

*Supramolecular Catalysis:  
Chemistry within Well-Defined  
Self-Assembly Hosts*

*Staffan Torssell  
MacMillan Group Meeting  
10-15-08*



## *Supramolecular Catalysis: An Introduction*

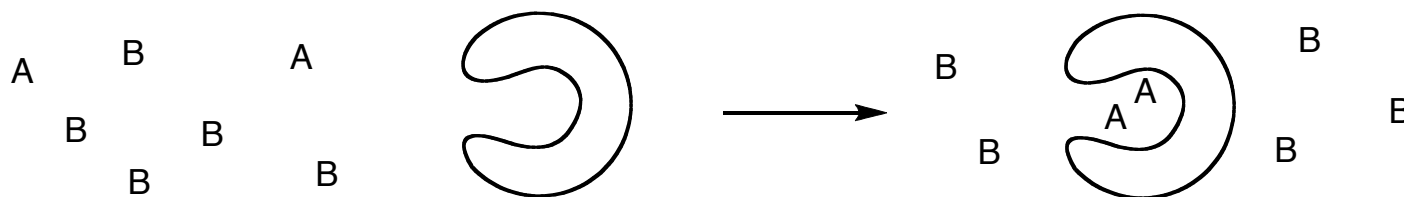
- In Nature: Highly efficient, well orchestrated cascades that takes places in well-defined reaction environments
- Lessons learned from Nature arises from the observation and understanding of enzyme catalysis
- Early work focused on the synthesis of macrocycles for molecular recognition and culminated with the Nobel prize in Chemistry (1987) to Donald Cram, Jean-Marie Lehn and Charles Pedersen for "their development and use of molecules with structure-specific interactions of high selectivity"
- Occasionally enormous accelerations were noted, change in selectivity but applications in synthetic chemistry remained elusive
- Main drawback: Tedious synthesis of host molecules with catalytic entities
- Last decade: New biomimetic approaches have arised which avoid elaborate syntheses
- Self-assembly of higher-order capsules by pre-designed interactions such as H-bonding and metal-ligand coordination

### *Important literature covering supramolecular catalysis:*

- *Supramolecular Catalysis*; van Leeuwen, P. W. N. M., Ed.; Wiley-VCH: Weinheim, 2008
- *Modern Supramolecular Chemistry*; Diederich, F.; Stang, P. J. Tykwinski, R. R., Eds.; Wiley-VCH: Weinheim, 2008
- Vriezema, D. M.; Comellas Aragonés, M.; Elemans, J. A. A. W.; Cornelissen, J. J. L. M.; Rowan, A. E.; Nolte, R. J. M. *Chem. Rev.* **2005**, *105*, 1445-1489

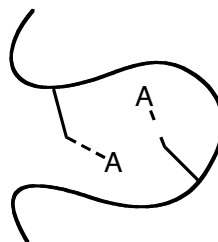
## Criteria for Artificial "Enzymes"

### ■ Molecular recognition: Selective recognition of desired substrate



### ■ Binding affinity: Cavity/site where substrate can bind

- 1) H-Bonding
- 2)  $\pi$ - $\pi$  Stacking
- 3) Cavity effect



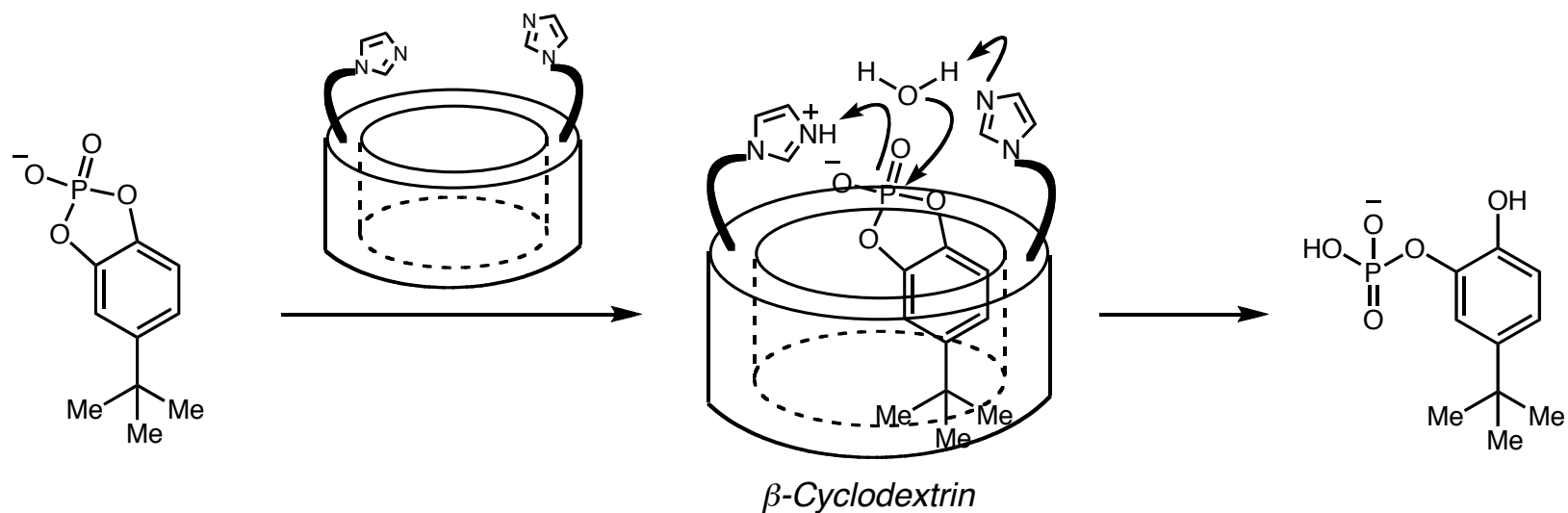
### ■ Reactive site: Proximal to binding site in order to react with substrate

- 1) Unimolecular reactions: More TS-like conformations
- 2) Bimolecular reactions: Proximity effects leads to very high effective molarities  $\Rightarrow$  entropic advantage

### ■ Product release: Regeneration of host in order to achieve catalyst turn-over

Usual bottle-neck in many artificial supramolecular models

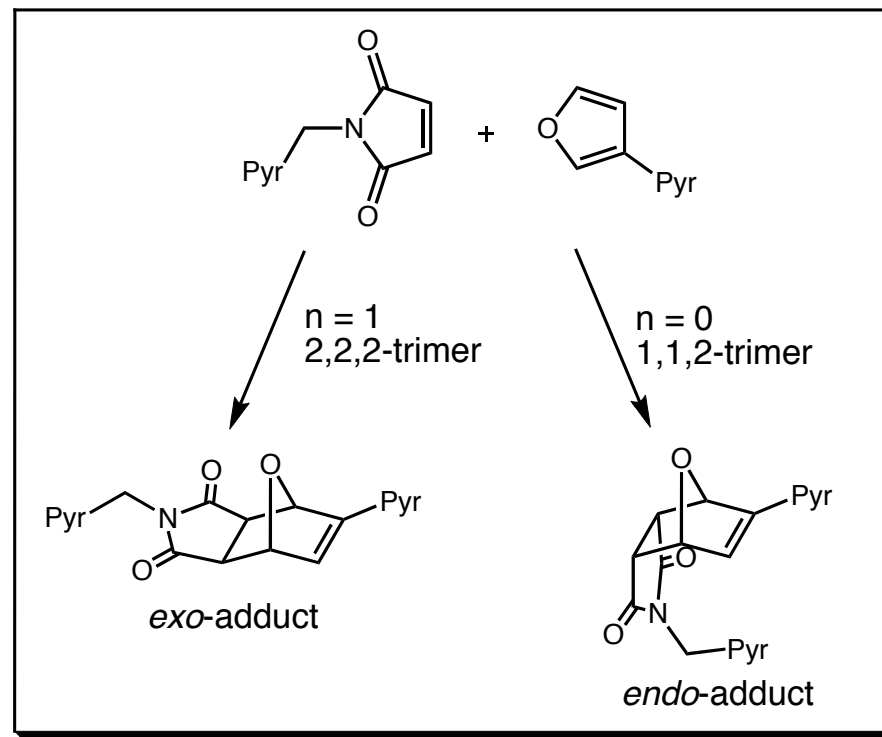
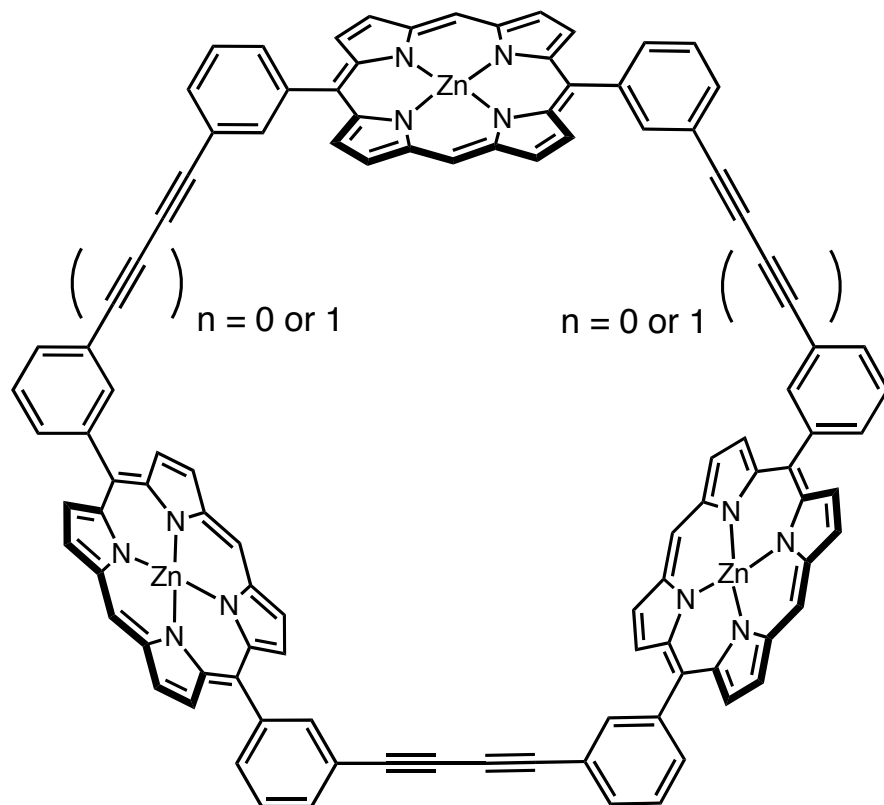
## Early Examples: Breslow's Ribonuclease Model System



- Functionalized  $\beta$ -cyclodextrin bearing two imidazole moieties
- The substrate binds into the cavity of the catalyst in water solution
- One imidazole acts as base and the other (protonated) acts as acid
- Catalyzed hydrolysis is 100 times faster and selective (>99%) comp. non-catalyzed

Breslow, R.; Doherty, J.; Guillot, G.; Lipsey, C. *J. Am. Chem. Soc.* **1978**, *100*, 3227  
Anslyn, E. V.; Breslow, R. *J. Am. Chem. Soc.* **1989**, *111*, 8931

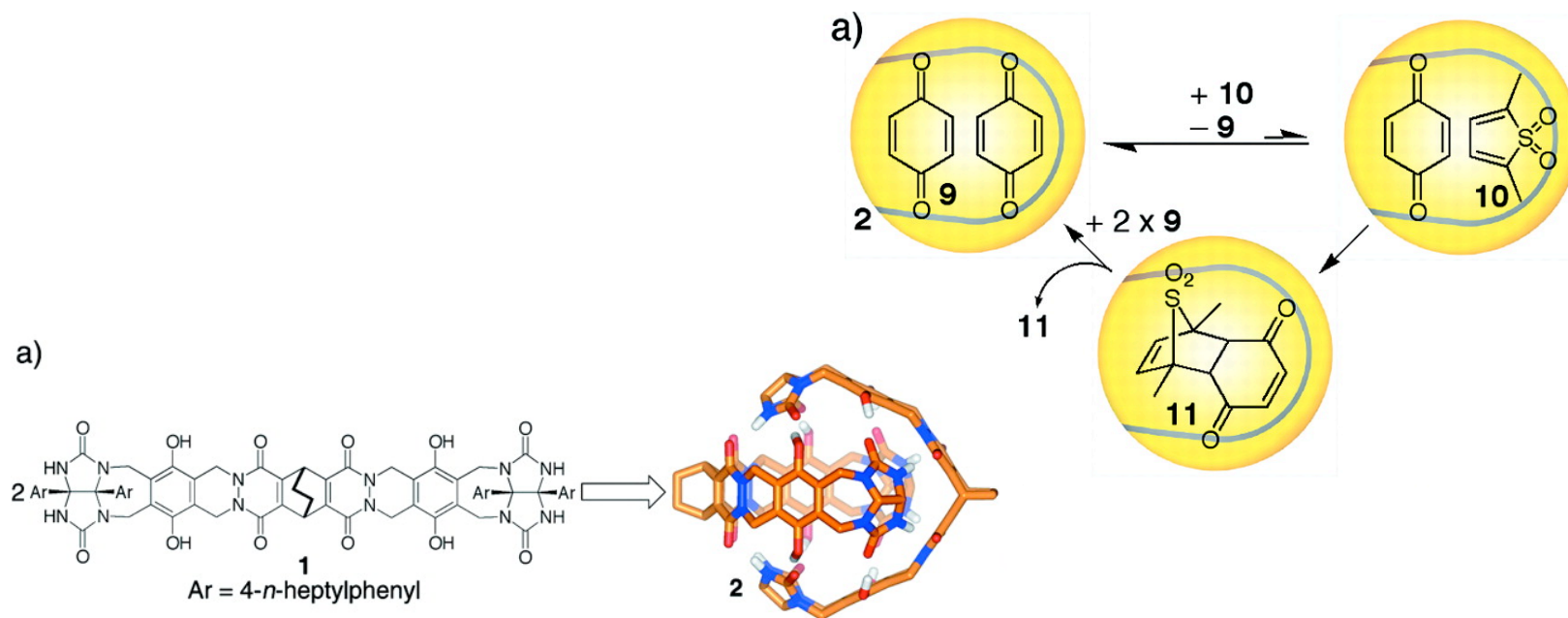
## Sanders' Zn(II) Porphyrin Trimer: Endo- or Exo-Selective Diels-Alder



- Complete *exo*-selectivity in 2,2,2-trimer due to correct binding distance for *exo*-product (15 Å)
- Complete *endo*-selectivity in 1,1,2-trimer due to correct binding distance for *endo*-product (12 Å)
- 200-fold acceleration compared to non-catalyzed reaction, product inhibition.
- Complete inhibition of the reaction when competitive binder is added

Walter, C. J.; Anderson, H. L.; Sanders, J. K. M. *Chem. Commun.* **1993**, 458  
Walter, C. J.; Sanders, J. K. M. *Angew. Chem. Int. Ed. Engl.* **1995**, 34, 217

## Rebek's "Soft Ball"-Catalyzed Diels-Alder



- Encapsulation by dynamic, reversible self-assembly of cage-like molecular complex
- Encapsulation forces the reacting components in close proximity (high local concentration)  
⇒ productive reaction pathway
- Reversible encapsulation leads to product release and catalyst turnover
- 75% conversion after 4 days, 10 fold acceleration compared to non-catalyzed reaction

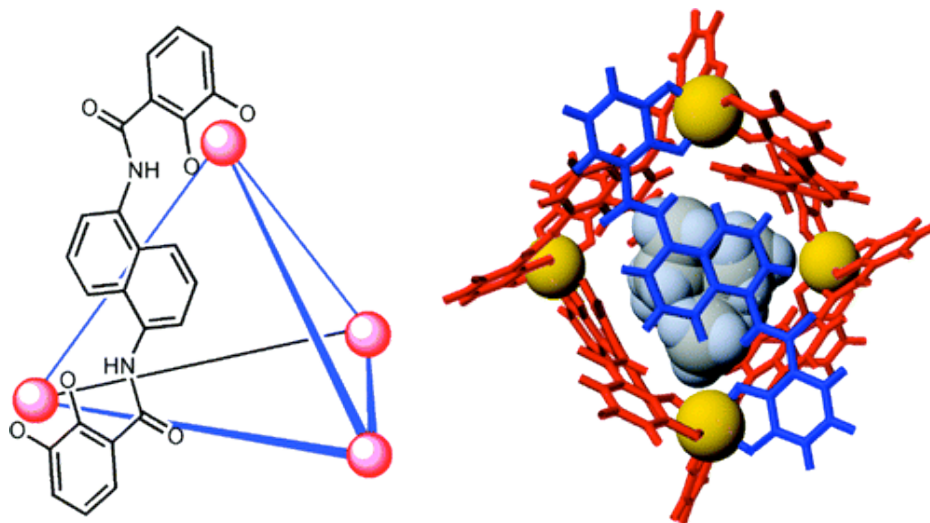
Kang, J.; Rebek, J., Jr. *Nature* **1997**, *385*, 50

Kang, J.; Santamaria, J.; Hilmersson, G.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1998**, *120*, 7389

*Prof. Kenneth N. Raymond  
Prof. Robert G. Bergman  
Department of Chemistry  
University of California, Berkeley*

*Catalysis within  $M_4L_6$  Self-Assembly Hosts*

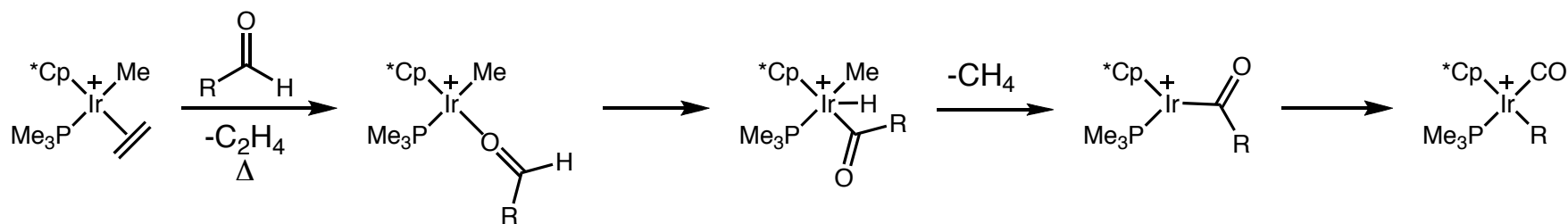
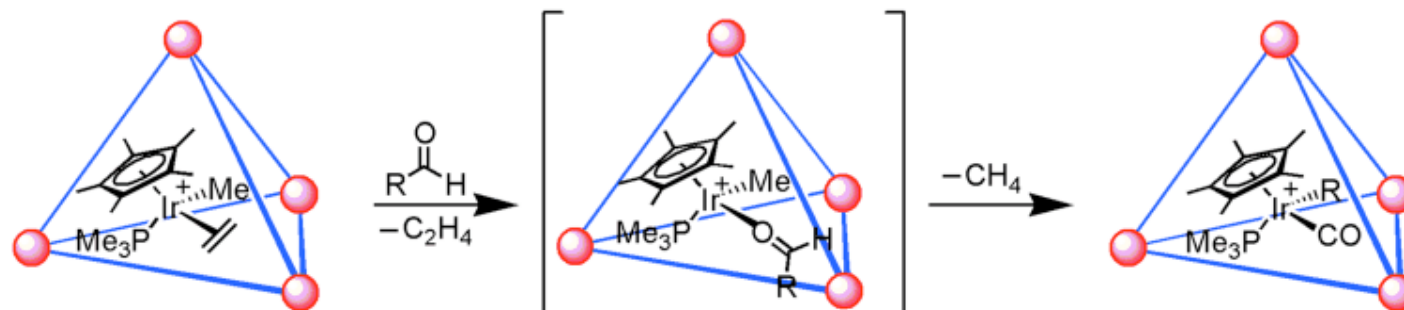
## The Raymond Group's $M_4L_6$ -Assembly



- $M_4L_6$  stoichiometry:  $M = Ga^{III}, Al^{III}, In^{III}, Fe^{III}, Ti^{IV}, Ge^{IV}$   
 $L = N,N'$ -bis(2,3-dihydroxybenzoyl)-1,5-diaminonaphthalene
- Well-defined, chiral self-assembling tetrahedron
- Tris-bidentate coordination @ metal  $\Rightarrow$  stereogenic center
- -12 overall charge  $\Rightarrow$  water solubility. Naphthalene residues  $\Rightarrow$  hydrophobic cavity.
- Hydrophobic, polyanionic host  $\Rightarrow$  stabilization of reactive cations by encapsulation



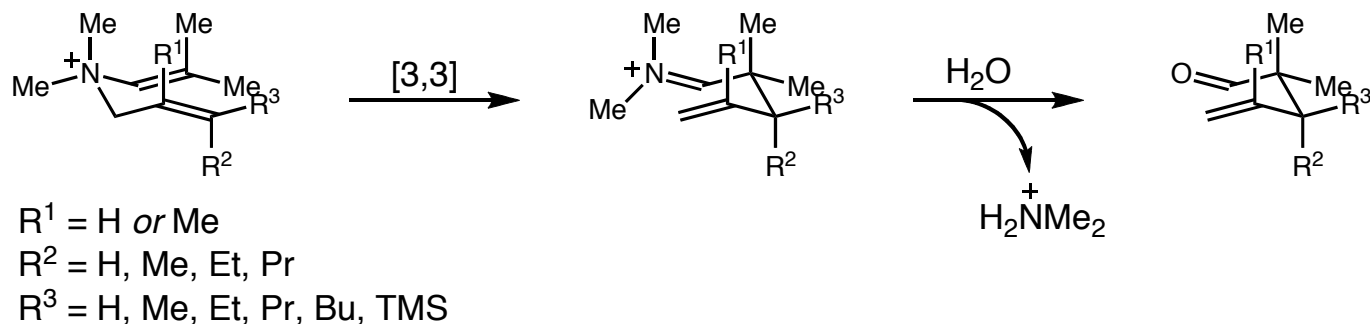
## C-H-bond activation by Encapsulated Ir(III)-Catalysts



- Polyanionic host and cationic, hydrophobic organometallic guest ⇒ driving force for encapsulation
- Host-guest complexes with up to 70:30 d.r. obtained when using *cis*-butene pre-catalyst
- Heating liberates olefin ligand and generates active Ir-comp
- Addition of aldehyde ⇒ C-H insertion and release of CH<sub>4</sub> and generation of Ir-acyl complex
- Migratory deinsertion of Ir-acyl ⇒ chiral cationic Ir alkyl carbonyl product with d.r. up to 70:30

Leung, D. H.; Fiedler, D.; Bergman, R. G.; Raymond, K. N. *Angew. Chem. Int. Ed.* **2004**, 43, 963  
 Leung, D. H.; Bergman, R. G.; Raymond, K. N. *J. Am. Chem. Soc.* **2006**, 128, 9781

## [3,3] aza-Cope Rearrangements of Allyl Enammonium Salts



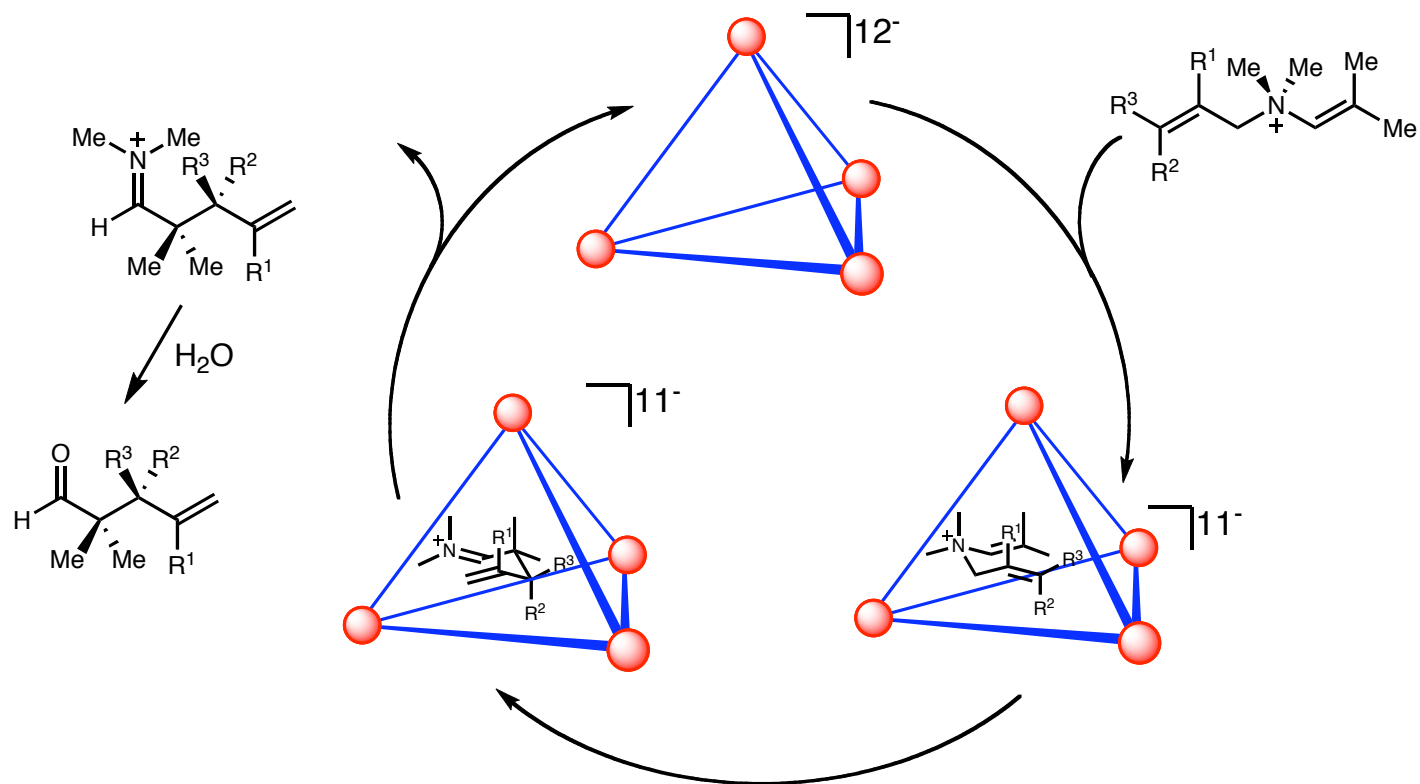
- Cationic enammonium = driving force for encapsulation
- Neutral product = no driving force for re-encapsulation  $\Rightarrow$  catalyst turn-over
- Rate acceleration = up to 3 orders of magnitude
- Investigation of energetic parameters showed a decreased entropy barrier ( $\Delta S^\ddagger$ ) as well as a decreased enthalpic barrier for larger substrates ( $\Delta H^\ddagger$ )
- ( $\Delta S^\ddagger$ ): Encapsulation of only tightly packed conformations that resembles the TS. Several degrees of freedom lost  $\Rightarrow$  decreased entropic barrier
- ( $\Delta H^\ddagger$ ): Encapsulation of larger substrates forces the substituents closer together. Ground-state energy increased  $\Rightarrow$  decreased enthalpic barrier

Fiedler, D.; Bergman, R. G.; Raymond, K. N. *Angew. Chem. Int. Ed.* **2004**, *43*, 6748

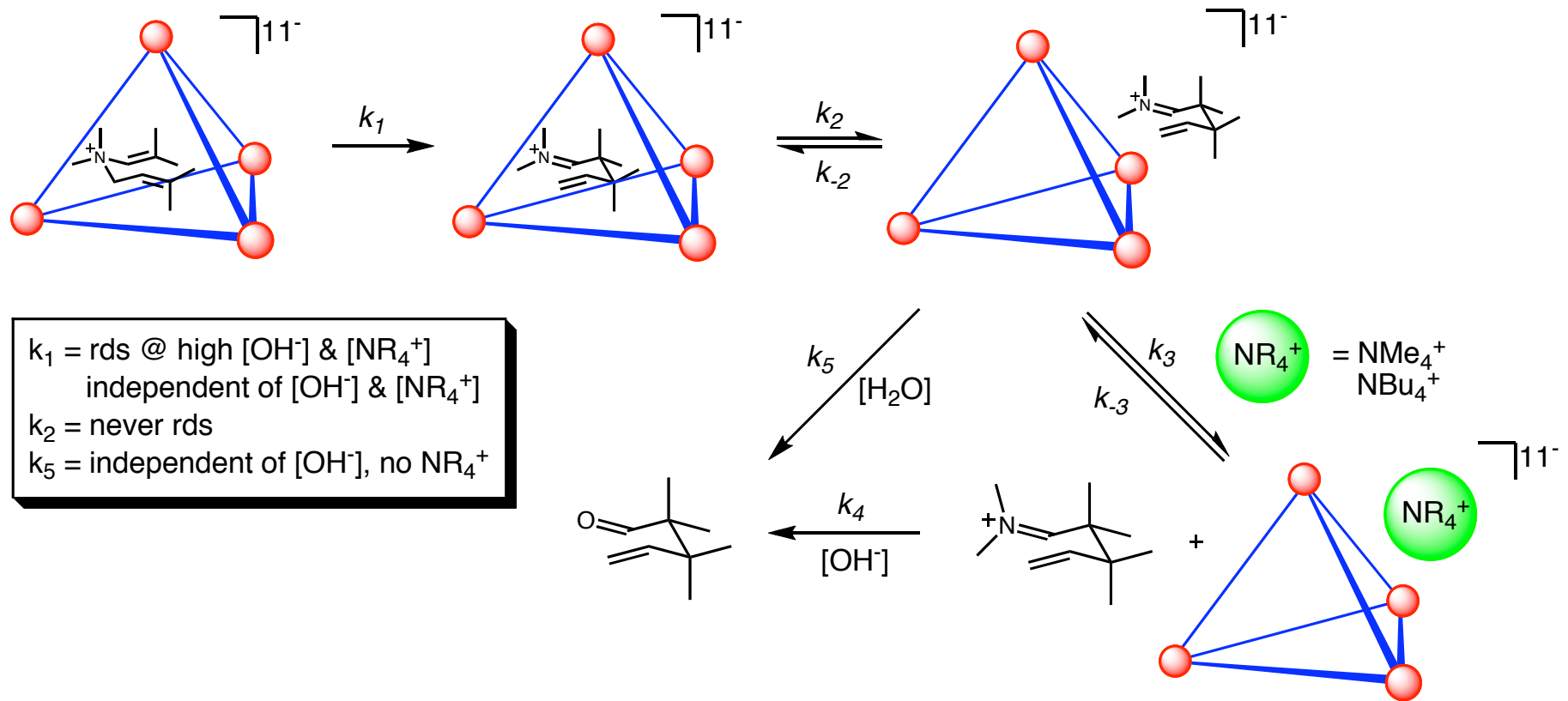
Fiedler, D.; van Halbeek, H.; Bergman, R. G.; Raymond, K. N. *J. Am. Chem. Soc.* **2006**, *128*, 10240

Hastings, C. J.; Fiedler, D.; Bergman, R. G.; Raymond, K. N. *J. Am. Chem. Soc.* **2008**, *130*, 10977

# Mechanism for [3,3] aza-Cope rearrangement of enammonium substrates

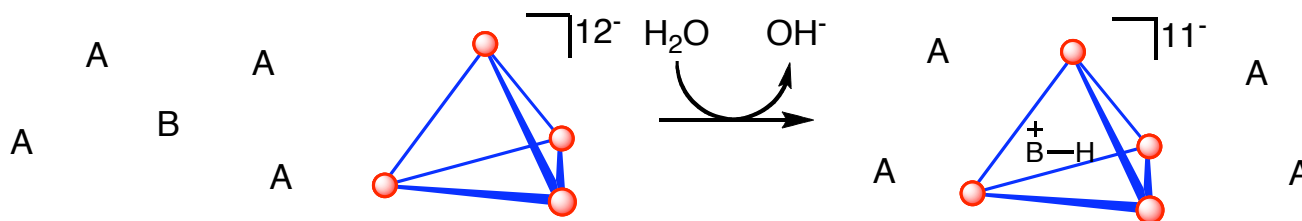


## Mechanism for hydrolysis of the iminium product



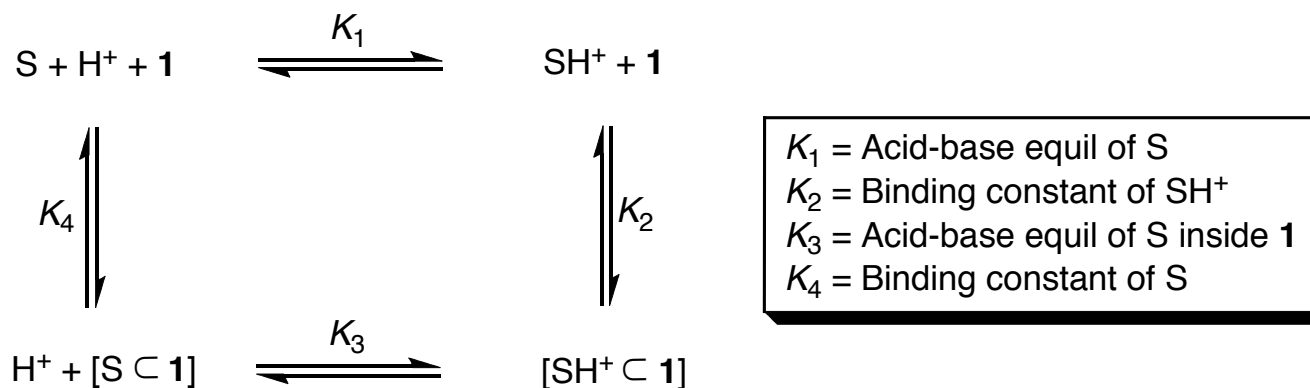
- Experiment series 2: High pH, varying  $[\text{NMe}_4^+]$  from low to high
- Rate of hydrolysis is first-order in  $[\text{NMe}_4^+]$ . Saturation @ high  $[\text{NMe}_4^+]$
- Ion association of  $\text{NMe}_4^+$  on the outside facilitates the displacement of iminium into the solution
- Explains the pH dependance when ammonium salt present since  $\text{OH}^-$  only exists in the bulk phase

## Acid Catalyzed Reactions



- $M_4L_6$ -complex bind/stabilizes cationic species over neutral  $\Rightarrow$  stabilization of cationic TS?
- Acid catalyzed reaction = prime candidate. High-energy, monocationic intermediate
- Would widen the scope of transformations to neutral substrates
- Biomimetic approach: In Nature, electrostatic interactions can lead to  $pK_a$  shifts up to 5 units due to precise stabilization of charged intermediates *via* H-bonding networks.

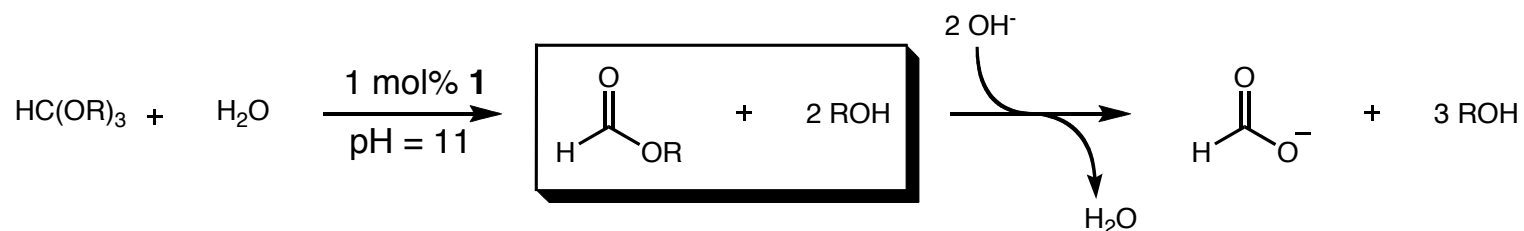
## Acid Catalyzed Reactions



- Protonated amines remained encapsulated even when pH were higher than the  $\text{pK}_a$  of the protonated amine  $\Rightarrow$  encapsulated guest is significantly stabilized by **1**
- Fast self-exchange rates confirms thermodynamic encapsulation rather than kinetic
- To determine the magnitude of stabilization, the encapsulation was monitored as a function of pH
- The  $\text{pK}_a$  of the amine and the binding constant gives the effective basicity of the encapsulated amine
- $\text{pK}_a$  shifts with up to 4.5 units, largest ever seen in synthetic hosts

## Acid Catalyzed Hydrolysis of Orthoformates and Acetals under Basic Conditions

### Hydrolysis of orthoformates

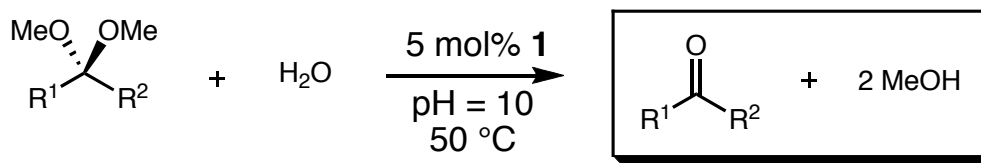


Quantitative: R = Me, Et, Pr, *i*-Pr, *n*-Bu, *i*-Bu

Pluth, M. D.; Bergman, R. G.; Raymond, K. N. *Science* **2007**, *316*, 85

Pluth, M. D.; Bergman, R. G.; Raymond, K. N. *J. Am. Chem. Soc.* **2008**, *130*, 11423

### Hydrolysis of acetals



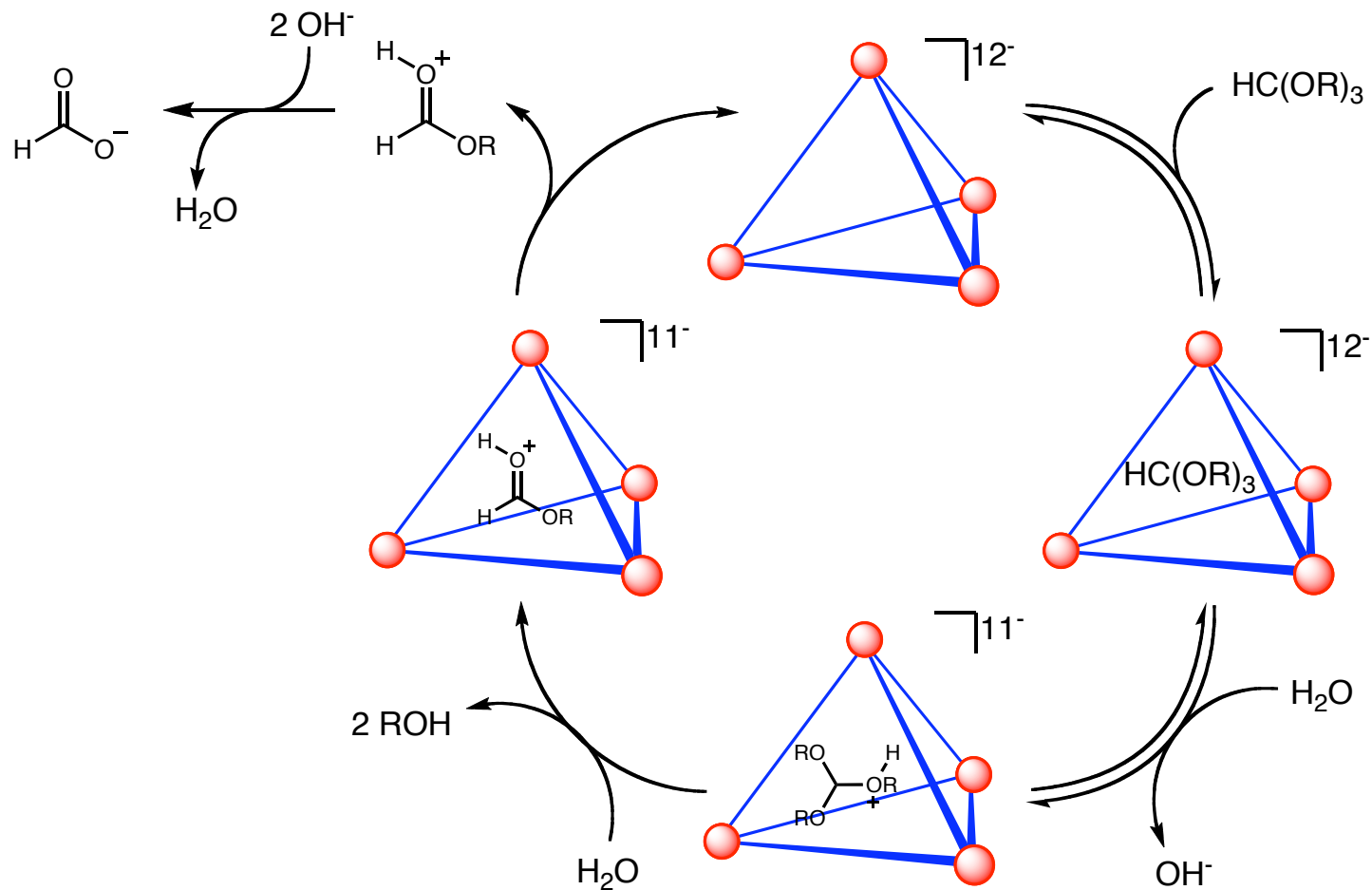
Quantitative: R<sup>1</sup> = H or C<sub>1</sub>H<sub>3</sub> to C<sub>3</sub>H<sub>7</sub> and R<sup>2</sup> = C<sub>1</sub>H<sub>3</sub> to C<sub>6</sub>H<sub>13</sub>

R<sup>1</sup> = H and R<sup>2</sup> = *cyclo*-pentane, hexane

*cyclo*-pentanone, hexanone, adamantanone

Pluth, M. D.; Bergman, R. G.; Raymond, K. N. *Angew. Chem. Int. Ed.* **2007**, *46*, 8587

## Mechanism for hydrolysis of orthoformates



- Step 4: Protonated formate ester is ejected and further hydrolyzed in the solution
- Reaction obeys Michaelis-Menten kinetics in similarities to enzymes with a pre-equilibration step  $\Rightarrow$  substrate saturation followed by a first-order rate-limiting step (hydrolysis)



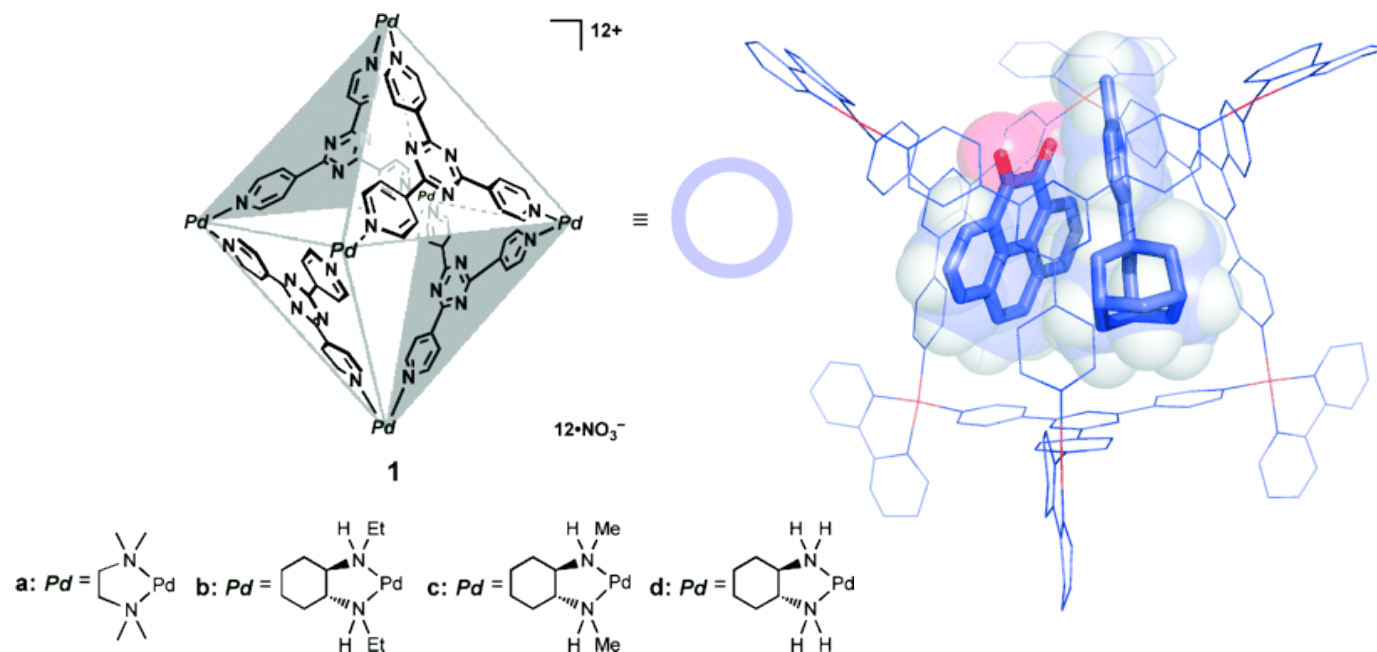
## *Conclusions: $M_4L_6$ Self-Assembly Hosts*

- Chiral anionic hosts can be utilized for incapsulation of chiral cationic organometallic complex with moderate to good diastereoselectivity. Exemplified with Ir-cat C-H bond activation of aldehydes
- Anionic hosts accelerates and catalyzes unimolecular rearrangements of cationic substrates. Exemplified with [3,3] aza-Cope rearrangements of allyl enammonium salts
- The scope of cation stabilization was further widen to neutral substrate participating in acid-catalyzed processes. Exemplified with acid-catalyzed hydrolysis of orthoformates and acetals in basic media

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*Department of Applied Chemistry*  
*University of Tokyo*  
*Japan*

*Chemistry within  $M_6L_4$  Self-Assembly Hosts*

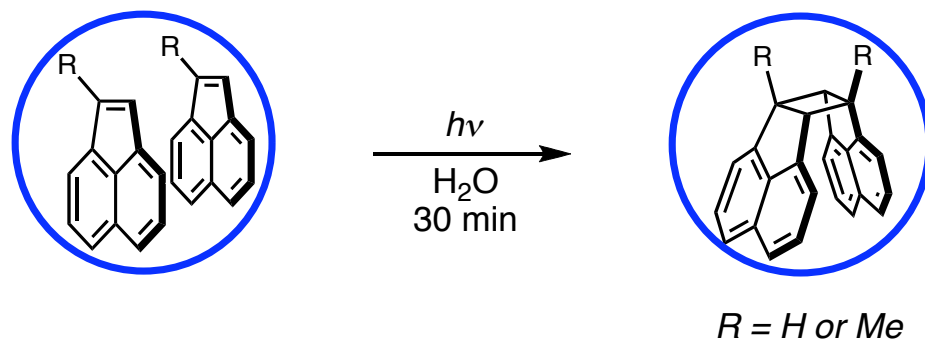
## The Fujita Group's $M_6L_4$ -Assembly



- $M_6L_4$  stoichiometry:  $M = \text{Pd}^{\text{II}}$ .  $L = 2,4,6\text{-tri(pyridin-4-yl)-1,3,5-triazine}$
- Well-defined, self-assembling octahedral
- Possibility for using chiral diamine- $\text{Pd}^{\text{II}}$  complexes  $\Rightarrow$  chiral enantiomerically pure assembly
- +12 overall charge  $\Rightarrow$  water solubility. Hydrophobic electron deficient ligands  $\Rightarrow$  hydrophobic cavity with strong affinity for electron-rich guests.
- Mediates photo-induced electron transfer for guest to the host due to electron-deficient ligands

First report: Fujita, M.; Oguro, D.; Miyazawa, M.; Oka, H.; Yamaguchi, K.; Ogura, K *Nature*, **1995**, *378*, 469

## [2+2] Photoadditions

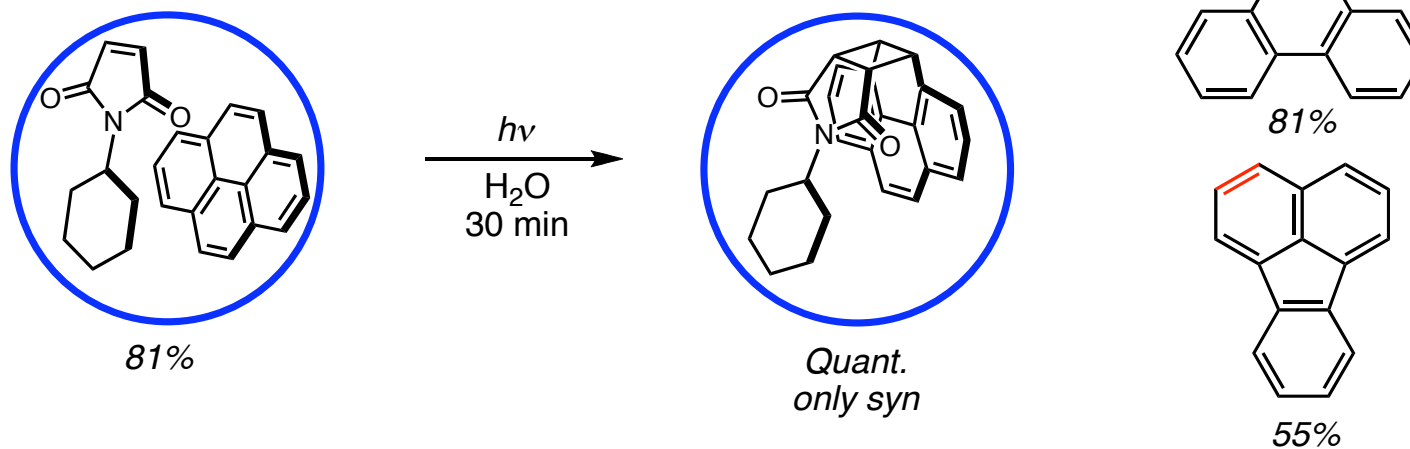


- R = H: In solution phase, low yield & *syn, anti* mixture
- R = H: Quantitative host-guest formation, 100% conversion in 30 min and only *syn*-isomer
- R = Me: No reaction in solution phase
- R = Me: 100% conversion, only *syn* head-to-tail isomer

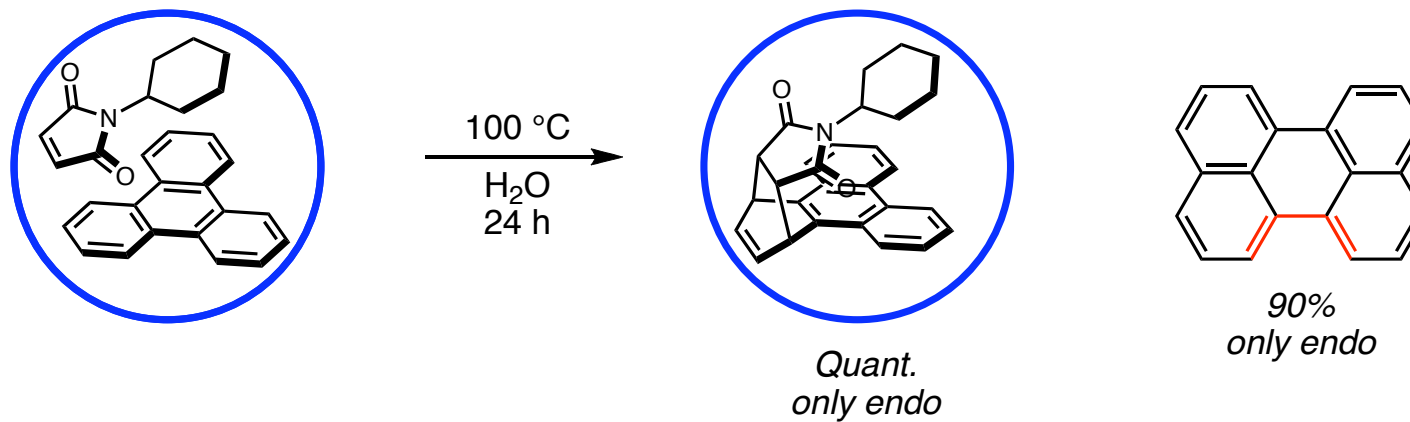
Yoshizawa, M.; Takeyama, Y.; Kusakawa, T.; Fujita, M. *Angew. Chem. Int. Ed.* **2002**, *41*, 1347  
Takaoka, K.; Kawano, M.; Ozeki, T.; Fujita, M. *Chem. Commun.* **2006**, 1625

## Unusual [2+2] & [4+2] Cycloadditions

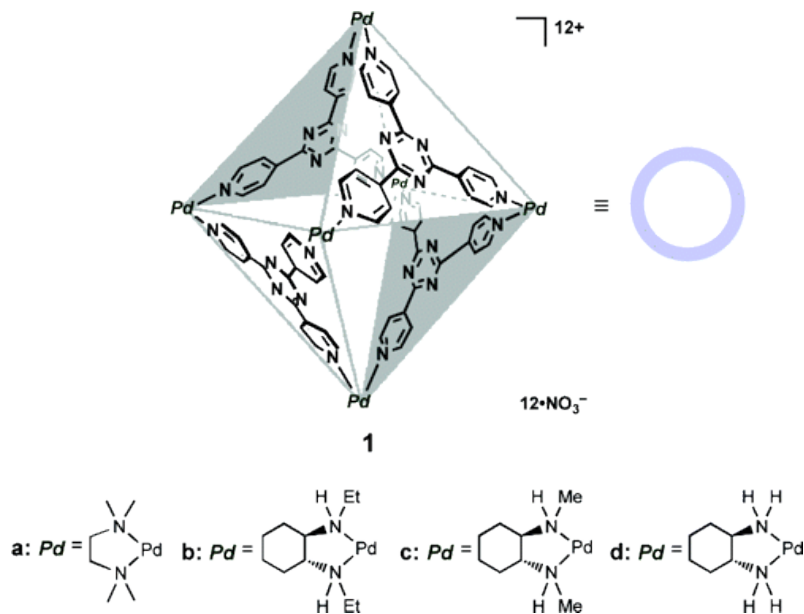
### ■ Unusual [2+2] photoaddition



### ■ Unusual thermal [4+2] cycloaddition

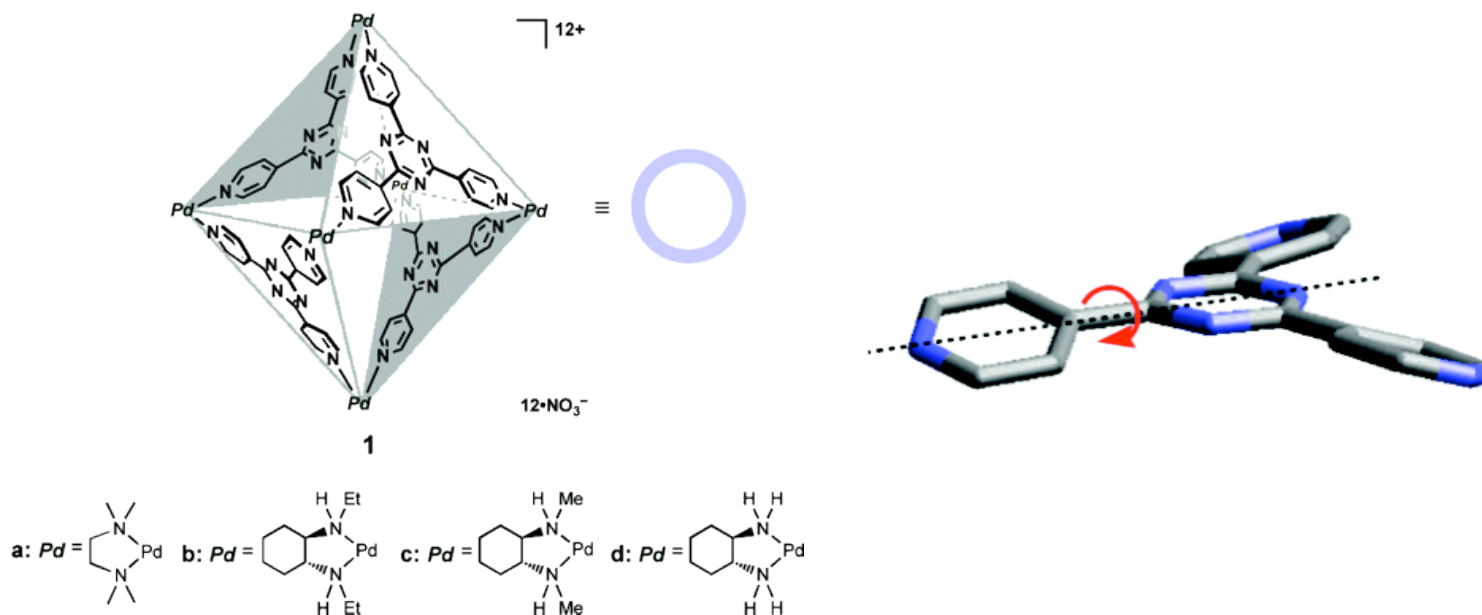


## Asymmetric [2+2] Photoadditions in Chiral Self-Assembled Hosts



- Asymmetric synthesis in chiral cavities are relatively unexplored
- Difficult to prepared large self-assembly hosts in enantiomerically pure form
- $\text{M}_6\text{L}_4$ -Pd(II) complexes with chiral diamine end-caps are easily prepared

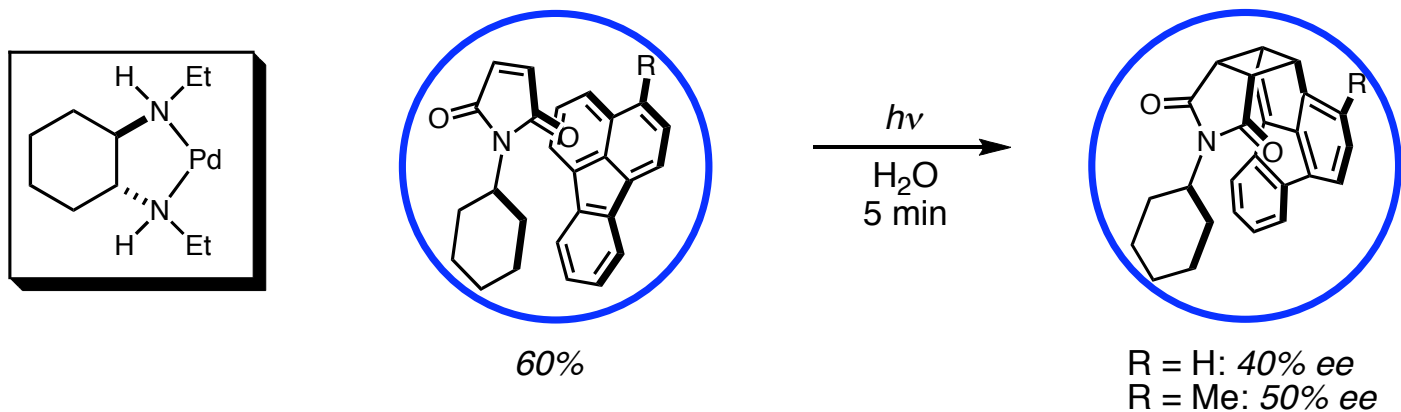
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- M<sub>6</sub>L<sub>4</sub>-Pd(II) complexes with chiral diamine end-caps are easily prepared
- TMEDA-Pd(II) ⇒ co-planar triazine ligands (X-ray)
- Cyclohexane-1,2-diamine-Pd(II) ⇒ deformation of triazine ligand leading to chiral cavities  
Titled up to 17° with *N*-Et (calculations)

Nishioka, Y.; Yamaguchi, T.; Kawano, M.; Fujita, M. *J. Am. Chem. Soc.* **2008**, *130*, 8160

## Asymmetric [2+2] Photoadditions in Chiral Self-Assembled Hosts

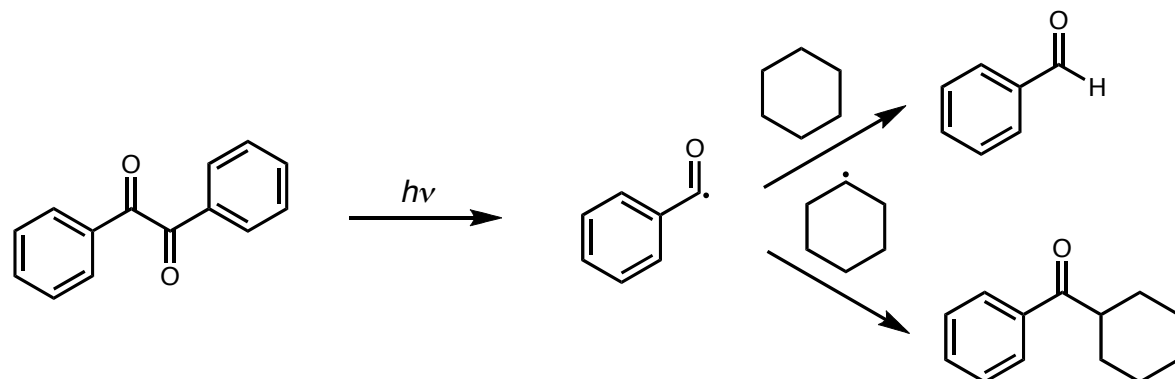


- Remarkable high asymmetric induction considering the remote location of the chiral ligand
- Substituent on N important: *N*-Et 50% ee, *N*-Me 20% ee, *N*-H 5% ee
- Confirms that, like in enzymes, indirect cavity-control by remote chiral ligands can be an important and viable strategy in asymmetric synthesis

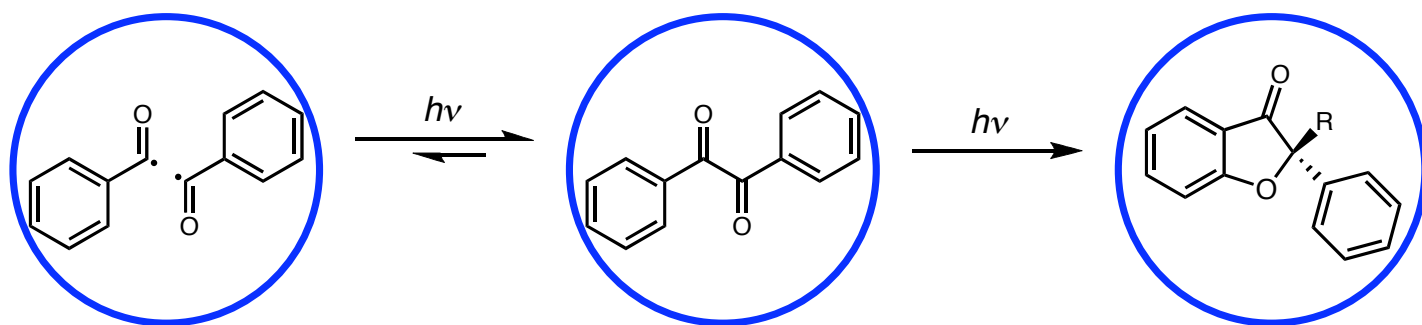


## Photocyclizations Through Kinetically Unfavored Pathways

### ■ Photoreaction of diphenylethanedione in degassed cyclohexane



### ■ Photoreaction of diphenylethanedione in $M_6L_4$ self-assembly host

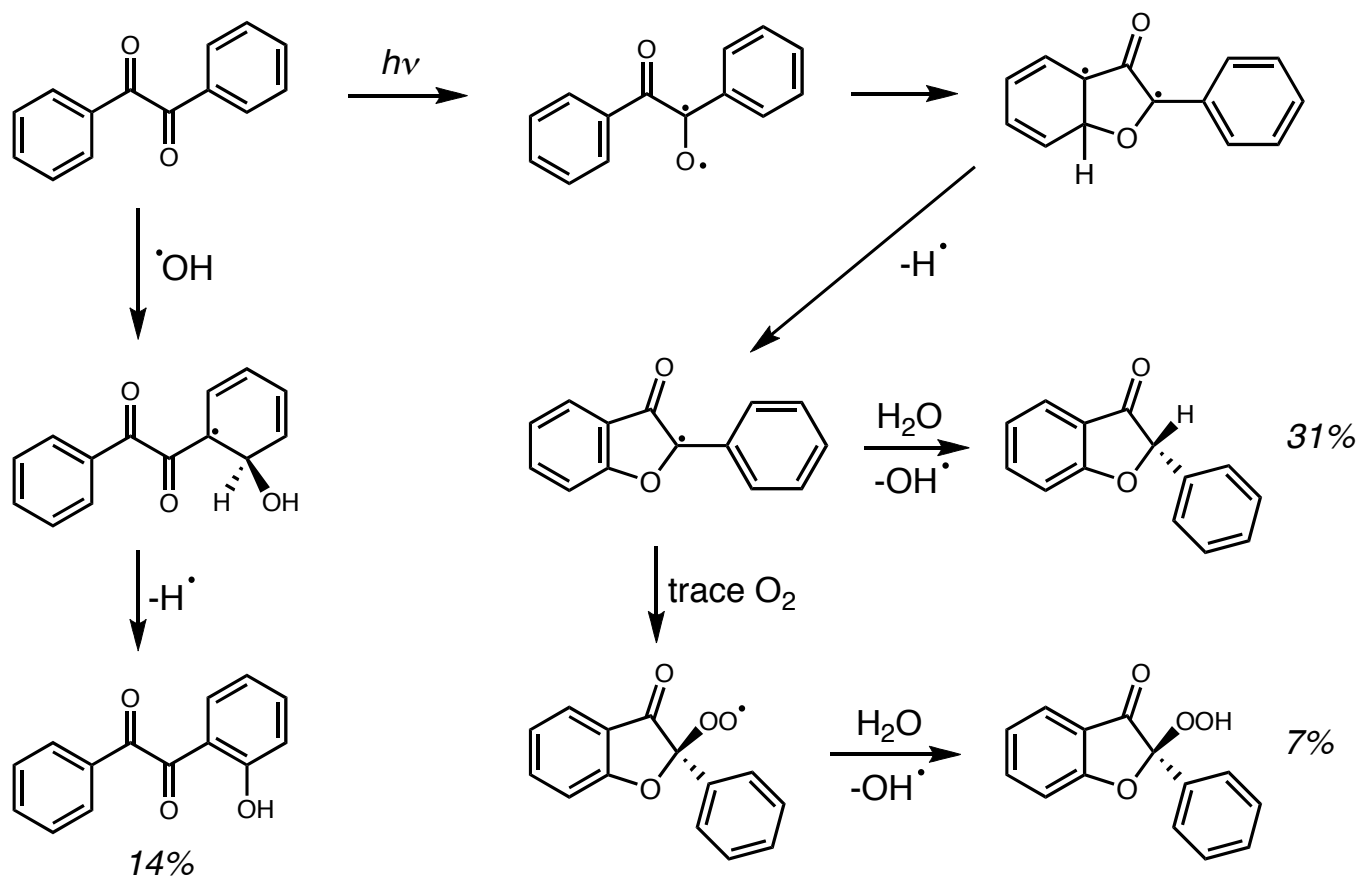


$R = H \text{ or } OOH$

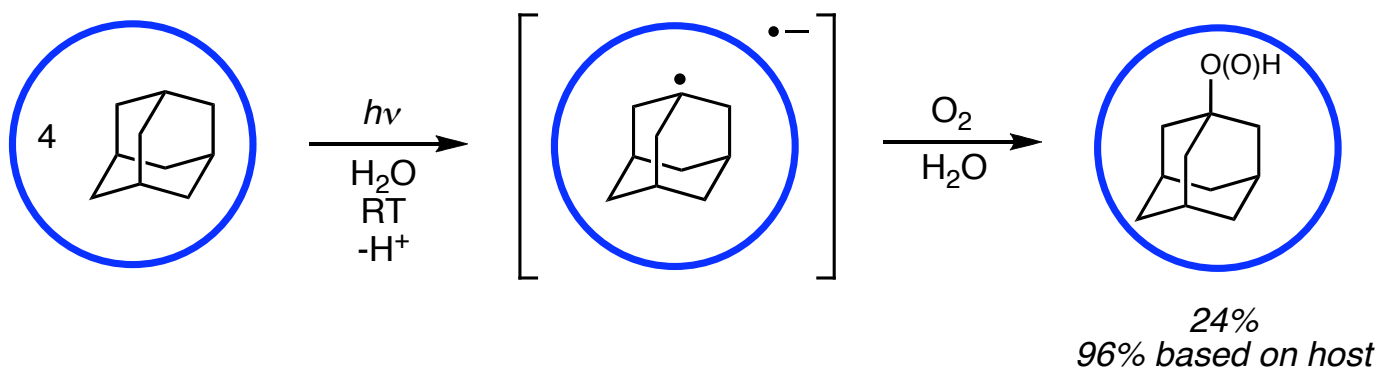
*Unprecedented intramolecular photocyclization*

# Photocyclizations Through Kinetically Unfavored Pathways

## Proposed mechanism

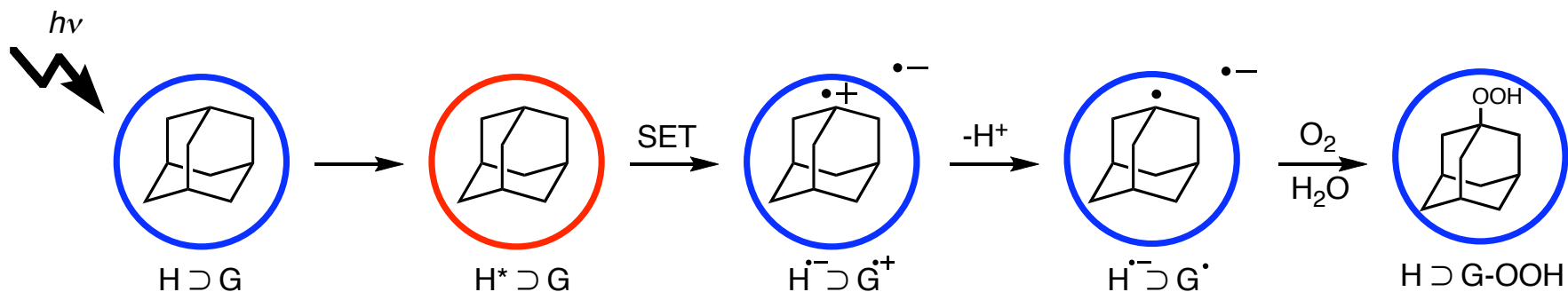


## Alkane Photo-Oxidation via Host-Guest Electron Transfer



- Irradiation ( $>300$  nm) of an aqueous sol. of 1:4 host:adamantane complex gives blue color
- Formation of adamantan-1-ol in 24 % yield (1 out of 4 guests are oxidized)
- First one-electron reduction potential of the cage is considerably low  $\Rightarrow$  suggesting a cage-mediated electron transfer

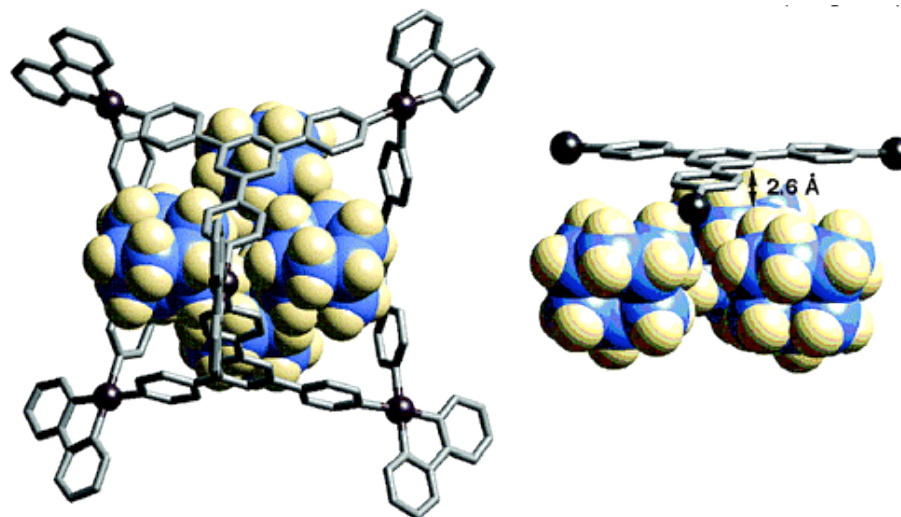
## Alkane Photo-Oxidation via Host-Guest Electron Transfer



- Step 1: Photochemical excitation of the triazine ligand with a low lying LUMO
- Step 2: One-electron transfer from the bridgehead C-H @ adamantane to the ligand
- Step 3: Adamantane radical cation dissociated to an adamantane radical and  $H^+$
- Step 4: Radical traps  $O_2$  or  $H_2O$ .

Yoshizawa, M.; Miyagi, S.; Kawano, M.; Ishiguro, K.; Fujita, M. *J. Am. Chem. Soc.* **2004**, *126*, 9172

## Mechanistic Elucidation of Alkane Photo-Oxidation



- X-Ray analysis of H $\supset$ G complex shows very short distances between C-H $\cdots$  $\pi$ -system (triazine)
- Control experiment 1: Host counterion ( $\text{NO}_3^-$  to  $\text{PF}_6^-$ ) or solvent ( $\text{H}_2\text{O}$  to MeCN) = no effect
- Control experiment 2: Exchanging triazine for benzene = no photoreactivity
- Conclusion: Radical should be generated on the ligands.
- $^{18}\text{O}$ -labeled  $\text{O}_2$  or  $\text{H}_2\text{O}$  led to  $^{18}\text{O}$ -incorp. prod  $\Rightarrow$  suggests adamantyl radical

Yoshizawa, M.; Miyagi, S.; Kawano, M.; Ishiguro, K.; Fujita, M. *J. Am. Chem. Soc.* **2004**, *126*, 9172

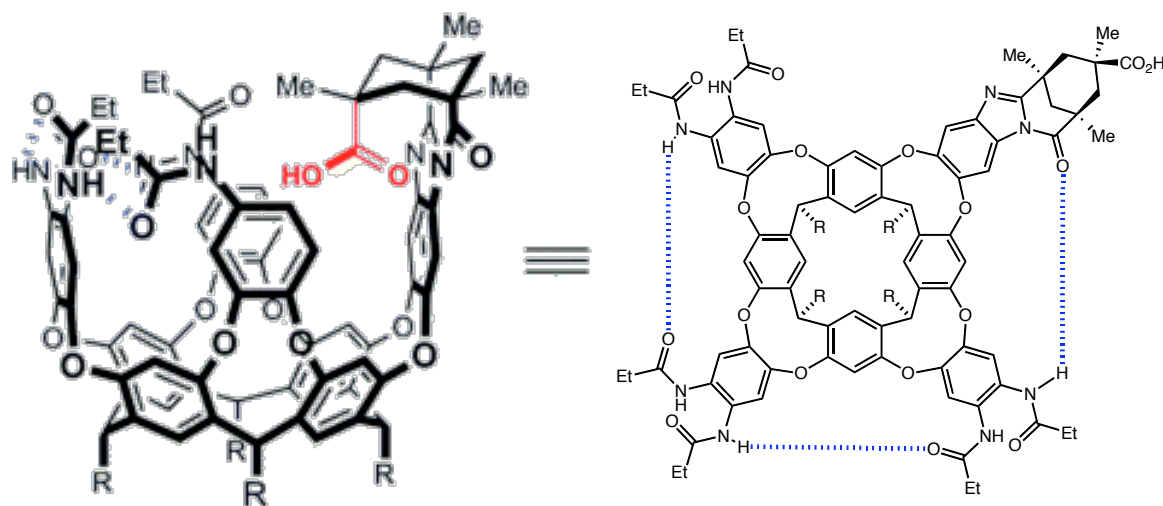
## *Conclusions: $M_6L_4$ Self-Assembly Hosts*

- Cationic Pd(II) hosts can encapsulate electron-rich aromatic substrates and be used to facilitate unusual and otherwise unfavored cycloadditions by geometrical control leading to TS-like encapsulation conformations
- The scope was then widen to asymmetric photoadditions using chiral diamine end-caps leading moderate enantioselectivities
- Then hosts has also been shown to facilitate kinetically unfavored and unprecedented photochemical cyclization by geometrical control
- The cage also mediates photo-induced electron transfer from guest to the electron-poor ligands

*Prof. Julius Rebek, Jr*  
*The Skaggs Institute for Chemical Biology*  
*And Department of Chemistry*  
*The Scripps Research Institute*

*Stabilization and Acceleration of Reactions in Cavitands*

## The Rebek Group's Open-Ended Cavitand

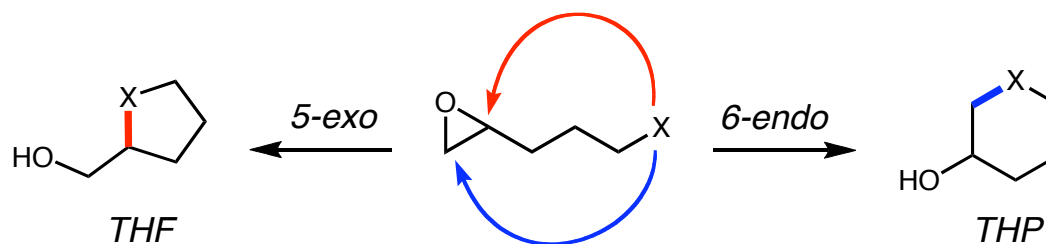


- The cavitand is a vase-shaped structure built up from a resorcinarene scaffold and widely used in molecular recognition
- The conformation is stabilized by a seam of hydrogen bonds conferred by a cyclic array secondary amides around the rim
- The rim is readily functionalized with reagents such as Kemp's triacid to bind to guests
- Amides makes a polar region within the cavitand  $\Rightarrow$  hydrogen bonding with guests
- Benzene rings in the walls  $\Rightarrow$  electron-rich  $\pi$ -surface to bound substrates

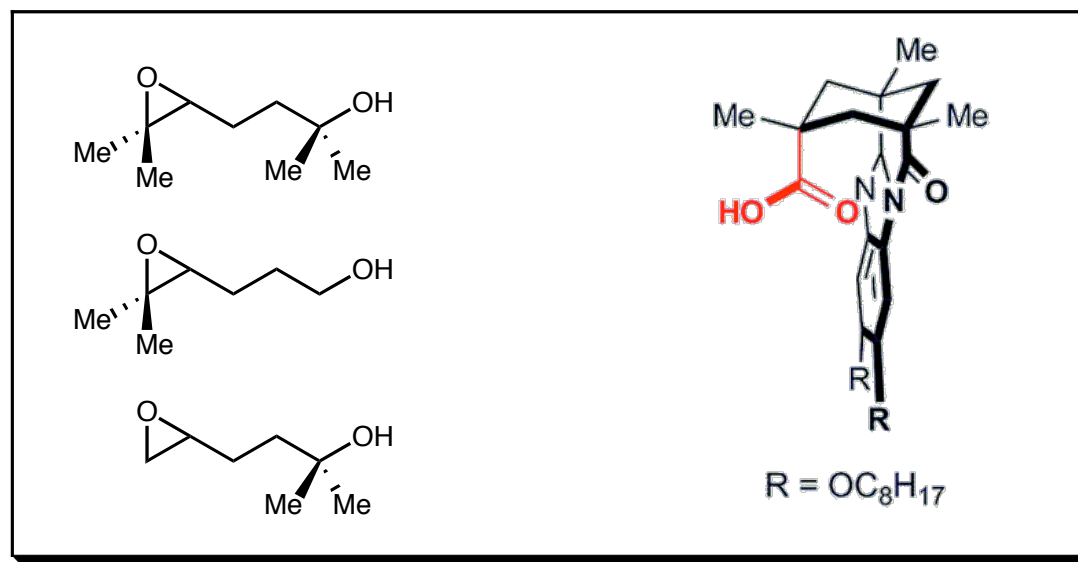


## Organocatalysis In a Synthetic Receptor: Regioselective Opening of Epoxy Alcohols

- Brønsted acid catalyzed intramolecular ring-opening of 1,5-epoxy alcohols

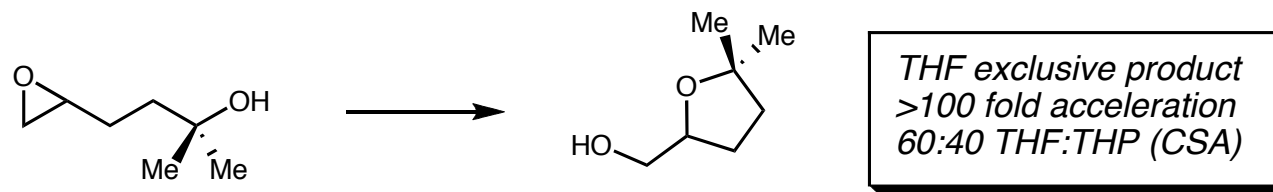
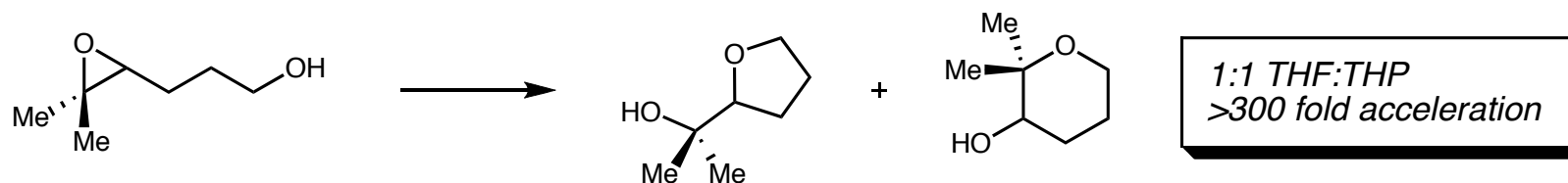
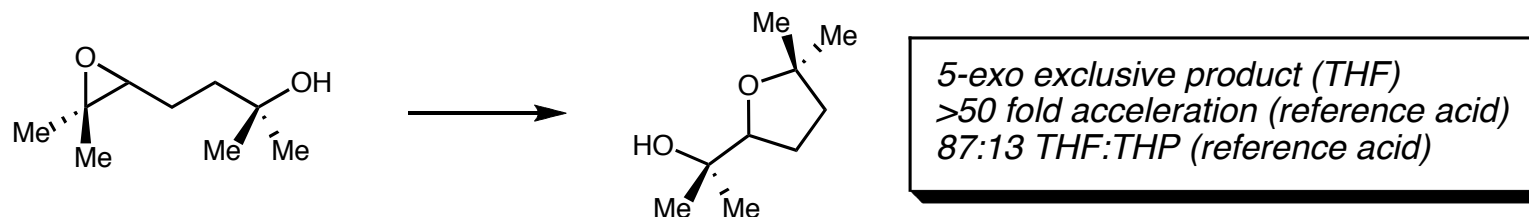


- Model substrates and reference acid

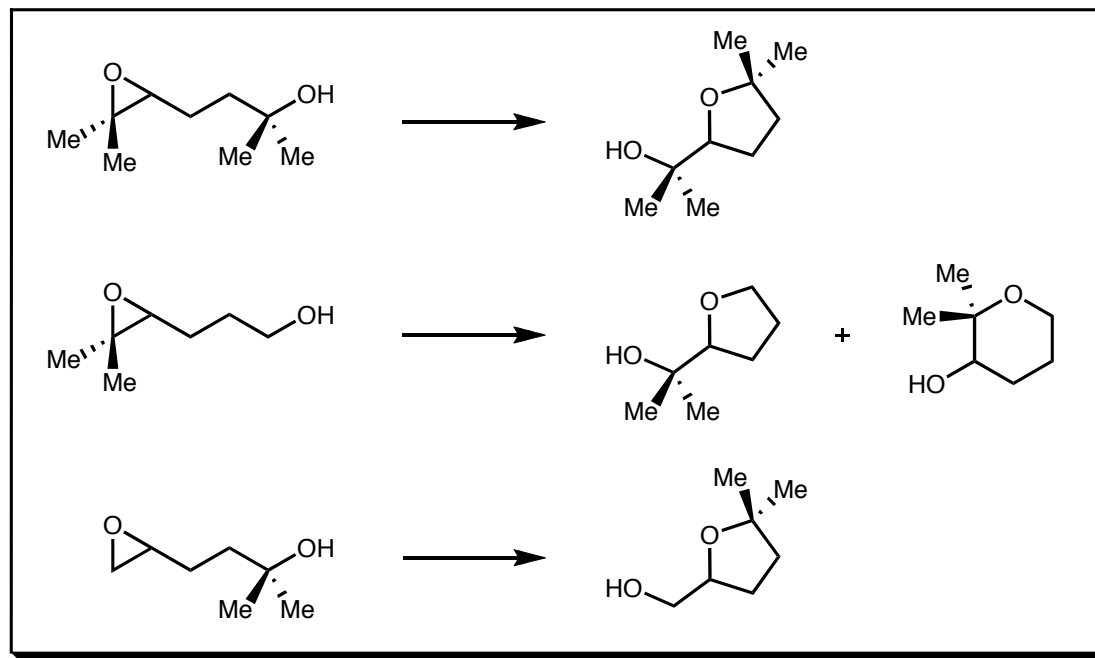


## Organocatalysis In a Synthetic Receptor

### ■ Epoxide opening within Kemp's triacid-derived cavitand in mesitylene- $d_{12}$



## Organocatalysis In a Synthetic Receptor



- Complexation exposes the epoxide to a local high concentration of the acid
- CH- $\pi$  interactions between  $\pi$ -surface of the host and alkyl groups of the guest induced coiling leading to TS-like conformations
- Multiple CH- $\pi$  interactions with geminal methyl groups @ OH-terminus  $\Rightarrow$  compressed TS giving THF products

Shenoy, S. R.; Pinacho Crisóstomo, F. R.; Iwasawa, T.; Rebek, J., Jr. *J. Am. Chem. Soc.* **2008**, *130*, 5658

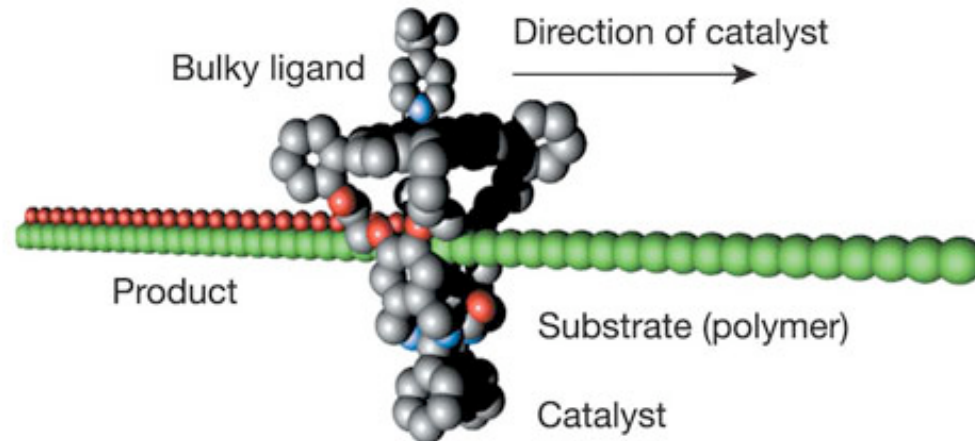
## *Conclusions: Self-Assembly Open-Ended Cavitands*

- The resorcinarene-based cavitands are held together by a seam of H-bonding through a cyclic array of secondary amides situated on the rim
- The rim is readily functionalized to incorporated binding sites for substrates with reagent such as Kemp's triacid
- Accelerates and catalyzes Brønsted acid mediated reactions. Exemplified with regioselective opening of 1,5-epoxy alcohols

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*Prof. Roeland J. M. Nolte*  
*Institute for Molecules and Materials*  
*Radboud University, Nijmegen*  
*The Netherlands*

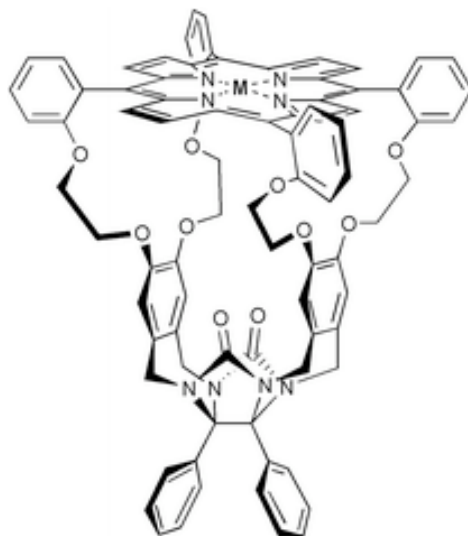
*Bio-Inspired Supramolecular Catalysis*

## *Development of Processive Enzyme Mimics using Cavity-Containing Catalysts*



- Processive enzymes: Plays an essential role in DNA synthesis and degradation
- DNA polymerase operate by threading the biopolymer through the catalyst cavity
- After threading several rounds of catalysis occurs before the enzyme (catalyst) dissociates

## Epoxidation of Stilbene using Mn(III) Porphyrin-Based Hosts

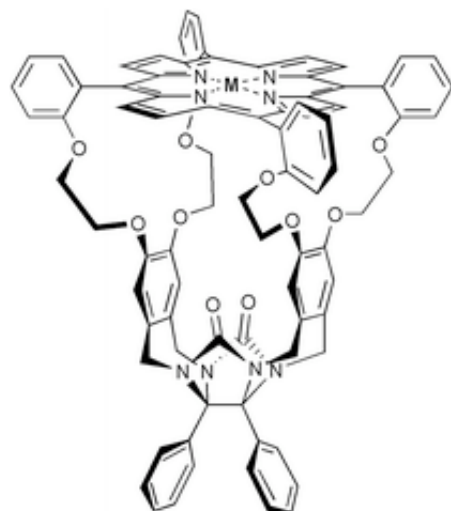


H<sub>2</sub>1: M = 2H  
Zn1: M = Zn(II)  
Mn1: M = Mn(III)Cl

- Cavity-containing catalyst with porphyrin "roof"
- Cavity: ca. 9 Å in diameter suitable to complex small aromatic guests
- Complexed by electrostatic and  $\pi$ - $\pi$  stacking interactions ( $K_a = 10^5$ - $10^6$  M<sup>-1</sup>, MeCN/CHCl<sub>3</sub>)  
Ex: Pyridine,  $K_a = 1.1 \cdot 10^5$  M<sup>-1</sup> (cavity Zn-porphyrin),  $K_a = 1000$  M<sup>-1</sup> (Zn-porphyrin)

Elemans, J. A. A. W.; Claase, M. B.; Aarts, P. P. M.; Rowan, A. E.; Schenning, A. P. H. J.; Nolte, R. J. M.  
*J. Org. Chem.* **1999**, *64*, 7009

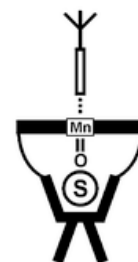
## Epoxidation of Stilbene using Mn(III) Porphyrin-Based Hosts



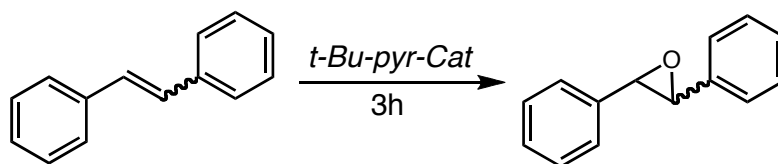
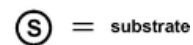
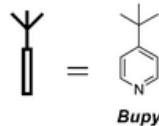
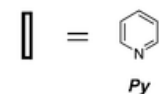
H<sub>2</sub>1: M = 2H  
 Zn1: M = Zn(II)  
 Mn1: M = Mn(III)Cl



Approach A



Approach B



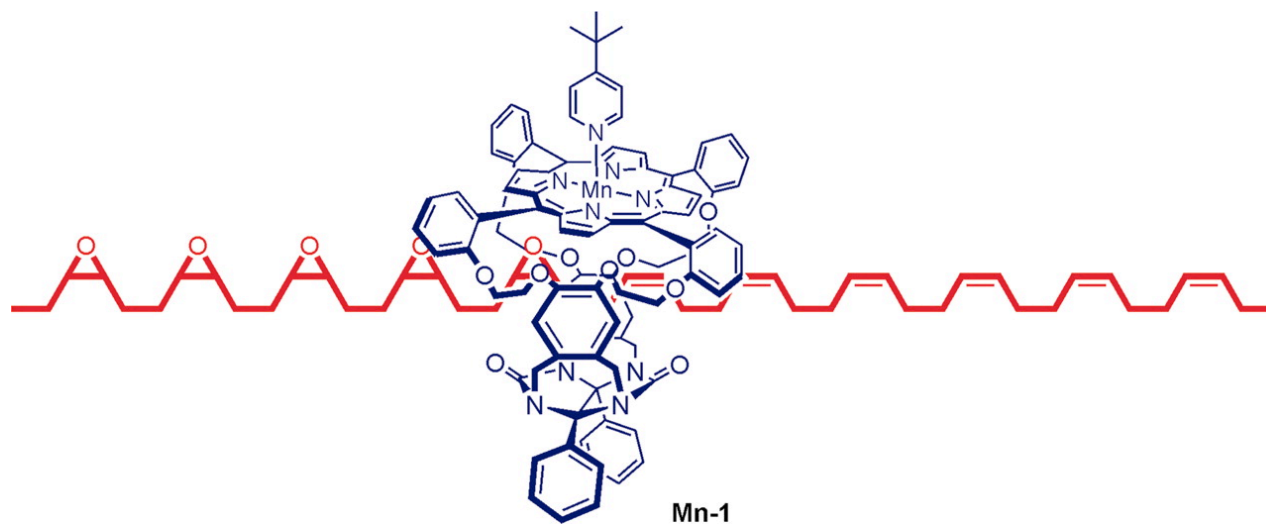
*cis*-Stilbene: 57% (90% *cis*)  
*trans*-Stilbene: 72% (100% *trans*)

- Pyridine replaced with *t*-Bu-Pyr: Bulky ligand that coordinates axially on the outside
- Catalyst decomposition completely suppressed
- Catalysis occurs inside the cavity with impact on the stereochemistry
- Rate of *trans*-stilbene epoxidation twice as high as *cis* due to sterical hinderance

Elemans, J. A. A. W.; Bijsterveld, E. J. A.; Rowan, A. E.; Nolte, R. J. M. *Chem. Commun.* **2000**, 2443



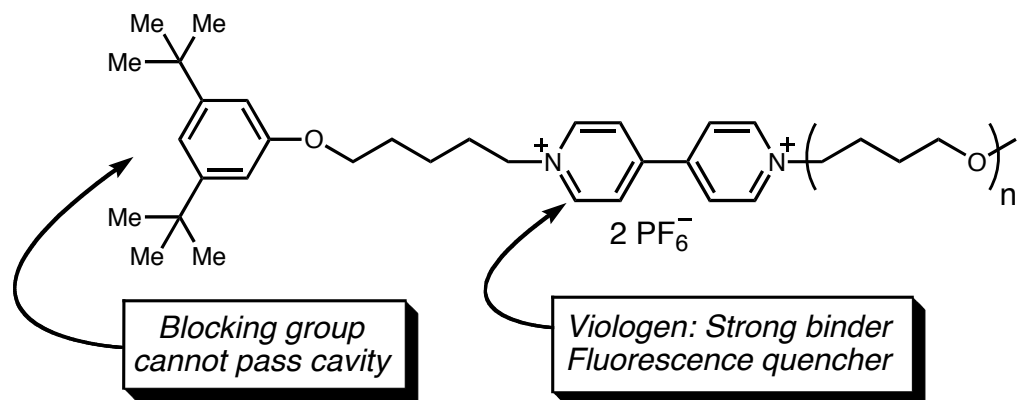
## Mn(III) Porphyrin-Based Hosts as Processive Enzyme Mimics



- Reaction performed in  $\text{CHCl}_3$  with PhIO as stoichiometric oxidant
- Polybutadiene ( $M_w = 300000$ , >98% *cis*) used as substrate
- Polyepoxide product (80% *trans*), catalyst turnover 140/h (cavity-catalyst)
- Polyepoxide product (78% *cis*), Mn(III)-porphyrin reference catalyst

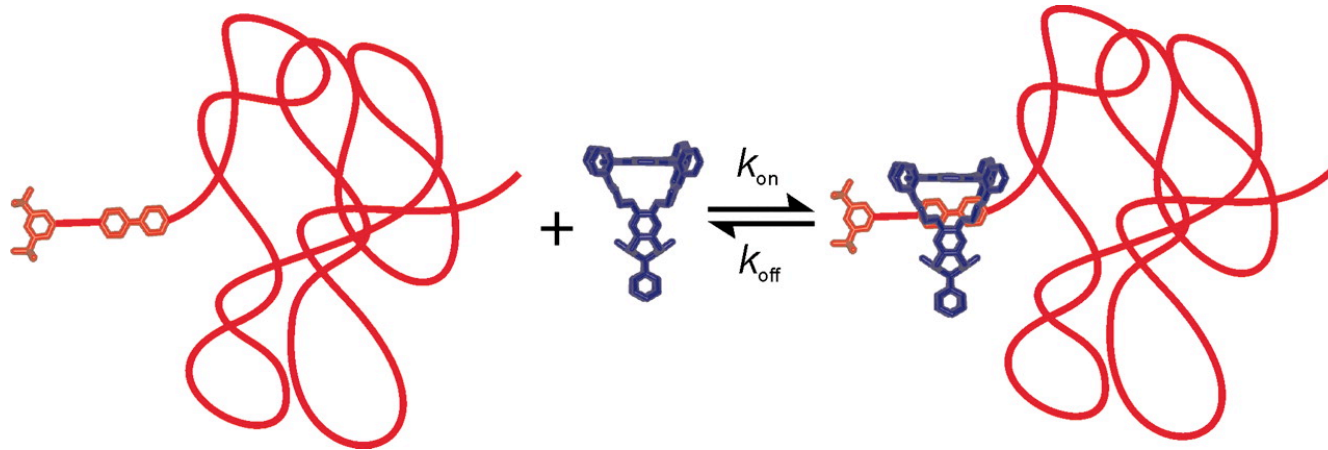
Thordardson, P.; Bijsterveld, E. J. A.; Rowan, A. E.; Nolte, R. J. M. *Nature*, **2003**, 424, 915

## Investigation of the Threading Mechanism



- Polytetrahydrofuran viologen (fluorescence quencher) traps used to investigate the threading mechanism

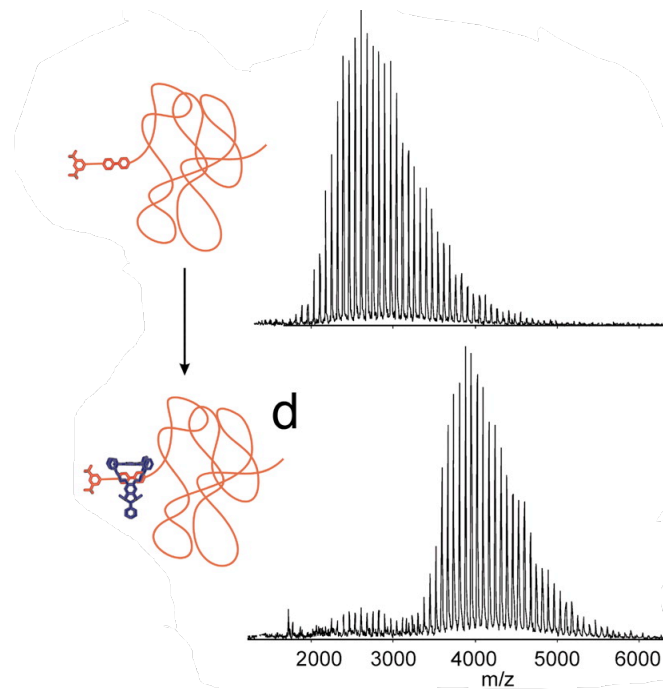
## Investigation of the Threading Mechanism



- Polytetrahydrofuran viologen (fluorescence quencher) traps used to investigate the threading mechanism
- Monitoring quenching/time showed: Second-order kinetics for threading and first-order for de-threading (fast dilution). Rate decreased when polymer length increased

Coumans, R. G. E.; Elemans, J. A. A. W.; Nolte, R. J. M.; Rowan, A. E. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 19647

## Investigation of the Threading Mechanism



- Polytetrahydrofuran viologen (fluorescence quencher) traps used to investigate the threading mechanism
- Monitoring quenching/time showed: Second-order kinetics for threading and first-order for de-threading (fast dilution). Rate decreased when polymer length increased
- Evidence for threading obtained using MALDI-TOF (1:1 complex),  $^1\text{H-NMR}$ : -2.29 to -4.25 ppm complexation induced shifts for aromatic viologen peaks due to complexation

Coumans, R. G. E.; Elemans, J. A. A. W.; Nolte, R. J. M.; Rowan, A. E. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 19647

## *Conclusions: Processive Enzyme Mimics*

- Cavity-containing Mn(III) porphyrin catalyst has been developed for *in-cavity* epoxidation of stilbene by activation using bulky axially-coordinating *t*-Bu-pyridine ligands
- Successfully used as a processive enzyme mimic for the epoxidation of polybutadiene by threading
- Extensive elucidation of threading kinetics using fluorescence quenching & MALDI-TOF mass spectroscopy & <sup>1</sup>H-NMR spectroscopic analysis of host-guest complexes confirms threading of only one host

## *Summary and Outlook: Supramolecular Catalysis Within Self-Assembly Hosts*

- Supramolecular enzymes models are always smaller and simpler than their biological counterparts but it is not necessarily a drawback
- Using simpler systems can open for the possibility to estimate the relative importance of different factor contributing to catalysis
- Synthetic model are also easily manipulated in a systematic fashion which is more difficult in biological systems
- Encapsulation has in recent years lead to the discovery of several unprecedented reaction pathways and clearly shows that otherwise unfavored pathways are possible
- The use of chiral, enantiomerically pure self-assembly hosts is still a largely unexplored area which can lead to the development of several new interesting reactions. For example with Fujita's chiral  $M_6L_4$  complexes
- The development of more general processive enzyme mimics can open up for the possibility of rapid post-polymerization functionalization of polymers and biopolymers