Chemistry I (Organic)

Aromatic Chemistry

LECTURE 3 – Electrophilic Substitution (part 2)

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Format and scope of presentation

- **Electrophilic aromatic substitution (SₖAr) – part 2:**
  - Friedel-Crafts alkylation and acylation, nitrosation (diazonium salt formation & diazo-coupling, Sandmeyer reactions),
  - Directing effects (*ortho*-/*para*- ratios, *ipso*-substitution)
Electrophilic Aromatic Substitution ($S_e\text{Ar}$) - Mechanism
Friedel-Crafts alkylation

• **Typical conditions:** alkyl halides in the presence of Lewis acid promotors

\[ \text{alkyl halide-Lewis acid complex} = E \]

- ‘Plagued’ by rearrangements (Wagner-Meerwein 1,2-hydride and alkyl shifts)
- Substantially reversible and therefore can de-alkylate!
- Products are activated relative to starting materials hence extensive poly-alkylation
- Alkyl halide-Lewis acid complex is a weak electrophile and deactivated aromatics do not react
- The Lewis acid is a catalytic promotor

Order of Lewis acid effectiveness: $\text{AlCl}_3 > \text{FeCl}_3 > \text{BF}_3 > \text{TiCl}_3 > \text{ZnCl}_2 > \text{SnCl}_4$
Friedel-Crafts acylation

- **Typical conditions**: acid chlorides or anhydrides ± Lewis acid promotor:

  ![Chemical Structure](image)

- Lewis acid not required for activated aromatics
- **stoichiometric LAs**: $\text{AlCl}_3 > \text{FeCl}_3 > \text{BF}_3 > \text{TiCl}_3 > \text{ZnCl}_2 > \text{SnCl}_4$
  - Generally can’t be recycled via aqueous extraction
- **catalytic Lewis acids**: lanthanide(III) halides/triflates e.g. $\text{GaCl}_3$, $\text{InCl}_3$, $\text{Hf(OTf)}_4$

  ![Chemical Reaction](image)

  **N.B.**: NOT catalytic in Lewis acid because it complexes to product ketone
Formylation

- **Aryl aldehyde formation**: formyl chloride (HOCI) is not stable so ‘standard’ F-C acylation is not possible. A number of classical approaches have been developed:

  ![Chemical structure](image)

  **Vilsmeier-Haack formylation**: (activated aromatics only)
Nitrosation

- Typical conditions: sodium nitrite and hydrochloric acid

![Chemical reaction diagram]

- Nitrosonium ion is weak electrophile: only ring nitrosates activated aromatics (e.g. phenols)
- N-Alkyl anilines give N-nitroso anilines (i.e. N-nitrosation not ring nitrosation)
- N-Nitroso anilines can undergo Fischer-Hepp rearrangement on heating to ring nitrosated products
- Anilines give diazonium salts via initial N-nitrosation
Diazotisation & Sandmeyer reactions

- **Mechanism of formation:**

  
  \[
  \text{NH}_2 \quad \text{NO}^+ \quad \overset{\text{OH}}{\text{N}} \quad \text{H}_2\text{O} \quad \text{N}^+ \quad \text{N}^+ \quad \text{R} \quad \text{R} \quad \text{N}^+ \quad \text{N}^+ \quad \text{H}_2\text{O} \quad \text{diazonium salt}
  \]

- **Nucleophilic ipso-substitution (Sandmeyer reactions):**
Diazotisation & diazo-coupling

- **Nucleophilic attack can also occur at the terminal nitrogen of diazonium ions** (cf. at the ipso-carbon in Sandmeyer reactions)
  - *e.g.* triazine synthesis using **amines** as nucleophiles:

  ![](image1.png)

  - *e.g.* diazo-compound synthesis (dyes) using **phenols** as C-nucleophiles:

  ![](image2.png)
Aromatics as ambident nucleophiles

- cf. Aryl diazonium ions as ambident electrophiles:

- Aromatics as ambident nucleophiles (‘directing effects’):

What governs position of reactivity?