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Interconversion of molecular face-rotating polyhedra through turning inside out

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1 Supplementary Methods

Synthesis of FRP 1. The racemic enantiomers of **1** were prepared from the reaction of hexabutyl trialdehydetruxene (TR) and ethylenediamine as described previously[1]. (*CCCC*)-**1** and (*AAAA*)-**1** were separated by HPLC in the mobile phase of hexane:ethyl acetate = 83:17 (v/v) with 0.1% diethylamine. The isolated enantiomers showed a high stability in the mobile phase of HPLC, and thus allowed us to obtain the solid enantiomers and the corresponding solutions in toluene and dichloromethane.

Characterization of kinetics. Solutions of racemic enantiomers of **1** in toluene or dichloromethane (*ca.* 2 mL) were made at accurate concentrations with the rapid determination from UV-Vis spectra, and 5% TFA (*i.e.*, 5 μM TFA for 100 μM cage) was added to activate the imine bonds. The racemization took place in 5 mL pressure vessels at different temperatures. At regular intervals (15 minutes to 2 hours depending on the reaction rates), each 40 μL reaction solutions were extracted into 360 μL ethyl acetate to quench the racemization for the following HPLC and CD measurements. HPLC analyses were performed on a Shimadzu LC-16A instrument, using Daicel Chiralcel IE Columns in the mobile phase of hexane:ethyl acetate = 83:17 (v/v) with 0.1% diethylamine. CD spectra were collected on JASCO J-810 circular dichroism spectrometer at 298 K. CD spectra were measured in toluene or dichloromethane according to the solvents for racemization.

Deduction of the kinetics of interconversion and racemization. The racemization of (*AAAA*)-**1** essentially contains two opposing reactions[2–4], *i.e.*, the forward reaction from (*AAAA*)-**1** to (*CCCC*)-**1** and the reverse reaction from (*CCCC*)-**1** to (*AAAA*)-**1**, as shown in Eq. 1.

$$\begin{aligned} (AAAA)\text{-}\mathbf{1} &\xrightarrow{k_{\text{obs}}} (CCCC)\text{-}\mathbf{1} \\ (AAAA)\text{-}\mathbf{1} &\underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} (CCCC)\text{-}\mathbf{1} \end{aligned} \tag{1}$$

in which the k_{obs} is the observed rate constant of the racemization, and the k_1 and k_{-1} are the rate constants of the forward and reverse reactions, respectively. The deduction for the kinetics of general opposing reactions can be found in textbooks[5], based on which we give following deduction for the racemization of (*AAAA*)-**1**.

The forward and reverse reactions should have the same reaction order and the same the rate constant, $k_1 = k_{-1}$. For first order forward and reverse reactions, we have:

$$\vec{r} = k_1[(AAAA)\text{-}\mathbf{1}]; \quad \overleftarrow{r} = k_{-1}[(CCCC)\text{-}\mathbf{1}]$$

Therefore, we have the variation of $(AAAA)$-**1** as:

$$d[(AAAA)\text{-}\mathbf{1}] = -k_1[(AAAA)\text{-}\mathbf{1}] \cdot dt + k_{-1}[(CCCC)\text{-}\mathbf{1}] \cdot dt$$

Using $k_1 = k_{-1}$ and $[(AAAA)\text{-}\mathbf{1}] = [(AAAA)\text{-}\mathbf{1}]_0 - [(CCCC)\text{-}\mathbf{1}]$, in which $[(AAAA)\text{-}\mathbf{1}]_0$ is the initial concentration of $(AAAA)$-**1**, we have

$$d[(AAAA)\text{-}\mathbf{1}] = k_1[(AAAA)\text{-}\mathbf{1}]_0 - 2[(AAAA)\text{-}\mathbf{1}] \cdot dt$$

After integration, it gives

$$-2k_1t = ln\frac{2[(AAAA)\text{-}\mathbf{1}] - [(AAAA)\text{-}\mathbf{1}]_0}{[(AAAA)\text{-}\mathbf{1}]_0}$$

Using the expression of normalized CD intensity:

$$[\mathrm{CD}] = \frac{[(AAAA)\text{-}\mathbf{1}] - [(CCCC)\text{-}\mathbf{1}]}{[(AAAA)\text{-}\mathbf{1}]_0} = \frac{2[(AAAA)\text{-}\mathbf{1}] - [(AAAA)\text{-}\mathbf{1}]_0}{[(AAAA)\text{-}\mathbf{1}]_0}$$

we have the relationships between the CD intensity and racemization time:

$$ln[\mathrm{CD}] = -2k_1t$$

, which can be written as:

$$ln[\mathrm{CD}] = -k_{\mathrm{obs}}t \text{ and } k_{\mathrm{obs}} = 2k_1$$

2 Supplementary Figures

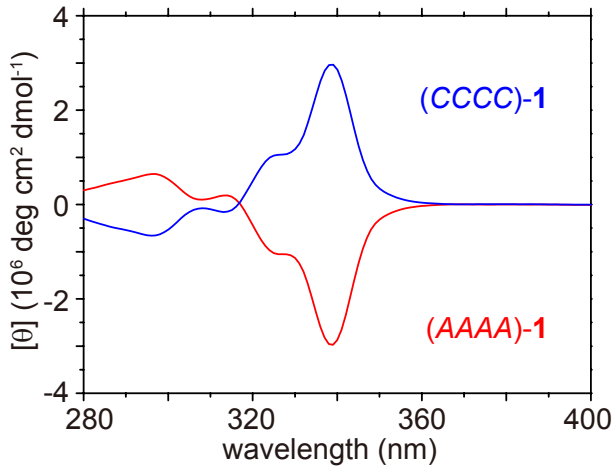

Figure S1: CD spectra of the isolated $(CCCC)$-**1** and $(AAAA)$-**1** in toluene at the concentration of 100 μM. The isolated enantiomers showed a high stability in the mobile phase of HPLC (hexane:ethyl acetate = 87:13), and thus allowed us to obtain the solid enantiomers and the corresponding toluene solutions.

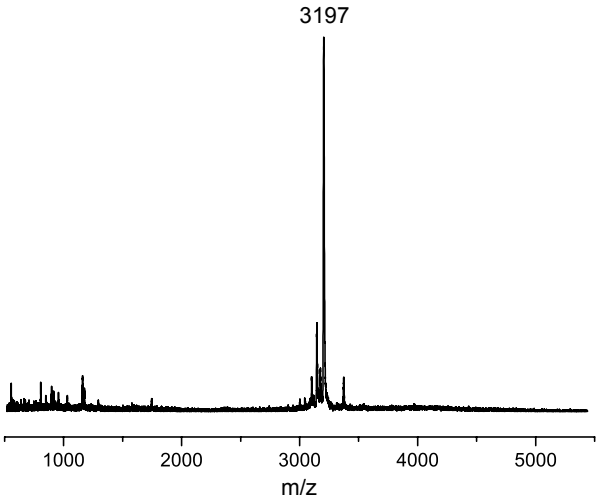

Figure S2: MALDI-TOF spectroscopy of the $(AAAA)$-**1** solution in toluene after heated at 333 K for 24 hours. The peak at 3197 m/z indicates that the enantiomers remain their cage structure.

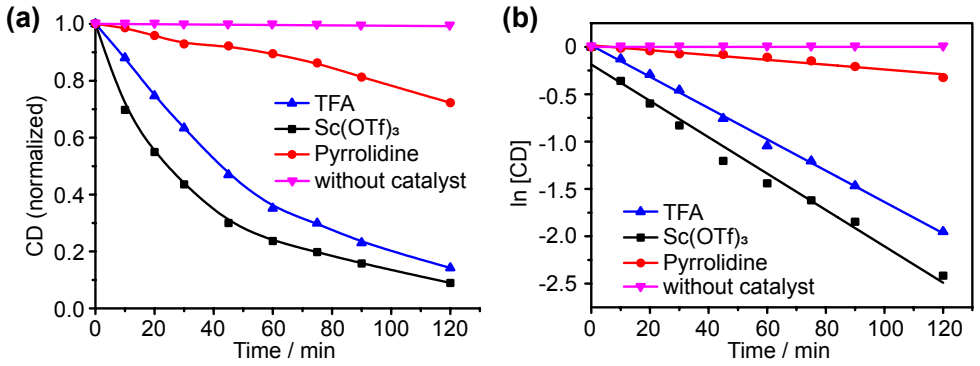

Figure S3: Normalized CD intensity (a) and logarithm of the CD intensity (b) versus reaction time during the racemization of (*AAAA*)-**1** (100 μM, 338 K) in toluene without or with different catalysts (5 μM). From the entry (b), k_{obs} values for TFA, $Sc(OTf)_3$ and pyrrolidine are calculated to be 2.8 $\times$ 10^{-4} s^{-1}, 3.2 $\times$ 10^{-4} s^{-1} and 4.2 $\times$ 10^{-5} s^{-1}, respectively.

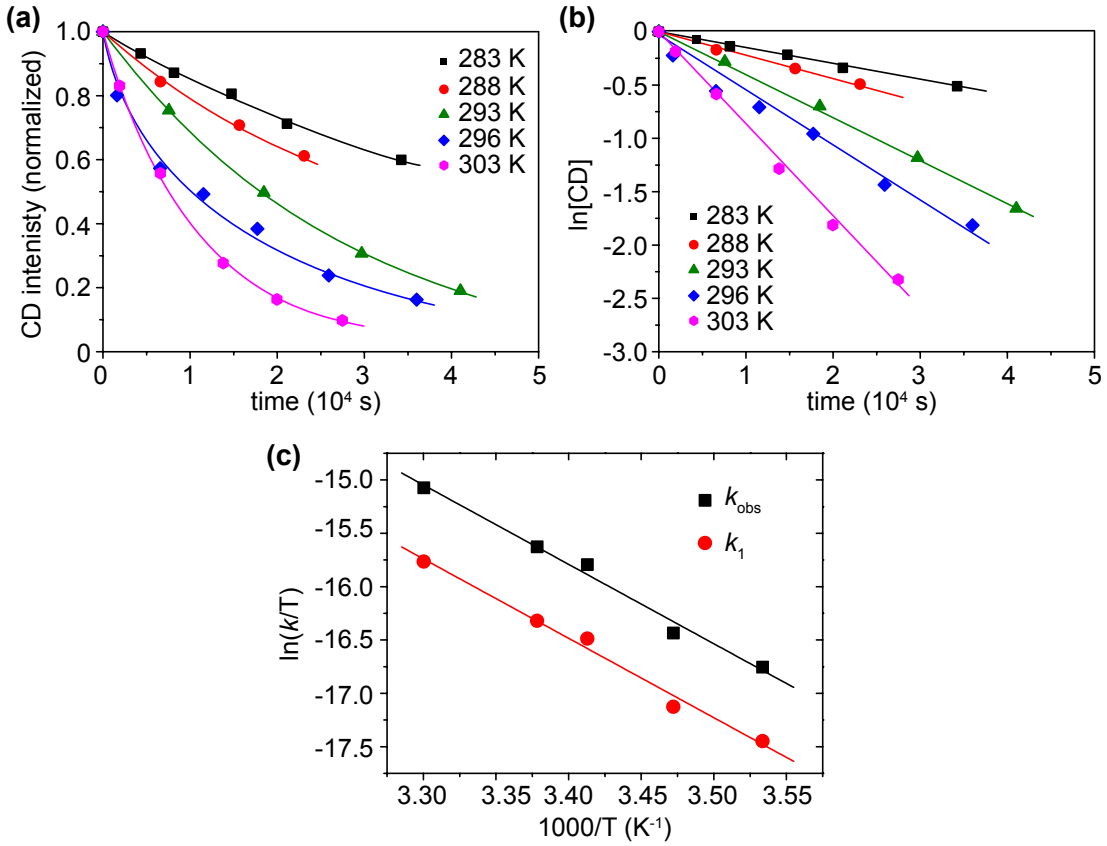

Figure S4: Normalized CD intensity (a) and logarithm of the CD intensity (b) versus reaction time during the racemization of (*AAAA*)-**1** in dichloromethane at the concentration of 100 μM under various temperatures. (c) Rate constants of the racemization of (*AAAA*)-**1** in dichloromethane at different temperatures fitted by the Eyring equation. Through the Eyring equation, the kinetics parameters are calculated as: $\Delta H^{\ddagger}_{\mathrm{obs}}(DCM) = 61.9$ kJ mol^{-1} and $S^{\ddagger}_{\mathrm{obs}}(DCM) = -118.5$ J mol^{-1} K^{-1}.

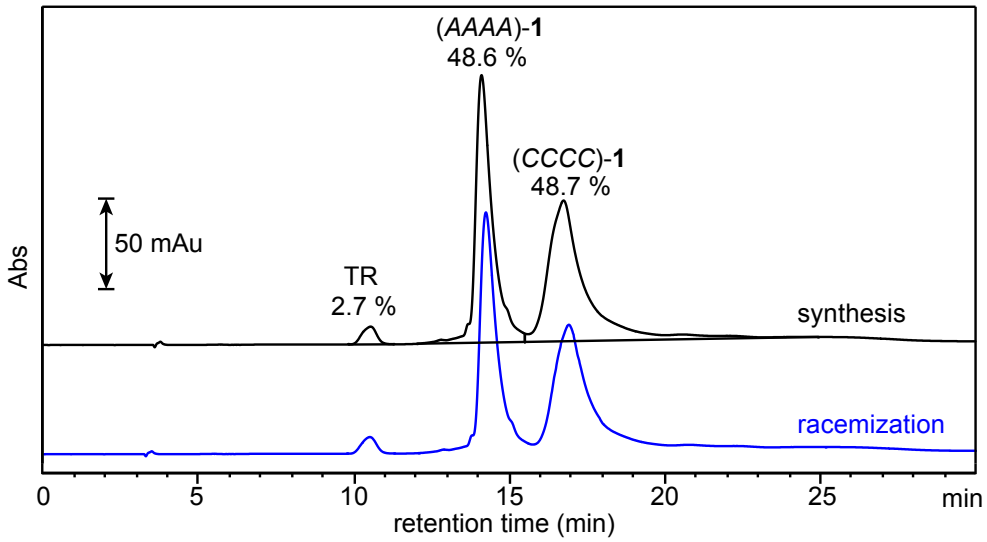

Figure S5: HPLC spectra of the equilibrium products of synthesis (black line) and racemization (blue line) of cage **1** (100 μM) in toluene at 343 K with the catalysis of trifluoroacetic acid (5 μM). The energy difference between the reactants and products was calculated in Table S3.

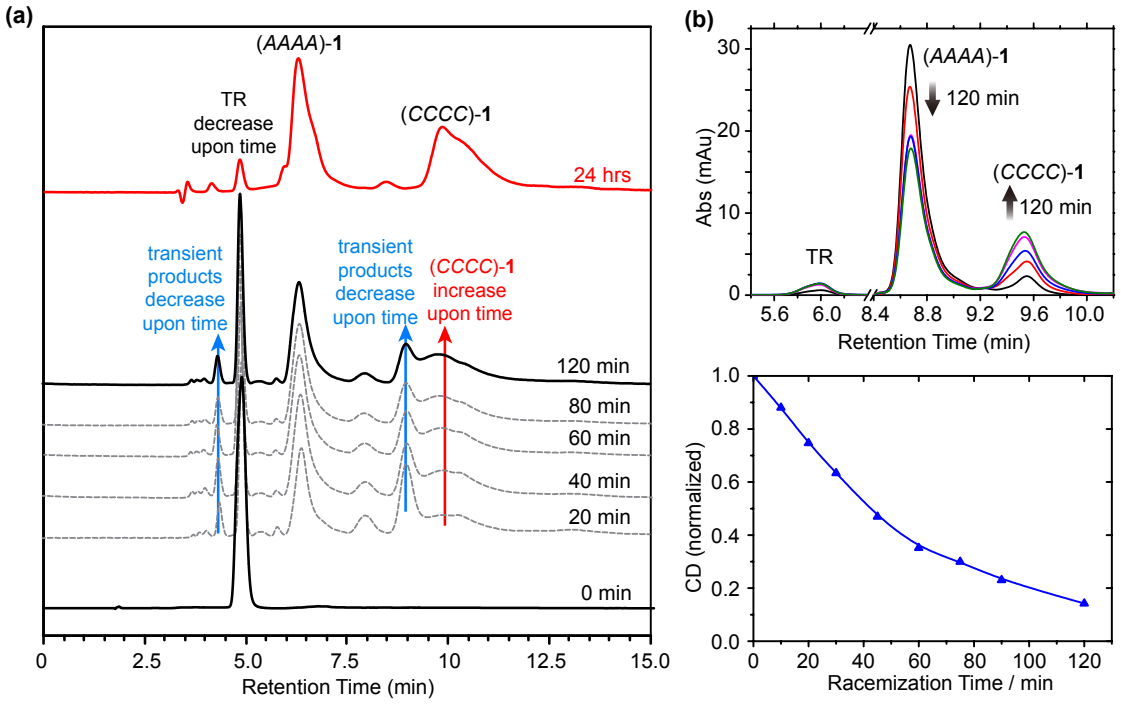

Figure S6: Kinetics comparison of the synthesis of cage **1** and the racemization of (*AAAA*)-**1** with the same constitutional dynamic library to the racemization of 100 μM cage. For both cases, the overall cage concentration was set to 100 μM, the temperature was set to 338 K, and toluene with 5% TFA was used as solvent. (a) HPLC spectra at different reaction time during the synthesis of cage **1**. At 120 min, there are still a great amount of transient products (probably dimers, trimers, and oligomers) in the dynamic library, and only a small fraction of (*CCCC*)-**1** has been formed, suggesting the cage synthesis process is still far away from completion. (b) HPLC spectra and normalized CD intensity during the racemization of (*AAAA*)-**1**. At 120 min, CD intensity has decreased to 15%, indicating the racemization process has proceeded to a large extent.

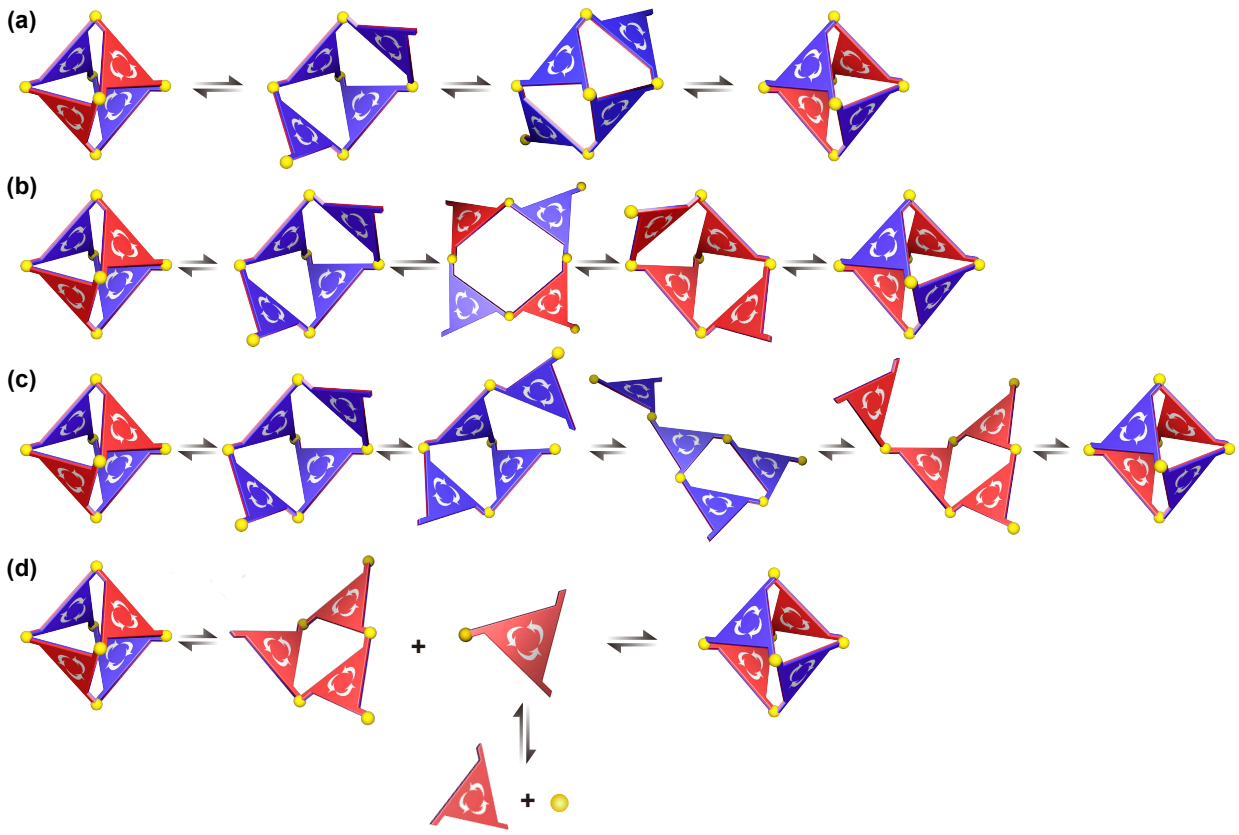

Figure S7: Representative possible pathways through partially disassembled cage fragments. (a) pathway through the cleavage of only one imine bond. (b) pathway through the cleavage of two imine bonds on two opposite vertices. (c) pathway through the cleavage of two imine bonds on two adjacent vertices. Pathways a and b do not involve the formation of monomer intermediates, nevertheless, due to the nature of dynamic covalent chemistry, other pathways involving the cleavage of more imine bonds might also be possible, *e.g.*, pathway (d). (d) pathway through the cleavage of three imine bonds on three adjacent vertices, forming two fragments which might further reversibly convert into EDA and TR monomers.

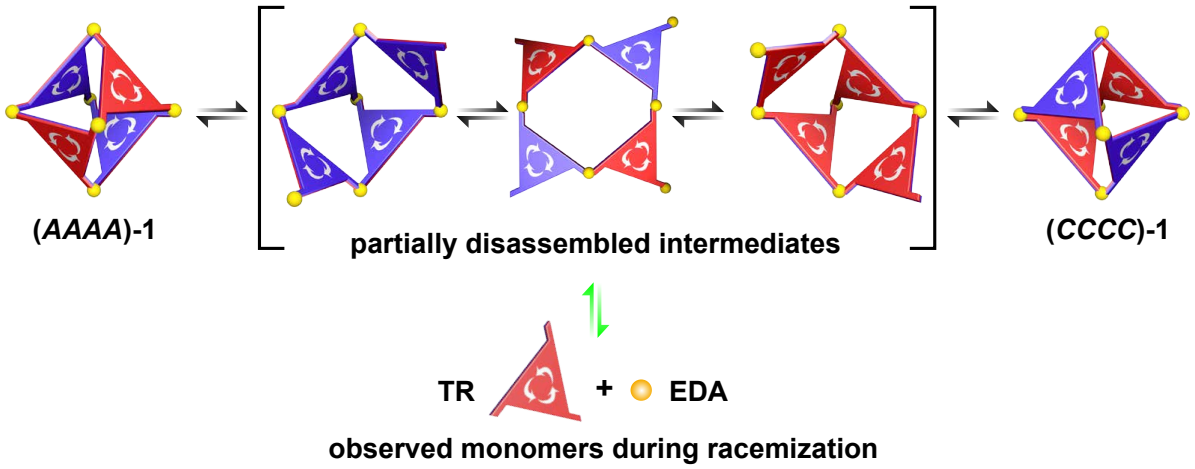

Figure S8: Schematic of the concurrent disassembly of a small amount of cage during the racemization of $(AAAA)$-**1**. The main pathway during the racemization of $(AAAA)$-**1** is through the partially disassembled intermediates, as shown in Figure S7 and the black arrows here as an example. Nevertheless, for dynamic imine chemistry, the constitutional library at the equilibrium state inevitably contains some the amine and aldehyde monomers. Therefore, a small amount of cage was completely disassembled into TR and EDA monomers during the racemization. And this minor pathway to completely disassembled monomers should also go through the partially disassembled intermediates, as shown by the green arrow.

3 Supplementary Tables

Table S1: Rate constant k_{obs} and k_1 (with error Δk_{obs} and Δk_1) at a concentration of 100 μM in toluene as a function of temperature.

T(K)	k_{obs} (s^{-1})	Δk_{obs} (s^{-1})	k_1 (s^{-1})	Δk_1 (s^{-1})	R^2
323	5.112E-05	1.28E-06	2.556E-05	6.41E-07	0.997
328	9.950E-05	1.03E-06	4.975E-05	5.15E-07	0.999
333	1.603E-04	2.72E-06	8.014E-05	1.36E-06	0.999
338	2.755E-04	5.94E-06	1.378E-04	2.97E-06	0.997
343	4.276E-04	4.38E-06	2.138E-04	2.19E-06	1.000

Table S2: Rate constant k_{obs} and k_1 (with error Δk_{obs} and Δk_1) at a concentration of 100 μM in dichloromethane as a function of temperature.

T(K)	k_{obs} (s^{-1})	Δk_{obs} (s^{-1})	k_1 (s^{-1})	Δk_1 (s^{-1})	R^2
283	7.003E-04	3.7E-05	3.502E-04	1.8E-05	0.984
288	1.335E-03	1.8E-05	6.673E-04	9.2E-06	0.999
293	2.118E-03	9.6E-05	1.059E-03	4.8E-05	0.990
296	2.559E-03	1.4E-04	1.280E-03	6.8E-05	0.986
303	5.171E-03	1.5E-04	2.585E-03	7.5E-05	0.996

Table S3: Calculation of the energy difference between the reactants and products of the synthesis of Cage **1** in toluene at 343 K.

$[TR]_0$ (M)	4.00E-4	Cage ratio (%)	97.3
$[EDA]_0$ (M)	6.00E-4	TR ratio (%)	2.7
$[Cage]_{eq}$ (M)	9.73E-5	$[TR]_{eq}$ (M)	1.08E-5
$[EDA]_{eq}$ (M)	1.62E-5	$[H_2O]_{eq}$ (M)	1.17E-3
$4\ TR + 6\ EDA \ \rightarrow \ Cage + 12\ H_2O$			
$\Delta G_{343K} = -RTln\frac{[Cage]_{eq}[H_2O]_{eq}^{12}}{[TR]_{eq}^{4}[EDA]_{eq}^{6}} = -61.8\ kJ\ mol^{-1}$			

4 Supplementary References

[1] X. Wang, Y. Wang, H. Yang, H. Fang, R. Chen, Y. Sun, N. Zheng, K. Tan, X. Lu, Z. Tian, X. Cao, *Nature Commun.* **2016**, *7*, 12469.

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