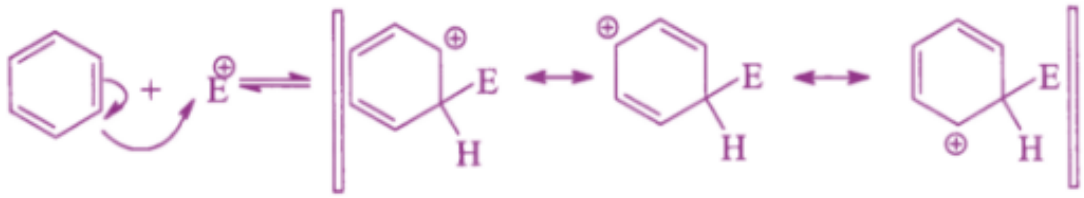
Electrophilic aromatic substitution

Electrophilic Aromatic Substitution: Effect of Substituent Groups

Overview:

- Electrophilic Aromatic Substitution (EAS) is a type of reaction where an electrophile replaces a hydrogen atom on an aromatic ring.



- The nature of substituent groups already present on the aromatic ring plays a crucial role in determining both the reactivity of the ring and the position (orientation) where the new group will be introduced.

Substituent Effects:

- Substituent groups can be classified based on how they influence:
  - **Rate** of reaction (activating or deactivating the ring)
  - **Orientation** of incoming electrophile (ortho, meta, para positions)

Types of Effects:

1. Inductive Effect (I-effect):

- Electron-withdrawing or electron-donating character through sigma bonds.
- **Example:** $-NO_2$ exerts a strong –I effect, pulling electrons away from the ring.
- **Example:** $-CH_3$ exerts a +I effect, pushing electrons toward the ring.

2. Resonance Effect (R-effect or Mesomeric effect):

- Delocalization of electrons via π-bond systems.
- Electron-donating via resonance (+R) groups: –OH, $-NH_2$, –OR
- Electron-withdrawing via resonance (–R) groups: $-NO_2$, –CHO, –COOH

Combined Effect:

- The overall effect of a substituent is a combination of its inductive and resonance behavior.
- **Example:** Halogens like –Cl and –Br have –I effect (electron-withdrawing) but also +R effect (donate lone pairs into the ring). This creates unique behavior (deactivating yet ortho/para directing).

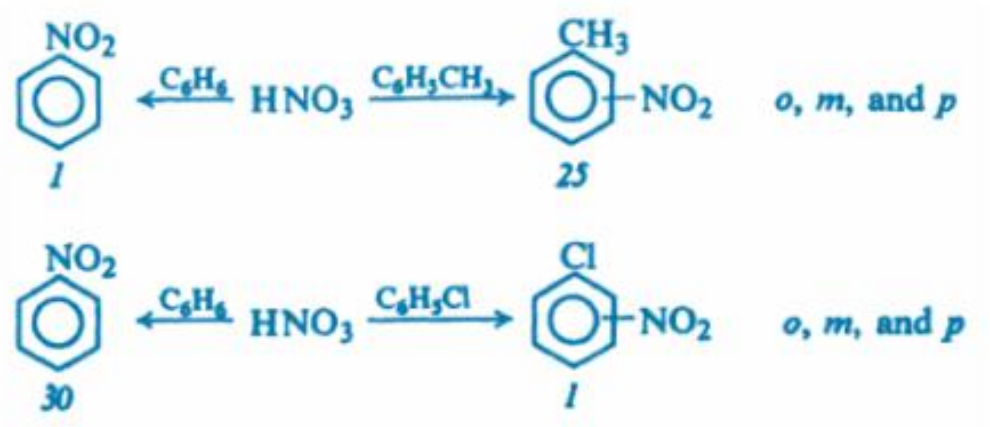
Examples:

- **Phenol (–OH group):** The –OH group donates electron density via resonance, activating the ring and directing new substituents to the ortho and para positions.
- **Nitrobenzene (–NO_2 group):** The –NO_2 group withdraws electron density via both inductive and resonance effects, deactivating the ring and directing incoming groups to the meta position.

Determination of Orientation in EAS

Overview

- Orientation refers to the position on the aromatic ring where the incoming electrophile is directed due to the influence of existing substituent(s).
- There are three main positions for substitution relative to an existing substituent on a monosubstituted benzene ring:
  - **Ortho (o):** Adjacent carbon (1,2-position).
  - **Meta (m):** One carbon away (1,3-position).
  - **Para (p):** Opposite carbon (1,4-position).



Orientation depends on the nature of the substituent already present:

1. Ortho/Para Directing Groups (Activating):

- **Examples:** –OH, –NH_2, –CH_3, –OCH_3.
- These groups have lone pairs or are electron-releasing, increasing electron density at ortho and para positions through +R effect.
- Stabilize the intermediate sigma complex (arenium ion) at o/p positions better.

2. Meta Directing Groups (Deactivating):

- **Examples:** –NO_2, –CN, –SO_3H, –COOH, –CHO.
- These groups are electron-withdrawing, lowering electron density at ortho and para positions.
- Meta positions become relatively more reactive.

- Stabilize the intermediate sigma complex best when the electrophile attacks the meta position.

3. Halogens (–X):

- Halogens like –Cl, –Br, –I are deactivating but ortho/para directing.
- Due to their lone pairs, they exhibit a +R effect (resonance donation) but also a strong –I effect (inductive withdrawal).
- The net result: overall slower reaction (due to deactivation), but when it occurs, it goes to o/p positions.

Why is this important?

- Understanding the orientation allows chemists to predict the product of electrophilic aromatic substitution and control regioselectivity in synthetic pathways.

Example Cases:

- **Toluene (CH_3–benzene)** reacts with nitrating agents to form ortho- and para-nitrotoluene due to +I and weak +R effects.
- **Nitrobenzene (NO_2–benzene)** reacts slowly with further substitution favoring meta-nitro positions due to strong –I and –R effects.

Determination of Relative Reactivity in EAS

- The relative reactivity of a substituted benzene ring in EAS reactions is governed by the electron density in the aromatic ring.
- Substituent groups either activate or deactivate the ring:
  - Activating groups make the ring more reactive than benzene.
  - Deactivating groups make the ring less reactive than benzene.

Mechanism Behind Reactivity Differences:

- During EAS, the aromatic ring temporarily loses its aromaticity when it forms a carbocation intermediate (sigma complex).
- Stability of this intermediate is crucial.

Reactivity Influenced by:

1. Activating Groups:

- Donate electron density into the ring.
- Stabilize the carbocation intermediate via resonance or hyperconjugation.
- Lower the activation energy for the reaction.
- Increase reaction rate.

- **Examples (ranked from strongly to weakly activating):**
  - $-NH_2 > -OH > -OR > -NHR > -CH_3 >$ benzene.

2. Deactivating Groups:

- Withdraw electron density from the ring.
- Destabilize the carbocation intermediate.
- Increase the activation energy.
- Decrease reaction rate.
- **Examples (ranked from strongly to weakly deactivating):**
  - $-NO_2 > -CF_3 > -CN > -COOH > -CHO >$ halogens > benzene.

3. Comparison with Benzene:

- Benzene is the reference point for reactivity.
- Substituted benzenes are compared in terms of their relative rate of reaction with a given electrophile under identical conditions.

Experimental Determination:

- Relative reactivities are often determined using competitive substitution reactions.
- Equal amounts of substituted benzenes are allowed to react with an electrophile, and the product ratios reveal their relative reactivity.

Classification of Substituent Groups in EAS

- Substituent groups attached to the benzene ring influence both the rate and orientation of electrophilic aromatic substitution (EAS) reactions.
- These groups are classified based on their electronic effects and their directive influence.

Based on Reactivity:

1. Activating Groups:

- Increase the electron density on the benzene ring, making it more reactive towards electrophiles.
- Usually donate electrons via +I (inductive) and/or +R (resonance) effects.
- **Examples**:
  - Strongly activating: $-OH$, $-NH_2$, $-OCH_3$
  - Moderately activating: $-NHR$, $-NHCOCH_3$, $-CH_3$
- **Reaction Rate**: Faster than benzene.

2. Deactivating Groups:

- Withdraw electron density from the ring, making it less reactive towards electrophiles.
- Withdraw electrons via **–I** and/or **–R** effects.
- **Examples**:
  - Strongly deactivating: $–NO_2$, $–CF_3$, $–SO_3H$, –CN
  - Moderately deactivating: –CHO, –COOH, –COOR
  - Weakly deactivating: Halogens (e.g., –Cl, –Br)
- **Reaction Rate**: Slower than benzene.

Based on Orientation:

1. Ortho/Para Directing Groups:

- Direct incoming electrophile to ortho and para positions.
- Typically electron-donating groups (EDGs).
- Also includes halogens (special case – see below).
- **Examples**: $–CH_3$, –OH, $–NH_2$, $–OCH_3$, –Cl, –Br

2. Meta Directing Groups:

- Direct incoming electrophile to meta position.
- Typically electron-withdrawing groups (EWGs).
- **Examples**: $–NO_2$, –COOH, –CHO, –CN, $–SO_3H$

Special Case – Halogens:

- Halogens (–Cl, –Br, –I, –F) are deactivating due to strong –I effect.
- However, they are ortho/para directing due to lone pair donation via +R (resonance).

Substituent	Reactivity	Orientation
–OH, $–NH_2$, –OR	Activating	Ortho/Para
$–CH_3$, $–C_2H_5$	Activating	Ortho/Para
–X (Cl, Br, I)	Deactivating	Ortho/Para
$–NO_2$, –CN, –COOH	Deactivating	Meta
–CHO, $–COCH_3$	Deactivating	Meta

Mechanism of Nitration

- **Nitration** is a classic electrophilic aromatic substitution where a **nitro group ($–NO_2$)** is introduced onto an aromatic ring.
- **Overall Reaction:**

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