

Encapsulation of a guest molecule in a strained form: an extended 36-membered dodecanuclear manganese metallamacrocycle that accommodates a cyclooctane in the S_4 symmetry conformation†

Rohith P. John, Jaejoon Park, Dohyun Moon, Kyungjin Lee and Myoung Soo Lah*

Received (in Cambridge, UK) 31st May 2006, Accepted 11th July 2006

First published as an Advance Article on the web 31st July 2006

DOI: 10.1039/b607675k

An extended 36-membered dodecanuclear manganese metallamacrocycle with S_{12} symmetry has been synthesized using the ligand *N*-cyclohexanoylsalicylhydrazide ($H_3chxshz$) by a self-assembly that accommodates a cyclooctane of conformationally strained S_4 symmetry in its hydrophobic cavity.

Metallamacrocycles are an interesting class of compounds because of their diverse molecular architectures,¹ their utilization as motifs for coordination networks² and their potential as host systems in guest inclusion chemistry.³ Diaza-bridged macrocycles^{4–9}—termed metalladiazamacrocycles^{4a}—have received considerable interest because of their potential as secondary building blocks for the construction of two- or three-dimensional network structures.^{2c–e} These compounds can be readily assembled using the trianionic pentadentate ligand *N*-acylsalicylhydrazide with a metal ion such as manganese,^{4,5} iron,^{5–7} cobalt⁸ or gallium.⁷ We recently reported a dodecanuclear manganese metallamacrocycle with pentadentate ligand *N*-*trans*-2-pentenoysalicylhydrazide that could offer a geometric restriction at the *N*-terminal position of the ligand.^{4a} Even though the metalladiazamacrocycle is a 36-membered ring system, ring puckering led to the macrocycle containing no meaningful inner cavity for the accommodation of a guest.

To prepare metalladiazamacrocycles with a large inner cavity, we need to use a ligand with both a sterically rigid and bulky *N*-terminal group to prevent ring puckering. During our investigations, by modifying the *N*-terminal group to influence the size and nuclearity of metallamacrocycles, we identified that a cyclohexyl group would lead to a new type of dodecanuclear structure with a large enough hydrophobic inner cavity to accommodate small organic molecules. Even though several metallamacrocyclic systems with a central cavity have been reported, most of them are for anion or cation sequestration.^{3a–e} The inclusion of a hydrophobic organic molecule within the cavity of a metallamacrocycle is very rare.^{3f}

In this work we report a new 36-membered dodecanuclear manganese metalladiazamacrocycle, obtained by the use of steric restraint at the *N*-terminal position of the ligand. We also discuss the recognition of small hydrophobic organic molecules, such as benzene, cyclohexane and cyclooctane, and their behavior within the cavity.

Department of Chemistry and Applied Chemistry, Hanyang University, Ansan, Kyunggi-do, 426-791 Korea. E-mail: mslah@hanyang.ac.kr; Fax: +82 31 407 3863; Tel: +82 31 400 5496

† Electronic supplementary information (ESI) available: Experimental procedures and crystallographic details for the structure determination. See DOI: 10.1039/b607675k

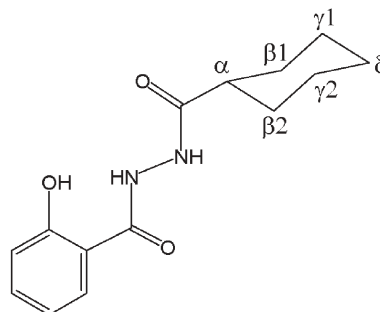


Fig. 1 Schematic diagram of the ligand $H_3chxshz$ with carbon atom labelling for the *N*-terminal group.

The ligand *N*-cyclohexanoylsalicylhydrazide ($H_3chxshz$) (Fig. 1) was synthesized by a procedure reported previously.⁴ Dark brown single crystals of $[Mn_{12}(chxshz)_{12}(MeOH)_{12}]$ (**1**) were obtained by slow diffusion of manganese(II) acetate into a solution of $H_3chxshz$.‡ The ligand binds to the metal in a back-to-back fashion, resulting in a dodecanuclear cyclic structure with successive metal centers in an alternating $\cdots\Lambda\Delta\Lambda\Delta\Lambda\Delta\cdots$ -type configuration, where the metallamacrocycle that lies at the crystallographic S_4 axis in $P4_2/n$ space group has three Mn–ligand moieties as an asymmetric unit (Fig. 2 and Fig. S1†). This alternating configuration of metal centers drives the extended

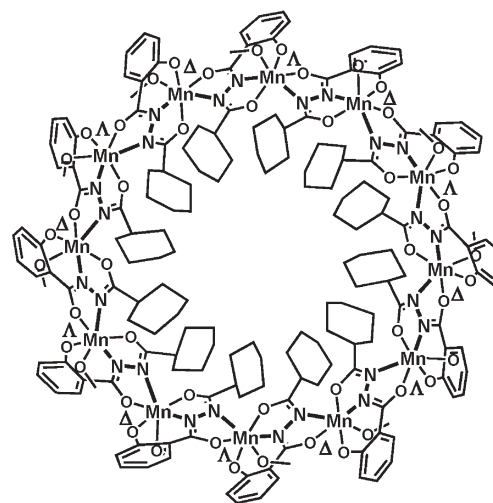


Fig. 2 Schematic diagram of a 36-membered dodecanuclear manganese metalladiazamacrocycle with Λ and Δ configurations for the alternating manganese centers.

structure to close at some point, resulting in a cyclic system. As all the *N*-cyclohexyl groups point to the inner core of the macrocycle, close contact interactions occur between alternate *N*-cyclohexyl groups. The size of the *N*-terminal group and its geometrical disposition determines the extent of close contact interactions. The choice of cyclohexyl as the *N*-terminal group offers directionally-rigid α , β , γ and δ carbon atoms, the arrangement of which leads to the formation of a dodecanuclear metallamacrocycle in an extended conformation. The adoption of a sequence of chiralities by a certain kind of macrocycle is triggered by the tendency of the system to choose the lowest energy macrocycle. In the case of the *N*-terminal group *N*-*trans*-2-pentenyl, a puckered dodecanuclear system of S_6 symmetry is the choice for the lowest energy macrocycle, where the chirality of the macrocycle varies in a $\cdots\Lambda\Lambda\Delta\Delta\Lambda\Lambda\Delta\Delta\cdots$ -type configuration. In the present instance, the preferred system is the extended dodecanuclear structure of S_{12} symmetry. This is due to the sterically rigid orientation of the two β -carbons, which the former lacks. The extended dodecanuclear metallamacrocycle system leaves a large enough hydrophobic inner cavity of the same S_{12} symmetry (the cavity dimensions are ~ 4 Å portal diameter, ~ 7 Å inner diameter and ~ 6 Å height) for the encapsulation of small organic molecules.

The crystal structure of **1** shows the presence of a disordered solvent molecule in the cavity, where the methyl group of the disordered methanol is in close contact with the *N*-cyclohexyl group of the ligand (Fig. S1†). This prompted us to probe the hydrophobic guest inclusion behavior of the macrocycle. As a follow-up, we tried to insert benzene into the cavity. The structural analyses of the isolated crystals, either prepared with benzene as a co-solvent or from the addition of benzene to the mother liquor after the growth of the crystals, did not show any evidence for the accommodation of benzene molecules in the inner cavity. However, in the case of cyclohexane as guest, we were able to isolate statically disordered cyclohexane trapped in the inner cavity of the dodecanuclear metallamacrocycle, regardless of the method of insertion (Fig. S2†). Even though the size of a cyclohexane molecule approximately matches that of the cavity, the guest's S_6 symmetry does not match the cavity's S_{12} or S_4 symmetry. The symmetry mismatch explains the static disorder of the captured cyclohexane within the cavity.

To investigate the shape or symmetry recognition of the host for guest molecules, we tried to insert a molecule of cyclooctane as a guest into the macrocyclic cavity, and were able to isolate crystals that comfortably accommodated it (Fig. 3). Even though the symmetry of cyclooctane in its most stable conformation is the extended S_8 symmetry, the cavity accommodates a disordered

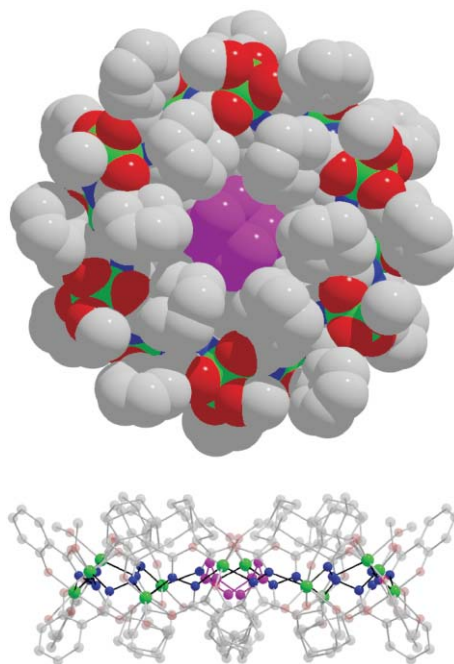


Fig. 3 Top: The CPK diagram of $[\text{Mn}_{12}(\text{chxshz})_{12}(\text{MeOH})_{12}] \supset \text{cyclooctane}$. The encapsulated cyclooctane is shown in purple. Bottom: A ball-and-stick diagram of a side view. The guest at the center of the metallamacrocycle (in purple) represents one of two disordered cyclooctane sites in a strained S_4 symmetry conformation. Mn (green), N (blue), O (red) and C (gray).

cyclooctane molecule in two different half-occupancy sites, both in their strained S_4 symmetry conformations (Fig S3†). This happens because the strained S_4 symmetry conformation of the guest matches one of the allowed cavity symmetries.

The guest encapsulation has a small effect on the overall host framework geometry. When the local geometry around the metal centers and the overall features of the macrocycle, such as the adjacent Mn1–Mn2 distance, the next-adjacent Mn1–Mn3 distance, the inversion symmetry-related Mn–Mn distances and the Mn1–Mn2–Mn3 angle, were compared, the differences in the average values were found to be within experimental error ranges (Table 1 and Fig. S4†). However, the cavity dimensions of the metallamacrocycles changed, depending on the size and shape of the guest molecule. When a cyclohexane was accommodated, small increases in portal diameter and height of the cavity were observed but were within experimental error range (Table 1). However, when the cyclooctane was encapsulated in the cavity in a

Table 1 Comparisons of the geometrical features of the metalladiazamacrocycles with guest molecules

	1	1 ⊃ cyclohexane	1 ⊃ cyclooctane
Mn1–Mn2/Å ^a	4.84(3)	4.85(4)	4.83(4)
Mn1–Mn3/Å ^b	8.90(7)	8.94(7)	8.91(6)
Mn–Mn/Å ^c	17.78(3)	17.86(10)	17.80(9)
Mn1–Mn2–Mn3/°	134(2)	134(2)	134(2)
Portal diameter of cavity/Å ^d	~4.1(1)	~4.2(1)	~4.4(2)
Cavity height/Å ^e	~6.0(2)	~6.1(1)	~6.4(1)

^a The distance between adjacent metal centers in the ring system. ^b The distance between next-adjacent metal centers in the ring system. ^c The distance between inversion symmetry-related metal centers in the ring system. ^d The portal of the cavity was formed of the six C_6 symmetry-related γ -hydrogen atoms of the *N*-terminal cyclohexyl groups. ^e The height of the cavity was calculated from the distance between the close-lying γ -carbons (S_{12} symmetry-related γ carbons) of cyclohexyl groups located on opposite sides of the portal cavity.

strained S_4 symmetry conformation, marginal increases both in the portal diameter and the height of the cavity were observed. The increase in the cavity dimensions were achieved by modulation of the rather flexible N -cyclohexyl groups of the ligands.

In this study, we were able to prepare a metallamacrocyclic with a large enough hydrophobic cavity to accommodate small organic molecules. The encapsulation of guest molecules of sizes larger than the portal diameter suggests that the portal has some degree of flexibility. In addition, the cavity distinguishes guest molecules based on their size and shape/symmetry. The failure to observe benzene encapsulation might be due to the smaller size of the guest compared to the cavity size. Cyclohexane, of matching size, could be accommodated in a chair conformation with disorder, even though the symmetry of the guest did not match that of the cavity. Meanwhile, cyclooctane could be encapsulated only in its conformationally-strained S_4 symmetry conformation.

This work was supported by KRF (KRF-2005-070-C00068), ITEP (M1-0213-03-0004), KOSEF (R01-2005-000-10490-0) and CBMH. The authors also acknowledge PAL for beam line use (2005-3063-10).

Notes and references

‡ **Crystal data for $[\text{Mn}_{12}(\text{chxshz})_{12}(\text{MeOH})_{12}] \cdot 12(\text{DMF}) \cdot 2(\text{H}_2\text{O}) \cdot 4.5(\text{MeOH})$ (1):** $\text{Mn}_{12}\text{C}_{220.5}\text{H}_{334}\text{N}_{36}\text{O}_{66.5}$, $M = 5212.54 \text{ g mol}^{-1}$, tetragonal, space group $P4_2/n$, $a = b = 27.0406(3)$, $c = 18.7658(3) \text{ \AA}$, $V = 13721.4(3) \text{ \AA}^3$, $T = -173(2) \text{ }^\circ\text{C}$, $Z = 2$, $\mu(\text{synchrotron}, \lambda = 0.82657 \text{ \AA}) = 0.592 \text{ mm}^{-1}$, 55375 reflections measured, 7501 unique ($R_{\text{int}} = 0.0355$) which were used in all calculations. The final $R1$ was 0.0874 for observed data with $I > 2\sigma(I)$. Structure refinement following modification of the data with the SQUEEZE routine in PLATON:¹⁰ $R1 = 0.0548$ ($I > 2\sigma(I)$), $wR2 = 0.1777$, $\text{GOF} = 1.091$, max./min. residual electron density $0.693/-0.420 \text{ e \AA}^{-3}$. CCDC 298633.

Crystal data for 1 \supset cyclohexane: $\text{Mn}_{12}\text{C}_{186}\text{H}_{240}\text{N}_{24}\text{O}_{48}$, $M = 4239.30 \text{ g mol}^{-1}$, tetragonal, space group $P4_2/n$, $a = b = 27.189(3)$, $c = 18.904(4) \text{ \AA}$, $V = 13974(3) \text{ \AA}^3$, $T = -173(2) \text{ }^\circ\text{C}$, $Z = 2$, $\mu(\text{Mo-K}\alpha, \lambda = 0.71073 \text{ \AA}) = 0.580 \text{ mm}^{-1}$, 67612 reflections measured, 16082 unique ($R_{\text{int}} = 0.0683$). The final $R1$ was 0.1403 for observed data with $I > 2\sigma(I)$. Structure refinement following modification of the data with the SQUEEZE routine in PLATON:¹⁰ $R1 = 0.0853$ ($I > 2\sigma(I)$), $wR2 = 0.1957$, $\text{GOF} = 1.057$, max./min. residual electron density $0.796/-0.617 \text{ e \AA}^{-3}$. CCDC 298634.

Crystal data for 1 \supset cyclooctane: $\text{Mn}_{12}\text{C}_{188}\text{H}_{244}\text{N}_{24}\text{O}_{48}$, $M = 4267.35 \text{ g mol}^{-1}$, tetragonal, space group $P4_2/n$, $a = b = 27.073(2)$, $c = 18.909(3) \text{ \AA}$, $V = 13860(3) \text{ \AA}^3$, $T = -173(2) \text{ }^\circ\text{C}$, $Z = 2$, $\mu(\text{Mo-K}\alpha, \lambda = 0.71073 \text{ \AA}) = 0.586 \text{ mm}^{-1}$, 71393 reflections measured, 16854 unique ($R_{\text{int}} = 0.0745$). The final $R1$ was 0.1438 for observed data with $I > 2\sigma(I)$. Structure refinement following modification of the data with the SQUEEZE routine in PLATON:¹⁰ $R1 = 0.0948$ ($I > 2\sigma(I)$), $wR2 = 0.2394$, $\text{GOF} = 1.061$, max./min. residual electron density $0.873/-0.711 \text{ e \AA}^{-3}$. CCDC 298635.

For crystallographic data in CIF or other electronic format see DOI: 10.1039/b607675k

- (a) V. L. Pecoraro, A. J. Stemmler, B. R. Gibbney, J. J. Bodwin, H. Wang, J. W. Kampf and A. Barwinski, *Prog. Inorg. Chem.*, 1997, **45**, 83–177; (b) T. Liu, E. Diemann, H. Li, A. W. M. Dress and A. Müller, *Nature*, 2003, **426**, 59–62; (c) C.-Y. Su, Y.-P. Cai, C.-L. Chen, M. D. Smith, W. Kaim and H.-C. Loye, *J. Am. Chem. Soc.*, 2003, **125**, 8595–8613; (d) A. J. Tasiopoulos, A. Vinslava, W. Wernsdorfer, K. A. Abboud and G. Christou, *Angew. Chem., Int. Ed.*, 2004, **43**, 2117–2121; (e) C. L. M. Pereira, E. F. Pedroso, H. O. Stumpf, M. A. Novak, L. Ricard, R. R. Garcia, E. Riviere and Y. Journaux, *Angew. Chem., Int. Ed.*, 2004, **43**, 956–958; (f) R.-D. Schnebeck, E. Freisinger, F. Glahe and B. Lippert, *J. Am. Chem. Soc.*, 2000, **122**, 1381–1390; (g) K. Campbell, C. A. Johnson, II, R. McDonald, M. J. Ferguson, M. M. Haley and R. R. Tykwinski, *Angew. Chem., Int. Ed.*, 2004, **43**, 5967–5971; (h) U. Patel, H. B. Singh and G. Wolmershäuser, *Angew. Chem., Int. Ed.*, 2005, **44**, 1715–1717; (i) L. F. Jones, A. Batsanov, E. K. Brechin, D. Collison, M. Helliwell, T. Mallah, E. J. L. McInnes and S. Piligkos, *Angew. Chem., Int. Ed.*, 2002, **41**, 4318–4321; (j) O. Hallale, S. A. Bourne and K. R. Koch, *CrystEngComm*, 2005, **7**, 161–166.
- (a) S. R. Halper and S. M. Cohen, *Angew. Chem., Int. Ed.*, 2004, **43**, 2385–2388; (b) C.-Y. Su, X.-P. Yang, B.-S. Kang and T. C. W. Mak, *Angew. Chem., Int. Ed.*, 2001, **40**, 1725–1728; (c) M. Moon, I. Kim and M. S. Lah, *Inorg. Chem.*, 2000, **39**, 2710–2711; (d) D. Moon, J. Song, B. J. Kim, B. J. Suh and M. S. Lah, *Inorg. Chem.*, 2004, **43**, 8230–8232; (e) D. Moon and M. S. Lah, *Inorg. Chem.*, 2005, **44**, 1934–1940.
- (a) G. Mezei, P. Baran and R. G. Raptis, *Angew. Chem., Int. Ed.*, 2004, **43**, 574–577; (b) R. V. Slone, K. D. Benkstein, S. Bélanger, J. T. Hupp, I. A. Guzei and A. L. Rheingold, *Coord. Chem. Rev.*, 1998, **171**, 221–243; (c) J. J. Bodwin, A. D. Cutland, R. G. Malkani and V. L. Pecoraro, *Coord. Chem. Rev.*, 2001, **216–217**, 489–512; (d) M. Willermann, C. Mulcahy, R. K. O. Sigel, M. M. Cerdà, E. Freisinger, P. J. S. Miguel, M. Roitzsch and B. Lippert, *Inorg. Chem.*, 2006, **45**, 2093–2099; (e) K. Severin, *Coord. Chem. Rev.*, 2003, **245**, 3–10; (f) J. Overgaard, B. B. Iversen, S. P. Pali, G. A. Timco, N. V. Gerbeleu and F. K. Larsen, *Chem.–Eur. J.*, 2002, **8**, 2775–2786; (g) M.-L. Lehaire, R. Scopelliti and K. Severin, *Inorg. Chem.*, 2002, **41**, 5466–5474.
- (a) R. P. John, K. J. Lee and M. S. Lah, *Chem. Commun.*, 2004, 2660–2661; (b) R. P. John, K. J. Lee, B. J. Kim, B. J. Suh, H. Rhee and M. S. Lah, *Inorg. Chem.*, 2005, **44**, 7109–7121; (c) B. Kwak, H. Rhee, S. Park and M. S. Lah, *Inorg. Chem.*, 1998, **37**, 3599–3602; (d) B. Kwak, H. Rhee, S. Park and M. S. Lah, *Polyhedron*, 2000, **19**, 1985–1994.
- S.-X. Liu, S. Lin, B.-Z. Lin, C.-C. Lin and J.-Q. Huang, *Angew. Chem., Int. Ed.*, 2001, **40**, 1084–1087.
- S. Lin, S.-X. Liu, Z. Chen, B.-Z. Lin and S. Gao, *Inorg. Chem.*, 2004, **43**, 2222–2224.
- I. Kim, B. Kwak and M. S. Lah, *Inorg. Chim. Acta*, 2001, **317**, 12–20.
- S. Lin, S.-X. Liu, J.-Q. Huang and C.-C. Lin, *J. Chem. Soc., Dalton Trans.*, 2002, 1595–1601.
- Y. Bai, D. Dang, C. Duan, Y. Song and Q. Meng, *Inorg. Chem.*, 2005, **44**, 5972–5974.
- A. L. Spek, *Acta Crystallogr., Sect. A: Found. Crystallogr.*, 1990, **46**, 194–201.