_3
\]

b. \[
\text{Br}^+ + \text{AlCl}_3 \rightarrow \text{Br} \quad \text{AlCl}_3
\]

c. \[
\text{Cl}^+ + \text{AlCl}_3 \rightarrow \text{Cl} \quad \text{AlCl}_3
\]
5. Give the curved arrow mechanism for each E.A.S. reaction.

a. 

b.

6. Give the complete curved arrow mechanism for each Friedel Crafts reaction.

a.
7. Would each compound react faster or slower than benzene in a halogenation reaction?

<table>
<thead>
<tr>
<th>Compound</th>
<th>Faster / Slower</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCH₂CH₃</td>
<td>Faster</td>
</tr>
<tr>
<td>CH₃C₆H₄⁺CH₃</td>
<td>Slower</td>
</tr>
<tr>
<td>BrC₆H₄</td>
<td>Slower (X deactivator)</td>
</tr>
<tr>
<td>NH₂C₆H₄</td>
<td>Faster</td>
</tr>
<tr>
<td>COC₆H₄</td>
<td>Faster</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Faster / Slower?</th>
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<th>Slower</th>
<th>Slower (X deactivator)</th>
<th>Faster</th>
<th>Faster</th>
</tr>
</thead>
<tbody>
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<td>OCH₂CH₃</td>
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<td></td>
<td>Slower</td>
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</tr>
<tr>
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<td></td>
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<td></td>
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<td></td>
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<td>COC₆H₄</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Faster</td>
</tr>
</tbody>
</table>

8. Rank each set in order of increasing rate of reaction towards Cl₂ and FeCl₃. (Hint: how do the substituents affect the energy of the intermediate?) Explain the trend in detail.

- a. OCH₂CH₃ | slowest | fastest

  The rate of an E.A.S. reaction is related to the stability of the carbocation intermediate (sigma complex): if the cation is low energy the reaction will have a low Eₐ (activation barrier) and be fast.

  The carbonyl is an electron withdrawing group (EWG), so its presence will increase the energy of the cationic intermediate (removing electron density from an already electron deficient center is “bad” or increases the energy). This makes this reaction slower.

  The alkyl group is an electron donating group (EDG), so will stabilize the cationic intermediate (donating electron density to an electron deficient center “helps” or lowers its energy). This makes the alkyl reaction faster than benzene, which has no group affecting the energy of its sigma complex.

- b. OCH₃ | CF₃

  CF₃ is a strong EWG due to the high electronegativity of fluorine. The CF₃ group therefore removes electron density from the carbocation intermediate, increasing its energy. This makes the E.A.S. reaction slower.

  The OCH₃ group is an EDG, which stabilizes the carbocation intermediate, lowering its energy. This makes the E.A.S. reaction faster.
9. Reaction of phenol with $\text{Cl}_2$ / $\text{FeCl}_3$ can theoretically form three products: from ortho, meta and para addition.

a. Draw resonance structures of the intermediate that leads to each product.

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Resonance Structures of the Intermediate</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{Phenol} + \text{Cl}_2, \text{FeCl}_3 \rightarrow \text{p-chlorophenol} (86.6%) + \text{o-chlorophenol} (11.4%) + \text{meta} (0%)$</td>
<td></td>
</tr>
</tbody>
</table>

The para product is the major because it is formed faster: the reaction has the lowest activation barrier.

The carbocation leading to both the ortho and para product are low energy because the cation is placed directly next to the OH. This allows for a fourth very stabilizing resonance structure where all atoms have an octet. The carbocation leading to the meta product has only 3 resonance structures so is not as stabilized. This is why ortho, para $>$ meta.

Para $>$ ortho due to less steric repulsion from the Cl and OH in the carbocation intermediate.
10. Use resonance structures to rationalize the product distribution for this reaction.

\[ \text{Toluene} + \text{PhCOCl}, \text{AlCl}_3 \rightarrow \text{para} (89.2\%) + \text{meta} (1.5\%) + \text{ortho} (9.3\%) \]

The carbocation leading to both the ortho and para products are low energy because the cation is placed directly next to the \( \text{CH}_3 \) in the intermediate. This allows for the cation to be stabilized well through hyperconjugation (or it allows for a 3\textdegree carbocation whereas there are only 2\textdegree carbocations in the meta intermediate).

\( \text{Para} > \text{ortho} \) due to less steric repulsion in the carbocation intermediate.

11. Use resonance structures to explain why nitration of acetophenone (PhCOCH\(_3\)) adds the nitro group \textit{meta} to the carbonyl instead of ortho or para.

The carbocation leading to both the ortho and para products are high energy because the cation is placed directly next to the EWG (the carbonyl, which has a partial positive right next to the cation). This destabilizes the cationic intermediate, increasing the activation barrier and making the ortho/para products form at a slower rate.

The \textit{meta} product is major because the cation is never directly next to the carbonyl in any of the resonance structures.
12. Gives the reagents necessary to complete each reaction.

a. \[
\text{Ph}OCH_3 + \text{AlCl}_3 \rightarrow \text{PhOCH}_3
\]
b. \[
\text{BrPh} + \text{FeBr}_3 \rightarrow \text{BrPh}
\]
c. \[
\text{C}_2H_4 + \text{AlCl}_3 \rightarrow \text{PhC}_2H_4
\]
d. \[
\text{PhCH}_2Cl + \text{AlCl}_3 \rightarrow \text{PhCH}_2Cl
\]

13. Give the major organic product for each reaction, showing only the monosubstitution product.

a. \[
\text{CF}_3 + \text{HNO}_3 + \text{H}_2\text{SO}_4 \rightarrow \text{CF}_3\text{NO}_2
\]
b. \[
\text{O}_2\text{C}_6\text{H}_5 + \text{Cl} + \text{AlCl}_3 \rightarrow \text{O}_2\text{C}6\text{H}_5\text{Cl}
\]
c. \[
\text{PhCOOCH}_3 + \text{Cl}_2 + \text{FeCl}_3 \rightarrow \text{PhCOOCH}_3
\]
d. \[
\text{PhC}_6\text{H}_5 + \text{HNO}_3 + \text{H}_2\text{SO}_4 \rightarrow \text{PhC}_6\text{H}_5\text{O}_2\text{N}
\]
e. \[
\text{O}_2\text{NPh} + \text{Cl} + \text{AlCl}_3 \rightarrow \text{O}_2\text{NPh}
\]
f. \[
\text{PhNCH}_2\text{CH}_2\text{Ph} + \text{Br}_2 \rightarrow \text{PhNCH}_2\text{CH}_2\text{Ph}
\]
14. In each reactant below there are two aromatic rings, yet one ring preferentially undergoes substitution. Briefly explain why one ring is more reactive than the other, then give the expected major product from monosubstitution.

Ring A (left) has a carbonyl attached (EWG) which deactivates that ring (makes it react slower). Ring B (right) has an oxygen attached (EDG) which activates that right (makes it react faster). Therefore reaction occurs on ring B.

**Argument 1:** Ring A (left) has two alkyl groups (EDG) while ring B (right) has 4 alkyl groups. Considering the ability of hyperconjugation to stabilize the cationic intermediate, Ring B’s intermediate would be more stabilized. Therefore Ring B is more activated, so reacts faster.

**Argument 2:** It can also be argued that sterics play a large role in this reaction. Despite Argument 1, placement of a t-buty1 group ortho to two alkyl groups may carry a high repulsive load. Therefore Ring A may react faster if sterics are most important to the product distribution.

### ACTIVATORS AND OVERSUBSTITUTION

15. Phenols and anilines are so strongly activating that they sometimes don’t need catalysts in order to undergo substitution reactions, and they often over-substitute. Explain why a hydroxyl group is such a strong activator, while a methyl group is a weak activator. Use resonance structures with your explanation.

Both OH and CH$_3$ are activators because they’re EDG’s and stabilize the cationic intermediate. However the carbocation is MORE stabilized by OH (so much that a catalyst may not be needed) because a fourth very important resonance structure is present where all atoms have an octet.
16. Explain why multiple-alkylation is common under the conditions of reaction (1), but does not occur in reaction (2).

Alkyl groups are activators, so once an R group is added, the product is more reactive than the starting material. There is a lower $E_a$ for the reaction of toluene than the reaction of benzene, so it tends to overalkylate.

Carbonyl groups are deactivators, meaning the product of reaction (2) is less reactive than benzene. There is a higher $E_a$ for reaction of the product, so it further reaction only occurs on the initial reactant.

17. Assign the peaks in each $^1$H NMR spectrum to hydrogen atoms in each structure. Then use resonance structures to help explain your assignment for the aromatic hydrogen atoms (why are certain H more shielded than others)?

The carbonyl is an EWG through resonance and makes the positions ortho and para to it $\delta^+$. These spots are the most electron poor, so should show up to the left on the spectrum (highest ppm). From this reasoning “b” and “c” should be the $\delta^+$ centers and the splitting can be used to determine which is which. (Also “b” is closest to both carbonyls so should be furthest left.)

OH is a stronger directing group than Cl, so will influence the electron density of the ring the most. Considering resonance structures involving the OH, the positions ortho and para to the OH are electron rich and should therefore absorb at low ppm (to the right in the spectrum). There are no H para to the OH, so only the ortho positions are affected.
18. Explain in detail the following observations:

a. No E.A.S. reaction occurs in the conditions below.

![Diagram showing the reaction between amines and AlCl3](image)

Amines are good bases and so react with AlCl3 (a Lewis acid). This reaction converts the nitrogen into a \( \text{N}^+ \) group, which is a deactivator. Friedel Crafts alkylations are “sensitive” and cannot work with a deactivated ring as they are not nucleophilic enough. No E.A.S. reaction happens, only an acid-base.

b. The meta product is formed in this reaction, even though the \(-\text{NH}_2\) is an ortho-para director.

![Diagram showing the nitration reaction](image)

Nitration conditions are acidic, so an acid-base reaction will occur with the amine (base) and the \( \text{H}_2\text{SO}_4 \). Protonation turns the \(-\text{NH}_2\) group into a \(-\text{NH}_3^+\) group, which is an EWG and meta director.

### REACTIONS OF SYNTHETIC UTILITY

19. Gives the reagents necessary to complete each reaction.

a. ![Diagram showing the reaction between benzene and Zn, HCl](image)

b. ![Diagram showing the reaction between benzene with NO2 and H2, Pd](image)

c. ![Diagram showing the reaction between benzene with HSO4 and H+](image)

d. ![Diagram showing the reaction between benzene and Cl2, FeCl3](image)

[2 steps]

d. ![Diagram showing the reaction between benzene with Zn and HCl](image)
20. For each problem, choose which sequence of reagents would effectively perform the desired synthesis. Then explain why the other sequence is not as efficient or wouldn’t work.

a. \[ \text{Route 1: } \begin{align*} &\text{a) } \text{Cl}_2, \text{FeCl}_3 \\ &\text{b) } \text{HNO}_3, \text{H}_2\text{SO}_4 \end{align*} \]

\[ \text{Route 2: } \begin{align*} &\text{a) } \text{HNO}_3, \text{H}_2\text{SO}_4 \\ &\text{b) } \text{Cl}_2, \text{FeCl}_3 \end{align*} \]

If the nitro group is added first, as in Route 2, you end up with the wrong substitution. A nitro group is an EWG and so a meta director. The correct substitution occurs with Route 1.

b. \[ \text{Route 1: } \begin{align*} &\text{a) } \text{Br}_2, \text{FeBr}_3 \\ &\text{b) } \text{CH}_3\text{CH}_2\text{CH}_2\text{Br}, \text{AlCl}_3 \end{align*} \]

\[ \text{Route 2: } \begin{align*} &\text{a) } \text{CH}_3\text{CH}_2\text{COCl, AlCl}_3 \\ &\text{b) } \text{Zn, HCl} \\ &\text{c) } \text{Br}_2, \text{FeBr}_3 \end{align*} \]

The Friedel Crafts alkylation in step b) of Route 1 will produce mostly the rearranged alkyl chain (isopropyl group). Some product with propyl substitution will also form, but the yield will be split. Route 2 is more efficient.
21. Starting with **benzene or toluene**, design a synthesis for each compound, showing all reagents and intermediates. Assume monosubstitution for each E.A.S. reaction. Some syntheses may require reactions other than E.A.S. reactions.

<table>
<thead>
<tr>
<th>Target Compound</th>
<th>Synthesis</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Bromonitrobenzene" /></td>
<td><img src="image" alt="Synthesis" /></td>
</tr>
<tr>
<td><img src="image" alt="Bromonitroanisole" /></td>
<td><img src="image" alt="Synthesis" /></td>
</tr>
<tr>
<td><img src="image" alt="Anisidin" /></td>
<td><img src="image" alt="Synthesis" /></td>
</tr>
<tr>
<td><img src="image" alt="Ortho-diaminotoluene" /></td>
<td><img src="image" alt="Synthesis" /></td>
</tr>
</tbody>
</table>
22. Give the major organic product for each reaction, assuming conditions that encourage reaction of only 1 equivalent in all cases where multiple could occur.

a. \( \text{HI at } 50^\circ C \)

b. \( \text{NC-CN at } 180^\circ C \)

c. \( \text{CH}_3\text{OH} \) with \( \text{AlCl}_3 \)

d. \( \text{H}_2\text{SO}_4 \) and \( \text{HNO}_3 \) with \( \text{CF}_3 \)

\[
\begin{align*}
a. & \quad \text{benzene} \xrightarrow{\text{HI at } 50^\circ C} \text{products} \\
b. & \quad \text{benzene} \xrightarrow{\text{NC-CN at } 180^\circ C} \text{product} \\
c. & \quad \text{dioxane} \xrightarrow{\text{CH}_3\text{OH with } \text{AlCl}_3} \text{product} \\
d. & \quad \text{molecule} \xrightarrow{\text{H}_2\text{SO}_4 \text{ and } \text{HNO}_3 \text{ with } \text{CF}_3} \text{product}
\end{align*}
\]