Supporting Information

Efficient optical resolution of water-soluble self-assembled tetrahedral M_4L_6 cages with 1,1'-bi-2-naphthol

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1. General

The NMR spectra were measured with a Bruker Unity 500 MHz spectrometer using TMS as an internal standard for ^{1}H NMR and a Bruker Unity 850 MHz spectrometer using 2-methyl-2-propanol as an internal standard for ^{13}C NMR. Circular dichroism (CD) spectra were measured with a Jasco J-810 spectropolarimeter. The slit band width of CD spectra measurements was set at 2 nm. Mass spectral data were acquired using a Bruker Fourier transform ICR spectrometer. Fluorescence spectra were recorded on a F-7000 fluorescence spectrophotometer at an excitation wavelength of 280 nm with both of excitation and emission monochromators set at 2.5 nm. Elemental analyses for C, H, and N were performed on an Elementar Vario EL III elemental analyzer. Racemic $(Me_4N)_4[Fe_4L_6]$ and $(Me_4N)_4[Ni_4L_6]$ were synthesized according to literature.[S1,S2] The $[Ru(phen)_3](PF_6)_2$ was synthesized and resolved according to published procedures.[S3,S4] Solvents and commercially available reagents were used without further purification.

2. Resolution of cage T with Leu^+ and $Bcic^+$.

Rac-$(Me_4N)_4[Fe_4L_6]$ 36 mg and Leu^+ 12 mg ($Bcic^+$ 17 mg) were added to a 50 mL flask containing methanol 15 mL. The reaction was stirred for 1 h at 50 ℃. The less soluble salt (ΛΛΛΛ-T) was collected by centrifugation, washed with a small portion of methanol, and dried under vacuum. The remaining methanolic solution was concentrated on a rotational evaporator and the more soluble salt was obtained. The Leu^+ ($Bcic^+$) ions were exchanged against Me_4N^+ on a cation exchange column. $(Me_4N)_4[Fe_4L_6]$ with enantiomer excess were isolated by slow vapor diffusion of acetone into their aqueous solutions.

3. Resolution of cage T with $[Ru(phen)_3](PF_6)_2$

Rac-$(Me_4N)_4[Fe_4L_6]$ 36 mg and $[Ru(phen)_3](PF_6)_2$ 9 mg were added to a 50 mL flask containing methanol 15 mL. The reaction was stirred for 1 h at 50 ℃. The less soluble salt (ΛΛΛΛ-T) was collected by centrifugation, washed with a small portion of methanol, and dried under vacuum. The remaining methanolic solution was concentrated on a rotational evaporator and the more soluble salt was obtained. The $[Ru(phen)_3]^{2+}$ ions were exchanged against Me_4N^+ on a cation exchange column. $(Me_4N)_4[Fe_4L_6]$ with enantiomer excess were isolated by slow vapor diffusion of acetone into their aqueous solutions.

4. Resolution of cage T with BINOL.

Rac-$(Me_4N)_4[Fe_4L_6]$ 108 mg and (*S*)-BINOL (or (*R*)-BINOL) 36 mg were added to a 25 mL flask containing 6 mL water/methanol (v/v = 1:1). The reaction was stirred for 1 h at 50 ℃. The less soluble diastereoisomer was collected by centrifugation and washed with water (3 × 2mL) and then with acetone, after that dried in vacuum, and last dissolved in 4 mL water/methanol (v/v = 1:1). ΔΔΔΔ-**T** was obtained by slow vapor diffusion of acetone into the water/methanol solution

for several days. Yield: 35%. ΛΛΛΛ-**T** was obtained from slow vapor diffusion of acetone into the filtrate. Yield: 45%. ^{1}H NMR (500 MHz, 298 K, D_2O): δ = 9.29 (s, 12H, imine), 8.66 (d, 12H, 3-pyridine), 8.34 (t, 12H, 4-pyridine), 7.72 (t, 12H, 5-pyridine), 7.50 (d, 12H, 6-pyridine), 7.09 (d, 12H, 6,6'-benzidine), 6.38 (s, 12H, 3,3'-benzidine), 5.78 (d, 12H, 5,5'-benzidine), 3.30 ppm (s, $[NMe_4]^+$). ^{13}C NMR (212.5 MHz, 298 K, D_2O, referenced to 2-methyl-2-prop-anol at 29.5 ppm as internal standard): δ = 176.0, 157.9, 155.7, 150.0, 143.1, 139.7, 135.9, 132.0, 131.9, 129.8, 121.7, 120.8. HR-ESI-MS: m/z: 1123.0083 ($[Fe_4L_6]^{4-} + Na^+$), 548.0199 ($[FeL_2]^{2-}$), 836.0117 ($[Fe_2L_3]^{2-}$), 1124.5048 ($[Fe_3L_4]^{2-}$), 1412.9976 ($[Fe_4L_5]^{2-}$). Elemental analysis calcd for $C_{160}H_{144}N_{28}Fe_4O_{36}S_{12}\cdot Me_2CO\cdot 20(H_2O)$: C 48.20, H 4.72, N 9.66; found C 48.31, H 4.80, N 9.50.

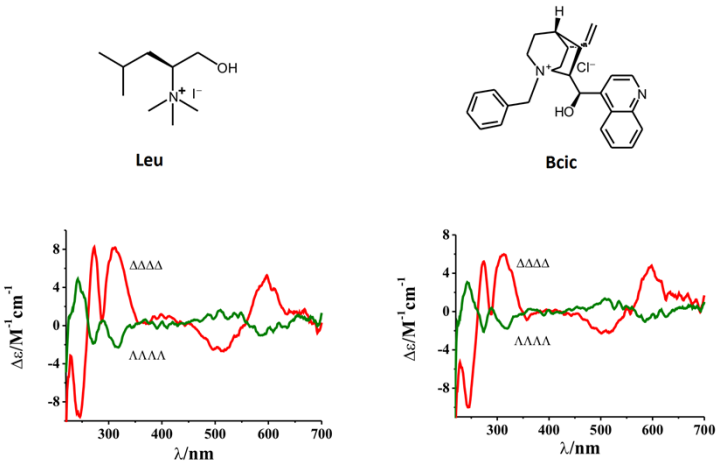
5. Resolution of cage $[Ni_4L_6]^{4-}$ with BINOL.

Rac-$(Me_4N)_4[Ni_4L_6]$ 108 mg and (*S*)-BINOL (or (*R*)-BINOL) 36 mg were added to a 25 mL flask containing 6 mL water/methanol (v/v = 1:1). The reaction was stirred for 1 h at 50℃. The less soluble diastereoisomer was collected by centrifugation and washed with water (3 × 2 mL) and then with acetone, after that dried in vacuum, and last dissolved in 4 mL water/methanol (v/v = 1:1). ΔΔΔΔ-$(Me_4N)_4[Ni_4L_6]$ was obtained by slow vapor diffusion of acetone into the water/methanol solution for several days. Yield: 30%. ΛΛΛΛ-$(Me_4N)_4[Ni_4L_6]$ was obtained from slow vapor diffusion of acetone into the filtrate. Yield: 40%. HR-ESI-MS: m/z: 1143.7192 ($[Ni_4L_6]^{4-} + Me_4N^+$), 839.0130 ($[Ni_2L_3]^{2-}$), 1128.0081 ($[Ni_3L_4]^{2-}$), 1418.0025 ($[Ni_4L_5]^{2-}$).

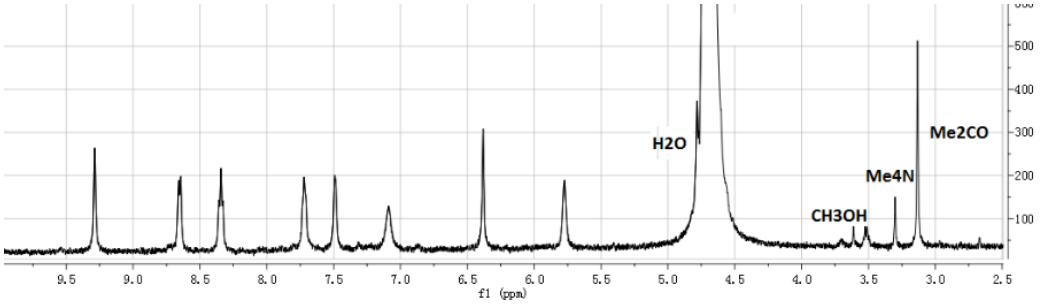
6. The chiral stability of resolved cages upon complexation of cyclohexane.

Aqueous solution of ΔΔΔΔ-**T** (2.5 mL, 1.4×10^{-5} M^{-1}) and excess cyclohexane (0.1 mL, 1.52 mmol) were added to a cuvette. The sealed cuvette was heated in a water bath to 323 K for 6 h, and reaction progress was monitored by CD spectra.

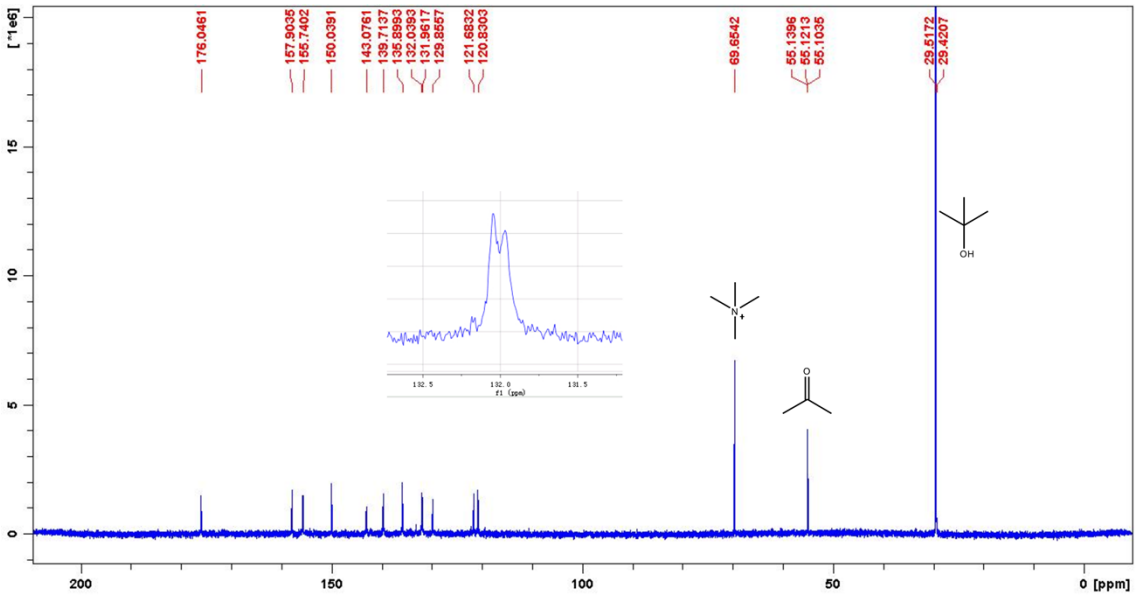
7. ***Figure S1.*** CD spectra of cage **T** resolved by Leu^+ and $Bcic^+$.



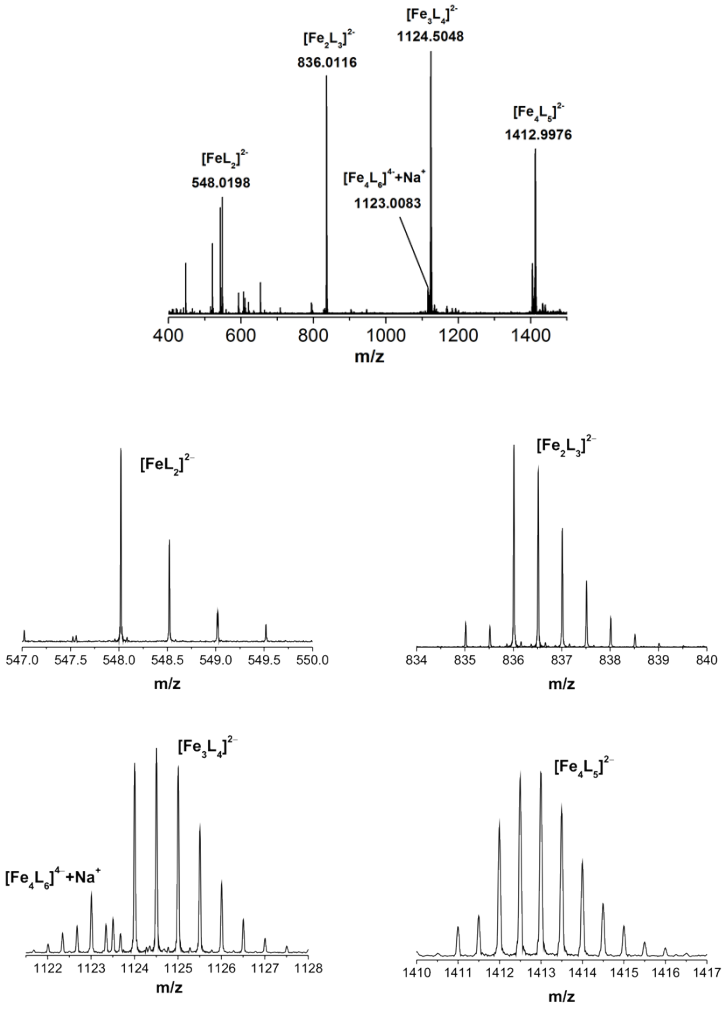
8. ***Figure S2.*** ^1H NMR spectrum of the resolved cage **T.**



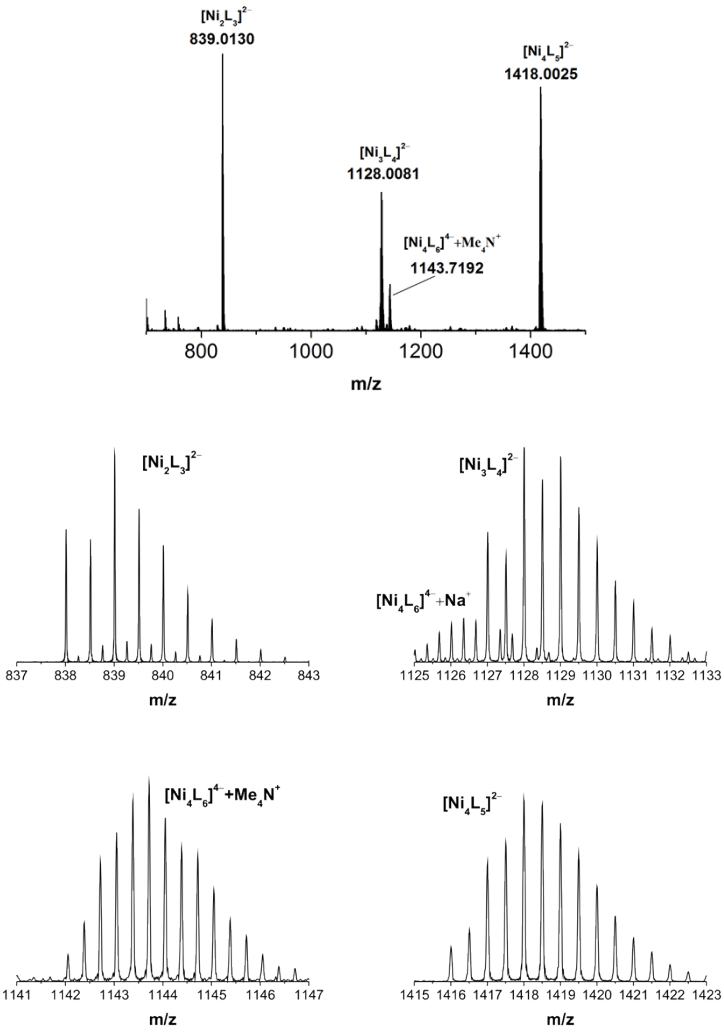
9. ***Figure S3.*** ^{13}C NMR spectrum of the resolved cage **T.**



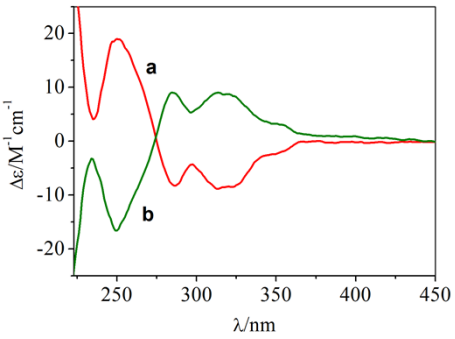
10. ***Figure S4*****.** HR-ESI-MS of the resolved cage **T.**



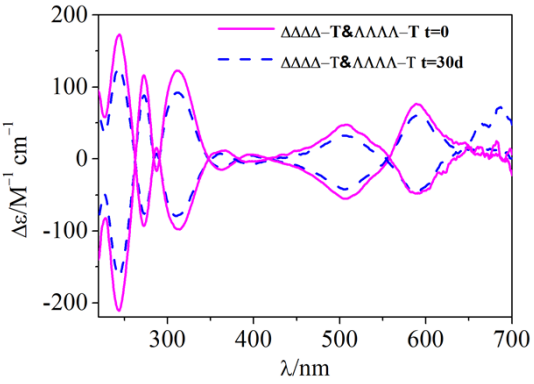
11. ***Figure S5.*** HR-ESI-MS of the resolved cage $(Me_4N)_4[Ni_4L_6]$.



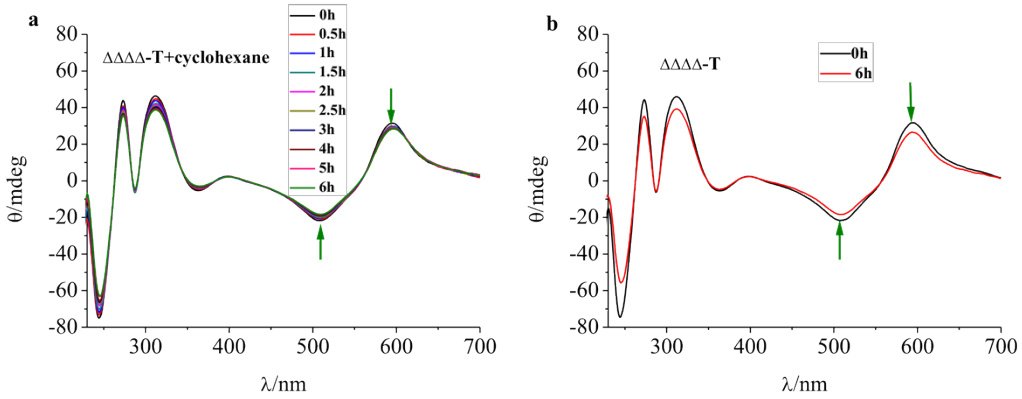
12. ***Figure S6.*** CD spectra of the resolved tetranuclear cluster $[Ni_4L_6]^{4-}$: ΔΔΔΔ (a) and ΛΛΛΛ (b) forms.



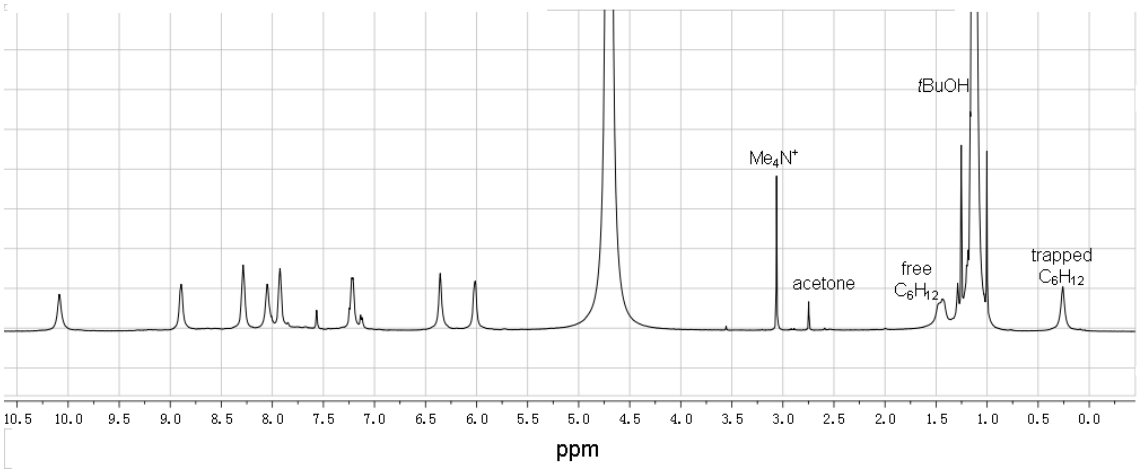
13. ***Figure S7.*** Dynamic CD spectra of ΔΔΔΔ-**T** and ΛΛΛΛ-**T** taken immediately after preparation of the 0.01 mM solution and after 30 days.



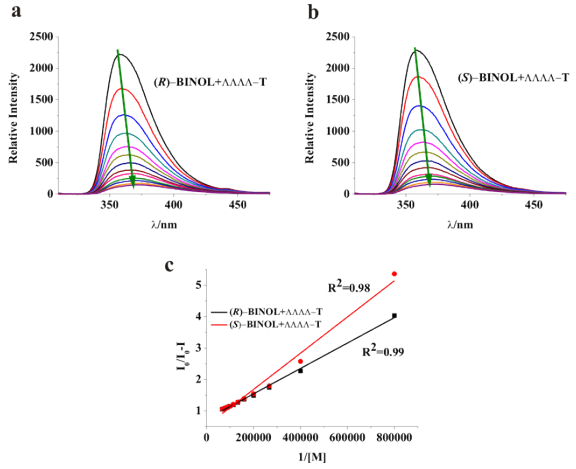
14. ***Figure S8***. CD spectra of ΔΔΔΔ-T varied with time at 323 K: a) in the presence of cyclohexane (C_6H_{12}); b) in the absence of C_6H_{12}.



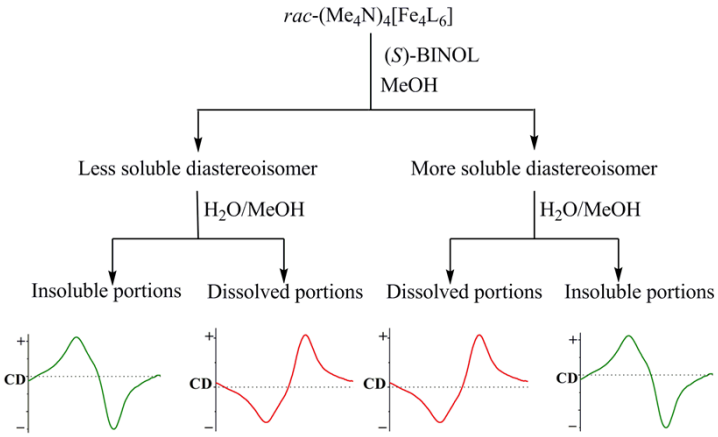
15. ***Figure S9***. The ^{1}H NMR spectrum of C_6H_{12}⊂ΔΔΔΔ-T.



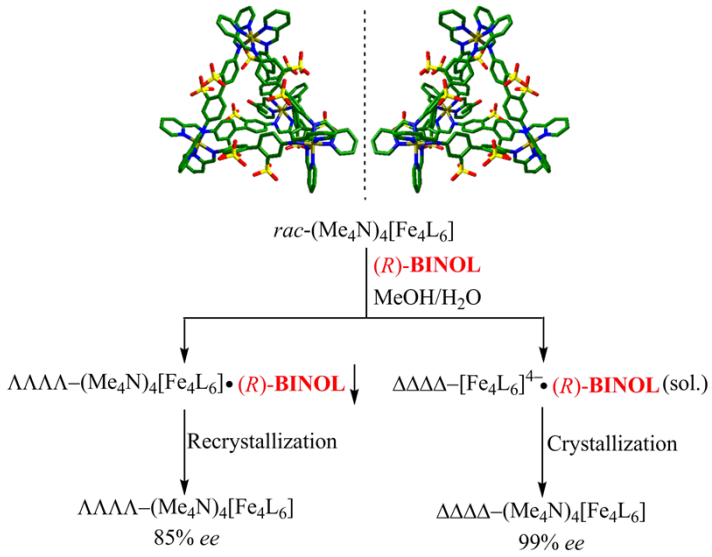
16. ***Figure S10***. Fluorescence responses of (a) (*R*)-BINOL (2×10^{-5} M) and (b) (*S*)-BINOL (2×10^{-5} M) upon addition of ΛΛΛΛ-**T** at 1.25×10^{-6} M intervals; (c) the Benesi-Hildebrand plots.



17. ***Scheme S1***. Optical resolution of **T** using (*S*)-BINOL in methanol.



18. ***Scheme S2***. Optical resolution of **T** using (*R*)-BINOL in 1:1 water-methanol solution followed by removal of (*R*)-BINOL during crystallization.



19. Reference

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[S4] K. A. McGee, K. R. Mann, *J. Am. Chem. Soc.* 2009, **131**, 1896-1902.