Cage Compounds

Rational Design of Tightly Closed Coordination Tetrahedra that are Stable in the Solid State, in Solution, and in the Gas Phase**

Iris M. Müller, Daniela Möller, and*
Christoph A. Schalley

Molecular "Lego" utilizing simple building blocks with a rationally programmed arrangement of binding sites permits the construction of complex coordination cages by self-assembly,[1] among them different types of coordination

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[*] Dr. I. M. Müller, Dipl.-Chem. D. Möller
Lehrstuhl für Analytische Chemie, NC 4/27
Ruhr-Universität Bochum
44780 Bochum (Germany)
Fax: (+49) 234-321-4420
E-mail: iris.m.mueller@rub.de

Priv.-Doz. Dr. C. A. Schalley
Kekulé-Institut für Organische Chemie und Biochemie
Universität Bonn, 53121 Bonn (Germany)

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tetrahedra (Figure 1). The oldest and most common $[M_4L_6]$ systems combine four metal centers at the corners with six bridging ligands as edges (Figure 1 a).[2] $[M_4L_4]$ tetrahedral cages, whose faces are covered by ligands with threefold symmetry (Figure 1 b) have been reported more rarely.[3] Nearly all $[M_6L_4]$ systems are truncated tetrahedra or adamantanoid cages (Figure 1 c) with rather wide openings at their corners allowing encapsulated guest molecules to be exchanged.[4] To our knowledge, only one $[M_6L_4]$ tetrahedron with an almost completely closed surface has been reported.[5] In this case, M is a $(CdO)_2$ four-membered ring and an $[Et_4N]^+$ ion is securely trapped within the octaanionic capsule.

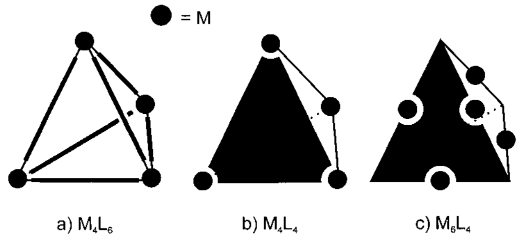
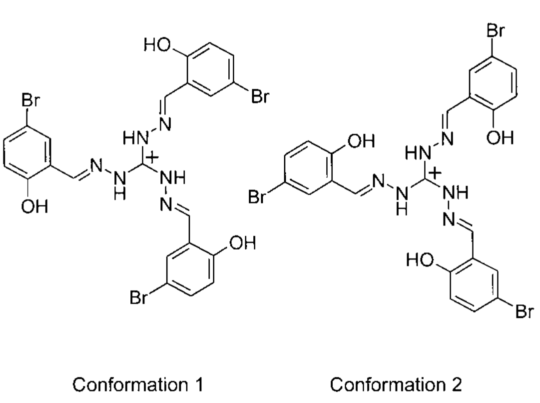


Figure 1. Tetrahedral cage molecules with different topologies.

The structural characterization of such large cage compounds by X-ray crystallography is often difficult owing to rapid solvent loss and severe disorder of counterions and solvent molecules. The introduction of heavy atoms with their higher scattering power into the ligands should help to improve the resolution and quality of the X-ray data. With tris[(5-bromo-2-hydroxybenzylidene)amino]guanidinium chloride ($[H_6Br_3L]Cl$ (**1**)), we herein present a new ligand suitable for the formation of chiral (although racemic), tightly closed tetrahedral cages with the formal $[M_6L_4]$ topology.

Compound **1** is easily obtained by a Schiff base reaction of 5-bromosalicylaldehyde and triaminoguanidinium chloride.[6] Diffusion of HCl into an acetonitrile solution of **1** leads to orthorhombic pale yellow crystals of $[H_6Br_3L]Cl\cdot3\,CH_3CN\cdot H_2O$ (**1a**).[7] In the solid state **1a** adopts conformation 1 (Scheme 1) which is unfavorable for the coordination of metal centers and which is stabilized through hydrogen bonding with the Cl^- counterions and solvent molecules (see Supporting Information). In slightly basic solution, a change to conformation 2 is observed.[6] To examine whether metalation of **1** has the same effect, we allowed a mixture of $CdCl_2$ and **1** to react in acetone at 88 °C. The solid-state structure of the pale yellow crystals of the resulting complex $[H_6Br_3L]_2[CdCl_4]\cdot6(CH_3)_2CO\cdot H_2O$ (**1b**) showed no change in conformation of **1**.[8] In **1b** there are two $[H_6Br_3L]^+$ ligands together with a $[CdCl_4]^{2-}$ counterion in the asymmetric unit.



Scheme 1. Unfavorable and favorable conformation for the coordination of metal centers to **1**.

A similar reaction of $CdCl_2$ and **1** in methanol in the presence of Et_4NCl (as a tetrahedral counterion) and Et_3N as base leads to the formation of bright yellow crystals.[9] This time, the ligand is fully deprotonated and binds three CdCl units. All observed bond lengths and angles at the square pyramidal cadmium centers fall in the expected ranges (see Supporting Information) with three coordination sites taken by the ligand $[Br_3L]^{5-}$ and one by a Cl^- ligand. The fifth site is occupied by a phenolate oxygen atom of a neighboring $[(CdCl)_3Br_3L]$ building block so that a chiral cage with the formula $(Et_4N)_5(Et_3NH)_3[\{(CdCl)_3Br_3L\}_4]$ (**2**), is formed as shown in Figure 2 with each $[(CdCl)_3Br_3L]^{2-}$ unit color coded differently. Although the ligand $[H_6Br_3L]^+$ is fully deprotonated and coordinating three Cd^{2+} centers in **2** the observed bond lengths and angles remain at the 3σ level the same as those found in **1a** and **1b**. Only the propeller-like distortion becomes more distinct, with dihedral angles of 16.9–36.4°. Not unexpectedly, this avoids close Br···Br contacts at the tightly packed tetrahedron corners with their already short Br···Br separations of 3.72(2)–4.89(2) Å (Figure 3). The cage dimensions can be determined by an imaginary inner sphere that is defined by the four central carbon atoms ($r = 4.31(8)$ Å). The theoretical edge length (a) is calculated to be 21.1(4) Å, the height (h) to be 17.2(3) Å (Scheme 2, Table 1). The observed edge length can be gauged by the H···Br separation (d) which has values of 15.46(3)–15.99(3) Å, so that only the ends of the corners remain uncovered. This situation also confirms that the $[(CdCl)_3Br_3L]$ units are triangular building blocks, each of which covers almost completely one face of the tetrahedron leaving effectively no opening at the cage corners. In the asymmetric unit of **2**, two cages and 16 counterions can be found, two of the $[Et_4N]^+$ ions are located in the cavities of the two cage anions. The remaining 14 cations (six $[Et_3NH]^+$, eight $[Et_4N]^+$) are located outside the cages with the $[Et_3NH]^+$

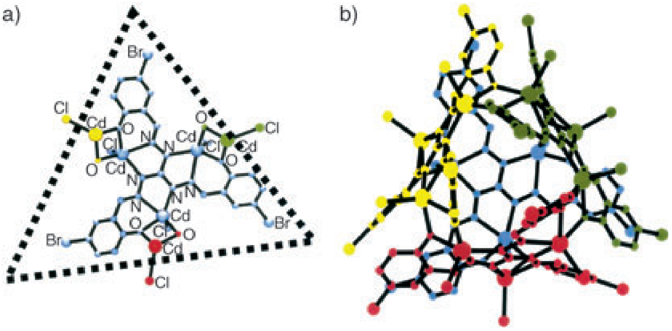


Figure 2. a) Connectivity of one $[(CdCl)_3Br_3L]$ unit. b) Crystal structure of $[\{(CdCl)_3Br_3L\}_4]^{8-}$, hydrogen atoms and counterions are omitted for clarity.

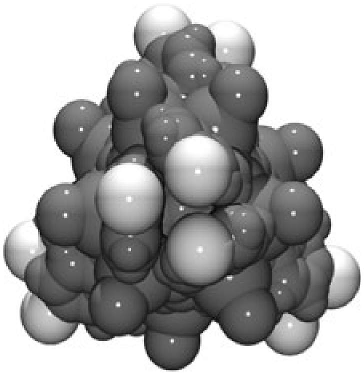
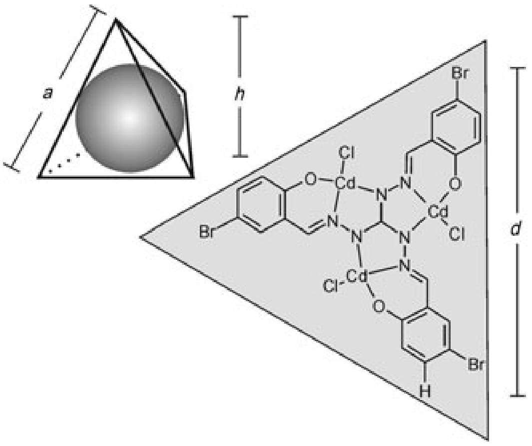


Figure 3. Space-filling model of $[\{(CdCl)_3Br_3L\}_4]^{8-}$ in **2**, view towards the corner of the cage (counterions not shown).



Scheme 2. Definition of the cage dimensions in **2**.

Table 1: Theoretical and observed dimensions [Å] of the tetrahedral cages **2**–**4**.

Dimension[a]	**2**	**3**	**4**
r	4.31(8)	4.36(8)	4.36(5)
a	21.1(4)	21.3(4)	21.3(3)
h	17.2(3)	17.5(3)	17.4(2)
Br···Br	3.72(2)–4.89(2)	3.77(2)–4.72(2)	3.85(2)–4.56(2)
d	15.46(3)–15.99(3)	15.60(3)–16.02(3)	15.68(3)–15.96(3)

[a] See Scheme 2.

ions forming hydrogen bridges to the Cl ligands of the tetrahedra (N···Cl = 3.13(2) Å).

To learn more about the influence of the size and geometry of the counterion, $[Et_4N]^+$ was replaced by larger $[Ph_4P]^+$ ions in a second reaction of $CdCl_2$ and $[H_6Br_3L]Cl$ with Et_3N performed under identical conditions. Again bright yellow crystals were obtained which according to the crystal-structure analysis correspond to a tetrahedral cage with the formula $(PPh_4)_{1.33}(Et_3NH)_{6.67}[\{(CdCl)_3Br_3L\}_4]$ (**3**)[10] and of the same size as **2**. An $[Et_3NH]^+$ ion is located inside the cage. Encouraged by these results, the experiment was repeated without the addition of any tetrahedral cations. Again, bright yellow crystals suitable for crystal-structure analysis were obtained corresponding to $(Et_3NH)_8[\{(CdCl)_3Br_3L\}_4]\cdot x\,H_2O$ (**4**).[11] Again, all crystallographically observed bond lengths and angles fall in the expected ranges and show no additional distortion compared with **2** or **3**. An $[Et_3NH]^+$ ion is captured inside tetrahedron **4**, together with a water molecule, which is hydrogen bonded to the cation (N···O 2.66(9) Å). Apparently, the size of the guest is more important than its symmetry for efficiently templating the tetrahedron formation.

Cage **4** is quite stable in solution. The ^1H NMR spectrum of **4** in $[D_6]$acetone shows different signals for the $[Et_3NH]^+$ ions inside (methyl groups, $\delta_H = 0.95$ ppm) and outside (methyl groups, $\delta_H = 1.27$ ppm) the cage, which indicates that their exchange is slow on the NMR timescale.

Electrospray ionization Fourier-transform ion-cyclotron-resonance (ESI-FT-ICR) mass spectrometry provides a soft method for the ionization of intact tetrahedra **4** and other metallosupramolecular assemblies.[12] When sprayed from acetonitrile or acetone, doubly, triply, and quadruply charged anions are generated by successively stripping off $[Et_3NH]^+$ counterions (Figure 4a). Although the spectra are complex, they can be analyzed in detail. In addition to the $[M-nEt_3NH]^{n-}$ ions, losses of Et_3N and Et_3NHCl are observed (Figure 4b). An exact comparison of the experimental spectrum with that simulated on the basis of natural isotope abundances reveals that each of these ions is accompanied by an ion bearing exactly one water molecule although dry acetonitrile was used as the spray solvent. In marked contrast, no such ions bearing water molecules are observed in the mass spectrum of **2** obtained under the same conditions (Figure 4c). This finding rules out incomplete desolvation as the reason for the presence of a water molecule in the spectra of **4** and points to its presence as a guest inside the cage, thus providing evidence for the intact structure of the tetrahedron even in the gas phase. Consequently, it can safely be assumed that the much larger $[Et_3NH]^+$ guest is also still inside the cage in these ions.

In conclusion, a tightly closed tetrahedral cage successfully self-assembles around templating cations as long as these cations have a suitable size. While $[Et_4N]^+$ almost exactly fills the space inside, $[Et_3NH]^+$ leaves enough space for an additional water molecule, which is co-encapsulated in the cavity of the tetrahedron. The crystal structures of several tetrahedra are in excellent agreement with data from solution and the gas phase which provide evidence for their existence as stable, discrete entities. It is particularly surprising, that ESI mass spectrometry is capable of identifying the encapsulated water molecule, which may also be interpreted as an effect of the tightly closed surfaces of the tetrahedra, which impose a considerable barrier for the water expulsion from the interior. The tetrahedra are chiral, although they form as a racemic mixture. As cations template their formation, a diastereoselective formation of one tetrahedron enantiomer around an enantiopure guest cation might be possible.

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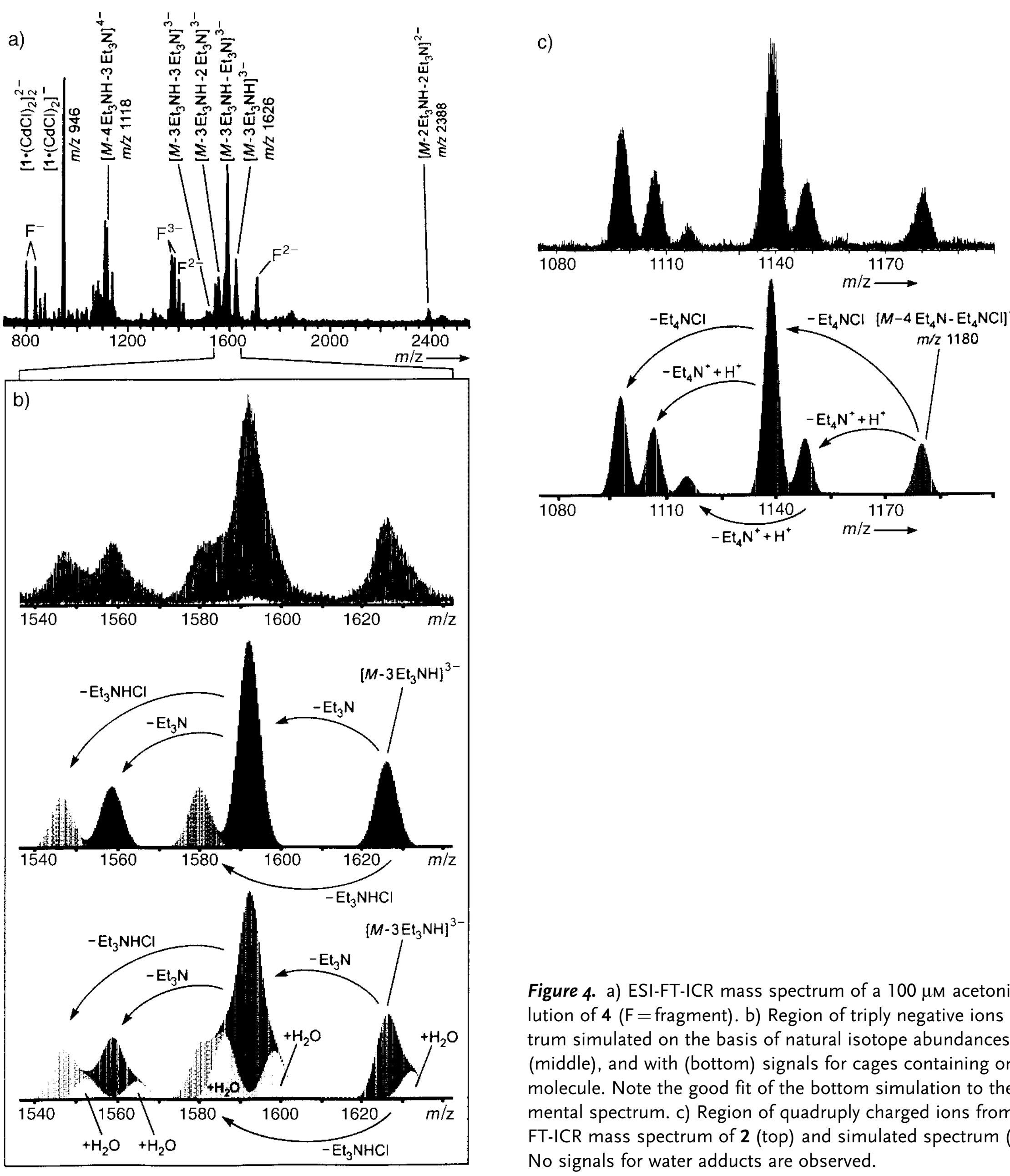

Figure 4. a) ESI-FT-ICR mass spectrum of a 100 µM acetonitrile solution of **4** (F = fragment). b) Region of triply negative ions (top), spectrum simulated on the basis of natural isotope abundances without (middle), and with (bottom) signals for cages containing one water molecule. Note the good fit of the bottom simulation to the experimental spectrum. c) Region of quadruply charged ions from the ESI-FT-ICR mass spectrum of **2** (top) and simulated spectrum (bottom). No signals for water adducts are observed.

Keywords: cadmium · cage compounds · mass spectrometry · self-assembly · structure elucidation

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[7] Experimental details are given in the Supporting Information. $0.16 \times 0.19 \times 0.25$ mm^3, orthorhombic, $Pbcn$, $a = 28.649(6)$, $b = 15.133(3)$, $c = 15.739(3)$ Å, $V = 6823(2)$ Å^3, $\rho_{calcd} = 1.617$ g cm^{-3}, $2\theta_{max} = 62.08°$, $\lambda = 0.71073$ Å, $T = 100$ K, 63876 measured reflections, 10825 independent reflections ($R_{int} = 0.0701$), 7685 observed reflections ($I > 2\sigma(I)$), $\mu = 3.673$ mm^{-1}, numerical absorption correction, $T_{min} = 0.460$, $T_{max} = 0.591$, 406 parameters, $R_1(I > 2\sigma(I)) = 0.0492$, wR_2(all data) $= 0.0856$, max./min. residual electron density 0.63/−0.48 e Å^{-3}.[13]

[8] Experimental details are given in the Supporting Information. $0.24 \times 0.18 \times 0.14$ mm^3, triclinic, $P\bar{1}$, $a = 16.437(7)$, $b = 16.746(6)$, $c = 16.889(7)$ Å, $\alpha = 80.529(9)$, $\beta = 74.212(5)$, $\gamma = 61.36(1)°$, $V = 3923(3)$ Å^3, $\rho_{calcd} = 1.633$ g cm^{-3}, $2\theta_{max=}47.50°$, $\lambda = 0.71073$ Å, $T = 213$ K, 18324 measured reflections, 11762 independent reflections ($R_{int} = 0.0805$), 5118 observed reflections ($I > 2\sigma(I)$), $\mu = 3.534$ mm^{-1}, empirical absorption correction, $T_{min} = 0.472$, $T_{max} = 0.608$, 560 parameters, $R_1(I > 2\sigma(I)) = 0.0767$, wR_2(all data) $= 0.1947$, max./min. residual electron density 0.76/−0.97 e Å^{-3}.[13] Owing to the weak scattering power of **1b**, the large number of solvent molecules and the poor reflection to parameter ratio, all solvent molecules as well as the phenyl groups were refined isotropically. The bond lengths in the solvent molecules were fixed to literature values.

[9] Experimental details are given in the Supporting Information. $0.08 \times 0.14 \times 0.14$ mm^3, triclinic, $P\bar{1}$, $a = 19.7629(1)$, $b = 31.7856(1)$, $c = 34.1879(2)$ Å, $\alpha = 107.491(2)$, $\beta = 94.548(2)$, $\gamma = 96.091(2)°$, $V = 20227.0(2)$ Å^3, $\rho_{calcd} = 1.748$ g cm^{-3}, $2\theta_{max} = 50.50°$, $\lambda = 0.71073$ Å, $T = 100$ K, 248756 measured reflections, 73078 independent reflections ($R_{int} = 0.0697$), 50612 observed reflections ($I > 2\sigma(I)$), $\mu = 3.819$ mm^{-1}, empirical absorption correction, $T_{min} = 0.597$, $T_{max} = 0.732$, 3026 parameters, $R_1(I > 2\sigma(I)) = 0.0634$, wR_2(all data) $= 0.1984$, max./min. residual electron density 1.07/−1.14 e Å^{-3}.[13]

[10] Experimental details are given in the Supporting Information. $0.15 \times 0.19 \times 0.19$ mm^3, trigonal, $R3c$, $a = 34.764(1)$, $c = 94.689(1)$ Å, $V = 99102(1)$ Å^3, $\rho_{calcd} = 1.664$ g cm^{-3}, $2\theta_{max} = 47.74°$, $\lambda = 0.71073$ Å, $T = 100$ K, 140050 measured reflections, 28466 independent reflections ($R_{int} = 0.0517$), 26602 observed reflections ($I > 2\sigma(I)$), $\mu = 3.520$ mm^{-1}, numerical absorption correction, $T_{min} = 0.476$, $T_{max} = 0.571$, 1476 parameters, $R_1(I > 2\sigma(I)) = 0.0585$, wR_2(all data) $= 0.1553$, max./min. residual electron density 1.38/−1.00 e Å^{-3}.[13]

[11] Experimental details are given in the Supporting Information. $0.10 \times 0.19 \times 0.22$ mm^3, monoclinic, $C2/c$, $a = 65.484(1)$, $b = 20.4154(4)$, $c = 33.0347(6)$ Å, $\beta = 113.215(1)°$, $V = 40588(1)$ Å^3, $\rho_{calcd} = 1.703$ g cm^{-3}, $2\theta_{max} = 50.50°$, $\lambda = 0.71073$ Å, $T = 100$ K, 128167 measured reflections, 36682 independent reflections ($R_{int} = 0.0381$), 27665 observed reflections ($I > 2\sigma(I)$), $\mu = 3.805$ mm^{-1}, numerical absorption correction, $T_{min} = 0.470$, $T_{max} = 0.683$, 1499 parameters, $R_1(I > 2\sigma(I)) = 0.0510$, wR_2(all data) $= 0.1630$, max./min. residual electron density 0.94/−1.10 e Å^{-3}.[13]

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[13] CCDC-248614–248618 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).