Lecture VI

Previously:
1. Electrophilic Aromatic Substitution
2. Nucleophilic " "
3. Radical " "

Today:
1. Benzyne as an Intermediate Formation
2. Reactivity
3. Substituent Effects

1. John Roberts (Caltech) first suggested the existence of benzyne (dehydrobenzene):

\[
\begin{align*}
&\text{HC,} \\
&\text{C}_6\text{H}_4 \\
&\text{cumulene structure} \\
&\text{biradical structure} \\
&\text{most important contributor}
\end{align*}
\]

Calculations suggest bond localization:
- 1.42 Å vs 1.22 Å

Benzyne has a very strained alkyne:
- \( \Delta H_f = +118 \pm 5 \text{ kcal mol}^{-1} \)

Benzyne has been observed at low temperatures, and has been trapped in hemicarcerand (UCLA):
- Warmuth, R. AcIEE 1977, 36, 1347

- \( ^1\text{H-NMR (in carcerand)} \): 4.99, 4.31
- \( ^{13}\text{C-NMR (in carcerand)} \): 121.33, 125.45
- \( ^1\text{H-extrapolated for 5e} \): 7.69, 7.01

Based on coupling constants, NMR is more consistent with cumulenic structure, but a real model is still absent.

How is benzyne formed?
John Roberts (Caltech)
-born in 1918
-went to UCLA when they did not have a PhD program
-JOC, 2009, 74, 4897

First order in Ar-Br, and in base. Concerted E2-analog better with better LGs. However, with a poor LG, elimination becomes rate-limiting:

Hofmann
Dehydrobenzene and cycloalkynes

2) Benzene reactivity - essentially an electrophile
Addition of C-nucleophiles:

Although this could be radical in character too.

If benzyl is generated in the absence of bases, it can act like an electrophile:
Finally, concerted reactions:

\[
\begin{align*}
\text{[4+2]} \quad & \quad \text{Diels-Alder} \\
\text{[2+2]} \quad & \quad \text{[2+2]} \\
\text{[2+1]} \quad & \quad \text{[2+1]} \\
\end{align*}
\]

Ene-reaction

\[
\begin{align*}
\text{[2+2]} & \quad \text{[2+2]} \\
\text{[2+1]} & \quad \text{[2+1]} \\
\end{align*}
\]

should work, but getting two short-lived intermediates together is improbable

3) Substituent effects

a) Where does C=C bond form?

\[
\begin{align*}
\text{[acidity of eliminating proton is crucial: } Y=EWG \rightarrow \text{A; } Y=EOG \rightarrow \text{B} \\
\text{Only!} \\
\end{align*}
\]

b) Where does nucleophile attack?

 favored if Y=EWG

 favored if Y=EOG (but weakly)

too far, weak effects, mixtures
here, Y affects both steps

weak selectivity

Y = CH₃ → all three products!