

Tetrahedral Anion Cage: Self-Assembly of a $(\text{PO}_4)_4\text{L}_4$ Complex from a Tris(bisurea) Ligand**

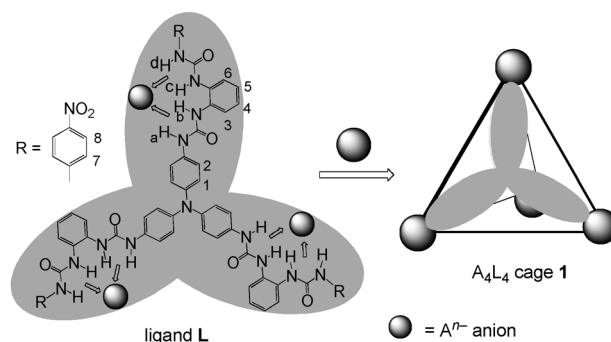
Biao Wu,* Fengjuan Cui, Yibo Lei, Shaoguang Li, Nader de Sousa Amadeu, Christoph Janiak, Yue-Jian Lin, Lin-Hong Weng, Yao-Yu Wang, and Xiao-Juan Yang

Anion coordination chemistry has developed rapidly in recent years because of the important roles anions play in many biological, environmental, and chemical processes.^[1,2] Studies have shown that the coordination behavior of the anions, although less-well defined, is quite similar to the coordination of transition metals; for example, anions also display “coordination geometry” and “coordination number”.^[2] These analogies provide promising ideas for the self-assembly of novel supramolecular systems based on anion coordination.

In the past few decades, zero-dimensional, aesthetically pleasing metal coordination complexes, such as molecular squares, capsules, tetrahedra, and other complex polyhedral shapes, have attracted much interest.^[3,4] Tetrahedral cages that contain an isolated space have been intensely studied as mimics of the microenvironments of bioprocesses, in stabilizing reactive intermediates, and as catalysts for chemical transformations.^[5] There are two typical approaches for constructing tetrahedral metal cages: By using C_2 -symmetric bis-chelating ligands and octahedral metal ions, M_4L_6 -type species (with four metal ions at the vertices and six ligands along the edges) can be obtained.^[6] The other type of tetrahedral cages, the M_4L_4 compounds, is less common and can be assembled from C_3 -symmetric tris-chelating ligands which are positioned on the faces of the tetrahedron.^[7] In addition, there are also covalent organic cages comprised of a single molecule.^[8]

In contrast to the rich chemistry of metal-based systems, supramolecular architectures driven by anion coordination are underdeveloped, although anions can play crucial roles in templating exciting structures (e.g. the starlike helicates).^[9] In recent years, anion-centered structures, such as catenanes, rotaxanes, foldamers, and helices, have emerged;^[10] however, the well-defined cage complexes have not yet been explored. Compared to the transition-metal complexes, the assembly/disassembly process of anion-based supramolecular systems may be controlled under mild conditions (e.g. by acid/base modulation or by solvent polarity), which may be more promising for biological processes.

As part of our studies on anion coordination we recently developed a series of *ortho*-phenylene-bridged oligourea ligands, which display excellent affinity and complementarity to the tetrahedral sulfate and phosphate anions.^[11] More importantly, the fully deprotonated phosphate ion (PO_4^{3-}) shows a strong tendency for “coordination saturation” (12 hydrogen bonds), a characteristic of tetrahedral anions that is proven both theoretically and experimentally.^[11,12] This property can ensure the formation of desired structures by hydrogen bonding six urea groups to its six edges. Hence, we designed the tris(bisurea) ligand **L** (Scheme 1) by attach-



Scheme 1. Assembly of the A_4L_4 tetrahedral anion cage from phosphate anions and ligand **L**.

ing three bisurea moieties to a central C_3 -symmetric triphenylamine platform. Here we report the assembly of the first tetrahedral anion cage ($[A_4L_4]$ -type ($A = \text{anion}$); **1**) and a unique pinwheel helical $[A_3L_2]$ complex (**2**) from ligand **L** and PO_4^{3-} and SO_4^{2-} ions, respectively.

Ligand **L** was synthesized by the reaction of *p*-nitrophenylisocyanate with N,N',N'' -(nitrilotri-4,1-phenylene)-tris(2-aminophenylurea). Treatment of **L** with an equimolar quantity of $(\text{TMA})_3\text{PO}_4$ (generated in situ from $(\text{TMA})\text{OH}$

[*] Prof. B. Wu, Dr. Y. Lei, Prof. Y.-Y. Wang
Key Laboratory of Synthetic and Natural Functional Molecule
Chemistry of the Ministry of Education
College of Chemistry and Materials Science, Northwest University
Xi'an 710069 (China)
E-mail: wubiao@nwu.edu.cn

Dr. F. Cui, Dr. S. Li, Prof. X.-J. Yang
State Key Laboratory for Oxo Synthesis & Selective Oxidation,
Lanzhou Institute of Chemical Physics, CAS
Lanzhou 730000 (China)

Dr. N. S. Amadeu, Prof. Dr. C. Janiak
Institut für Anorganische Chemie und Strukturchemie
Universität Düsseldorf
Universitätsstrasse 1, 40225 Düsseldorf (Germany)

Prof. Y.-J. Lin, Prof. L.-H. Weng
Shanghai Key Laboratory of Molecular Catalysis and Innovative
Material, Department of Chemistry
Fudan University, Shanghai, 200433 (China)

[**] This work was supported by the National Natural Science
Foundation of China (Grant No. 21271149).

Supporting information for this article is available on the WWW
under <http://dx.doi.org/10.1002/anie.201209930>.

and H_3PO_4 ; TMA = tetramethylammonium ion) afforded a yellow crystalline product in almost quantitative yield. The compound is readily soluble in common solvents such as acetone, acetonitrile, DMF, and DMSO. NMR spectroscopy, ESIMS, and elemental analysis proved that this species $(\text{TMA})_{12}[(\text{PO}_4)_4\text{L}_4]$ (**1**) was the unique product, with no evidence for the occurrence of other stoichiometries (see below for solution studies).

Complex **1** crystallizes from diethyl ether/acetonitrile in the centrosymmetric cubic space group $P\bar{4}3n$.^[13] The structure has the ideal T symmetry with one twelfth of the tetrahedral molecular cage (one third of a phosphate ion, one third of the ligand, one TMA as the counter cation) appearing in the asymmetric unit. The four C_3 -symmetric ligands position on the four triangular faces of the tetrahedron, and each vertex is defined by a phosphate ion which is coordinated by three bisurea arms (Figure 1). The four axial-chiral PO_4^{3-} centers

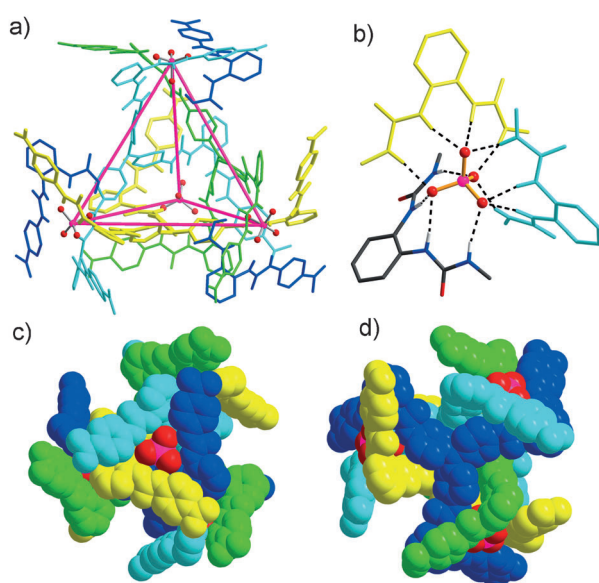


Figure 1. a) The tetrahedral cage $[(\text{PO}_4)_4\text{L}_4]^{12-}$ in the crystal structure of **1**, with the dark-blue facial ligand truncated so that the interior and opposite PO_4 corner can be seen; b) hydrogen bonds around the PO_4^{3-} ion; c,d) space-filling representation of the tetrahedron with a view onto a corner (c) or a face (d). Only a P enantiomer is shown, and non-acidic hydrogen atoms are omitted for clarity.

have the same configuration ($\Delta\Delta\Delta\Delta$ or $\Lambda\Lambda\Lambda\Lambda$) in the tetrahedron. However, as in most M_4L_4 tetrahedra with achiral ligands,^[7] both P - and M -handed $[\text{A}_4\text{L}_4]$ enantiomers are present in the crystal lattice of complex **1**.

The tetrahedral cage **1** represents the first example of a new class of anion-coordination supramolecular hosts. Each phosphate ion is bound to six urea groups from three different ligands through 12 strong $\text{N}\cdots\text{H}\cdots\text{O}$ hydrogen bonds ($\text{N}\cdots\text{O}$ distances range from 2.811(5) to 2.827(5) Å, average 2.817 Å; $\text{N}\cdots\text{H}\cdots\text{O}$ angles range from 157 to 168°, average 163°; see Figure 1 and Table S2 in the Supporting Information). Altogether there are 48 $\text{N}\cdots\text{H}\cdots\text{O}$ hydrogen bonds. In addition, there is also a $\text{C}\cdots\text{H}\cdots\text{O}$ hydrogen bond ($\text{C}\cdots\text{H}$: 3.340(5) Å; $\angle\text{CHO}$: 133°) from one o -CH proton of each

nitrophenyl group to the anion. The combination of all these weak interactions results in a rather stable complex $[(\text{PO}_4)_4\text{L}_4]^{12-}$, which shows a large dissociation energy of approximately $-1709 \text{ kcal mol}^{-1}$, as revealed by DFT studies.^[14]

In the tetrahedral cage, the $\text{PO}_4\cdots\text{PO}_4$ separation is about 15 Å, and the internal volume was estimated with the VOIDOO program to be about 181 \AA^3 .^[15] The volume of the counteranion TMA was calculated to be approximately 121 \AA^3 by DFT using the B3LYP/6-31G* method. An optimum encapsulation of about 55% was observed in many host-guest systems (for neutral guests),^[16] and it would be expected that the tetrahedral cage is too small to include the TMA ion. Indeed, there is no guest inside the cage, and in the crystal structure the TMA cations and solvent molecules are found outside the cage.

Treatment of **L** with $[\{\text{K}(\text{[18]crown-6})\}_2]\text{SO}_4$ afforded the sulfate complex $[\{\text{K}(\text{[18]crown-6})\}_6][(\text{SO}_4)_3\text{L}_2]\cdot 3 \text{ CH}_3\text{COCH}_3$ (**2**). Complex **2** ($C2/c$) shows a pinwheel-like helical structure, in which the bisurea arms cross over the $\text{SO}_4^{2-}\text{--SO}_4^{2-}$ axes (Figure 2 a).^[17] The ligand adopts a conformation such that the

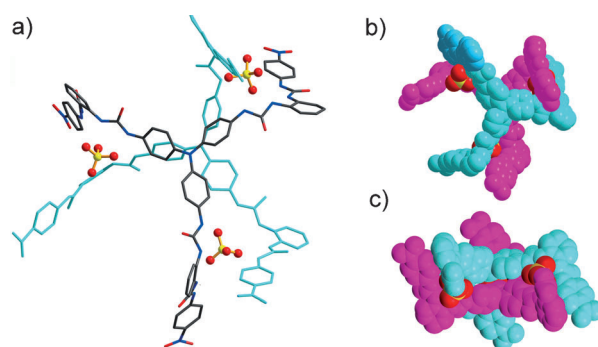


Figure 2. a) The “pinwheel” helical sulfate complex $[(\text{SO}_4)_3\text{L}_2]^{6-}$ in the crystal structure of **2**; b,c) top and side view of the space-filling representation. Only an M enantiomer is shown.

three terminal urea arms deviate from the triangular plane and point to the same side of the plane. Two ligands stack in a face-to-face fashion, with three SO_4^{2-} ions between. Notably, the structure is not C_3 -symmetric in the solid state. The $\text{S}\cdots\text{S}$ separations are 12.7 and 14.0 Å, and the central $\text{N}\cdots\text{N}$ separation between two ligands is 5.50 Å. Each sulfate ion is bound by four urea groups through eight $\text{N}\cdots\text{H}\cdots\text{O}$ hydrogen bonds (see Figure S8 and Table S3 in the Supporting Information). Moreover, $\text{C}\cdots\text{H}\cdots\text{O}$ hydrogen bonds also occur with the anions (see Figure S8 in the Supporting Information), and T-shaped $\text{CH}\cdots\pi$ interactions are formed between the terminal nitrophenyl rings and the o -phenylene planes, with $\text{CH}\cdots\text{plane}$ distances of 3.67–3.98 Å (see Figure S7b in the Supporting Information).

Notably, although the tetrahedral sulfate and phosphate ions can both potentially accept a maximum of 12 hydrogen bonds,^[12] we found that they lead to significantly different solid-state structures. The trianionic phosphate ion tends to accept 12 hydrogen bonds and, thus, can coordinate with three bisurea fragments, while the dianionic sulfate ion does not

reach saturated coordination. This difference was also observed in the assembly of the triple anion helicate in the presence of a phosphate ion, whereas the sulfate ion only leads to a single-stranded 1:2 complex.^[11d] The reason might be the higher negative charge density and stronger basicity of the phosphate ion which requires more hydrogen bonds for efficient binding.

The assembly of **L** and PO_4^{3-} in solution was investigated. The ^1H NMR spectrum of complex **1** in $[\text{D}_6]\text{DMSO}/5\%$ water (v/v) revealed very large downfield shifts of the signals corresponding to all the urea NH protons ($\Delta\delta = 2.75\text{--}3.58$ ppm) compared to the free ligand, thus indicating strong hydrogen bonds to the PO_4^{3-} ions. When 1.0 equivalent of PO_4^{3-} ions (as the $[\text{K}(\text{[18]crown-6})]^+$ salt) were titrated into a solution of **L** (5×10^{-3} M), similar downfield shifts of the NH protons were observed (Figure 3 and see Figure S9 in the

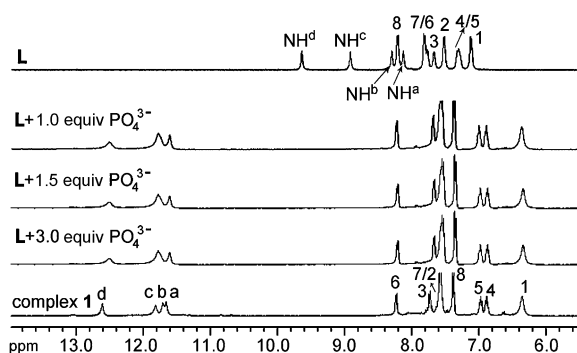


Figure 3. ^1H NMR titration of **L** (5×10^{-3} M) with $[\{\text{K}(\text{[18]crown-6})\}_3]\text{PO}_4$ in $[\text{D}_6]\text{DMSO}/5\%$ H_2O and the spectrum of complex **1** in $[\text{D}_6]\text{DMSO}$ (400 MHz, 298 K).

Supporting Information). No further changes appeared with more PO_4^{3-} , thus indicating that the 1:1 (4:4) binding mode is persistent in solution. In addition, a clear upfield shift of the signal corresponding to the H8 proton ($\Delta\delta = -0.80$ ppm) occurred because of the shielding effects in the anion complex. Notably, the TMA counteranion showed only one signal in the normal range (2.99 ppm), with no upfield-shifted peak, which implies that no TMA ion is encapsulated within the cage, and is in agreement with the crystal structure.

The high-symmetry structure of **1** is reflected in its simple ^1H NMR spectrum. In the NOESY spectrum (see Figure S11a,b in the Supporting Information), cross-peaks are formed between all adjacent NH protons as well as between H6–H7/H8, H4/H5–H7, and H4/H5–H8, which are not found in the TOCSY spectrum (see Figure S12a in the Supporting Information) and, thus, are caused by the through-space coupling in **1**. These interactions are also indicated by the spatial proximity of the nitrophenyl and *o*-phenylene groups in the crystal structure (see Figure S7a in the Supporting Information). Moreover, the ^{31}P NMR spectrum of **1** in $[\text{D}_6]\text{DMSO}$ (see Figure S13 in the Supporting Information) showed one signal that is substantially downfield shifted to 8.03 ppm relative to the free PO_4^{3-} ion (2.96 ppm) because of the strong hydrogen bonding, and there is no other phosphate species in solution.

Furthermore, 2D-DOSY was also performed in $[\text{D}_6]\text{DMSO}$ at 298 K. The DOSY spectrum of complex **1** (see Figure S14 in the Supporting Information) showed that all of the signals that correlate to the chemical shifts of ligand **L** are in a horizontal line, with a diffusion coefficient (D) of $9.0 \times 10^{-11} \text{ m}^2 \text{ s}^{-1}$. The hydrodynamic radius (r_s) of this species was calculated from the Stokes–Einstein equation to be about 12.0 Å, which is slightly smaller than that found in the crystal structure (see Figure S15 in the Supporting Information). The high-resolution ESI mass spectrum of $(\text{TMA})_{12}[(\text{PO}_4)_4\text{L}_4]$ exhibited intense signals for $[\text{A}_4\text{L}_4]$ species $[(\text{TMA})_x(\text{H})_y(\text{PO}_4)_z\text{L}_4]^{z-}$ at $m/z = 1068.707$ ($x=y=4, z=5$), 1083.326 ($x=4, y=5, z=5$), 1354.409 ($x=y=4, z=4$), and 1372.679 ($x=5, y=3, z=4$; see Figure S17 and Table S4 in the Supporting Information). The observed isotopic patterns agree well with the simulated ones. These results suggest that the tetrahedral structure also persists in solution.

The phosphate ion can be protonated or deprotonated to different states (PO_4^{3-} , HPO_4^{2-} , H_2PO_4^- , and H_3PO_4) when the external environment is changed, which could greatly influence the binding affinity and regulate the structure of the anion complex. Thus, a reversible formation of complex **1** was established by acid/base modulation and monitored by ^1H NMR spectroscopy ($[\text{D}_6]\text{DMSO}/5\%$ H_2O). The addition of HClO_4 to a solution of complex **1** resulted in the PO_4^{3-} ion being protonated gradually and the tetrahedral structure was disassembled (Figure 4). In contrast, when a base (TMAOH) was introduced, the protonated anions were deprotonated again, and the tetrahedral structure was reassembled (see Supporting Information for details). These results demonstrate that the assembly/disassembly of the anion-coordination-based cage can be readily controlled by the addition of acid or base. Moreover, the effects of other conditions such as temperature, solvent, and concentration on complex **1** were also examined, and the results revealed the complex to be

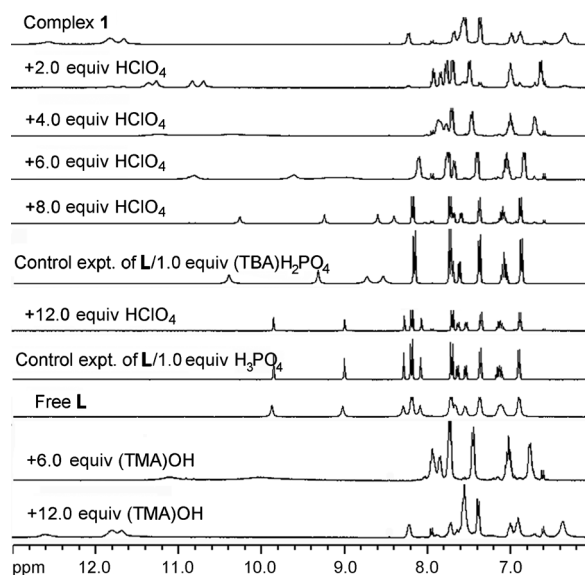


Figure 4. Details of ^1H NMR detection of the gradual assembly and disassembly of the tetrahedral cage **1** upon acid/base modulation in $[\text{D}_6]\text{DMSO}/5\%$ H_2O (400 MHz, 298 K, TBA = tetra-*n*-butylammonium).

remarkably stable. The variable-temperature ^1H NMR spectra recorded in $[\text{D}_6]\text{DMSO}$ showed that complex **1** is stable up to 80°C (see Figure S18 in the Supporting Information), and the cage can persist in different solvents (acetone, acetonitrile, DMSO), as indicated by NMR spectroscopy and ESIMS studies. Dilution of complex **1** in $[\text{D}_6]\text{DMSO}$ resulted in no signs of disassembly on the NMR scale (see Figure S19 in the Supporting Information).

The ^1H NMR spectrum of the sulfate complex **2** recorded in $[\text{D}_6]\text{DMSO}$ revealed that all of the resonances of the urea NH groups underwent downfield shifts ($\Delta\delta = 0.46\text{--}1.62$ ppm) relative to the signal of free ligand. The NOESY spectrum also demonstrated the formation of complex **2** (see Figure S11c,d in the Supporting Information). The DOSY results gave a diffusion coefficient of $D = 9.8 \times 10^{-11} \text{ m}^2 \text{ s}^{-1}$, which corresponds to an R_h value of about 11.0 \AA (see Figures S14 and S15 in the Supporting Information). The evolution of the spectrum was easy to follow in the ^1H NMR titration experiments (see Figure S10 in the Supporting Information). Detailed discussion of the titration process is given in the Supporting Information. Notably, the titration revealed both 2:3 and 1:3 (host to guest) binding modes. This difference between the binding stoichiometry in the solid state and solution is common and has been observed for many anion-binding receptors.

In conclusion, a C_3 -symmetric tris(bisurea) ligand (**L**) has been designed. Self-assembly of **L** and phosphate anions (PO_4^{3-}) affords the expected highly negatively charged $[\text{A}_4\text{L}_4]$ -type tetrahedral cage $[(\text{PO}_4)_4\text{L}_4]^{12-}$ (complex **1**) held together by 48 hydrogen bonds. In the complex, the phosphate ions occupy the vertices and the ligands lie on the faces. This conceptual study represents the first example of the successful assembly of tetrahedral cages through anion coordination, further proving the resemblance of metal coordination and anion coordination behavior in terms of the coordination number and geometry. Notably, the reversible assembly/disassembly of the tetrahedral cage **1** can be readily modulated under mild conditions by the addition of acid and base. Extension to bigger cages and higher polyhedra as well as investigation of their host-guest properties are currently underway.

Received: December 12, 2012

Published online: April 8, 2013

Keywords: anion coordination · oligourea · phosphate anion · self-assembly · tetrahedral cage

[1] For selected books and reviews on anion binding, see a) J. L. Sessler, P. A. Gale, W.-S. Cho, *Anion Receptor Chemistry*, Cambridge, 2006; b) P. D. Beer, P. A. Gale, *Angew. Chem.* 2001, 113, 502–532; *Angew. Chem. Int. Ed.* 2001, 40, 486–516; c) P. A. Gale, *Acc. Chem. Res.* 2006, 39, 465–475; d) E. A. Katayev, Y. A. Ustyniuk, J. L. Sessler, *Coord. Chem. Rev.* 2006, 250, 3004–3037; e) P. A. Gale, S. E. García-Garrido, J. Garric, *Chem. Soc. Rev.* 2008, 37, 151–190; f) for latest reviews on anion chemistry, see a thematic issue: *Chem. Soc. Rev.* 2010, 3581–4008.

- [2] a) J.-M. Lehn, *Acc. Chem. Res.* 1978, 11, 49–57; b) J.-M. Lehn, *Supramolecular Chemistry: Concepts and Perspectives*, VCH, Weinheim, 1995; c) K. Bowman-James, *Acc. Chem. Res.* 2005, 38, 671–678; d) *Anion Coordination Chemistry* (Eds.: K. Bowman-James, A. Bianchi, E. García-España) Wiley-VCH, Weinheim, 2011.
- [3] a) I. M. Oppel (née Müller), K. Föcker, *Angew. Chem.* 2008, 120, 408–411; *Angew. Chem. Int. Ed.* 2008, 47, 402–405; b) I. M. Müller, D. Möller, C. A. Schalley, *Angew. Chem.* 2005, 117, 485–488; *Angew. Chem. Int. Ed.* 2005, 44, 480–484; c) J. F. Bai, A. V. Virovets, M. Scheer, *Science* 2003, 300, 781–783; d) Q.-F. Sun, J. Iwasa, D. Ogawa, Y. Ishido, S. Sato, T. Ozeki, Y. K. Yamaguchi, M. Fujita, *Science* 2010, 328, 1144–1147.
- [4] a) H. Amouri, C. Desmarests, J. Moussa, *Chem. Rev.* 2012, 112, 2015–2041; b) R. Chakrabarty, P. S. Mukherjee, P. J. Stang, *Chem. Rev.* 2011, 111, 6810–6918; c) S. J. Dalgarno, N. P. Power, J. L. Atwood, *Coord. Chem. Rev.* 2008, 252, 825–841.
- [5] For selected reviews and articles, see a) M. D. Pluth, R. G. Bergman, K. N. Raymond, *Science* 2007, 316, 85–88; b) P. Mal, B. Breiner, K. Rissanen, J. R. Nitschke, *Science* 2009, 324, 1697–1699; c) T. S. Koblenz, J. Wassenaar, J. N. H. Reek, *Chem. Soc. Rev.* 2008, 37, 247–262; d) L. Trembleau, J. Rebek, Jr., *Science* 2003, 301, 1219–1221; e) M. D. Ward, *Chem. Commun.* 2009, 4487–4499; f) D. L. Caulder, K. N. Raymond, *Acc. Chem. Res.* 1999, 32, 975–982.
- [6] For examples of M_4L_6 cages, see a) R. W. Saalfrank, A. Stark, K. Peters, H. G. von Schnering, *Angew. Chem.* 1988, 100, 878–880; *Angew. Chem. Int. Ed. Engl.* 1988, 27, 851–853; b) M. D. Pluth, R. G. Bergman, K. N. Raymond, *Acc. Chem. Res.* 2009, 42, 1650–1659, and references therein; c) R. L. Paul, Z. R. Bell, J. C. Jeffery, J. A. McCleverty, M. D. Ward, *Proc. Natl. Acad. Sci. USA* 2002, 99, 4883–4888; d) N. Ousaka, J. K. Clegg, J. R. Nitschke, *Angew. Chem.* 2012, 124, 1493–1497; *Angew. Chem. Int. Ed.* 2012, 51, 1464–1468.
- [7] For examples of M_4L_4 cages, see a) A. J. Amoroso, J. C. Jeffery, P. L. Jones, J. A. McCleverty, P. Thornton, M. D. Ward, *Angew. Chem.* 1995, 107, 1577–1580; *Angew. Chem. Int. Ed. Engl.* 1995, 34, 1443–1446; b) D. L. Caulder, C. Bruckner, R. E. Powers, S. König, T. N. Parac, J. A. Leary, K. N. Raymond, *J. Am. Chem. Soc.* 2001, 123, 8923–8938; c) B. Birkmann, R. Fröhlich, F. E. Hahn, *Chem. Eur. J.* 2009, 15, 9325–9329.
- [8] a) E. Graf, J.-M. Lehn, *J. Am. Chem. Soc.* 1975, 97, 5022–5024; b) F. P. Schmidtchen, *Angew. Chem.* 1977, 89, 751–752; *Angew. Chem. Int. Ed. Engl.* 1977, 16, 720–721; c) K. Ichikawa, M. A. Hossain, *Chem. Commun.* 1996, 1721–1722; d) Q.-Q. Wang, V. W. Day, K. Bowman-James, *Angew. Chem.* 2012, 124, 2161–2165; *Angew. Chem. Int. Ed.* 2012, 51, 2119–2123; e) Q.-Q. Wang, V. W. Day, K. Bowman-James, *J. Am. Chem. Soc.* 2013, 135, 392–399.
- [9] a) M. Lankshear, P. D. Beer, *Coord. Chem. Rev.* 2006, 250, 3142–3160; b) B. Hasenknopf, J.-M. Lehn, G. Baum, B. O. Kneisel, D. Fenske, *Angew. Chem.* 1996, 108, 1987–1990; *Angew. Chem. Int. Ed. Engl.* 1996, 35, 1838–1840; c) J. S. Fleming, K. L. V. Mann, C.-A. Carraz, E. Psillakis, J. C. Jeffery, J. A. McCleverty, M. D. Ward, *Angew. Chem.* 1998, 110, 1315–1318; *Angew. Chem. Int. Ed.* 1998, 37, 1279–1281; d) B. Hasenknopf, J.-M. Lehn, N. Boumediene, A. Dupont-Gervais, A. Van Dorsselaer, B. O. Kneisel, D. Fenske, *J. Am. Chem. Soc.* 1997, 119, 10956–10962.
- [10] a) K. M. Mullen, P. D. Beer, *Chem. Soc. Rev.* 2009, 38, 1701–1713; b) M. R. Sambrook, P. D. Beer, J. A. Wisner, R. L. Paul, A. R. Cowley, F. Szemes, M. G. B. Drew, *J. Am. Chem. Soc.* 2005, 127, 2292–2302; c) H. Juwarker, K.-S. Jeong, *Chem. Soc. Rev.* 2010, 39, 3664–3674; d) J. Sánchez-Quesada, C. Seel, P. Prados, J. de Mendoza, *J. Am. Chem. Soc.* 1996, 118, 277–278; e) J. Keegan, P. E. Kruger, M. Nieuwenhuyzen, J. O'Brien, N. Martin, *Chem. Commun.* 2001, 2192–2193; f) S. J. Coles, J. G. Frey, P. A. Gale, M. B. Hurst-House, M. E. Light, K. Navakhun, G. L.

- Thomas, *Chem. Commun.* **2003**, 568–569; g) R. Custelcean, P. V. Bonnesen, B. D. Roach, N. C. Duncan, *Chem. Commun.* **2012**, 48, 7438–7440.
- [11] a) C. Jia, B. Wu, S. Li, Z. Yang, Q. Zhao, J. Liang, Q.-S. Li, X.-J. Yang, *Chem. Commun.* **2010**, 46, 5376–5378; b) C. Jia, B. Wu, S. Li, X. Huang, X.-J. Yang, *Org. Lett.* **2010**, 12, 5612–5615; c) C. Jia, B. Wu, S. Li, X. Huang, Q. Zhao, Q.-S. Li, X.-J. Yang, *Angew. Chem.* **2011**, 123, 506–510; *Angew. Chem. Int. Ed.* **2011**, 50, 486–490; d) S. Li, C. Jia, B. Wu, Q. Luo, X. Huang, Z. Yang, Q.-S. Li, X.-J. Yang, *Angew. Chem.* **2011**, 123, 5839–5842; *Angew. Chem. Int. Ed.* **2011**, 50, 5721–5724.
- [12] a) B. P. Hay, T. K. Firman, B. A. Moyer, *J. Am. Chem. Soc.* **2005**, 127, 1810–1819; b) R. Custelcean, B. A. Moyer, B. P. Hay, *Chem. Commun.* **2005**, 5971–5973; c) R. Custelcean, P. Remy, P. V. Bonnesen, D.-E. Jiang, B. A. Moyer, *Angew. Chem.* **2008**, 120, 1892–1896; *Angew. Chem. Int. Ed.* **2008**, 47, 1866–1870.
- [13] CCDC 909133 (**1**) and 909134 (**2**) contain 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.
- [14] The structure of the tetrahedral cage $[(\text{PO}_4)_4\text{L}_4]^{12-}$ was optimized at the B3LYP/6-31G level using the Gaussian03 program suit (for full citation, see the Supporting Information).
- [15] The cavity volume was calculated using the VOIDOO program, with a 1.4 Å diameter rolling ball on the crystal structure of complex **1**.
- [16] a) S. Mecozzi, J. Rebek, Jr., *Chem. Eur. J.* **1998**, 4, 1016–1022; b) R. A. Bilbeisi, J. K. Clegg, N. Elgrishi, X. de Hatten, M. Devillard, B. Breiner, P. Mal, J. R. Nitschke, *J. Am. Chem. Soc.* **2012**, 134, 5110–5119.
- [17] B. Conerney, P. Jensen, P. E. Kruger, C. MacGloinn, *Chem. Commun.* **2003**, 1274–1275.