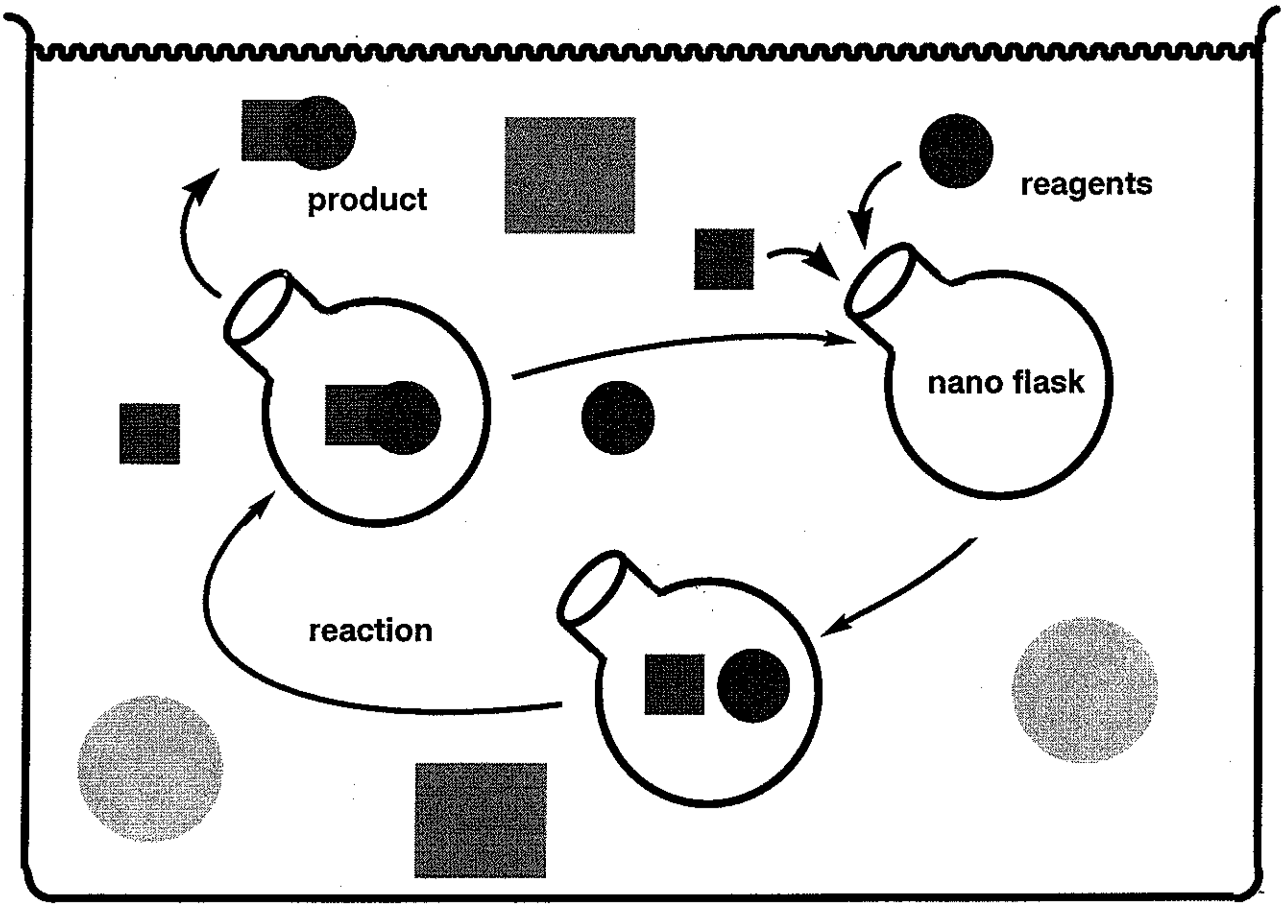
Literature Seminar (2008. Apr. 16th) Hisashi Mihara D3 (for D2)

Reaction in the molecular

~Using Self-Assembly Supramolecular Cluster~

○「Prologue」



— Contents —

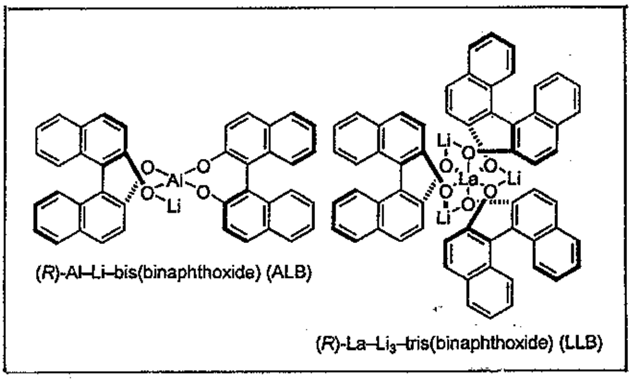
○「Introduction」

「Supramolecular Chemistry」

…. Supramolecular chemistry refers to the area of chemistry that focuses on the noncovalent bonding interactions of molecules.

In our group

- Heterobimetallic rare-earth-alkali-metal-binol catalyst



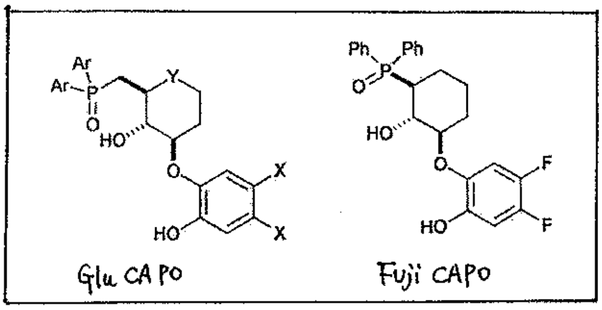
(R)-Al–Li–bis(binaphthoxide) (ALB)

(R)-La–Li_3–tris(binaphthoxide) (LLB)

○ J.A.C.S. 1992, 114, 4418

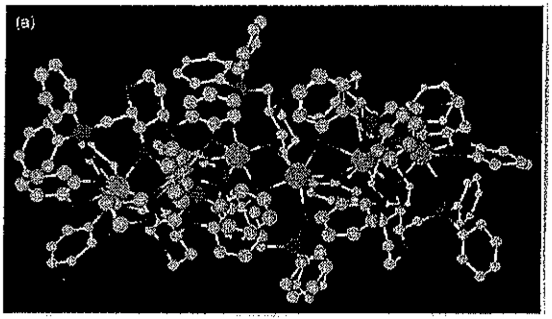
○ Angew. Chem. Int. Ed. Engl. 1997, 36, 1236

- Self-Assembled Poly Rare Earth Metal Complexes

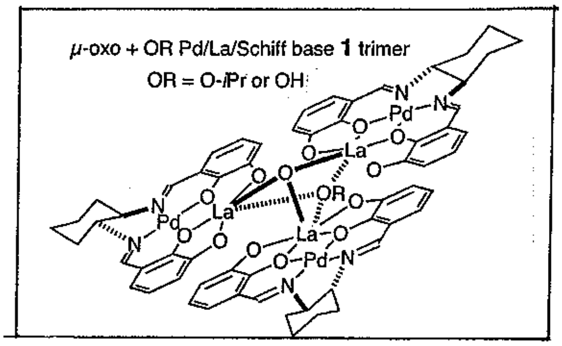


○ Org. Biomol. Chem. 2007, 5, 2027 (described in detail)

※ X-ray structure of crystal (La : Ligand 6 : 8)



- Schiff Base Complex



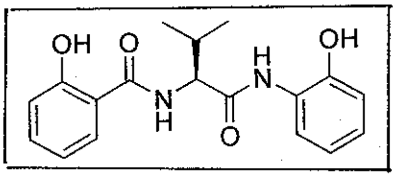
μ-oxo + OR Pd/La/Schiff base **1** trimer
OR = O-*i*Pr or OH

○ Angew. Chem. Int. Ed. 2008, 47, 3230

○ J. Am. Chem. Soc. 2008, 130, 2170

○ J. Am. Chem. Soc. 2007, 129, 4900

- Ligand / Rare Earth Metal Conglomerate



○ J. Am. Chem. Soc. 2008, 130, in press.

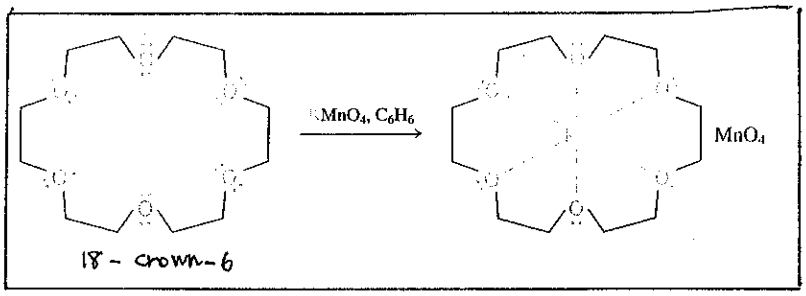
○ Tetrahedron Lett. 2008, 49, 272

○ J. Am. Chem. Soc. 2007, 129, 11342

o「The History of Supramolecular Chemisery」

1967. C. J. Pederson et al.

「Crown ether」 ref. J. Am. Chem. Soc. 1967, 89, 7017



cf. 12 - crown - 4
15 - crown - 5 etc.

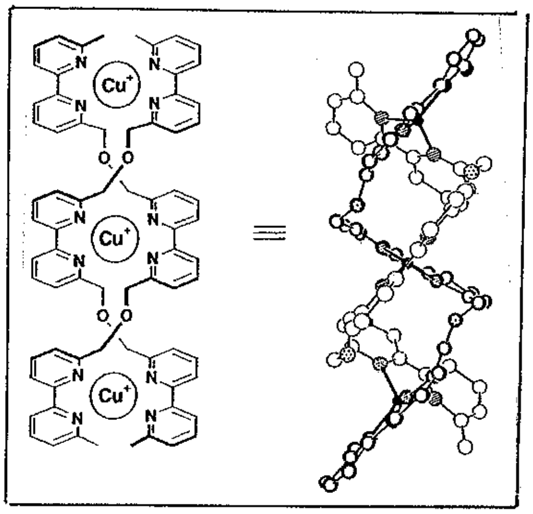
Crown ethers strongly bind certain cations forming complex.

⇨ This is the breakthrough for " Supramolecular Chemistry "

1987. J. M. Lehn et al. ref. Proc. Natl. Acad. Sci. USA 1987, 84, 2565

「Inorganic double helix」

→ This is the study that impressed it with a concept of the supramolecular definitely.



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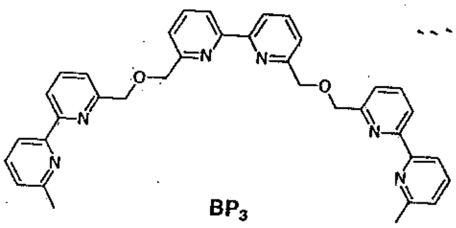


BP3

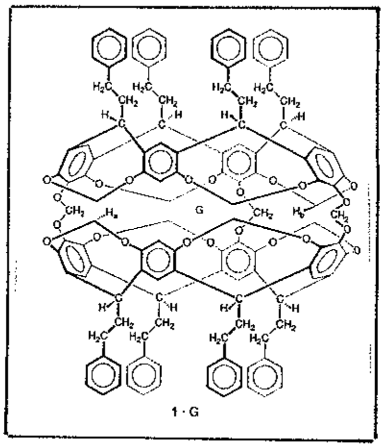
···· Poly bipyridine Ligand

\+

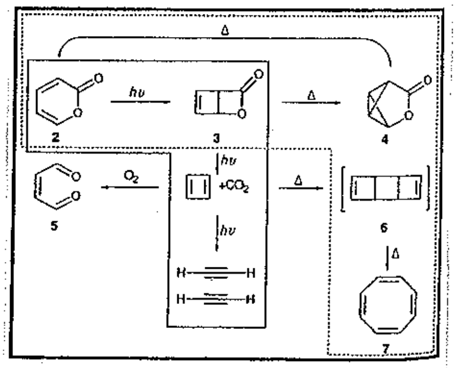
Cu(I) salt (CuOTf)

1991 D. J. Cram et al. ref Angew. Chem. Int. Ed. Engl 1991, 30, 1024

「Molecular encapsulation」



1·G



Scheme 1. Thermal and photochemical transformations of α-pyrone. The three frames contain reactions carried out: ---- historically in solution and gas phase; —— historically in an argon matrix at 8 K; —— in the inner phase of the hemicarcerand 1, and reported here (except cyclooctatetraene formation, which occurs outside).

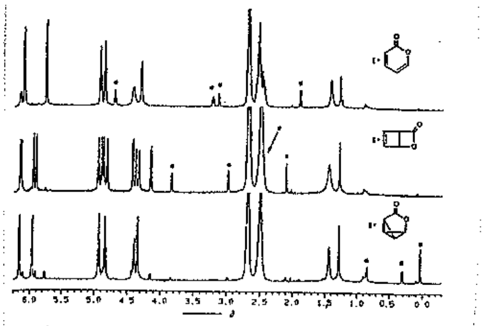


Fig. 1. ¹H NMR spectra (500 MHz, $CDCl_3$, 60°C) of hemicarceplexes 1·2, 1·3, and 1·4. Signals marked by stars are due to guests.

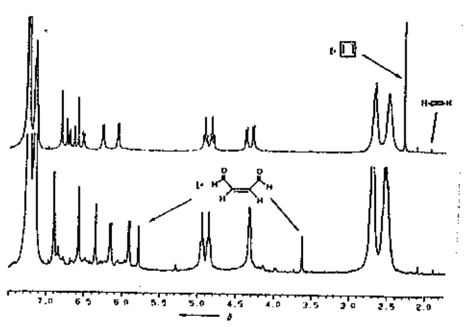
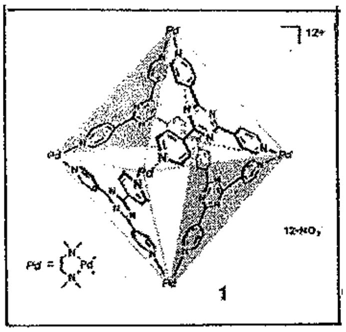


Fig. 2. ¹H NMR spectra (500 MHz, $CDCl_3$, 60°C) of hemicarceplexes 1·$(CH)_4$ and 1·(Z)-OHCCH=CHCHO.

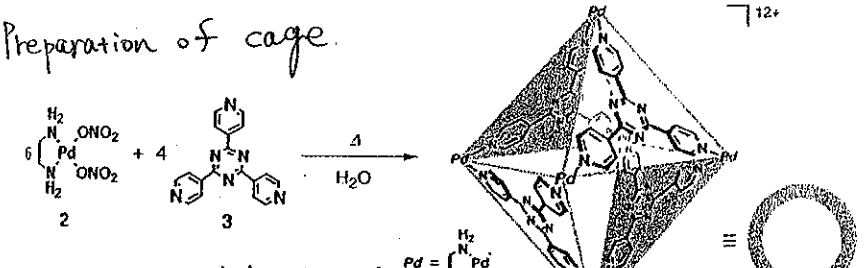
→ They report the synthesis and reactions of cyclobutadiene lodged in the cavity of the hemicarceplex 1.

○「Encapsulation into the molecular」

Fujta et al.



Preparation of cage



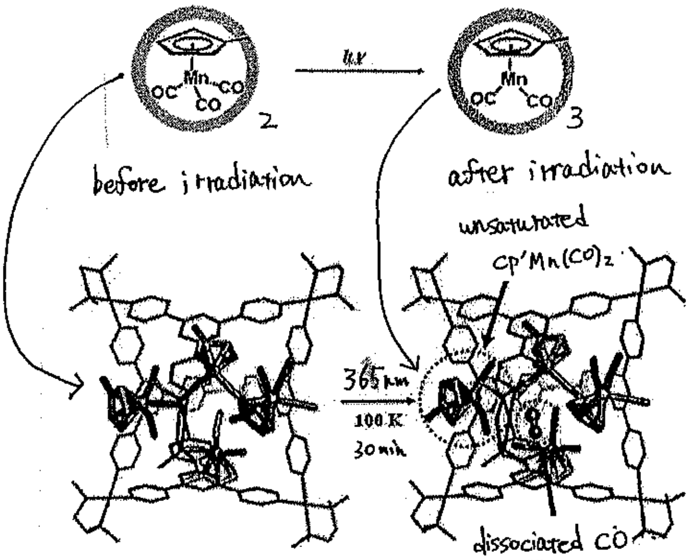
(Ligand 3 was suspended in H_2O solution of 2 and heated to 80°C.)

→ Nature 1995, 378, 469.

↳ pale yellow powder

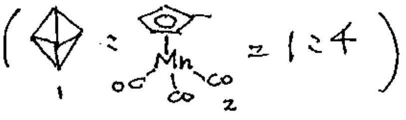
Direct Crystallographic Observation of a Coordinatively Unsaturated Transition-Metal Complex in situ Generated within a Self-Assembled Cage

→ J. Am. Chem. Soc. 2006, 128, 6558.



The reactive intermediates have never been investigated by crystallography. because of their labile nature.

→ The crystallographic analysis's confirmed the 1:4 complexation.



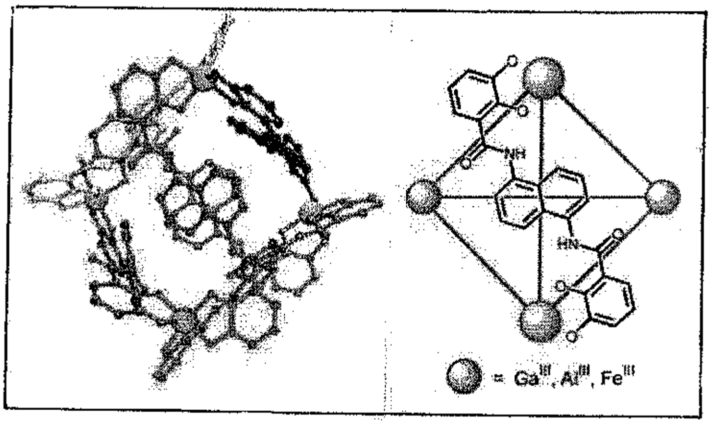
(1 : 2 = 1 : 4)

They successfully refined the molecular structure and observed the formation of coordinatively unsaturated Cp'Mn(CO₂)₂ (3) from one of four manganese complexes in the cage.

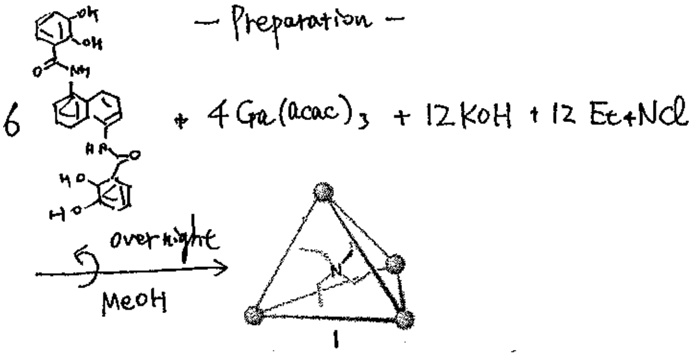
Raymond et al.

The Self-Assembly of a Predesigned Tetrahedral M_4L_6 Supramolecular Cluster**

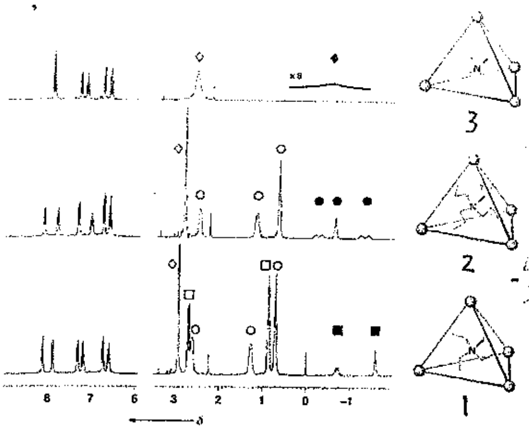
→ Angew. Chem. Int. Ed. 1998, 37, 1840



— Preparation —



L + Ga(acac)$_3$ + KOH + $\underline{\underline{Me_4NCl}}$ → 3



Pr$_4$NCl was added to 3

Et$_4$NCl was added to 2

◇ exterior Me$_4$N$^+$ ◆ interior Me$_4$N$^+$
○ exterior Pr$_4$N$^+$ ● interior Pr$_4$N$^+$
□ exterior Et$_4$N$^+$ ▨ interior Et$_4$N$^+$

Selective C–H Bond Activation by a Supramolecular Host–Guest Assembly**

→ Angew. Chem. Int. Ed. 2004, 43, 963

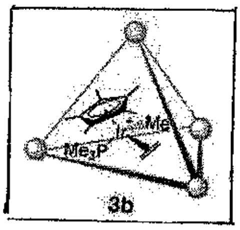
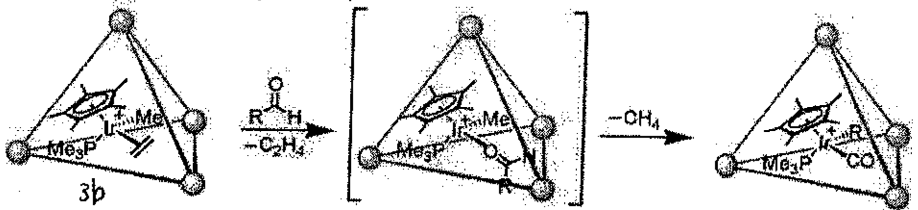
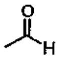
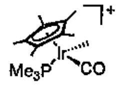
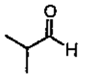
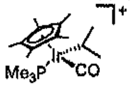
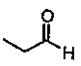
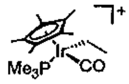
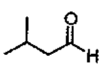
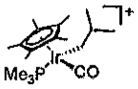
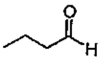
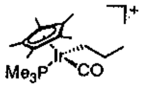
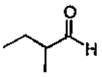
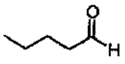
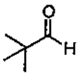
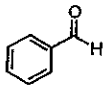


Table 1: Observed steric and diastereoselectivities in the C–H bond activation of aldehydes by the encapsulated iridium host–guest complex.



	Substrate	Guest product[a]	d.r.		Substrate	Guest product[a]	d.r.
4			60:40	9			55:45
5			65:35	10			58:42
6			70:30	11		n. r.	n/a
7		n. r.	n/a	12		n. r.	n/a
8		n. r.	n/a				

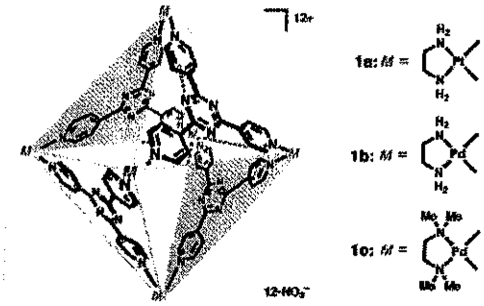
[a] n. r. = no reaction.

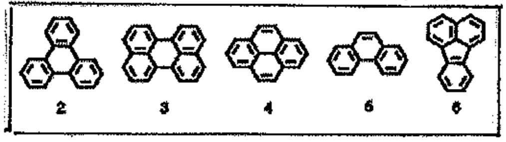
Table 1 showed size selectivity and shape selectivity plays a key role in the encapsulated C–H bond-activation reactions.

○「Reaction in the molecular

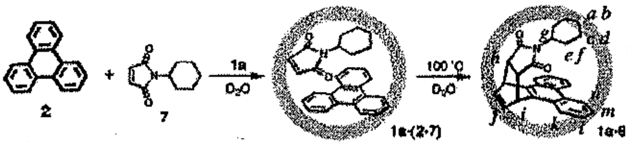
Unusual [2+4] and [2+2] Cycloadditions of Arenes in the Confined Cavity of Self-Assembled Cages

→ J. Am. Chem. Soc. 2007, 129, 7000

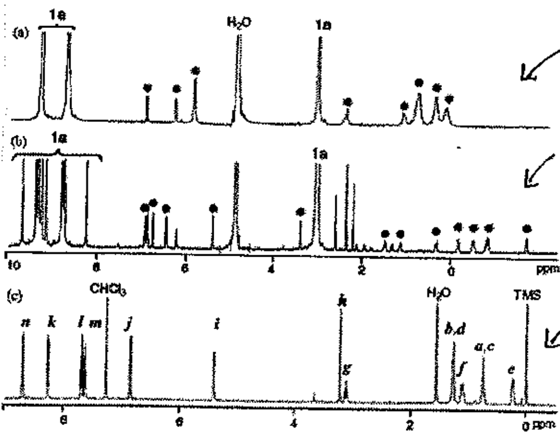




→ These compounds are inert under ordinary conditions.



↳ To date periodic reaction involving this substrate have not been reported.

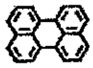


ternary complex 1a·(2·7)

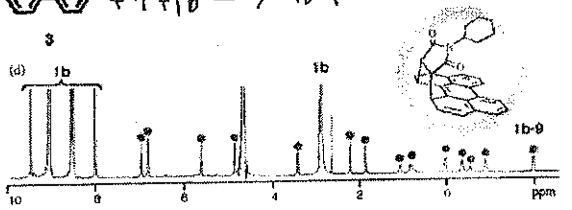
product 1a·8 (heated 100°C 24h)

Diels-Alder adduct 8 (extracted with CHCl$_3$)

similar condition (80°C, 24h)


3

+ 7 + 1b → 1b·9



crystal X-ray diffraction →

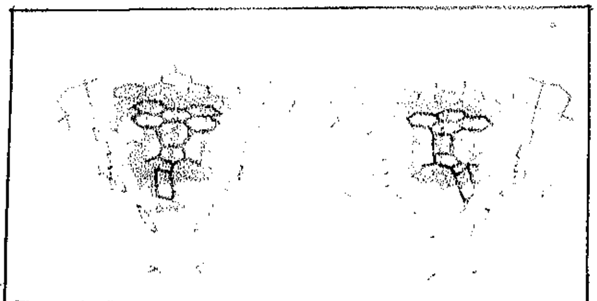
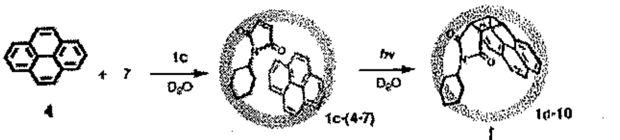
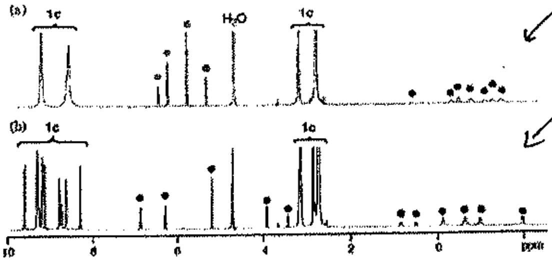


Figure 2. Crystal structures of (a) 1c·9 and (b) 1c·10.

※ 9 was extracted from the cage, the air oxidation was obserbed, however 9 was very stable toward oxidation inside the cage.



↓ crystal X-ray diffraction



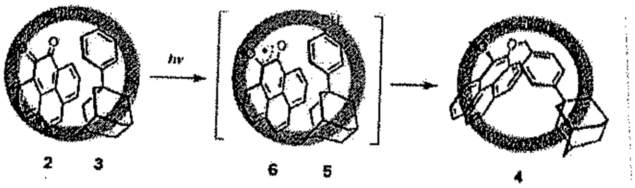
before irradiation

after irradiation

(500MHz, D_2O 27°C, 6h)

Highly Selective Photomediated 1,4-Radical Addition to *o*-Quinones Controlled by a Self-Assembled Cage**

→ Angew. Chem. Int. Ed. 2008, 47, 2067



(The proposed reaction mechanism involves the 1,4-addition of benzylic radical 5, formed by photoexcitation of quinone 2 and subsequent hydrogen abstraction from 3.


1a

+ 2+3 $\xrightarrow[30min]{80°C}$ 1a·(2·3)

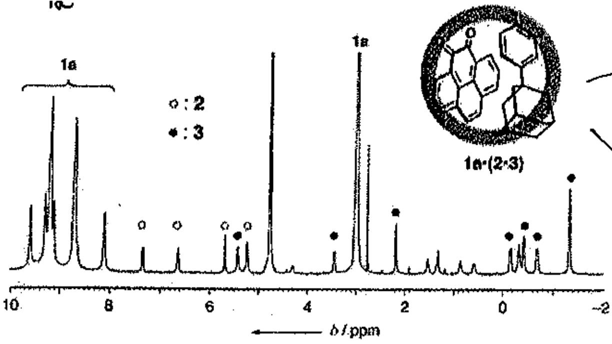


Figure 1. ¹H NMR spectrum of **1a**·(**2**·**3**) (500 MHz, D₂O, 300 K).

crystal X-ray diffraction →

one of carbonyl group of 2 is very close to methyl group of 3.

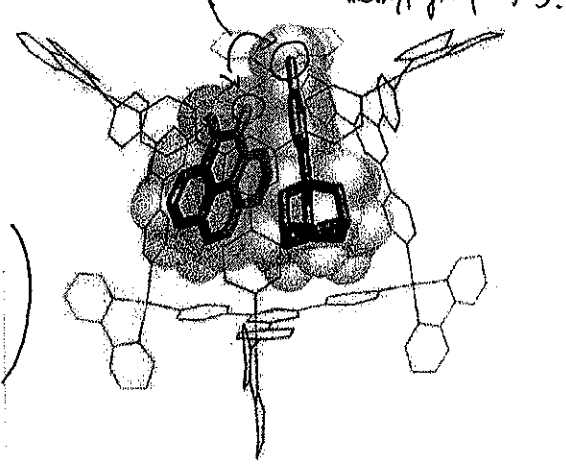
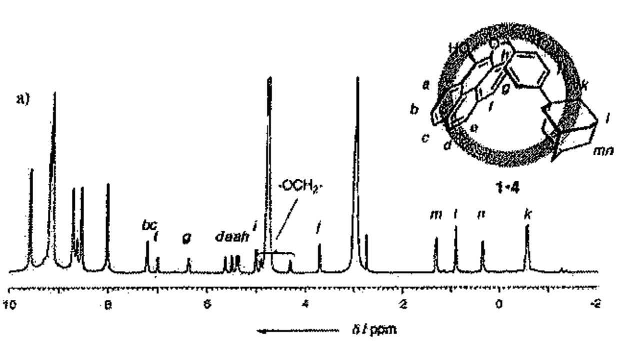


Figure 2. Crystal structure of **1b**·(**2**·**3**). For clarity, H atoms, anions and solvent molecules have been omitted. Cage **1b** is shown with thin lines, substrates **2** and **3** with thick lines. A space-filling depiction of **2** and **3** is shown in the background. C blue, O red, N black, Pd yellow.

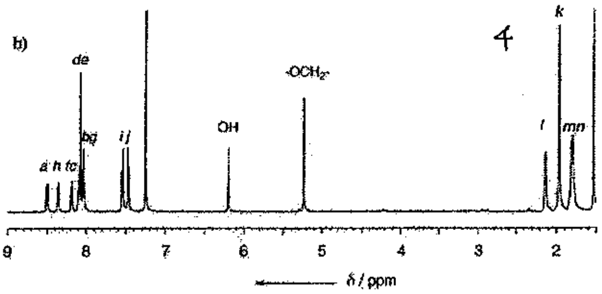
irradiation

(ultra-high-pressure mercury lamp 5min)



after purification

→ They obserbed the selective formation of a single product in the cavity.



。「Catalytic reactions」

Diels-Alder in Aqueous Molecular Hosts: Unusual Regioselectivity and Efficient Catalysis

→ science, 2006, 312, 251

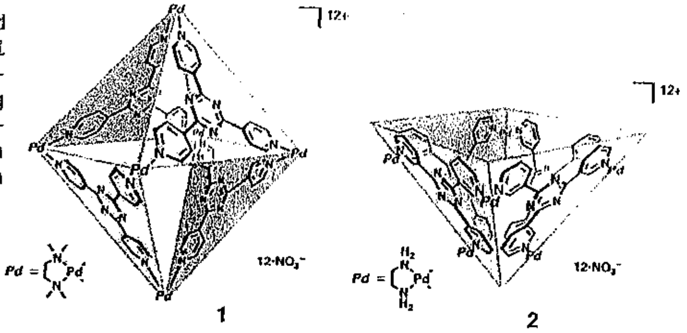
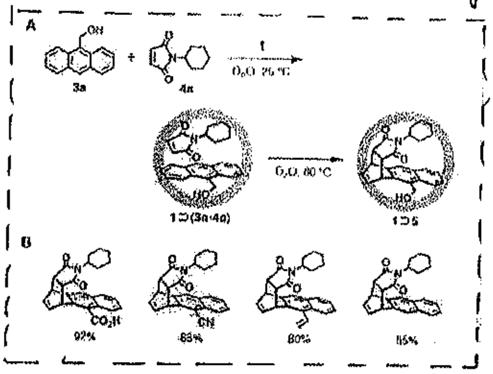


Fig. 1. Self-assembled coordination cages (1 and 2), which are prepared by simple mixing of an exo-tridentate organic ligand and an end-capped Pd(II) ion in a 4:6 ratio in water.

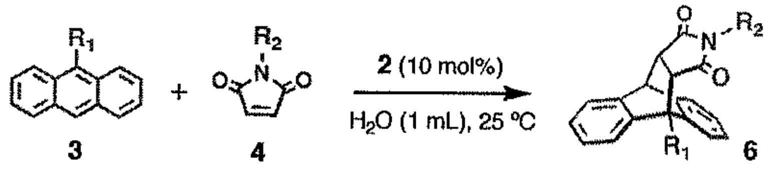
Syn 1,4 regio selective

Diels-Alder products within cage1.



They turned next to investigating Diels-Alder mediation by bowl-shaped host 2, and observed efficient catalytic turn over.

Table S1. Catalytic Diels-Alder reaction of 3 and 4 in the presence of 2 (10 mol%) in H_2O (1 mL) and control experiments in H_2O or $CDCl_3$ (1 mL) without 2.



Entry	Substrate 3 (R_1)	Substrate 4 (R_2)	Time	Yield(%) of 6 with 2	without 2	in $CHCl_3$[†]
1	$-CH_2OH$	propyl	5 h	>99	8	0
2	$-CH_2OH$	cyclohexyl	15 h	98	0	6
3	$-CH_2OH$	phenyl	5 h	>99[*,†]	3	9
4	$-CH_2OH$	phenyl	15 h	6	7	21
5	$-CH_2OH$	benzyl	5 h	>99	trace	0
6	$-CH_2OH$	xylyl	15 h	94	0	17
7	$-CH_3$	cyclohexyl	7 h	>99	0	5
8	$-CH_3$	phenyl	3 h	>99	5	17
9	$-CH=CH_2$	phenyl	1 d	88	0	trace
10	$-CH=CH_2$	benzyl	1 d	97	5	4
11	$-CO_2H$	benzyl	1 d	12	0	0
12	$-CH_2OH$	phenyl	1 d	>99[‡]	—	—

[*] (en)Pd$(NO_3)_2$: 10 mol% [†] without 2 [‡] 2 : 1 mol%, hexane (1 mL)

10 mol% of 2 was used.

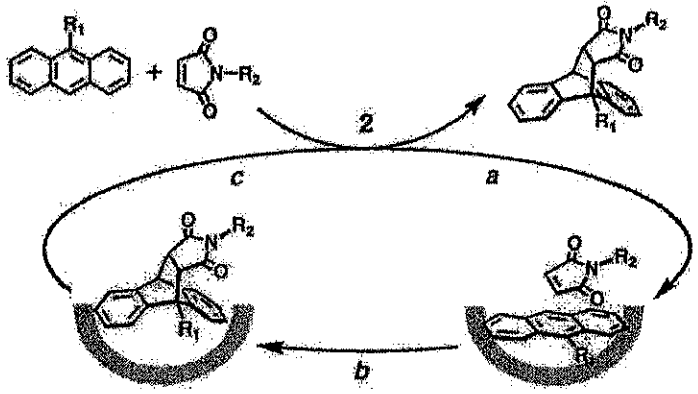
↓

- Diels-Alder adduct 6 formed quantitively.

  Surprisingly, even in the presence of 1mol% of 2, adduct 6 was obtained in >99% (Entry 12)

- In the absence of bowl 2, reaction hardly proceeded.

Proposed reaction mechanism.



a) Anthracene can stack onto the bowl 2 gaining considerable stabilization via aromatic-aromatic interaction

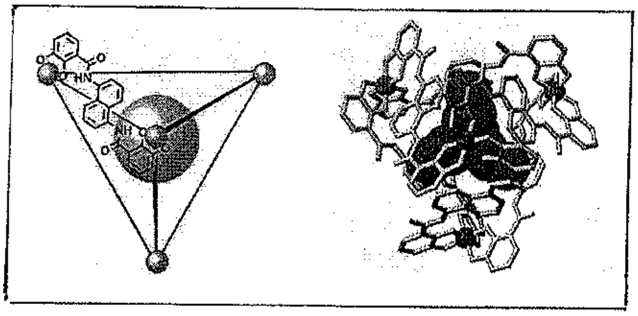
b) The reactant-like transition state is similary stabilized.

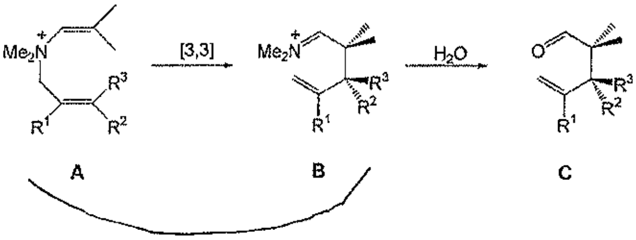
c) Once the reaction is complete, the product framework is bent at 9,10-position cutting off the host-guest aromatic stacking interaction

⇨ Accordingly, the encapsulated product is considerably destabilized and smoothly replaced by incoming reagent.

Supramolecular Catalysis of a Unimolecular Transformation: Aza-Cope Rearrangement within a Self-Assembled Host**

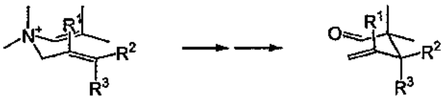
→ Angew. Chem. Int. Ed. 2004, 43, 6748.





cavity interior.

Table 1: Rate constants for free (k_{free}) and encapsulated (k_{encaps}) rearrangements (measured at 50 °C) and their acceleration factors.



Substrate	R^1	R^2	R^3	k_{free} [$\times 10^{-5}$ s^{-1}]	k_{encaps} [$\times 10^{-5}$ s^{-1}]	Acceleration
1	H	H	H	3.49	16.3	5
2	Me	H	H	7.61	198	26
3	H	Et	H	3.17	446	141
4	H	H	Et	1.50	135	90
5	H	*n*Pr	H	4.04	604	150
6	H	H	*n*Pr	1.69	74.2	44
7	H	*i*Pr	H	0.37	316	854

Remarkably, the encapsulated substrates rearranged faster in all cases.

↓

Thestoichiometric experiments had shown that in all cases of the host-mediated this reaction, leaving behind empty cavity.

↓

Raising the catalyst loading from 13 mol% to 27 mol% to 40 mol%

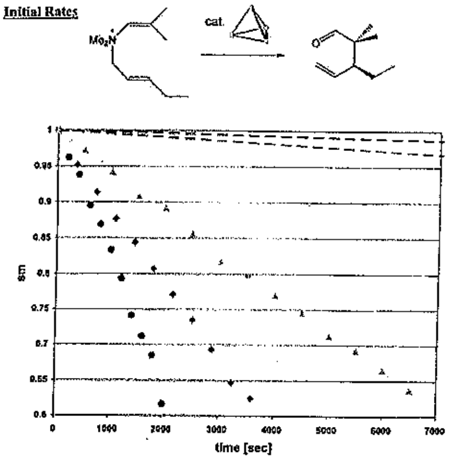
$k_{13mol\%} = 0.64 \times 10^{-4} s^{-1}$

$k_{27mol\%} = 1.17 \times 10^{-4} s^{-1}$

$k_{40mol\%} = 1.80 \times 10^{-4} s^{-1}$

(left graph)

Initial Rates



for the catalytic 3-Aza Cope rearrangement. ● = 40% catalyst loading; ◆ = ading; ▲ = 13% catalyst loading; -- = 40% catalyst loading, inhibited * uncatalyzed reaction.

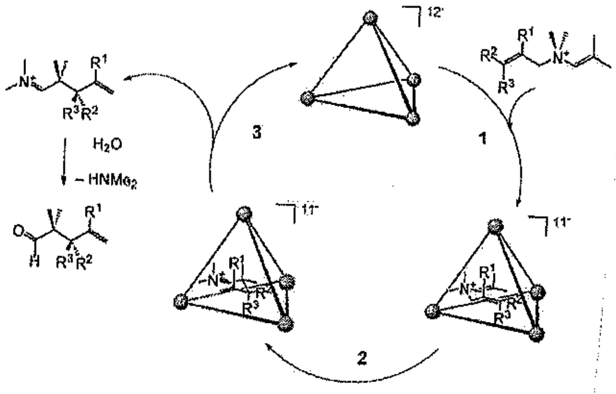
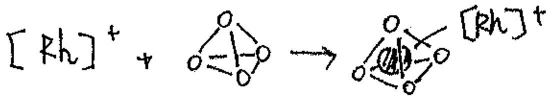


Figure 4. Proposed catalytic cycle for the cationic 3-aza-Cope rearrangement, see text for details.

Highly Selective Supramolecular Catalyzed Allylic Alcohol Isomerization

→ J. Am. Chem. Soc. 2007, 129, 2746



Addition of rhodium complexes to an aqueous solution of $Na_{12}[Ga_4L_6]$ host assembly, encapsulation was obserbe

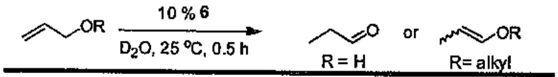
There is a sharp cutoff in size allowed for the encapsulation was observed.

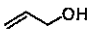
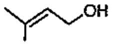
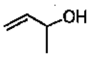
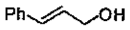
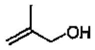
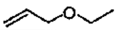
$(PEt_3)_2Rh(COD)^+$ were not encapsulated.

Table 1. Encapsulation Affinities for Rhodium Complexes in D_2O as Determined by ^1H NMR Spectroscopy

Guest	Encapsulation Guest Affinity (M^{-1})
(1) $(PMe_3)_2Rh(COD)^+$	5.2×10^2
(2) $(dmpe)Rh(COD)^+$	5.7×10^2
(3) $(PMe_3)_2Rh(NBD)^+$	1.2×10^2
(4) $(dmpe)Rh(NBD)^+$	1.2×10^2
(5) $(PEt_3)_2Rh(COD)^+$	not encapsulated

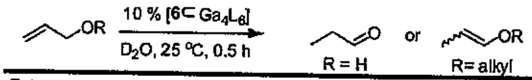
Table 2. Isomerization of Allylic Substrates by **6**

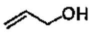
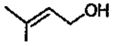
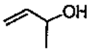
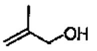


Entry	Substrate	Yield^a	Entry	Substrate	Yield^a
1		95 %	5		n. r.
2		95 %	6		n. r.
3		95 %	7		95 %^{b}
4		n. r.	8		95 %^{b}

^{a} Determined by ^{1}H NMR spectroscopy. ^{b}1:1 *E*:*Z* enol ether was obtained.

Table 3. Isomerization of Allylic Substrates by $[6 \subset Ga_4L_6]$



Entry	Substrate	Yield^a	Entry	Substrate	Yield^a
1		95 %	5		n. r.
2		n. r.	6		n. r.
3		n. r.	7		95 %^{b}
4		n. r.	8		n. r.

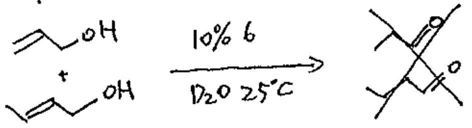
^{a} Determined by ^{1}H NMR spectroscopy. ^{b} 1:1 *E*:*Z* enol ether was obtained.

Table 2. unencapsulated results
Table 3 encapsulated results.

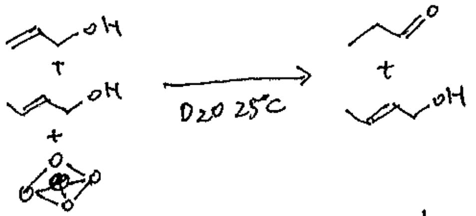
- To compare these results.

$[6 \subset Ga_4L_6]$ (Table 3)
Only alcohols of the correct size and shape are able to enter the host cavity and react.

- Crotyl alcohol behave as a catalyst inhibitor.



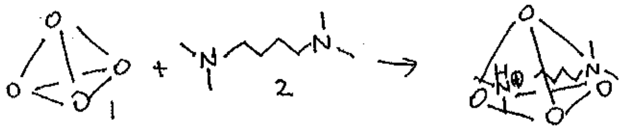
no isomerization



selective isomerization

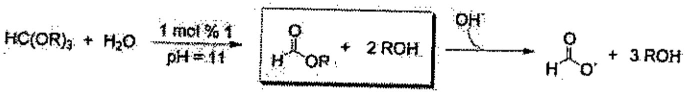
These selectivity results indicate that the highly specific substrate selectivites are enforced by encapsulation.
→ science, 2007, 316, 85.

Acid Catalysis in Basic Solution: A Supramolecular Host Promotes Orthoformate Hydrolysis



Amine 2 was encapsulated and protonated.
↓
H^+- amine
pka = 10.8 (in free solution)
= 14.3 (encapsulated)
⇒ Stabilization of protonated form by 1.

A



Quantitative:
R = Me, Et, Pr, *i*-Pr, *n*-Bu, *i*-Bu

No Reaction:
R = *n*-pentyl

- Hydrolysis of orthoformate ($HC(OR)_3$) in basic conditions.

They found that in the presence of a catalytic amount of 1 in basic solution several orthoformate is quickly hydrolyzed. ($HC(OEt)_3$ $t_{1/2}$ ~ 12min pH = 11.0. 22°C)
Substantial size selectivity was observed. (tripentyl orthoformate … No reaction)

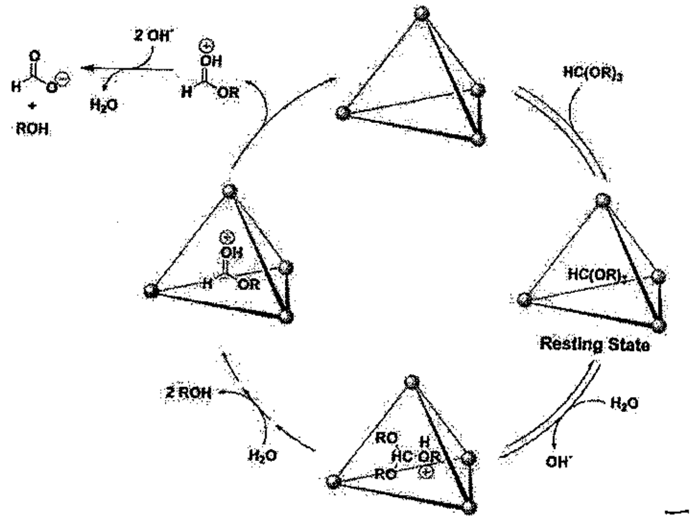


Fig. 3. Mechanism for catalytic orthoformate hydrolysis in the presence of catalytic **1**.

1) $HC(OR)_3$ was encapsulated
2) Protonated by deprotation of Water
3) Two succesive hydrolysis steps in the cavity liberating 2eq of alcohol.
4) protonated formate ester is ejected from 1.

・「Most recently examples」

Organocatalysis In a Synthetic Receptor with an Inwardly Directed Carboxylic Acid

→ J. Am. Chem. Soc. A.S.A.P
Rebek, Jr et al.

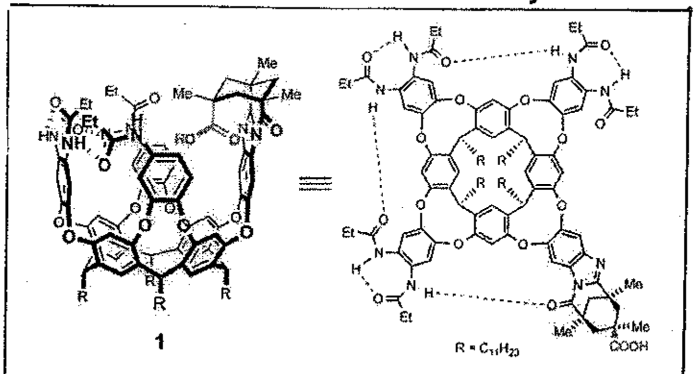


Figure 2. Cavitand 1 represented in its folded vase-like conformation (left) and as its detailed Lewis structure (right).

Figure 1. The 5-*exo* versus 6-*endo* modes of cyclization for epoxide ring-opening reactions.

→ The vase-like conformation of 1 is stabilized by hydrogen bonds.
The cavitand can fold guest molecules and present them with an inwardly directed carboxylic acid.

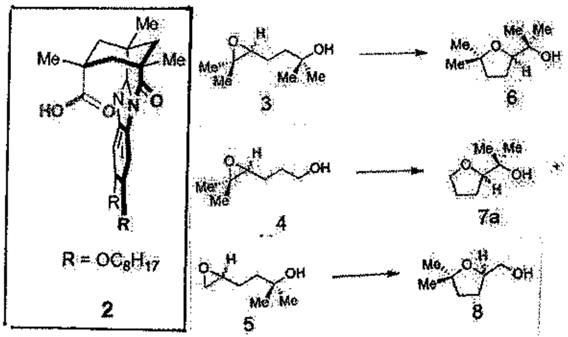


Figure 3. Model acid 2 and the 1,5-epoxyalcohols 3−5 used in this study.

These reactions were accelerated by 1.
In the cases of 3 and 5. regiocontrolled transformation were observed.

3 → 6 50-fold (using 2. 5exo : 6end 87 : 13)
4 → 7a, 7b 300-fold (using 1 5exo : 6end 1 : 1) (using 2 5exo : 6end 30 : 70)
5 → 8 100-fold (using 2 5exo : 6end 60 : 40)

Size-Selective Lewis Acid Catalysis in a Microporous Metal-Organic Framework with Exposed Mn^{2+} Coordination Sites

→ J. Am. Chem. Soc. A.S.A.P
Long et al.

→ Sodalite-type compound.
$Mn_3[(Mn_4Cl)_3(BTT)_8(CH_3OH)_{10}]_2$
H_3BTT = (1,3,5-benzenetristetrazol-5-yl)

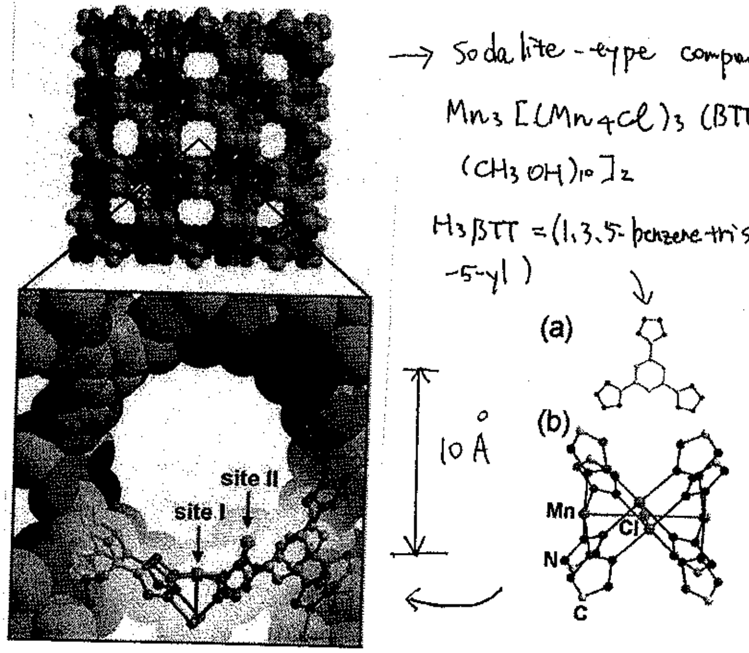
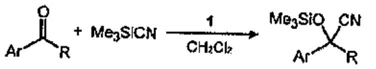


Figure 1. A portion of the crystal structure of 1 showing the two different types of Mn^{II} sites exposed within its three-dimensional pore system of 10 Å wide channels.[3e] Orange, green, gray, and blue spheres represent Mn, Cl, C, and N atoms, respectively; H atoms and bound MeOH molecules are omitted for clarity. Site I is five-coordinate, while site II is only two-coordinate; the separation between them is 3.420(8) Å.

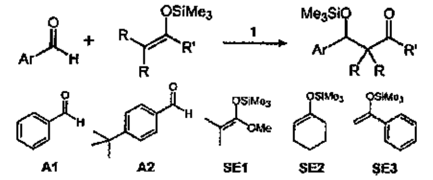
Table 1. Results for the Cyanosilylation of Carbonyl Substrates in the Presence of 1[a]



entry	Ar	R	time (h)	yield (%)[b]
1	phenyl	H	9	98
2	1-naphthyl	H	9	90
3	4-phenoxyphenyl	H	9	19
4	biphenyl	H	9	18
5	phenyl	CH_3	24	28
6	biphenyl	CH_3	24	1

[a] Reaction conditions: Me_3SiCN (3 mmol), aldehyde/ketone (1.5 mmol), CH_2Cl_2 (5 mL), 1 (0.04 g, 0.006 mmol), room temperature, under N_2. [b] Determined by ^1H NMR based on the carbonyl substrate.

Table 2. Results for the Mukaiyama−Aldol Reaction in the Presence of 1[a]



entry	aldehyde	silyl enolate	time (h)	solvent	yield (%)[b]
1	A1	SE1	99	CH_2Cl_2	63
2	A2	SE1	99	CH_2Cl_2	24
3	A1	SE2	99	CH_2Cl_2	<1
4	A1	SE3	99	CH_2Cl_2	<1
5[c]	A1	SE1	6	DMF	8[d]
6[c]	A1	SE1	6	DMF	51

[a] Reaction conditions: silyl enolate (2 mmol), aldehyde (1 mmol), solvent (5 mL), 1 (0.04 g, 0.006 mmol), room temperature, under N_2. [b] Determined by ^1H NMR based on the aldehyde. [c] Reaction at −45 °C. [d] No catalyst added.

Significant size selectivity effect is observed.
exa. Table1
entry 2 1-naphthyl … (9.7×8.4 Å^2) → 98% yield
3 4-phenoxyphenyl … (13.3×7.3 Å^2) → 19% yield

⇒ 10 Å wide pore system gave such size-selective reaction.

8 「Self-Assembly of chiral ligand」

Self-Assembly of Chiral Luminescent Lanthanide Coordination Bundles

→ J. Am. Chem. Soc. 2007, 129, 10986.

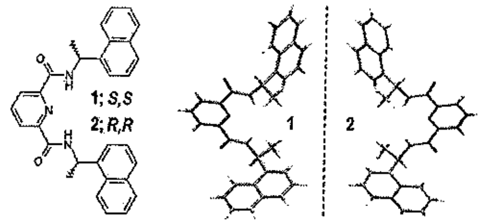


Figure 1. Ligands **1** (*S,S*) and **2** (*R,R*) and their corresponding solid-state structures, showing the enantiomeric nature of the two ligands. Solvent molecules of crystallization were omitted for clarity.

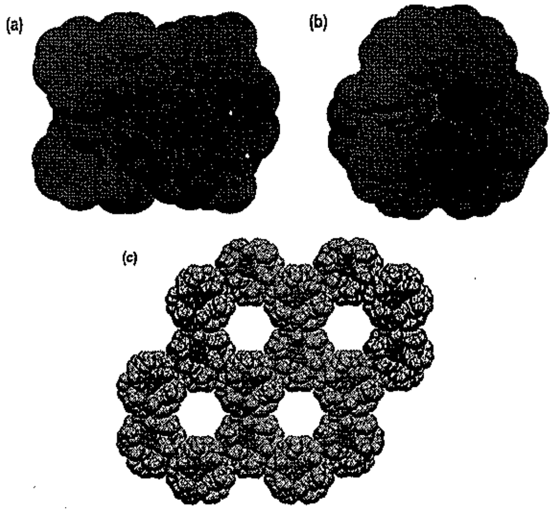


Figure 3. The X-ray crystal structure of the Tb·**2** sliotar showing the "helical" arrangement of the three ligands around Nd(III) (pink) as viewed down the crystallographic *a*-axis (a) and *c*-axis (b) and packing diagram viewed down the *c*-axis showing the channels (c). H-atoms, solvent molecules, and counter anions omitted for clarity.

Gunnlaugsson et al.

→ From simple chiral pyridyldiamide ligand. they demonstrated the formation of "The Trinity Sliotar".

The lanthanide complexes were synthesized by 1 or 2 with $Ln(OTf)_3$ = 3:1.

(ESI mass spectra was found to match the calculation.)

The chirality was also observed in the CD spectra of the complexs.

→ these complexes were luminescene in the solid state.

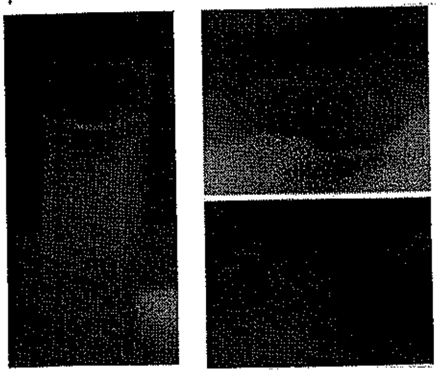


Figure S7. The Eu(III) emission from the complex of Eu(III) with **1**:
(A) In aqueous solution, [excite at 254 nm];
(B) As solid, [excite at 365 nm];
(C) As crystals [excite at 365 nm]

Reversible Interconversion of Homochiral Triangular Macrocycles and Helical Coordination Polymers

→ J. Am. Chem. Soc. 2007, 129, 7712.

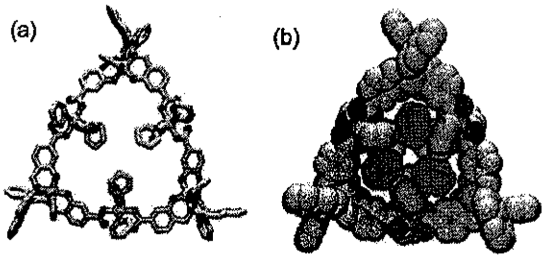
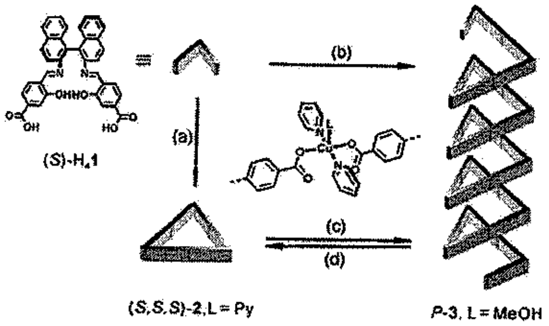


Figure 1. X-ray crystal structures of homochiral triangular complexes (a) (*S,S,S*)-**2** without guest pyridine molecules, (b) (*R,R,R*)-**2** including three pyridine guest molecules (pink) in the cavity. Hydrogen atoms are omitted for clarity.

Scheme 1. Solvent-Mediated Reversible Interconversion between the Triangular Macrocycle and the Helical Polymer (Inset: Coordination Environment of the Connecting Motif)^a



^{a} Conditions: (a) $Cu(OAc)_2 \cdot 6H_2O$, MeOH/pyridine = 3/10; (b) $Cu(OAc)_2 \cdot 6H_2O$, MeOH/pyridine = 10/1; (c) MeOH; (d) pyridine.

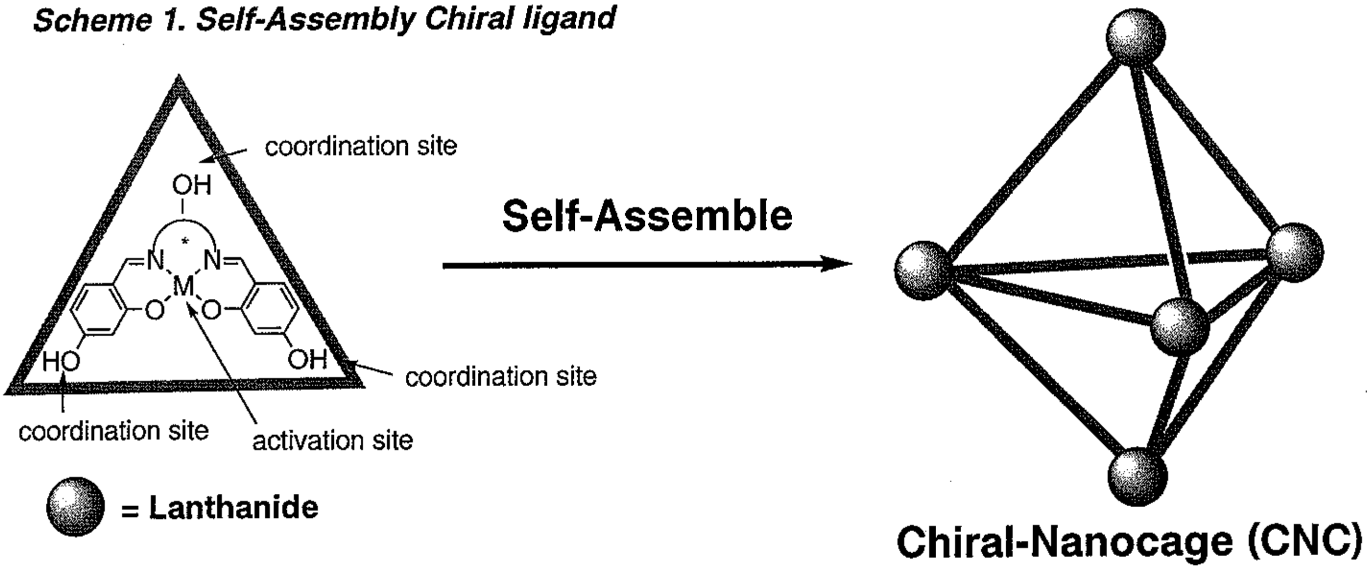
Mirkin et al.

→ From. chiral. Schiff-base complex (similar salen)

- Either cubic-or rod-shaped crystals were obtained, depending upon the solvent ratio.
- Interestingly, one not only can rationalize the formation of these two structures through this sequential bond breaking and reforming process but also realize it as a reversible chemical process.
- The helical channel inside is filled with solvent molecules. These guest molecules are helically aligned double-helix-like structure.

My Proposal

Scheme 1. Self-Assembly Chiral ligand



Dinamic Kinetic Resolution by Size- Shape - Enantio selective Catalysis

Scheme 2. Proposed mechanism