Lecture XXXIII: Supramolecular Catalysis


Today, lecture will be short because of evaluations at the end.

1. Approaches in supramolecular catalysis
   Examples of reactions in cavities
   Other examples of supramolecular catalysis
   Self-replication.

1. How can supramolecular chemistry help?

A) Proximity of binding site and reactive site:

- β-cyclodextrin
- Facilitates hydrolysis of p-nitrophenyl acetate

B) Preparation of catalyst through supramolecular interactions:

- Polymeric enzyme
- [M]
- [M]
- Supramolecular chelating ligand

C) Promotion of reactivity between two independently encapsulated species

\[ \text{A + B} \xrightarrow{\text{slow}} \text{A-B} \]

\[ \text{A + B} \xrightarrow{\text{fast}} \text{A-B} \]

- A - B necessary for catalytic turnover

- MORE EFFECTIVE
- AND MORE SELECTIVE
- THAN SIMPLE PROLINE

04/20/2010
Let's see some examples of these reactions proceeding in supramolecular cavities:

\[
\text{J} + \text{A} \rightarrow \text{normal 9,10-adduct}
\]

But in Makoto Fujita's octahedral capsule:

More recently:

\[
\text{J} + \text{A} \rightarrow \text{unusual 1,4-adduct in } H_2O
\]

Most common interpretation is a "compressed transition state."

Raynolds + Bergman:

\[
\text{HC(OEt)}_3 \xrightarrow{\text{pH 11}} H_2O + 3\text{EtOH} \quad \text{Science, 2007, 316, 85}
\]

Aromatic cavity stabilizes putrescine, but wait, orthoformates should be stable in basic solution.
pK_a (amine-H^+) ~ 10, but in the cavity it is ~14!

3. Some other examples

Using supramolecular interactions to identify the best catalyst:

\[ A + B \rightarrow [A-B]^+ \rightarrow A-B \]

\[ \uparrow \]

catalyst should bind to TS best, but you cannot isolate TS and screen it against hosts.

Sanders, Angew Chem Int Ed 2003, 42, 1270

\[ \text{TS analog} \]

\[ \text{similar in structure} \]

\[ P \text{ amplified one} \]

\[ \text{compound from the mixture of disulphides} \]

\[ \rightarrow \text{Shows moderate rate increases in O-A reaction} \]

Helping the stereoselectivity:

Thorsten Bach (LMU Munich)
Angew Chem Int Ed 2004, 43, 5849

79% ee

**Homework:**
Propose an explanation for this outcome.
In general, supramolecular catalysis has (so far) not been able to rival small-molecule or enzymatic catalysis. However, it can help with reactions in uncommon media (H₂O instead of organic solvents) and it can often change selectivities depending on structural and electronic parameters.

Finally: Self-replicating systems:
(autocatalytic)