

Chemistry I (Organic)

Aromatic Chemistry

LECTURE 3 – Electrophilic Substitution (part 2)

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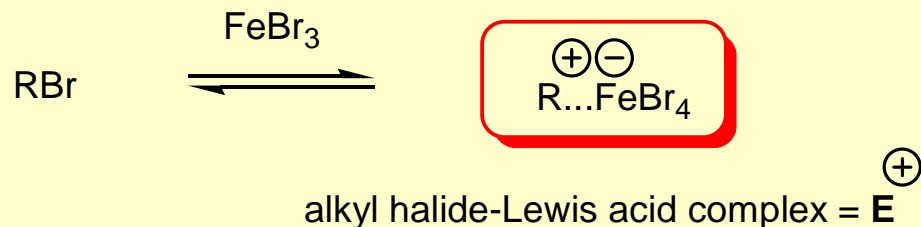
Dec 2009

Format and scope of presentation

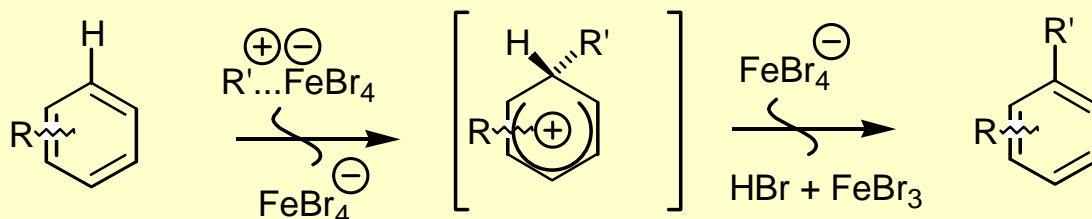
- ***Electrophilic aromatic substitution (S_EAr) – part 2:***
 - Friedel-Crafts alkylation and acylation, nitrosation (diazonium salt formation & diazo-coupling, Sandmeyer reactions),
 - Directing effects (*ortho-/para-* ratios, *ipso*-substitution)

Friedel-Crafts alkylation

- **Typical conditions:** alkyl halides in the presence of Lewis acid promoters



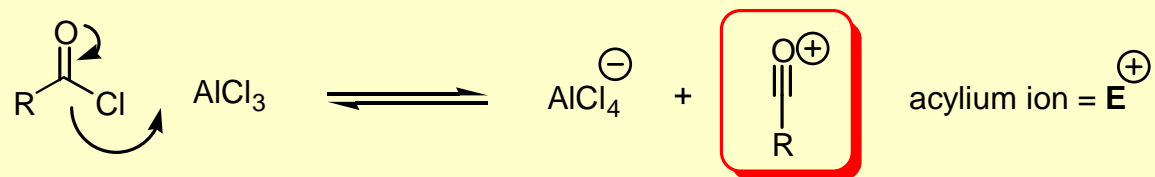
- ‘Plagued’ by rearrangements (Wagner-Meerwein 1,2-hydride shifts)
- Substantially reversible and therefore can de-alkylate!
- Products are activated relative to starting materials hence extensive poly-alkylation
- Alkyl halide-Lewis acid complex is a weak electrophile and deactivated aromatics do not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



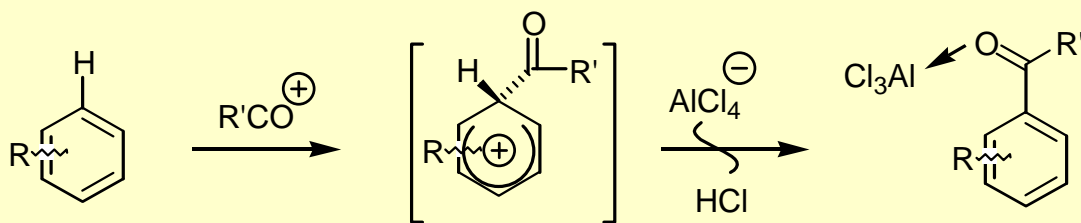
Order of Lewis acid effectiveness: $\text{AlCl}_3 > \text{FeCl}_3 > \text{BF}_3 > \text{TiCl}_3 > \text{ZnCl}_2 > \text{SnCl}_4$

Friedel-Crafts acylation

- **Typical conditions:** acid chlorides or anhydrides (also sulfonyl chlorides) \pm Lewis acid promotor :



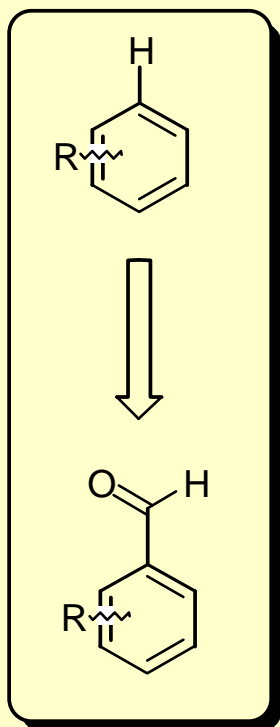
- Lewis acid not required for activated aromatics
- **stoichiometric LAs:** $AlCl_3 > FeCl_3 > BF_3 > TiCl_3 > ZnCl_2 > SnCl_4$
 - Generally can't be recycled *via* aqueous extraction
- **catalytic Lewis acids:** lanthanide(III) halides/triflates e.g. $GaCl_3, InCl_3, Hf(OTf)_4$



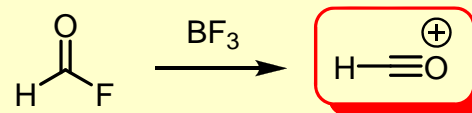
N.B. NOT catalytic in Lewis acid because it complexes to product ketone

Formylation

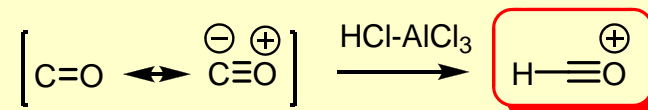
- Aryl aldehyde formation:** formyl chloride (HCOCl) is not stable so 'standard' F-C acylation is not possible. A number of classical approaches have been developed:



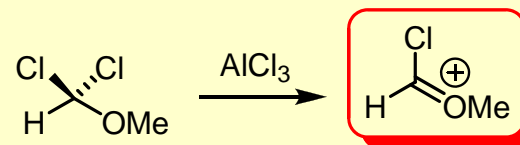
Olah-Kuhn formylation:



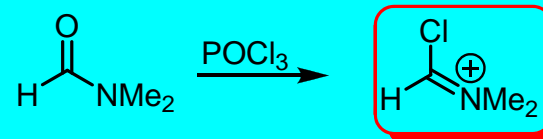
Gatterman formylation:



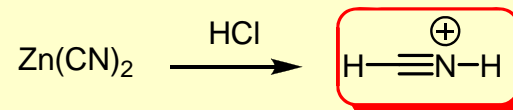
Rieche-Gross-Hoft formylation:



Vilsmeier-Haack formylation:
(activated aromatics only)

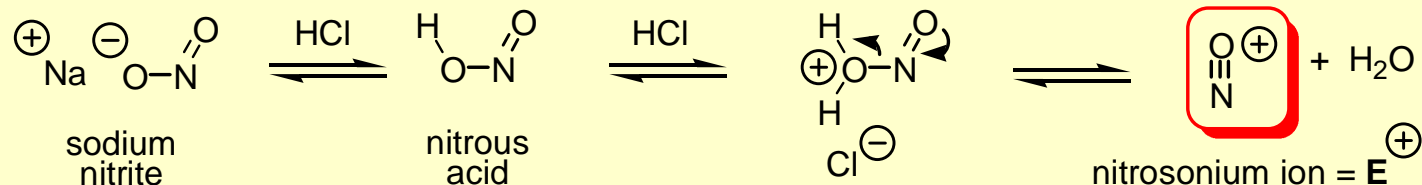


Gatterman-Koch formylation:

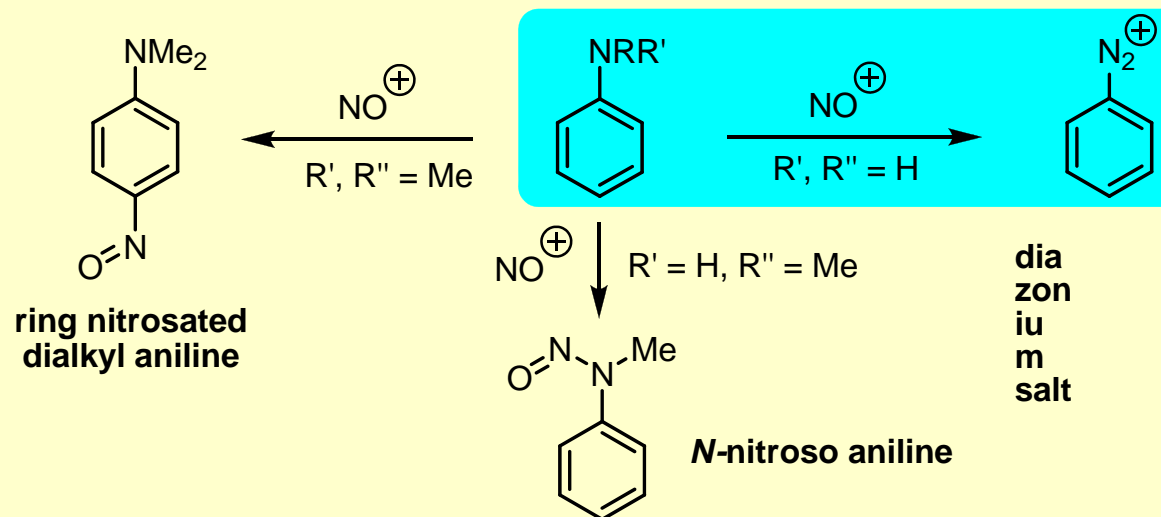


Nitrosation

- **Typical conditions:** sodium nitrite and hydrochloric acid

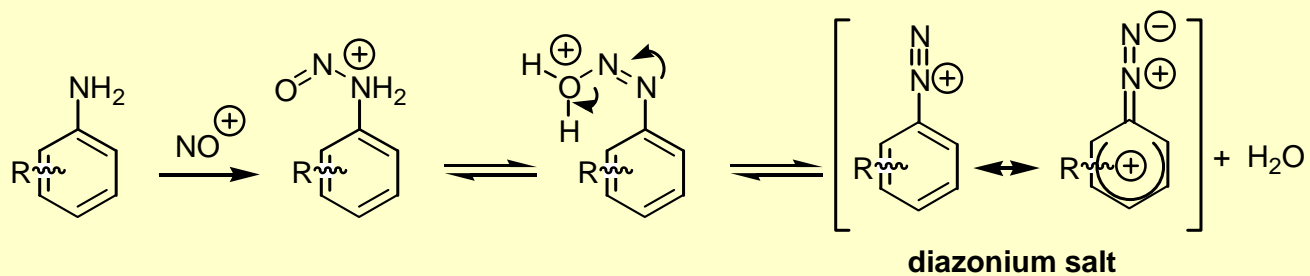


- Nitrosonium ion is weak electrophile: only ring nitrosates activated aromatics (e.g. phenols)
- *N*-Alkyl anilines give *N*-nitroso anilines (i.e. *N*-nitrosation not ring nitrosation)
- *N*-Nitroso anilines can undergo Fischer-Hepp rearrangement on heating to ring nitrosated products
- Anilines give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

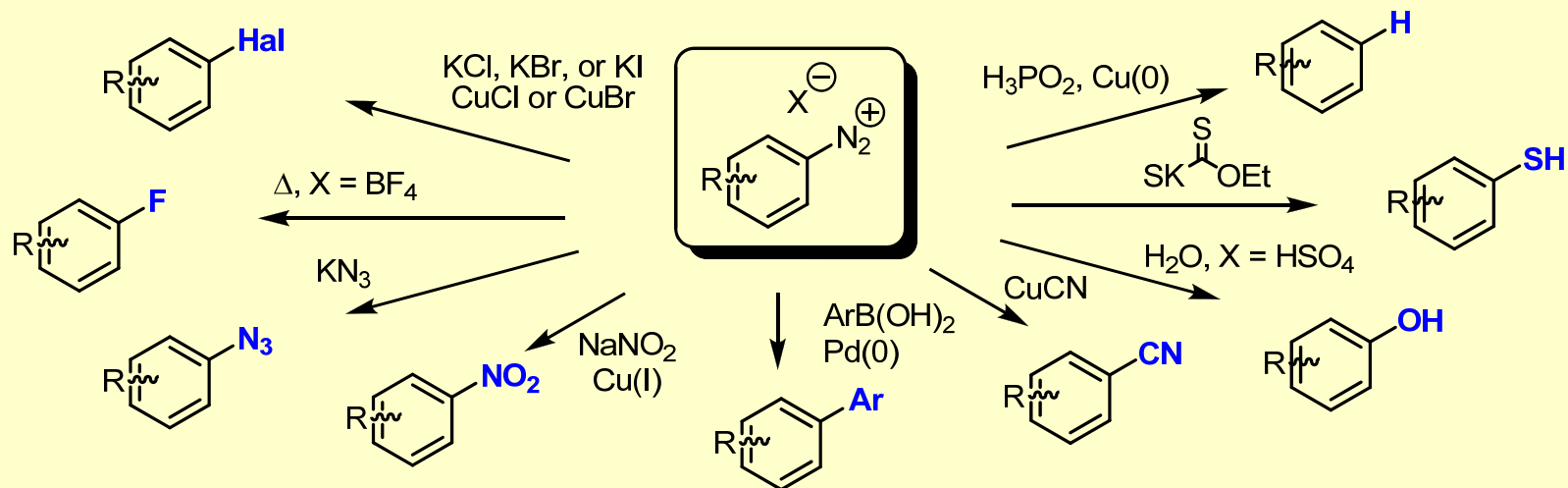


Diazotisation & Sandmeyer reactions

- Mechanism of formation:**

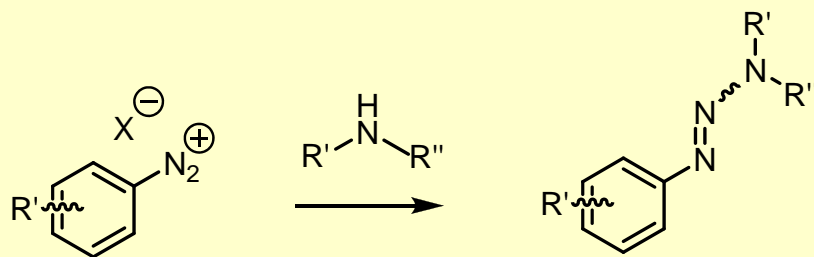


- Nucleophilic ipso-substitution (Sandmeyer reactions):**

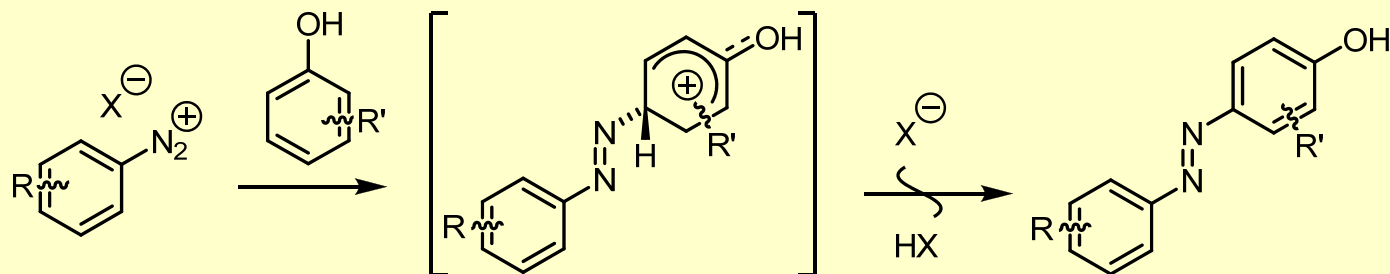


Diazotisation & diazo-coupling

- **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:

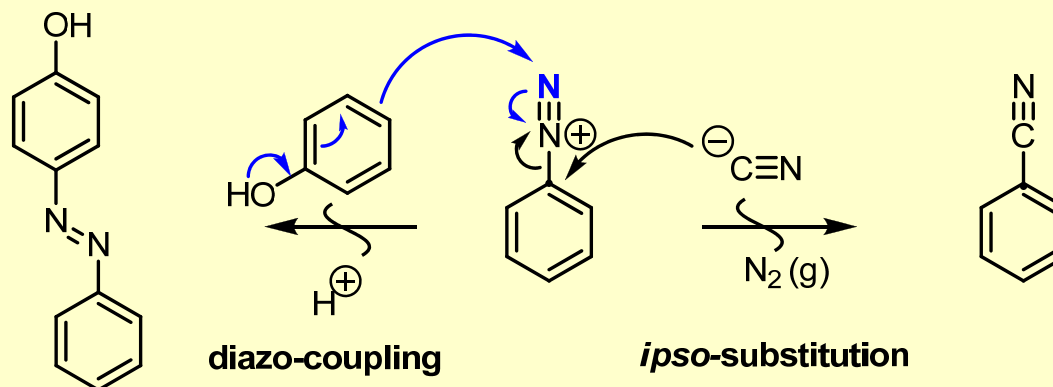


- e.g. diazo-compound synthesis (dyes) using **phenols** as C-nucleophiles:

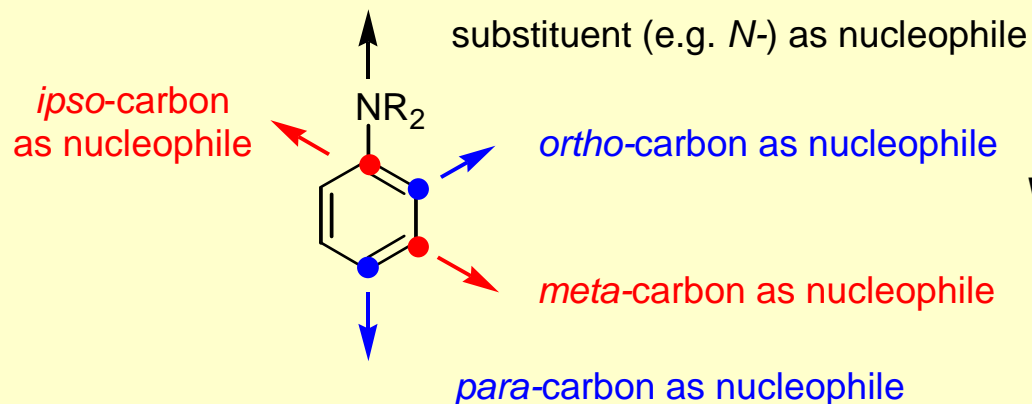


Aromatics as ambident nucleophiles

- cf. *Aryl diazonium ions as ambident electrophiles:*



- Aromatics as ambident nucleophiles ('directing effects'):*



What governs position of reactivity?