Lecture V

Previously:
1. Electrophilic Aromatic Substitution

Today
1. Nucleophilic Aromatic Substitution
2. Radical " " Complexes

1. Nucleophilic Aromatic Substitution (Sn2Ar) occurs when LG is σ- or π-
to one or more EWGs (CN, NO2)

No regioselectivity issues. Nu MUST attach to the former LG position.
Historically, a very important reaction!

\[
\begin{align*}
C_2NF + H_2N-CH_2-CH_- & \rightarrow C_2NF + H_2N-CH_2-CH_- \\
\end{align*}
\]

Frederic Sanger (Cambridge) N-terms identification

Often, Sn2Ar reactions involve single-electron transfer (SET), since they involve σ-rich
and e⁻-poor aromatic compound:

In some cases, LG is so good that it leaves without a strong nucleophile (Sn1 analogy)
-2nd order in Nu, 1st in Ar-LG:
However, the Sandmeyer reaction, although apparently similar, uses copper and involves electron transfer.

Vicarious $\text{Sn}_2\text{Ar}$ reactions:

\[
\begin{align*}
\text{R}_2\text{C} + \text{I} & \rightarrow \text{R}_2\text{C}^- + \text{I}^+ \\
\text{R}_2\text{C}^- + \text{NO}_2^+ & \rightarrow \text{R}_2\text{C} - \text{NO}_2 + \text{H}^+ \\
\text{R}_2\text{C} - \text{NO}_2 & \rightarrow \text{R}_2\text{C} + \text{NO}_2^-
\end{align*}
\]

$\text{LA}$ is a part of the incoming NO.

(2) Nucleophilic Substitutions on $\text{Cr}(\text{CO})_3$ Complexes of Arenes

\[\text{Cr}(\text{CO})_6 \xrightarrow{\Delta} \text{Cr}(\text{CO})_3 \text{or} \text{Cr}(\text{CO})_3(\text{MeCN})_3 \]

Nucleophilic substitutions are common on these complexes:

\[
\begin{align*}
\text{Cr}(\text{CO})_3 & \xrightarrow{\text{aq.} \text{OH}^- \text{ or EtOH}} \text{Cr}(\text{CO})_3 \rightarrow \text{Cr}(\text{CO})_3 \rightarrow \text{I}_2 (75\%) \\
\text{Cr}(\text{CO})_3 & \xrightarrow{\text{aq.} \text{OH}^- \text{ or EtOH}} \text{Cr}(\text{CO})_3 \rightarrow \text{Cr}(\text{CO})_3 \rightarrow \text{I}_2 (100\%)
\end{align*}
\]

we will see this compound again in supramolecular...
This complex offers other kinds of reactivity too:

\[
\begin{align*}
&\text{NuLi} \\
&\text{ipso SwAr} \\
&\text{Nu} \quad \text{NuLi} \\
&\text{Nu} \quad \text{NuLi} \\
&\text{Nu} \quad \text{NuLi} \\
&\text{Nu} \quad \text{NuLi} \\
\end{align*}
\]

3) Radical Aromatic Substitutions

-these are not just substitutions, but also other classes of reactions

a) SwAr \to \text{radical/nucleophilic}

Initiation:

\[
\begin{align*}
&\text{Nu} \rightarrow [\text{Nu}]^\Theta + \text{Nu}.
\end{align*}
\]

Propagation:

\[
\begin{align*}
&[\text{Nu}]^\Theta \rightarrow \text{Nu} + x^\Theta \\
&\text{Nu} + x^\Theta \rightarrow [\text{Nu}]^\Theta \\
&[\text{Nu}]^\Theta + x^\Theta \rightarrow [\text{Nu}]^\Theta + x^\Theta \\
\end{align*}
\]

Insensitive to EWG/EOG substituents, but highly sensitive to radical traps.

b) Benzylic position substitutions are sometimes radical in character, esp. with Cl.
\[ \text{O}_2 \text{N} \rightarrow \text{Cl} \xrightarrow{\text{Y}^+ \text{NO}_2} \text{O}_2 \text{N} \rightarrow \text{ONO}_2 \] 

Sn2 unlikely because of the bulk.

EOR confirms radical formation.

Stabilizes Ph\text{C\text{H}_{2}}^+ radical.

This is a synthetically useful process for building up highly substituted systems:

\[ \text{O}_2 \text{N} \rightarrow \text{Cl} \xrightarrow{\text{Y}^+ \text{NO}_2} \text{O}_2 \text{N} \rightarrow \text{ONO}_2 \] 

These are also chain processes.

d) Radical addition/eliminations, not involving chain reactions:

Either of the two steps can be rate-determining:

Regiochemistry: almost any substituent enhances the rate (EWG/EOG).

Smaller partial rate factors than for ionic substitutions, but with some trends.

Explanation: a) EWG/EOG is a charge-based argument so it affects more.

b) In radical reactions, 1st can be exothermic, while it is typically endothermic with ionic species.

Hence, little changes is radical is stabilized.