CHEMICAL COMMUNICATIONS

Sulfate-templated self-assembly of new M_4L_6 tetrahedral metal organic cages

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ELECTRONIC SUPPORTING INFORMATION

Experimental

Compound **1** (*N,N'*-bis(4-aminobenzyl)urea) was prepared according to a reported procedure.[1] To a stirred solution of 4-aminobenzylamine (20 g, 163.7 mmol) in 80 mL methanol was added *S,S'*-dimethyl dithiocarbonate (10 g, 81.8 mmol). The reaction mixture was heated at 60^{o}C for 24 h. When the reaction was complete, the reaction mixture was concentrated under reduced pressure, providing a crude solid which was further purified by recrystallization from methanol to give **1** as colorless crystals (13.2 g, yield: 60.0 %). ^{1}H NMR (500 MHz, DMSO-d$_6$) δ 6.89 (d, 4H), 6.49 (d, 4H), 6.04 (broad triplet, 2H), 4.91 (bs, 4H), 4.01 (d, 4H); ^{13}C NMR (125 MHz, DMSO-d$_6$) δ 158.2, 147.4, 128.2, 127.8, 113.9, 43.0.

Cage **3**: *N,N'*-bis(4-aminobenzyl)urea (48.7 mg, 0.18 mmol), 2-formylpyridine (38.6 mg, 0.36 mmol) and iron(II) sulfate heptahydrate (33.4 mg, 0.12 mmol) were added to 30 mL degassed methanol in a 100 mL flask. All starting materials dissolved, giving a purple solution. The reaction mixture was stirred for 18 h at 50^{o}C. The violet precipitate was collected as the product by discarding the supernatant solution and dried under vacuum (70.0 mg, yield: 70.7 %). ^{1}H NMR (500 MHz, D$_2$O, referenced to methanol) δ 8.97 (s, 12H), 8.55 (d, 12H), 8.35 (t, 12H), 7.68 (t, 12H), 7.40 (d, 12H), 7.20 (d, 24H), 5.18 (bs, 24H), 4.41 (d, 12H), 3.98 (d, 12H); ^{13}C NMR (125 MHz, D$_2$O, referenced to methanol) δ 180.7, 165.4, 164.9, 162.2, 156.0, 147.3, 146.1, 137.5, 136.0, 134.8, 128.4, 55.6. ESI-MS: found, m/z 501.6511 ($[Fe_4L_6 \cdot SO_4]^{6+}$), calculated, *m/z* 501.6499 ($[C_{162}H_{144}N_{36}SO_{10}Fe_4]^{6+}$); 552.1126 ($[Fe_2L_2 \cdot SO_4]^{2+}$); 610.9798 ($[Fe_4L_6 \cdot SO_4 \cdot HCOO]^{5+}$); 700.2707 ($[FeL_3]^{2+}$); 776.7158 ($[Fe_2L_3 \cdot SO_4]^{2+}$) (L= ligand **2**).

Cage **4**: *N,N'*-bis(4-aminobenzyl)urea (16.2 mg, 0.06 mmol), 2-formylpyridine (12.8 mg, 0.12 mmol) and nickel(II) sulfate hexahydrate (33.4 mg, 0.12 mmol) were added to 10 mL degassed methanol in a 50 mL flask. All starting materials dissolved, giving an orange solution. The reaction mixture was stirred for 18 h at 50^{o}C. The orange precipitate was collected as the product by discarding the supernatant solution and dried under vacuum (23.0 mg, yield: 69.5 %). ESI-MS: found, m/z 503.4879 ($[Ni_4L_6 \cdot SO_4]^{6+}$), calculated, *m/z* 503.4828 ($[C_{162}H_{144}N_{36}SO_{10}Ni_4]^{6+}$); 555.1089 ($[Ni_2L_2 \cdot SO_4]^{2+}$); 701.2654 ($[NiL_3]^{2+}$); 779.2106 ($[Ni_4L_6 \cdot (SO_{4)2}]^{4+}$) (L= ligand **2**).

Crystallographic Analyses

The data crystals of cage **3** and cage **4** were mounted onto the end of a thin glass fiber using Paratone-N. X-ray intensity data were measured with a Bruker SMART APEX2 CCD-based diffractometer using Mo Kα radiation (λ = 0.71073 Å).[2] The raw data frames were integrated with the SAINT+ program by using a narrow-frame integration algorithm.[2] Corrections for Lorentz and polarization effects were also applied with SAINT+. An empirical absorption correction based on the multiple measurement of equivalent reflections was applied using the program SADABS. The structure was solved by a combination of direct methods and difference Fourier syntheses, and refined by full-matrix least-squares on F^2, by using the SHELXTL software package.[3] All non-hydrogen atoms were refined with anisotropic displacement parameters unless otherwise stated. Hydrogen atoms were placed in geometrically idealized positions and included as standard riding atoms during the least-squares refinements. Crystal data, data collection parameters, and results of the analyses are listed in Table S1.

Purple single crystals of cage **3** suitable for x-ray diffraction analyses obtained by slow vapor diffusion of dioxane into the aqueous solution of cage **3** crystallized in the cubic crystal system. The systematic absences in the intensity data were consistent with the space groups $Im\bar{3}$, $I2_13$, and $I23$. The structure could only be solved in the chiral space group $I23$. With Z = 2, the Fe_4 cage complex has crystallographic *T* symmetry. The Flack parameter is 0.23(4); expected values are 0 (within 3 esd's) for correct and +1 for inverted absolute structures.[4] There is one SO_4^{2-} anion that is encapsulated in the Fe_4 cage and resides at the origin on the crystallographic *T* symmetry site. The remaining SO_4^{2-} counter anions are severely disordered and were modeled using a total of 9 geometric restraints (SHELX: DFIX, DANG instructions) and refined with isotropic thermal parameters. The oxygen atom O3 in this disordered group was refined with a fixed isotropic thermal parameter. At this stage the packing of the molecules of cage **3**, generates large cavities that are filled with disordered molecules from the solvent of crystallization. No reasonable disorder model could be obtained for these molecules despite many attempts. They were therefore accounted for by the SQUEEZE/PLATON program.[5] The program calculated a total solvent-accessible volume per unit cell of 2619.5 Å^3, or 24.2% of the total unit cell volume, corresponding to 878 e^-/cell. The contribution of these diffusely scattering species was removed from the structure factor calculations. The tabulated F(000), MW and density reflect the known unit cell contents only. It is not possible to estimate with any confidence (water, dioxane) what was removed by the SQUEEZE process.

Orange single crystals of cage **4** suitable for x-ray diffraction analyses obtained by slow vapor diffusion of dioxane into the aqueous solution of cage **4** crystallized in the trigonal crystal system. The systematic absences in the intensity data were consistent with either of the space groups $P\bar{3}$ or $P3$. The former space group was chosen and confirmed by the successful solution and refinement of the structure. With Z = 2, the Ni_4 cage complex has crystallographic 3 fold symmetry. There is one SO_4^{2-} anion that is encapsulated in the Ni_4 cage and resides also on a 3-fold symmetry site. The remaining SO_4^{2-} counter anions outside the cage are severely disordered and all attempts to locate, refine and model this group were unsuccessful. Also at this stage the packing of the molecules of cage **4**, generates large cavities that are filled with disordered molecules from the solvent of crystallization. No reasonable disorder model could be obtained for these molecules despite many attempts. They were therefore accounted for by the SQUEEZE/PLATON program.[5] The program calculated a total solvent-accessible volume per unit cell of 4213.6 Å^3, or 39.9.2% of the total unit cell volume, corresponding to 1237 e$^-$/cell. The contribution of these diffusely scattering species was removed from the structure factor calculations. The tabulated F(000), MW and density reflect the known unit cell contents only. It is not possible to estimate with any confidence (water, dioxane, sulfate) what was removed by the SQUEEZE process.

Although only the SO_4^{2-} counter ions that are encapsulated inside the cage in both structures could be located and refined satisfactorily from the difference map, the presence of three outer SO_4^{2-} counter anions per cage was confirmed by gravimetric experiments.

These data can be obtained free of charge from the Cambridge Crystallographic Data Centre (CCDC 891142 and 891143).

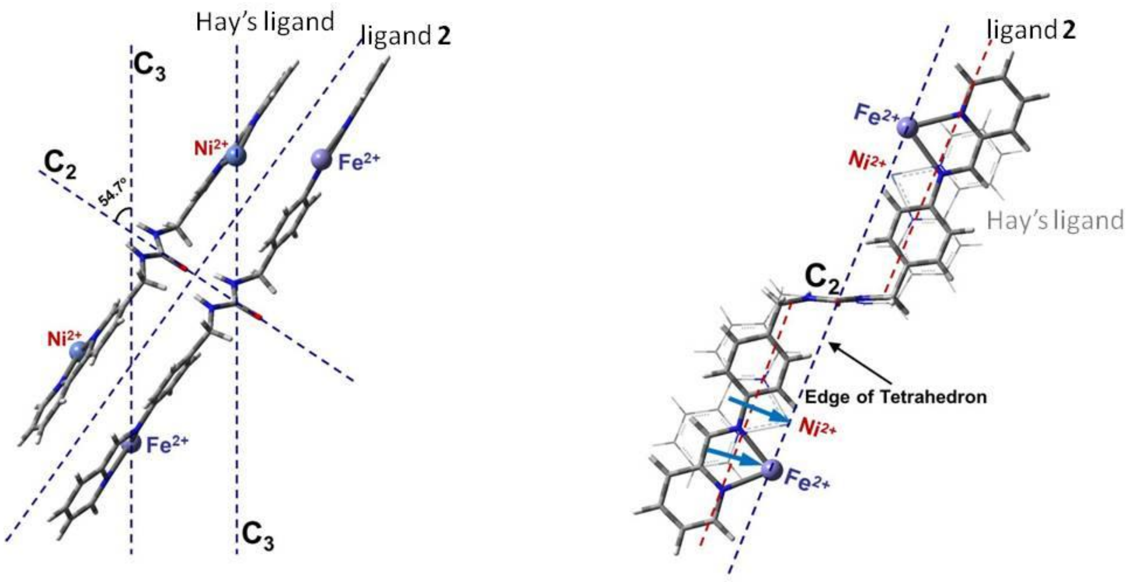


Figure S1. Comparison of Custelcean's ligand[6] and ligand **2**. Custelcean's ligand and its coordinated Ni^{2+} ions were picked up from the X-ray crystal structure of cage, while ligand **2** and its coordinated Fe^{2+} ions were created by molecular modeling. From this comparison, ligand **2** should also form a tetrahedral cage, which is supposed to have the same symmetry and functionalization as Custelcean's cage, but with relatively larger cavity volume.

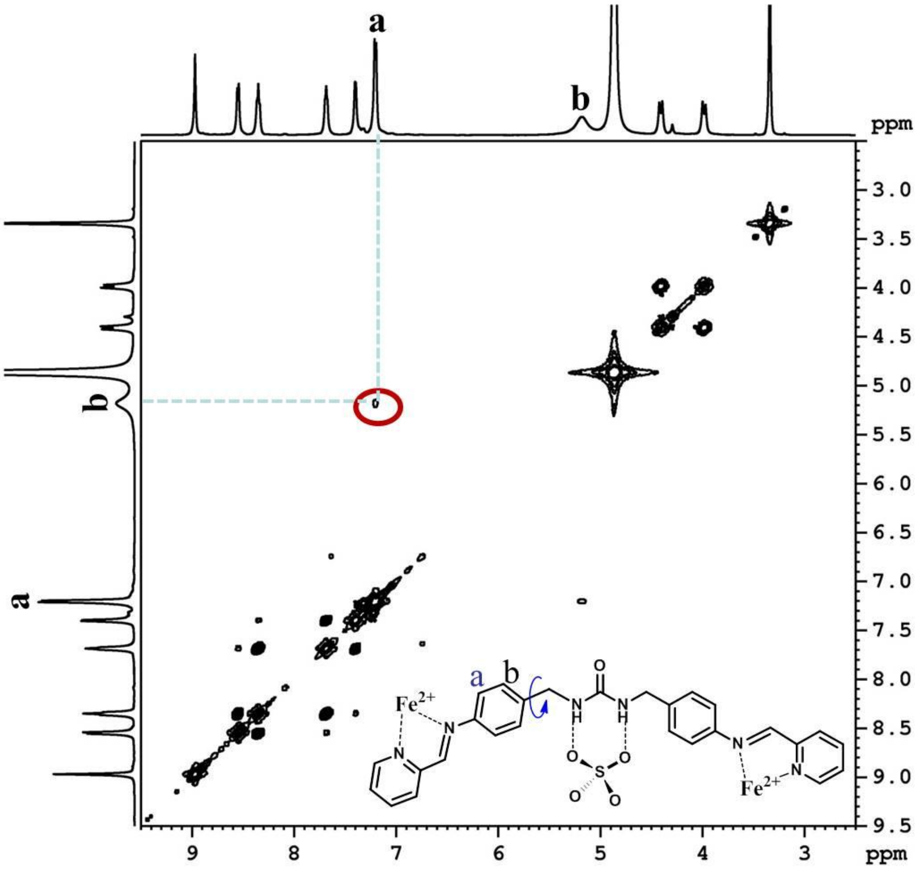


Figure S2. 2D COSY NMR (500 MHz) spectrum of cage **3** in D_2O.

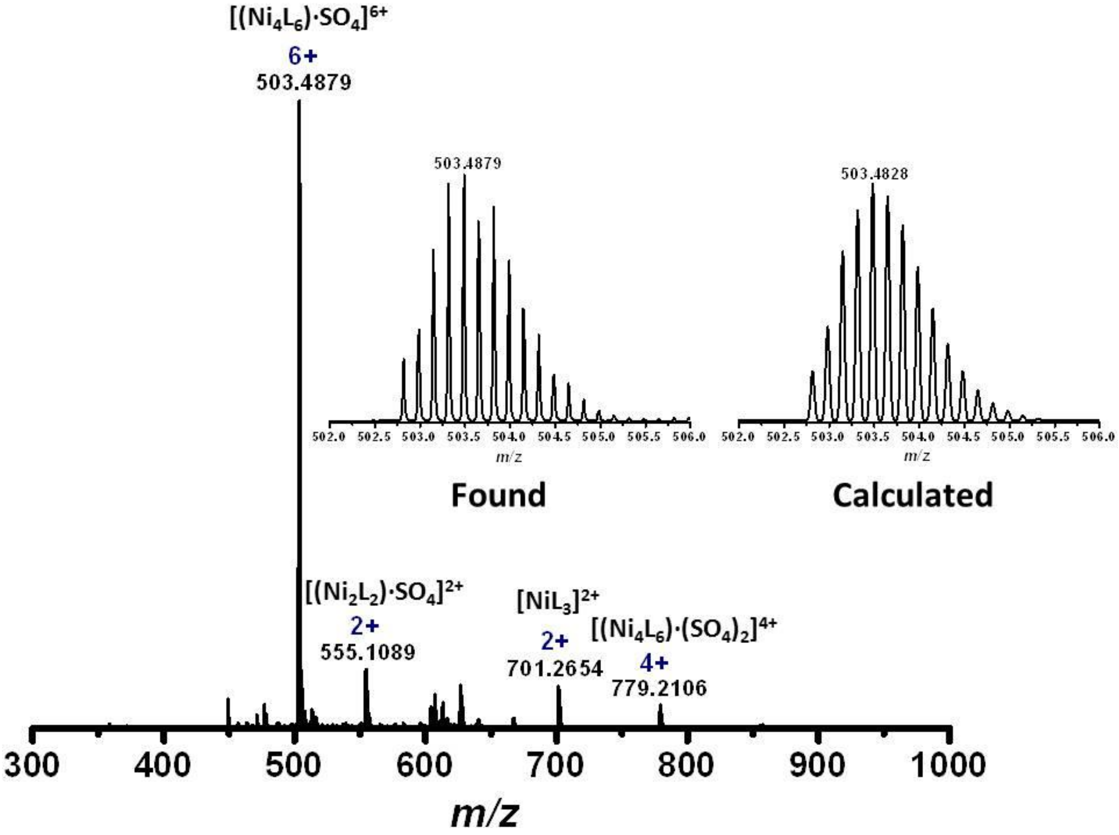


Figure S3. High resolution ESI-TOF mass spectrum of cage **4**. The insert shows the experimental and calculated isotopic distribution patterns for the most intense peak (L = ligand **2**).

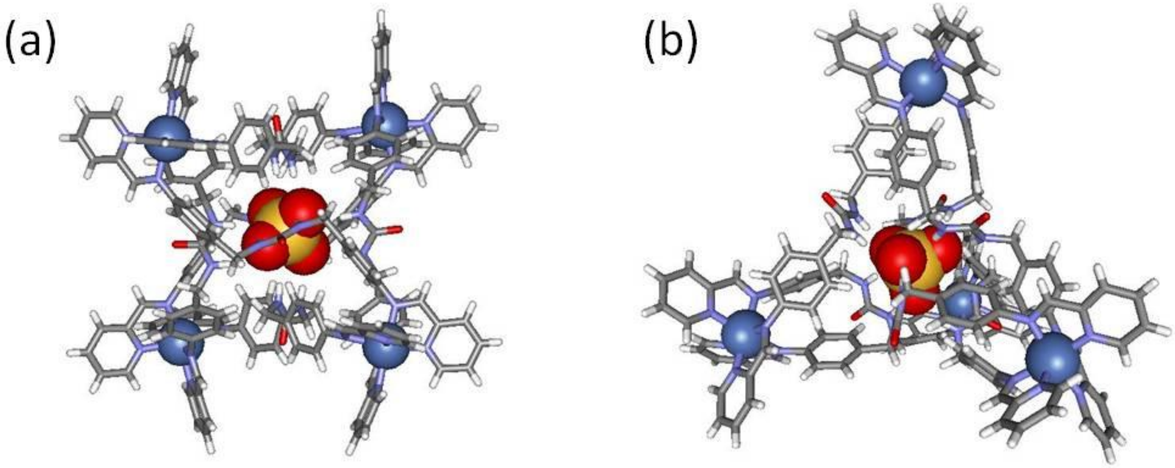


Figure S4. X-ray crystal structure of cage **4** from (a) top and (b) side views.

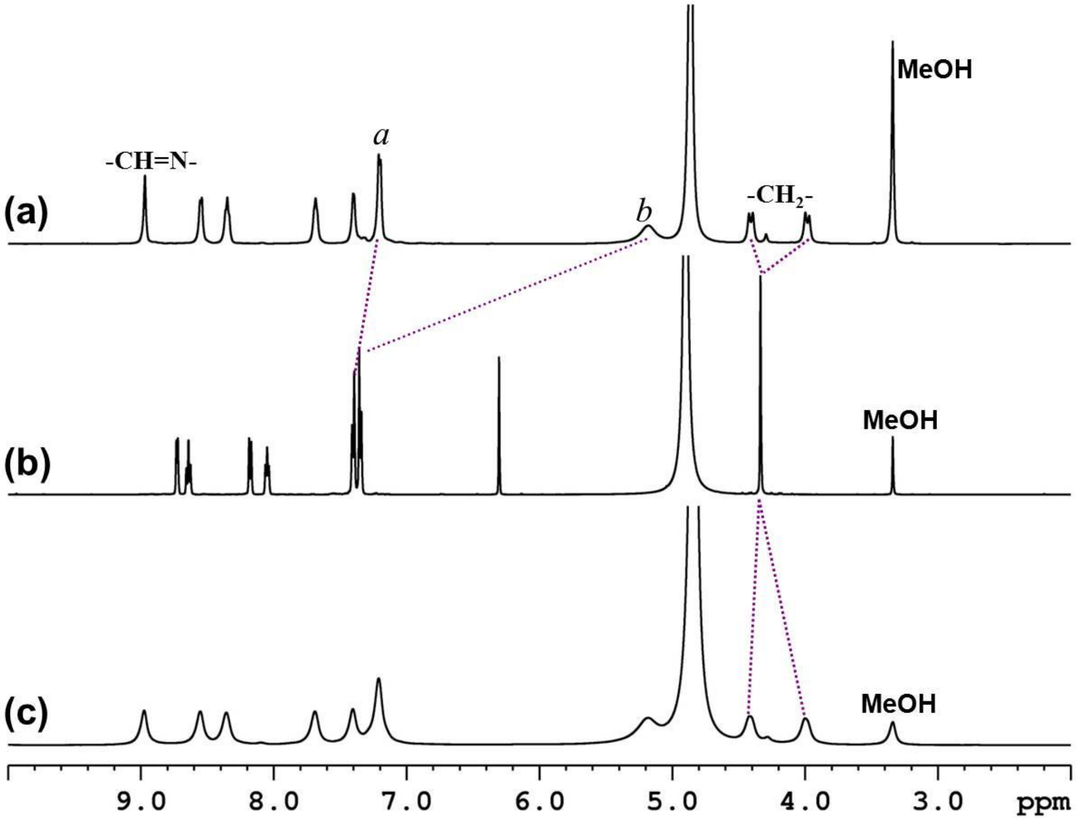
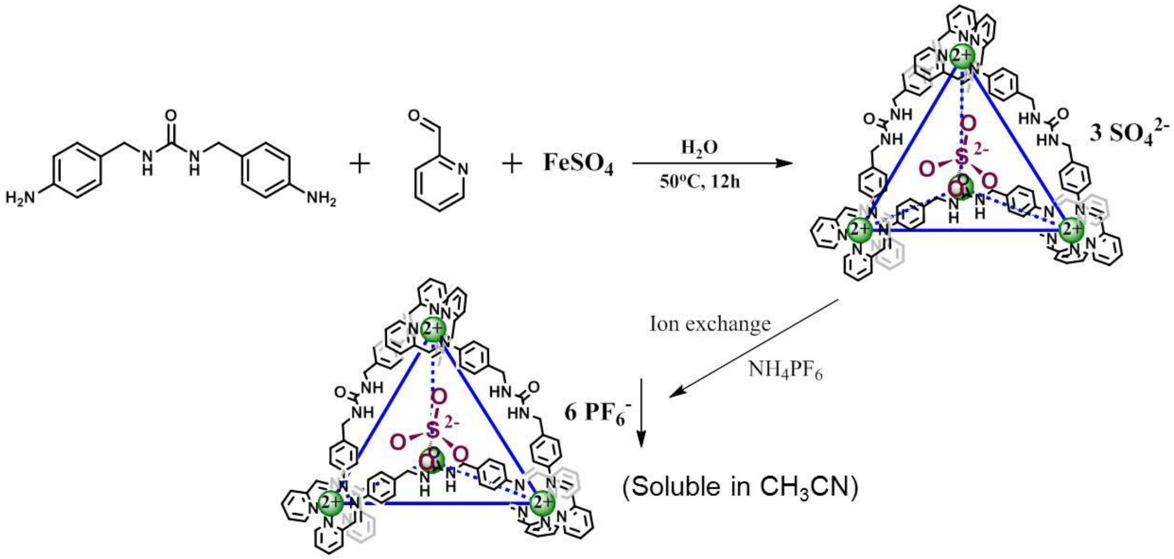


Figure S5. ^{1}H NMR (500 MHz) spectra (D_2O) of (a) cage **3**, (b) cage **3** after the addition of excess DCl (pD~3), (c) regeneration of cage **3** after addition of LiOD solution to (b) (pD~7).



Scheme S1. Precipitation of the sulfate-included cage **3** from aqueous solution through ion exchange.

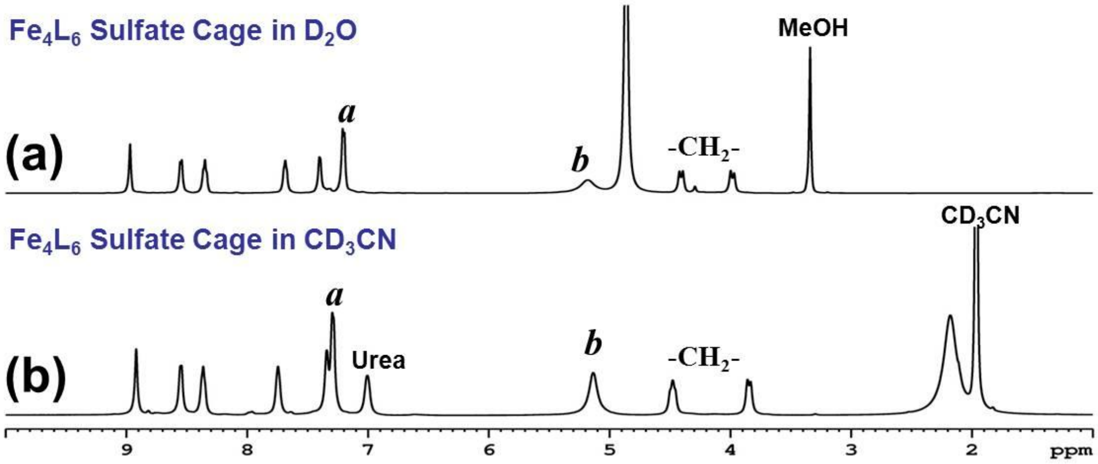


Figure S6. ^{1}H NMR (500 MHz) spectra of (a) cage **3** with SO_4^{2-} counterions in D_2O, (b) cage **3** with PF6$^-$ counterions in CD_3CN.

Table S1. Crystallographic Data for Cage 3 and Cage 4.

	Cage **3**	Cage **4**
Empirical formula	$Fe_4C_{162}H_{144}N_{36}O_{22}S_4$	$Ni_4C_{162}H_{144}N_{36}O_{10}S_1$
Formula weight	3298.77	3022.03
Crystal system	Cubic	Trigonal
Lattice parameters		
a (Å)	22.1233(8)	25.0734(12)
b (Å)	22.1233(8)	25.0734(12)
c (Å)	22.1233(8)	19.3734(9)
α (°)	90	90
β (°)	90	90
γ (°)	90	120
V (Å^3)	10828.0(7)	10547.8(9)
Space group	*I* 23 (# 197)	*P* $\bar{3}$ (# 147)
Z value	2	2
ρ_{calc} (g / cm^3)	1.012	0.952
μ (Mo Kα) (mm^{-1})	0.359	0.413
Temperature (K)	100	100
$2\Theta_{max}$ (°)	50.00	50.00
No. Obs. (I > 2σ(I))	2985	8761
No. Parameters	182	640
Goodness of fit	1.109	1.013
Max. shift in cycle	0.001	0.001
Residuals*:R1; wR2	0.0778; 0.2187	0.0593; 0.1634
Absorption Correction, Max/min	Multi-scan 0.7457/0.6689	Multi-scan 0.7457/0.6071
Absolute structure Flack parameter	0.23(4)	None
Largest peak in Final Diff. Map (e$^-$ / Å^3)	0.506	0.655

*$R = \Sigma_{hkl}(||F_{obs}| - |F_{calc}||)/\Sigma_{hkl}|F_{obs}|$; $R_w = [\Sigma_{hkl}w(|F_{obs}| - |F_{calc}|)^2/\Sigma_{hkl}wF_{obs}{}^2]^{1/2}$, $w = 1/\sigma^2(F_{obs})$; $GOF = [\Sigma_{hkl}w(|F_{obs}| - |F_{calc}|)^2/(n_{data} - n_{vari})]^{1/2}$.

References

[1] M. Leung, J. -L. Lai, K. -H. Lau, H. Yu, H. -J. Hsiao, *J. Org. Chem.* 1996, **61**, 4175.

[2] Apex2 Version 2.2-0 and SAINT+ Version 7.46A; Bruker Analytical X-ray System, Inc., Madison, Wisconsin, USA, 2007.

[3] (a) G. M. Sheldrick, SHELXTL Version 6.1; Bruker Analytical X-ray Systems, Inc., Madison, Wisconsin, USA, 2000. (b) G. M. Sheldrick, *Acta Cryst*. 2008**,** **A64**, 112–122.

[4] H. D. Flack and J. Bernardinelli, *J. Appl. Cryst*. 2000, **33**, 1143.

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[6] R. Custelcean, J. Bosano, P. V. Bonnesen, V. Kertesz, B. P. Hay, *Angew. Chem., Int. Ed.* 2009, **48**, 4025