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Core/Shell Oligometallic Template Synthesis of Macrocyclic Hexaoxime

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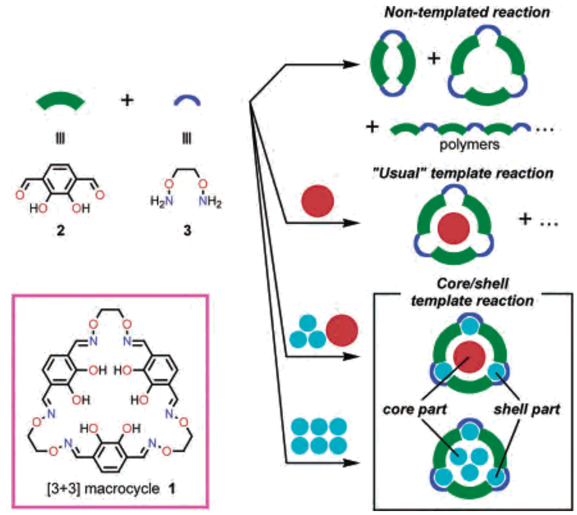
A 36-membered macrocyclic hexaoxime was quantitatively obtained by [3 + 3] condensation of dialdehyde **2** with diamine **3** using La^{3+} (core metal) and Zn^{2+} (shell metal) as a novel core/shell template, while the yield was very low in the absence of the metal ions. The high yield can be attributed to the efficient formation of a 3:3:1 complex of dialdehyde **2**, Zn^{2+}, and La^{3+}, which readily gives the macrocycle keeping the Zn_3La core/shell tetranuclear cluster structure.

Scheme 1. Concept of Core/Shell Oligometallic Template Macrocyclization



Macrocyclic polyimines are useful ligands to synthesize a variety of coordination compounds.[1] In most cases, such macrocycles are prepared by condensation of diamines and dialdehydes in the presence of appropriate metal ions as a template to avoid the formation of higher oligomeric or polymeric products. If several metal ions cooperatively act as a template for the macrocyclization, metal clusters incorporated in the macrocycles would form instantaneously. Indeed, template reaction using multiple (four,[2] five,[3] and six[4]) metal ions leads to [2 + 2], [3 + 3], or [4 + 4] macrocycles with a metal cluster core, which exhibits interesting magnetic or electrochemical properties. Most of the multiple-template syntheses employ only one kind of metal, and all of the template metal ions in the resulting clusters are located essentially in the same coordination environment. Although clusters[5] or nanoparticles[6] with a hierarchical core/shell structure have attracted much attention, there have been no reports on macrocyclization that is accompanied by the simultaneous formation of core/shell clusters. The macrocyclization should require a well-programmed building block that has suitable geometry not only to readily form a macrocycle but also to interact with both core and shell metals. Here we describe a one-pot synthesis of core/shell-type Zn_3La and Zn_6 clusters with a macrocyclic ligand using 2,3-dihydroxybenzene-1,4-dicarbaldehyde (**2**)[7] and 1,2-bis(aminooxy)ethane (**3**)[8] for the building blocks of the macrocyclic framework. A 36-membered [3 + 3] macrocyclic hexaoxime ligand **1** was obtained in high yield by the core/shell template reaction, though the yield was very low in the absence of the core and shell metal ions (Scheme 1).

We examined the condensation reaction of dialdehyde **2** with diamine **3**, which could give macrocyclic oligo(salamo)[9]

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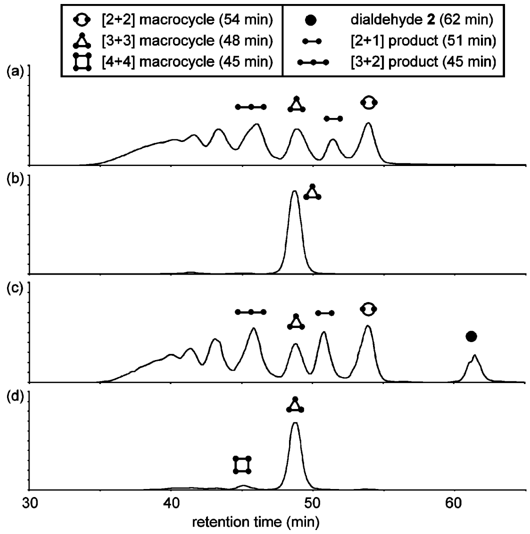

Figure 1. GPC profiles of the condensation products of dialdehyde **2** and diamine **3** in the presence of template metals monitored by UV absorption at 301 nm: (a) no metal; (b) Zn^{2+} (1 equiv) and La^{3+} ($^1/_3$ equiv); (c) La^{3+} ($^1/_3$ equiv); (d) Zn^{2+} (2 equiv).

ligands of various sizes. We have recently reported a nontemplate high-yield synthesis of the imine analogues, triangular tris(saloph) ligands,[7a,10] which are useful for the synthesis of core/shell-type homometallic Zn_7[10,11] and heterometallic Zn_3La[10a] clusters. Intramolecular hydrogen bonds and the reversibility of C═N bond formation are probably important for the high-yield macrocyclization.[7a,12]

Unlike the case of the imine analogues, the nontemplated condensation reaction of **2** with **3** [a chloroform−methanol (3:2) solution (2.0 mM)] gave [3 + 3] macrocycle **1**[13] in low yield. A gel permeation chromatography (GPC) profile of the reaction mixture showed several peaks corresponding to [2 + 2] (54 min) and [3 + 3] (48 min) macrocycles in addition to linear oligomers such as [2 + 1] and [3 + 2] condensation products (Figure 1a). The formation of higher oligomeric products is also evident from broad peaks around 33−40 min. The isolated yield of [3 + 3] macrocycle **1** was up to 15% even if a high-dilution technique was employed. The low selectivity is presumably due to conformational flexibility of the $-OCH_2CH_2O-$ moieties and stability of the oxime bonds, which resist C═N bond recombination.[9]

X-ray crystallographic analysis revealed the structure of [3 + 3] macrocycle **1** (Figure 2).[14] In the crystal structure, one (O5−O6) of the three catechol moieties directs outward and one (O3) of the six phenol O atoms did not form O−H···N hydrogen bonds to an oxime nitrogen (N2). This fact suggests that [3 + 3] macrocycle **1** does not always adopt a conformation suitable for complexation at three N_2O_2 and one O_6 sites.

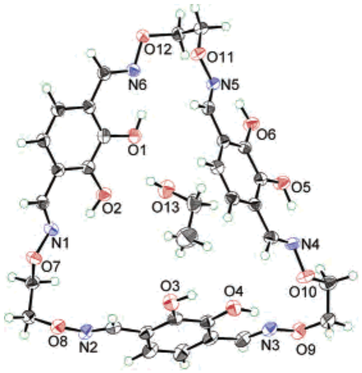

Figure 2. Crystal structure of [3 + 3] macrocycle **1** with thermal ellipsoids drawn at the 50% probability level. A cocrystallized ethanol molecule is also shown.

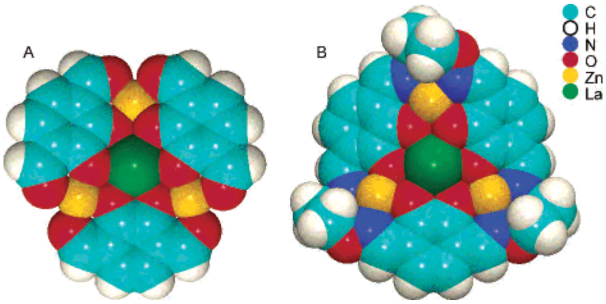

Figure 3. X-ray structures of (A) $[L^2{}_3Zn_3La]^{3+}$ and (B) $[L^1Zn_3La]^{3+}$. Counter anions and solvent molecules coordinating to the metal centers are omitted for clarity.

When the condensation reaction of **2** with **3** was carried out in the presence of $^1/_3$ equiv of La^{3+} (core metal) and 1 equiv of Zn^{2+} (shell metal) (Scheme 1), the yield of [3 + 3] macrocycle **1** was dramatically improved. The reaction afforded a yellow Zn−La mixed-metal complex, from which pure free [3 + 3] macrocycle **1** was obtained by demetalation with acid. The overall yield of [3 + 3] macrocycle **1** was 94%. No other macrocycles were observed in the chromatogram for the reaction mixture (Figure 1b).

The effectiveness of the Zn−La mixed-metal template can be explained by the formation of a Zn_3La tetranuclear complex of dialdehyde **2**. ^1H NMR and electrospray ionization mass spectrometry (ESI-MS) investigation showed that a discrete cluster $[L^2{}_3Zn_3La]^{3+}$ was formed quantitatively when dialdehyde **2** (=H_2L^2) was mixed with Zn^{2+} (1 equiv) and La^{3+} ($^1/_3$ equiv). X-ray crystallography revealed the structure of $[L^2{}_3Zn_3La]^{3+}$ in which the salicylaldehyde moieties of **2** coordinate to shell metal Zn^{2+} and the catechol moiety to the core metal La^{3+} (Figure 3A).[15,16] When the tetranuclear cluster $[L^2{}_3Zn_3La]^{3+}$ was allowed to react with diamine **3**, the complex was completely converted to the

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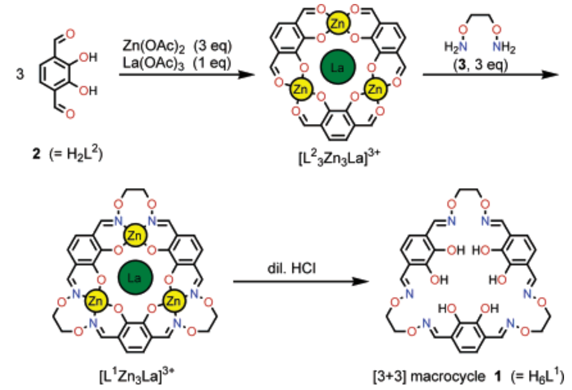
(13) **1**: colorless crystals, mp 231−233 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 4.51 (s, 12H), 6.65 (s, 6H), 8.19 (s, 6H), 9.67 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 73.75, 117.60, 120.70, 145.68, 151.32; ESI-MS obsd *m/z* 667.2 ($[M + H]^+$). Anal. Calcd for $C_{30}H_{30}N_6O_{12}$: C, 54.05; H, 4.54; N, 12.61. Found: C, 54.16; H, 4.64; N, 12.52.

(14) Crystallographic data for **1**·EtOH (712.67): monoclinic, $P2_1/n$, a = 7.5740(10) Å, b = 30.3840(10) Å, c = 15.2630(10) Å, β = 93.050(2)°, V = 3507.5(5) $Å^3$, Z = 4, T = 120 K, R1 = 0.0513 [$I > 2\sigma(I)$], wR2 = 0.1455 (all data).[20]

(15) Crystallographic data for $[L^2{}_3Zn_3La(NO_3)_2(MeOH)_6](NO_3)\cdot MeOH$ (1237.68): triclinic, $P\bar{1}$, a = 10.322(4) Å, b = 14.213(6) Å, c = 14.728(7) Å, α = 94.079(18)°, β = 92.159(16)°, γ = 95.342(15)°, V = 2143.8(15) $Å^3$, Z = 2, T = 120 K, R1 = 0.0445 [$I > 2\sigma(I)$], wR2 = 0.1027 (all data).[20]

Scheme 2. Efficient Formation of [3 + 3] Macrocycle **1** Using a Zn−La Mixed-Metal Template



corresponding macrocyclic complex $[L^1Zn_3La]^{3+}$. There is a surprising similarity between the X-ray crystal structures of $[L^2{}_3Zn_3La]^{3+}$ and $[L^1Zn_3La]^{3+}$ (Figure 3).[17,18] This indicates that the macrocyclization requires very little structural change in the dialdehyde moieties fixed by the Zn_3La metal centers. The complete conversion is probably due to the ready formation of seven-membered metallacycles (Scheme 2).

It is important to clarify whether both the core and shell metals are essential for the high-yield synthesis. When the core metal (La^{3+}, $^1/_3$ equiv) only was used as a template, the yield of [3 + 3] macrocycle was not improved (Figure 1c). On the other hand, the use of more than 2 equiv of Zn^{2+} (6 equiv per [3 + 3] macrocycle) considerably changed the product ratio. The GPC analysis showed that the mixture contains [3 + 3] macrocycle and a small amount of [4 + 4] macrocycle (45 min) (Figure 1d).

To elucidate the effect of Zn^{2+} in the absence of La^{3+}, the intermediary species in the reaction mixture was analyzed by spectrometric methods. Although the 1:2 mixture of dialdehyde **2** and $Zn(OAc)_2$ gave a complicated mixture, subsequent reaction with diamine **3** afforded a nearly single species. The MS spectrum indicates the formation of a hexanuclear cluster (m/z 1290.8, $[L^1Zn_6(OAc)_3(MeO)_2]^+$), and the ^1H NMR spectrum showed a simple C_s-symmetric spectral pattern. X-ray crystallographic analysis revealed that the Zn^{II} complex was a hexanuclear cluster L^1Zn_6 having the [3 + 3] macrocyclic ligand (Figure 4).[19] There are three Zn atoms (Zn4, Zn5, and Zn6) in the O_6 core site of the macrocycle in addition to ones in the shell N_2O_2 sites (Zn1, Zn2, and Zn3). The three Zn atoms in the core part are bridged with a μ_3-hydroxo group (O13). The hexanuclear structure is kept also in solution on the basis of the ESI-MS and ^1H NMR data.

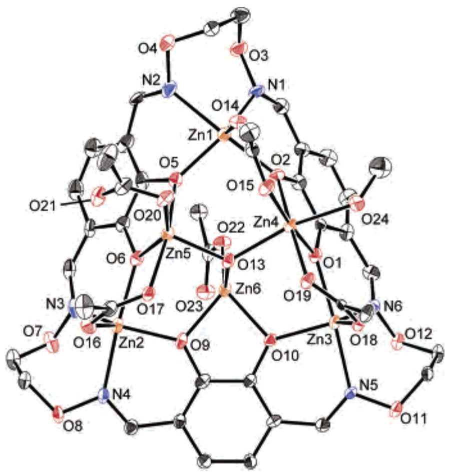


Figure 4. Crystal structure of $[L^1Zn_6(OAc)_5(OH)(MeOH)]$ with thermal ellipsoids drawn at the 30% probability level. One of the two crystallographically independent molecules is shown.

When the amount of Zn^{2+} was reduced to 1 equiv (i.e., 3 equiv per [3 + 3] macrocycle), the formation of insoluble materials considerably increased although [3 + 3] macrocycle **1** was still the major product. Obviously, Zn^{2+} acts as a template not only at the N_2O_2 site but also at the O_6 site. It is reasonable to consider that excess Zn^{2+} probably gathers three molecules of dialdehyde **2** to give a trimeric homometallic cluster $[L^2{}_3Zn_n]$. The subsequent treatment of the cluster with diamine **3** readily afforded the [3 + 3] macrocyclic complex $[L^1Zn_6]$, from which the metal-free [3 + 3] macrocycle **1** was isolated as a major product.

In summary, we synthesized [3 + 3] macrocyclic tris(salamo) ligand **1** by a one-pot procedure using a novel core/shell oligometallic template method. The method is applicable to the synthesis of well-defined homo- and heterometallic clusters, which may exhibit interesting magnetic and photochemical properties. Moreover, preliminary investigation showed that the isolated free [3 + 3] macrocycle again forms the $(3d)_6$ homometallic and $(3d)_3(4f)$ heterometallic clusters upon complexation with the corresponding 3d and/or 4f metal sources. Further investigation on such a metal-imprinting synthesis of clusters is now in progress.

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Supporting Information Available: X-ray crystallographic data for **1**·EtOH, $[L^2{}_3Zn_3La(NO_3)_2(MeOH)_6](NO_3)\cdot MeOH$, $[L^1Zn_3La(NO_3)_3(MeOH)_2]$, and $[L^1Zn_6(OAc)_5(OH)(MeOH)]\cdot 2MeOH\cdot 1.5H_2O$ in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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(17) Crystallographic data for $[L^1Zn_3La(NO_3)_3(MeOH)_2]$ (1245.69): orthorhombic, $Pca2_1$, a = 16.617(4) Å, b = 11.409(2) Å, c = 21.955(3) Å, V = 4162.3(14) Å^3, Z = 4, T = 120 K, R1 = 0.0232 [$I > 2\sigma(I)$], wR2 = 0.0511 (all data).[20]

(18) For related zinc−lanthanide complexes of salamo or acyclic oligo(salamo) ligands, see: (a) Akine, S.; Taniguchi, T.; Nabeshima, T. *Angew. Chem., Int. Ed.* **2002**, *41*, 4670−4673. (b) Akine, S.; Taniguchi, T.; Saiki, T.; Nabeshima, T. *J. Am. Chem. Soc.* **2005**, *127*, 540−541. (c) Akine, S.; Taniguchi, T.; Nabeshima, T. *Chem. Lett.* **2006**, *35*, 604−605. (d) Akine, S.; Taniguchi, T.; Matsumoto, T.; Nabeshima, T. *Chem. Commun.* **2006**, 4961−4963. See also ref 7b.

(19) Crystallographic data for $[L^1Zn_6(OAc)_5(OH)(MeOH)]\cdot 2MeOH\cdot 1.5H_2O$ (1488.15): triclinic, $P\bar{1}$, a = 14.503(5) Å, b = 18.608(5) Å, c = 21.841(6) Å, α = 101.521(10)°, β = 99.117(12)°, γ = 96.200(10)°, V = 5643(3) Å^3, Z = 4, T = 120 K, R1 = 0.0804 [$I > 2\sigma(I)$], wR2 = 0.2244 (all data).[20]

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