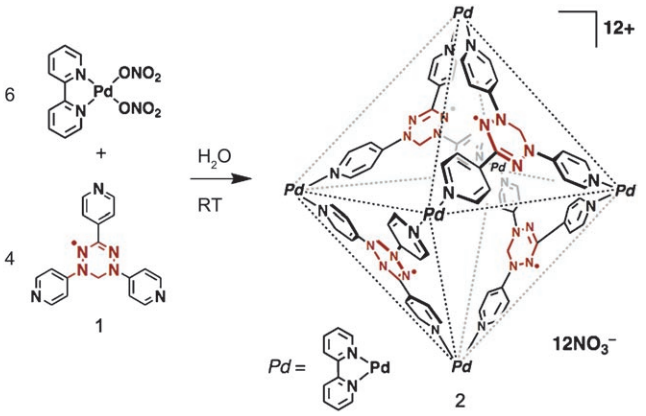
Molecular Recognition

DOI: 10.1002/anie.200704924

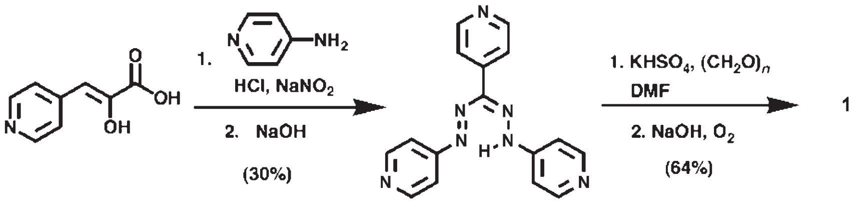
A Self-Assembled Spin Cage

*Koji Nakabayashi, Yusuke Ozaki, Masaki Kawano, and Makoto Fujita**

Cationic and anionic cage compounds can show unique molecular recognition capabilities as a consequence of their ionic nature.[1] In contrast, radical cages with unpaired electron spins in their frameworks are seldom prepared and their properties—with the exception of cagelike cluster compounds that have unpaired electrons at metal centers—particularly the interactions with radical guests, are largely unexplored.[2] This is mainly because of difficulties in introducing stable organic radicals at the core of the host frameworks. Here we report the facile self-assembly of a radical cage containing multiple spin centers around a cavity suitable for guest inclusion. We show that verdazyl radical-cored ligand **1** is quantitatively self-assembled into the large M$_6$L$_4$ spin cage **2** upon treatment with a Pd^{II} complex (Scheme 1). Similar to the analogous triazine-cored M$_6$L$_4$ complexes,[3] spin cage **2** is capable of binding neutral guests within the cavity in aqueous media. When radical guests are accommodated in the cavity of **2**, spin–spin interactions between the host and the guest are observed. We thus obtain a unique spin cage whose magnetic properties can be modulated by inclusion of a radical guest.



Scheme 1. Self-assembly of M$_6$L$_4$-type spin cage **2**.



Scheme 2. Synthesis of **1**.

Verdazyl radical ligand **1** was prepared by modified literature procedures (Scheme 2).[4] When a mixture of **1** (8 μmol) and [Pd(bpy)(NO$_3$)$_2$] (bpy = 2,2′-bipyridyl, 12 μmol) was stirred in water (2 mL) at room temperature for 2 h, the M$_6$L$_4$ complex **2** formed quantitatively, as indicated by CSI-MS and ESR studies.[5] After counterion exchange with PF$_6^-$ ions, CSI-MS measurements showed a series of prominent signals corresponding to [**2**-(PF$_6^-$)$_m$]$^{m+}$ (m = 4–7), from which the molecular weight of **2** (PF$_6$ salt) was determined to be 4580.2 Da (calculated as 4580.5 Da). After cage **2** had been decomplexed with base, the amount of radicals in the recovered ligand was measured to be 1.0, thus indicating that the radical does not degrade during the complexation and decomplexation.[6]

The structure of **2** was fully characterized by X-ray crystallographic analysis. Single crystals of **2** were obtained by the slow vapor diffusion of acetone into an aqueous solution of **2**.[7] The verdazyl panels are disordered and indistinguishable, as the C_{2v} symmetry of ligand **1** generates ten possible structural isomers. For clarity, only one of the isomers is shown in Figure 1. Although it involves severe disorder, the

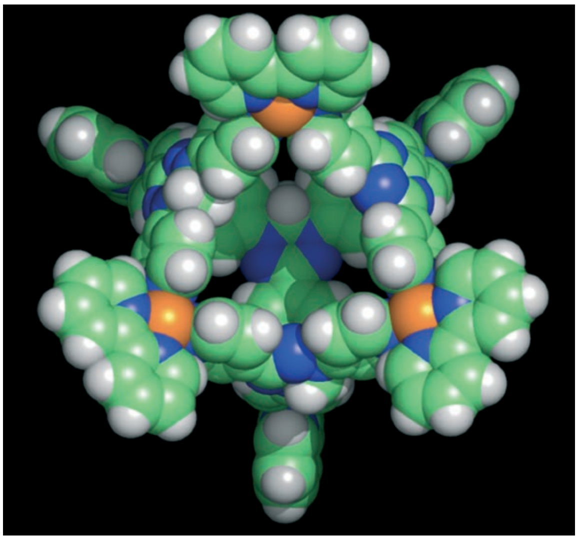


Figure 1. Crystal structure of spin cage **2**. Water molecules, nitrate ions, and hydrogen atoms are omitted for clarity.

---

[*] K. Nakabayashi, Y. Ozaki, Dr. M. Kawano, Prof. Dr. M. Fujita
Department of Applied Chemistry, School of Engineering
The University of Tokyo
and CREST
Japan Science and Technology Agency (JST)
7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656 (Japan)
Fax: (+81) 3-5841-7257
E-mail: mfujita@appchem.t.u-tokyo.ac.jp

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

crystal structure of **2** provides reliable evidence for the self-assembly of the M_6L_4 complex **2** with four spin centers.

The four spin centers of spin cage **2** show intramolecular magnetic interactions. Free ligand **1** shows nine sharp signals derived from four nitrogen nuclei (Figure 2a), which indicates that intermolecular exchange interactions are considerably weak compared to the hyperfine interaction ($a_N = 0.56$ mT).[2] In sharp contrast, the ESR spectrum of **2** shows only one broad signal (Figure 2b). The broadening of the signal is independent of concentration and temperature, and thus intermolecular interactions and motional broadening can be discounted.[8] The signal broadening is ascribed to the proximity of four spin centers on the ligands within the framework of **2**.[9] The observation of a $\Delta m_s = 2$ transition also supports the presence of intramolecular spin–spin interactions. The broad signal may contain not only a triplet transition but also other multiplet transitions from a quartet and a quintet derived from multiple interactions among the four radical ligands.

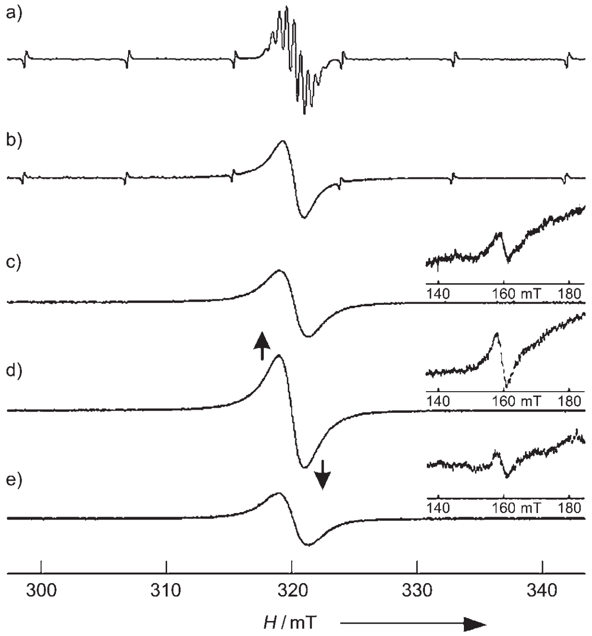
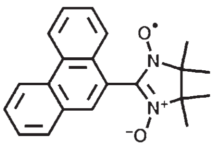


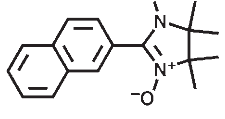
Figure 2. ESR spectra of a) ligand **1** (295 K, $CHCl_3$/MeOH = 4:1, 4 mM, $g = 2.003$), b) cage **2** (293 K, H_2O, 1 mM, $g = 2.003$); c) cage **2** (113 K, frozen H_2O, 1 mM, $g = 2.003$); d) complex **2·3** (113 K, frozen H_2O, 1 mM, $g = 2.004$); e) recovered **2** after extraction of **3** with $CHCl_3$ from **2·3** (113 K, frozen H_2O, 1 mM, $g = 2.003$). The intensity is normalized. The insets show the forbidden transition ($\Delta m_s = 2$) which was measured using 16 mW microwave power.

The magnetic character of the spin cage is affected by the enclathration of stable radicals in the large cavity of **2**. An excess of powdered nitrosyl radical **3** was suspended in an aqueous solution of **2** at 20 °C for 1 h to give, after filtration of surplus radical guest, the clathrate compound **2·3**.[10] The 1:1 host–guest stoichiometry was confirmed by elemental analysis and quantification of **3** after extraction with chloroform.[11] Complex **2·3** showed a considerably enhanced $\Delta m_s = 2$ transition, compared to empty cage **2**, and thus indicates the proximity of spin centers on the host and the guest in the cavity (Figure 2d). The original ESR spectrum of the cage was reproduced by removing the radical guest (Figure 2e). The magnetic susceptibility of **2** and **2·3** (measured by a superconducting quantum interference device (SQUID)) revealed that the spin–spin interactions in **2** are antiferromagnetic. After the encapsulation of **3**, the Weiss constant increased from −0.1 K to −0.4 K, which indicates the enhancement of spin–spin interactions by the presence of guest **3**.[12] Thus, the spin state of the cage can be controlled by inclusion of a radical guest. In this case, other multiplet transitions derived from the five spins of **2·3** could not be assigned, except for a triplet transition.



3

Similarly, the treatment of radical **4** with spin cage **2** resulted in the encapsulation of two guest molecules to give the complex **2·(4)**$_2$. Enhancement of the forbidden $\Delta m_s = 2$ transition compared with **2·3** was ascribed to both host–guest and guest–guest interactions.[10,11] We have previously reported the magnetic properties of a 1:2 complex of a triazine-cored M_6L_4 cage and **4**, where the ESR spectrum showed split doublet signals and a clear forbidden transition signal because of the proximity of the spin centers of radicals **4**.[13] Taking this fact into consideration, radicals **4** could be closely packed within spin cage **2** in a similar way. However, the **2·(4)**$_2$ complex showed one broad signal and a relatively weak forbidden transition signal (Figure 3) compared with the 1:2 complex of a triazine-cored M_6L_4 cage and **4**. It is very likely that this result may suggest multiple host–guest–guest–host interac-



4

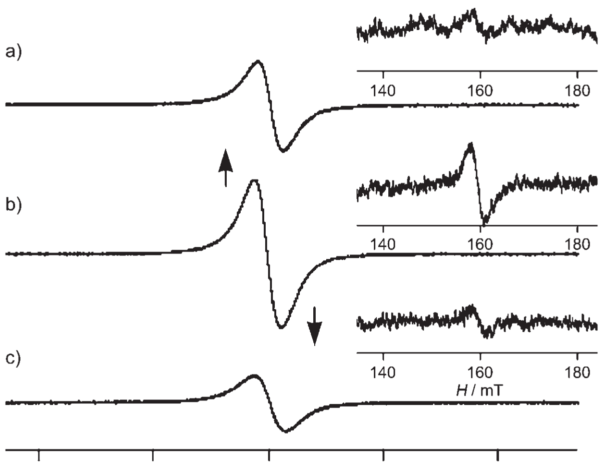


Figure 3. ESR spectra of a) cage **2** (113 K, frozen H_2O, 1 mM, $g = 2.003$); b) complex **2·(4)**$_2$ (113 K, frozen H_2O, 1 mM, $g = 2.004$); c) recovered **2** after extraction of **4** with $CHCl_3$ from complex **2·(4)**$_2$ (113 K, frozen H_2O, 1 mM, $g = 2.003$). The intensity is normalized. The insets show the forbidden transition ($\Delta m_s = 2$), which was measured using 1 mW microwave power.

tions, since six spins derived from one spin cage **2** and two guests **4** are accumulated in a restricted space. Various neutral molecules were also enclathrated by the spin cage,[14] but no significant change in the magnetic behavior of **2** was observed.

In summary, we have constructed a self-assembled radical cage with four spin centers. The inclusion of radical guests induced new spin–spin host–guest interactions. The water solubility of the spin cage will allow studies on organic radicals in aqueous media to enable the development of guest-tunable spin materials, such as new spin probe reagents and MRI contrast agents, that work in water.

Experimental Section

Spin cage **2**: *cis*-(2,2′-Bipyridine)dinitratopalladium(II) (4.61 mg, 12 μmol) and 1,3,5-tri(4-pyridyl)verdazyl (2.54 mg, 8 μmol) were mixed in distilled water (2 mL), stirred for 1 h at RT, and dried in vacuo to give **2** quantitatively. CSI-MS: m/z 509.53 $[M{-}7\,PF_6^-]^{7+}$, 618.29 $[M{-}6\,PF_6^-]^{6+}$, 771.10 $[M{-}5\,PF_6^-]^{5+}$, 1000.09 $[M{-}4\,PF_6^-]^{4+}$. Elemental analysis calcd for $C_{128}H_{104}N_{52}O_{36}Pd_6\cdot 18\,H_2O$: C 39.33, H 3.61, N 18.63; found: C 39.46, H 3.75, N 18.38. Crystal data for **2**: The very samll crystal size (80 × 20 × 20 μm) and poor crystallinity resulted in synchrotron radiation at the Photon Factory-Advanced Ring for Pulse X-rays (PF-AR) of the High Energy Accelerator Research Organization (KEK) being used. The diffraction data were measured at 80 K ($\lambda = 0.68890$ Å). $C_{129}H_{102}N_{47.66}O_{70.85}Pd_6$, $M_r = 4091.71$, trigonal, space group $P\bar{3}c1$, $a = b = 27.554(1)$, $c = 33.881(3)$ Å, $V = 22278(2)$ Å^3, $Z = 4$, $T = 80(2)$ K, $\rho_{calcd} = 1.220\ g\,cm^{-3}$; 146123 reflections were measured, of which 7514 were unique ($R_{int} = 0.1185$) and were used in all calculations. The structure was solved by direct methods (SHELXL-97) and refined by full-matrix least-squares methods on F^2 with 721 parameters. $R_1 = 0.1334$ for 3201 observed data ($I > 2\sigma(I)$) and $wR_2 = 0.3376$, GOF = 1.230, max./min. residual density 0.889/−0.974 e Å^{-3}. The trigonal crystal system results in one of the four ligands in **2** sitting on a threefold axis. Thus, the verdazyl core of this ligand was unable to be properly modeled. The refinement was done by modeling a C_3-symmetric triazine ring instead of the verdazyl ring; see the Supporting Information. CCDC 664973 (**2**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

Received: October 24, 2007

Keywords: host–guest systems · molecular recognition · palladium · radicals · self-assembly

---

[1] Self-assembled ionic hosts: a) M. Fujita, D. Oguro, M. Miyazawa, H. Oka, K. Yamaguchi, K. Ogura, *Nature* **1995**, *378*, 469–472; b) D. L. Caulder, K. N. Raymond, *Acc. Chem. Res.* **1999**, *32*, 975–982; c) S. Leininger, B. Olenyuk, P. J. Stang, *Chem. Rev.* **2000**, *100*, 853–908; d) M. Fujita, K. Umemoto, M. Yoshizawa, N. Fujita, T. Kusukawa, K. Biradha, *Chem. Commun.* **2001**, 509–518; e) F. A. Cotton, C. Lin, C. A. Murillo, *Acc. Chem. Res.* **2001**, *34*, 759–771; f) F. Hof, S. L. Craig, C. Nuckolls, J. Rebek, Jr., *Angew. Chem.* **2002**, *114*, 1556–1578; *Angew. Chem. Int. Ed.* **2002**, *41*, 1488–1508; g) M. Fujita, M. Tominaga, A. Hori, B. Therrien, *Acc. Chem. Res.* **2005**, *38*, 369–378; h) M. D. Pluth, R. G. Bergman, K. N. Raymond, *J. Am. Chem. Soc.* **2007**, *129*, 11459–11467.

[2] Cagelike compounds with spins at metal centers: Reviews: a) E. J. L. McInnes, S. Piligkos, G. A. Timco, R. E. P. Winpenny, *Coord. Chem. Rev.* **2005**, *249*, 2577–2590; b) G. Christou, *Polyhedron* **2005**, *24*, 2065–2075; radical cages: c) T. Okubo, S. Kitagawa, M. Kondo, H. Matsuzaka, T. Ishii, *Angew. Chem.* **1999**, *111*, 980–983; *Angew. Chem. Int. Ed.* **1999**, *38*, 931–933; d) L. Kröck, A. Shivanyuk, D. B. Goodin, J. Rebek, Jr., *Chem. Commun.* **2004**, 272–273; e) A. Rajca, S. Mukherjee, M. Pink, S. Rajca, *J. Am. Chem. Soc.* **2006**, *128*, 13497–13507; f) K. Igarashi, T. Nogamia, T. Ishida, *Chem. Commun.* **2007**, 501–503.

[3] a) T. Kusukawa, M. Fujita, *J. Am. Chem. Soc.* **2002**, *124*, 13576–13582; b) M. Yoshizawa, M. Tamura, M. Fujita, *J. Am. Chem. Soc.* **2004**, *126*, 6846–6847.

[4] a) R. Kuhn, F. A. Neugebauer, H. Trischmann, *Monatsh. Chem.* **1966**, *97*, 525–553; b) Y. A. Ibrahim, A. H. M. Elwahy, A. A. Abbas, *Tetrahedron* **1994**, *50*, 11489–11498; detailed conditions are described in the Supporting Information.

[5] The CSI-MS spectrum of **2** (PF_6 salt) and the ESR spectra of **2** recorded at several microwave powers are shown in Figures S1 and S2, respectively, of the Supporting Information.

[6] The titration experiment of radical ligand **1** into $[Pd(bpy)(NO_3)_2]$ is shown in Figure S3 of the Supporting Information.

[7] The quality of the crystals was improved by adding 1-adamantanol as a template.

[8] The ESR spectra of **2** recorded at different concentrations and temperatures are shown in Figures S4 and S5 of the Supporting Information.

[9] J. A. Weil, J. R. Bolton, *Electron Paramagnetic Resonance. Elementary Theory and Practical Applications*, 2nd ed., Wiley-Interscience, **2007**, pp. 322–324.

[10] The nitrosyl radicals **3** and **4** that were used as guests were prepared by the improved Ullman's procedure described in the following reference: C. Hirel, K. E. Vostrikova, J. Pecaut, V. I. Ovcharenko, P. Rey, *Chem. Eur. J.* **2001**, *7*, 2007–2014.

[11] **2**·**3**: Elemental analysis calcd for $C_{128}H_{104}N_{52}O_{36}Pd_6\cdot C_{21}H_{21}N_2O_2\cdot 21\,H_2O$: C 41.65, H 3.92, N 17.60; found: C 41.75, H 4.04, N 17.38. **2**·(**4**)$_2$: Elemental analysis calcd for $C_{128}H_{104}N_{52}O_{36}Pd_6\cdot 2\,C_{17}H_{19}N_2O_2\cdot 22\,H_2O$: C 42.78, H 4.12, N 17.25; found: C 42.82, H 4.10, N 17.11. The extraction experiments are described in Section 7 of the Supporting Information.

[12] The χT versus T plots of **2** and **2**·**3** are shown in Figure S6 of the Supporting Information.

[13] a) K. Nakabayashi, M. Kawano, M. Yoshizawa, S. Ohkoshi, M. Fujita, *J. Am. Chem. Soc.* **2004**, *126*, 16694–16695; b) K. Nakabayashi, M. Kawano, T. Kato, K. Furukawa, S. Ohkoshi, T. Hozumi, M. Fujita, *Chem. Asian J.* **2007**, *2*, 164–170.

[14] The enclathration of neutral molecules is described in the Supporting Information.