Self-Assembly

- TERMINOLOGY
- SELF-ASSEMBLING COORDINATION COMPOUNDS
- HYDROGEN BOND SELF-ASSEMBLIES
- INTERLOCKED MOLECULES
- APPLICATIONS
Self-Assembly

Templating:
Aid to the synthesis through the involvement of temporary or permanent “helper” species.

Templating a dynamic combinatorial library
Self-Assembly

Supramolecular self-assembly:
Recognition-directed, reversible spontaneous association of a limited number of molecular components (tectons) under intermolecular control of noncovalent interactions. Reversibility: crucial to form thermodynamically most favorable structure, self-repair and corrections of defects.

Recognition-directed self-assemblies

- Strict self-assembly (Tobacco-virus)
- Self-assembly with covalent modifications (Insulin)
Self-Assembly with Covalent Modifications

Biosynthesis of insulin by self-assembly followed by covalent modification.
Self-Assembly

Self-organization – interactions between constituents parts of self-assembled entities and the integration of those interactions leading to collective behavior such as phase changes.
Thermodynamics of Strict Self-Assembly
Thermodynamics

\[ K_a = 10^2 - 10^3 \text{ M}^{-1} \]

\[ K_a = 10^4 - 10^5 \text{ M}^{-1} \]

\[ K_a > 10^5 \text{ M}^{-1} \]

---

\[ \cdots \cdots \text{= (attractive) hydrogen bond} \]

\[ \leftrightarrow \text{= attractive secondary interaction} \]

\[ \leftrightarrow \text{= repulsive secondary interaction} \]
Template effect in Synthesis

- Metal ions as kinetic templates

Covalent template synthesis of an 18-membered macrocycle
Template Effect in Synthesis

- A catenane or rotaxane precursor:

- Interpenetration of an electron-rich guest with an electron-poor macrocycle
A Thermodynamic Model of Self-Assembly

Zinc Porphyrine Complexes:
Zn-pyridyl bond is labile in organic solvents

Also dimer and trimer due to the flexibility of the bridge
A Thermodynamic Model of Self-Assembly

Isac: lower self-assembly concentration

EM: effective molarity (concentration at what open oligomer formation starts to compete formation of cyclic oligomers)

i.e. $10^{-5}$ 0.6 (mol/l)
Self-Assembling Coordination Compounds

Naked Metal (divergent) + Convergent → Capsule

Protected metal (convergent) + Divergent → Capsule

Naked metal (divergent) + Divergent → Polymer
Self-Assembling Coordination Compounds

<table>
<thead>
<tr>
<th>Ditopic Subunit</th>
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<th>60°</th>
<th>90°</th>
<th>109.5°</th>
<th>120°</th>
<th>180°</th>
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<td>A</td>
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<td>180°</td>
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“Molecular Library” of polygons from ditopic units

Self-Assembling Coordination Compounds

A. POLYGONS: Trinuclear Structures

One of the units with 60°
Self-Assembling Coordination Compounds

\[ \text{Inorg. Chem. 2004, 43, 5335.} \]
Self-Assembling Coordination Compounds

A. POLYGONS: Tri- and Tetranuclear Structures

Less strained – major

Smaller entropy (smaller number of components)
– increasing fraction at lower concentrations

Equilibrium monitored by \(^1\text{H NMR}\)
Signals assigned in combination with Electron Spray MS
Molecular square (\(X=\text{nothing}\)) binds naphthalene

Self-Assembling Coordination Compounds

Macrocycle prevails at concentrations < 2 mM
Binds organic guests

Catenane prevails at concentrations > 50 mM

Pd: labile; Pt: inert

Self-Assembling Coordination Compounds

For Pt equilibrium is reached upon heating
Self-Assembling Coordination Compounds

A. POLYGONS: Tri- and Tetranuclear Structures

With more sterically demanding ligands squares are exclusively formed
Self-Assembling Coordination Compounds

- Cryptand synthesizable only through induced fit of a guest because the linkers are flexible
- Templated with phenylpropionic acid or adamantane-carboxylic acid, not with cations or xylene
- Stable even after synthesis and removal of the guest, not necessarily a thermodynamic product

(Adamantanecarboxylic acid)$_4$@[Pd(en)$_{12}$(7.16)$_8$]$^{12+}$, allosteric effect, 4.6 nm
Self-Assembling Coordination Compounds

CAGES (POLYHEDRONS)

“Molecular Library” for the formation of 3D-assemblies from ditopic and tritopic subunits.

Self-Assembling Coordination Compounds

Edge-Directed Self-Assembly

Face-Directed Self-Assembly

Self-Assembling Coordination Compounds

Cube

\[ \text{8} + \text{12} \rightarrow \text{Cube} \]

\[
\begin{align*}
\text{[RuCl}_2\text{Cl]} & \rightarrow \text{[RuL}_2\text{]} ^{2+} \\
\text{DMSO} \rightarrow 2 \text{AgOTf} - 2 \text{AgCl} \\
\text{4 weeks} \rightarrow 16^+ \text{OTf} \\
\end{align*}
\]
Self-Assembling Coordination Compounds

- Dodecahedra
Self-Assembling Coordination Compounds

- Trigonal bipyramids

Self-Assembling Coordination Compounds

- Truncated tetraheders

90° Ditopic corners

Planar tritopic linkers

Self-Assembling Coordination Compounds

- Molecular paneling
Self-Assembling Coordination Compounds

- Molecular paneling
Self-Assembling Coordination Compounds

- Nanoreactor
Self-Assembling Coordination Compounds

- Molecular paneling, face directed
Self-Assembling Coordination Compounds

Molecular Paneling, face directed, nanotubes
Self-Assembling Coordination Compounds

Other Arrays:

- Helicates
- Grids
- Racks
- Ladders
- Cylinders
- ......
Self-Assembly by Hydrogen Bonding

Tennis Ball:
Self-Assembly by Hydrogen Bonding

Tennis Ball, observed by:

- NMR Spectroscopy in CDCl$_3$: Shift of the NH protons
- Mass Spectrometry
- Vapour pressure osmometry
- X-Ray Crystallography
- Encapsulation of methane and ethane (K = 300 mol/l) in CDCl$_3$
- Bad host for dichloromethane (K = 4)
Self-Assembly by Hydrogen Bonding

Soft Ball:

\[ X = H: \quad (7.30) \]
\[ X = OH: \quad (7.31) \]
\[ R = \text{CO}_2-i\text{-penty}l \]

Templating guests

Guest encapsulation by ‘softball’ hosts is driven by entropic (solvophobic) effects.
Self-Assembly by Hydrogen Bonding

Soft Ball:

- "Catalysis" of Diels-Alder Reaction
- Self-inhibition: the product is a better guest than the reactants (Entropy-driven complexation)
- 55% of the cavity should be occupied by the guest to obtain the highest affinities in the absence of strong interactions (0.16 nm³ for the 0.34 nm³ cavity of soft ball)
- Similar value for liquids
Rosettes

Enthalpy vs. Entropy:

Enthalpically favourable:
-18 H-bonds formed
\( \Delta H = -100 \text{KJ/mol} \)

Entropically very unfavourable. (6 molecules bounded)

→ Stability: \( \frac{HB}{(N-1)} \)

\( HB = \) Number of hydrogen bonds
\( N = \) Number of molecules
Rosettes

Preorganisation by linking three units together

Peripheral crowding to inhibit tape and sheet formation
Rosettes

Calix[4]arene bismelamines

Barbituric or cyanuric acid

Double rosette

Rosettes

Complex with 3 molecules alizarin
Rosettes

Release of the guest with cyanuric acid
Alternatively, with protic solvent or a pH change (breaking of the capsule)
Interlocked Molecules

A. ROTAXANES
B. CATENANES
C. MOLECULAR KNOTS

[2]Rotaxane

[2]Pseudorotaxane

[2]Catenane

Trefoil knot
Rotaxanes: Synthesis

Threading

Snapping

Slipping

Clipping

Statistical approach ineffective: < 2 % y.
Rotaxanes

Synthesis: Clipping Approach

\[
\begin{align*}
\text{Si - O - O - O - O - Si} & \quad + \quad \text{Si - O - O - O - O - Si} \\
\text{N}^+ \quad \text{N}^+ & \quad + \quad \text{N}^+ \quad \text{N}^+ \\
\text{Br} \quad \text{Br} & \quad + \quad \text{MeCN, AgPF}_6, \text{RT, 7d} \\
\text{NH}_4\text{PF}_6, \text{H}_2\text{O} & \quad \xrightarrow{\text{MeCN, AgPF}_6, \text{RT, 7d}} \quad \text{N}^+ \quad \text{N}^+ \quad \text{N}^+ \quad \text{N}^+ \\
\end{align*}
\]
Rotaxanes

Synthesis: Slipping Approach

BPP34C10

MeCN /55°C / 10 Days

[2]Rotaxanes

<table>
<thead>
<tr>
<th>R</th>
<th>H</th>
<th>Me</th>
<th>Et</th>
<th>i-Pr</th>
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<tbody>
<tr>
<td>Yields (%)</td>
<td>52</td>
<td>45</td>
<td>47</td>
<td>0</td>
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J.F. Stoddart
Rotaxanes

Synthesis: Threading Approach

Rotaxanes

Synthesis: Threading/Snapping Approach
Catenanes

Synthesis via the clipping approach
Catenanes

Synthesis, Charge-Transfer Aided

1. Formation of the tricationic intermediate
2. Formation of a charge transfer complex
3. Self-organization to promote the catenation
4. The catenane is formed (in 70% yield)
Catenanes

Process I: Circumrotation of the crown ether through the bipyridinium macrocycle
Process II: Circumrotation of the bipyridinium macrocycle through the crown ether (values from the coalescence temperature of a VT NMR experiment.)
Catenanes

<table>
<thead>
<tr>
<th>$n$</th>
<th>$m$</th>
<th>Yield of [2]catenane (%)</th>
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<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>[31]crown-9</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
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<tr>
<td>3</td>
<td>3</td>
<td>[46]crown-14</td>
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Catenanes

Synthesis:
Auxiliary linkage approach
Catenanes

Synthesis:
Auxiliary linkage approach (covalently)
Catenanes

Coordination aided synthesis

Yield:
27 % in one step,
42 % in two steps

• Removal of Cu with CN⁻

• CV: Reversible reduction (in contrast to the open chain complex)
**Helicates**

\[
\begin{align*}
\text{Cu}_3(7.87e)_2 \\
\text{CO}_2\text{Et substituents omitted}
\end{align*}
\]

\[
\begin{align*}
isobestic points & \rightarrow \text{only two species present} \quad 55
\end{align*}
\]
Helicates

Strong positive cooperativity

\[ r = \text{average number of occupied sites} \]
Molecular Knots

$X_n$

$X$ – number of crosses

$n$ – order of the knot
Molecular Knots
Molecular Knots

Synthesis of a 84 membered macrocycle

Bis(1,10-phenanthroline)

Yield:
- a,b,c: less than 8%
- d: 29%
Molecular Knots

Doubly interlocked [2]catenane

Pentafoil knot

Triply interlocked [2]catenane
Catalytic Systems

Inhibited by the product

Self-assembling catalysis via a ternary complex involving a bisubstrate reaction template (after Kelly et al. 1989)
Self-Replicating Systems

Really autocatalytic since the ternary complex is more stable than the binary complex.