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Self-assembled Porphyrin-based Cage Complexes, M₁₁L₆ (M = Zn^{II}, Cd^{II}), with Inner Coordination Sites in Their Crystal Structure

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Herein we report self-assembled metallo-cage complexes, M_{11} (L1)₆ (M = Zn^{II}, Cd^{II}), formed from 4-fold-symmetric Zn^{II}-porphyrin-centered tetrakis-*meso*-(5'metallo-cage 23 methyl-2,2'-bipyridyl) ligands. The structures of these two 4 5 D_3 -symmetric cages have been characterized by 1D and 2D 6 NMR, ESI-MS, and XRD analyses. A common structural feature of these complexes is their inner molecular binding 8 site at the axial position of each square-pyramidal Zn 0 porphyrin in the crystal structure, which would provide a 10 method to place molecular coordination sites inside or 11 outside the cage complex with the minimum chemical 12 modification.

Keywords: Supramolecular Cage Complexes, Multi-metal Centers, Porphyrin

15 Coordination-driven self-assembly is a powerful tool to 16 construct cage-shaped metal complexes with a nano-sized 17 interior space as a platform for space-specific molecular 18 recognition and reactions. Although a large number of 19 excellent examples of metallo-cage complexes have been reported so far,¹⁻⁷ it is still a challenge to precisely arrange 20 molecular binding sites on the inner surface. A chemically 21 22 functionalized confined space with internal molecular 23 binding sites, as can be seen in the internal binding pockets 24 of a variety of metallo-enzymes, is a necessary requirement 25 to acquire functional spaces with high efficiency and 26 selectivity.

27 Recently, porphyrin-based self-assembled architectures, 28 in particular, cage complexes have attracted a lot of attention 29 because of the porphyrin-specific photochemical and redox functions.^{8–19} Typical examples are *O*-symmetric cubic cage 30 M₈L₆ complexes with eight chemically equivalent metal 31 centers as formed from 4-fold symmetric porphyrin-based ligands and metal ions.¹⁰⁻¹² In contrast, as we previously 32 33 reported,¹⁷ a self-assembled cage complex L0-Zn₁₁ with 34 similar 4-fold symmetric porphyrin-based ligands ($L0 = Zn^{II}$ -35 36 porphyrin-centered tetrakis-meso-(2,2'-bipyridyl) ligand, Figure 1a) has a lower symmetry with three types of metal 37 centers.²⁰ This D_3 symmetric $M_{11}L_6$ type complex, 38 39 $Zn_{11}(L0 \cdot H_2O)_6(H_2O)_{18}(OTf)_{22}$ (L0-Zn₁₁), formed from the C_{4v} symmetric porphyrin ligand L0 and Zn(OTf)₂, exhibits its 40 41 ability to unsymmetrically encapsulate guest molecules (Tf= 42 trifluoromethanesulfonyl).¹⁷ However, in the crystal structure, 43 the axial ligands bind only from outside the cage to the Zn^{II}-44 porphyrin centers, and there is no convincing evidence for 45 inward binding of coordinating molecules to the Zn^{II}-46 porphyrin center. Herein we report the effects of chemical modification of the porphyrin ligand from L0 to 47 48 tetramethylated L1 to improve the solubility and coordination 49 ability of the ligand. As a result, two isostructural $M_{11}(L1 \cdot CH_3OH)_6(H_2O)_{18}(OTf)_{22}$ (M = Cd^{II} or Zn^{II}) cage 50

51 complexes, L1- Zn_{11} and L1- Cd_{11} , having six sites to which

52 an included molecule is bonded were obtained (Figure 1b).



57 The Zn^{II} -porphyrin ligand L1·H₂O, a tetramethyl 58 derivative of L0 H₂O, was synthesized from 5'-methyl-2,2'-59 bipyridyl-5-carboxyaldehyde and pyrrole via Adler synthesis 60 and successive complexation with Zn(OAc)2 (H2O)2 in 6.6% 61 overall yield (Supporting Information S3), and characterized 62 by NMR, ESI-TOF MS, and elemental analyses. The C_{4y} 63 symmetric structure of L1 H₂O was confirmed by ¹H NMR 64 spectroscopy (Figure 2a).

65 Firstly, L1-Zn₁₁ was synthesized by complexation of 66 L1·H₂O with 11/6 eq. Zn(OTf)₂ in an aqueous mixed solvent, 67 $CHCl_3/CH_3OH/H_2O = 10.10.1 (v/v/v)$. The reaction mixture 68 was heated at 50 °C for 24 h. L1-Zn11 was isolated by 69 precipitation with Et₂O as a dark-green solid in 78% yield. 70 The ¹H NMR spectrum of L1-Zn₁₁ in CDCl₃/CD₃OD/D₂O = 71 10:10:1 (v/v/v) showed 32 signals in the aromatic region and 72 4 singlet signals in the alkyl region, suggesting the presence 73 of a C_1 symmetric L1 ligand in the self-assembled structure 74 (Figure 2b). This spectrum was in stark contrast with a simple 75 spectrum of ligand L1 with a C_{4v} symmetry. Each ¹H signal 76 was fully assigned by ¹H-¹H COSY (Figure S9) and ¹H-¹H 77 NOESY spectra (Figures S10 and S11). The interligand NOE

1 patterns of L1-Zn₁₁ (g_1 - g'_2 , g'_1 - g_2 , a_2 - a_4 , f_2 - f_4 , g_2 - f_4 , a_3 - f_3 , d_3 -2 g_3, d_3 -g'₃) were well matched with those of the previously 3 reported Moreover, the L0-Zn₁₁. presence of 4 $[Zn_{11}L1_6(OTf)_{22-n}]^{n+}$ (n = 5-7) in solution was verified by 5 ESI-MS spectrometry (Figure S14). L1-Zn₁₁ was further characterized by ¹H DOSY (Figure S12), ¹⁹F NMR (Figure 6 S13), and elemental analyses (Supporting Information S13). 7



Figure 2. a)–c) ¹H NMR spectra of L1·H₂O, L1-Zn₁₁, and L1-Cd₁₁ (500 10 MHz, 300 K, CDCl₃/CD₃OD/D₂O = 10:10:1 (v/v/v)). d) X-ray crystal structure of [L1-Cd₁₁]²²⁺ in which one Zn^{II}-porphyrin is highlighted and color-coded in red, yellow, green, and blue to illustrate a C_1 symmetry in [Cd₁₁L1₆]²²⁺. e) Chemical structure and assignment of each hydrogen atom of L1. Colours are coded according to the structure in (d).

8

15 Next, to examine the effects of metal exchange on the self-assembly, we selected Cd^{II} as a zinc group element. Cd^{II} 16 has a larger ionic radius (ca. 0.95 Å) in an octahedral 17 hexacoordinate geometry than that of Zn^{II} (ca. 0.74 Å).²¹ In 18 spite of the larger ionic radius of Cd^{II} and the smaller binding 19 20 constants of $Cd^{II}(bpy)_n$ compared with those of $Zn^{II}(bpy)_n$ 21 (log β for Cd^{II}(bpy)_n = 10.3 (n = 3) and 7.7 (n = 2); log β for $Zn^{II}(bpy)_n = 13.2 \ (n = 3) \text{ and } 9.5 \ (n = 2))^{22}$ an isostructural 22 23 L1-Cd₁₁ was successfully obtained. Ligand L1·H₂O was 24 reacted with 11/6 eq. Cd(OTf)₂·H₂O in a mixed solvent, 25 $CDCl_3/CD_3OD/D_2O = 10.10.1$ (v/v/v). The reaction mixture was heated at 50 °C for 17 h. L1-Cd11 was isolated by 26 27 precipitation with Et₂O as a purple solid in 70% yield. In 28 contrast, a mixture of ligand L0 H₂O without methyl 29 substituents of bipyridyl moieties and Cd^{II} did not afford any 30 isostructural cage complexes (Figure S24). The ¹H NMR 31 spectrum of isolated L1-Cd₁₁ in CDCl₃/CD₃OD/D₂O = 32 10:10:1 (v/v/v) showed 32 signals in the aromatic region and 33 4 singlet signals in the alkyl region, suggesting the presence of a C_1 symmetric L1·H₂O ligand in the self-assembled 34 35 structure (Figure 2c). Each ¹H signals were fully assigned by ¹H-¹H COSY (Figure S16) and ¹H-¹H NOESY spectra 36 37 (Figures S17 and S18). The interligand NOE patterns of L138 Cd_{11} , $(g_1-g'_2, g'_1-g_2, a_2-a_4, f_2-f_4, g_2-f_4, a_3-f_3, d_3-g_3, d_3-g'_3)$ were 39 identical with those of L1-Zn₁₁. However, in comparison 40 with these two complexes, some proton signals were 41 significantly shifted. For L1-Zn₁₁, the protons of the pyridyl 42 groups (e, f) attached to the Zn^{II}-porphyrin ring at the *meso* 43 positions showed downfield shift for f_3 and f_4 (0.28 and 0.19 44 ppm, respectively) and upfield shift for e_2 and e_4 (0.19 and 45 0.12 ppm, respectively). Some other signals also shifted. 46 though to lesser extent. However, it is rather difficult to give 47 a general explanation regarding the direction of the signal 48 shifts. This is because there are a few factors, affecting the 49 chemical environment of each proton, such as the different 50 electronic perturbation from Zn^{II} and Cd^{II}, and the structural 51 distortion due to the larger-sized Cd^{II}. Moreover, the presence 52 of $[Cd_{11}L1_6(OTf)_{22-n}]^{n+}$ (n = 5–7) in solution was verified by ESI-MS spectrometry (Figure S21). L1-Cd₁₁ was further 53 54 characterized by ¹H DOSY (Figure S19), ¹⁹F NMR (Figure 55 S20), and elemental analyses (Supporting Information S14). 56 The structures of L1-Zn₁₁ and L1-Cd₁₁ were 57 determined by single-crystal XRD analyses (Figure 3).22



Figure 3. X-ray crystal structures of a) $L1-Zn_{11}$ and b) $L1-Cd_{11}$. TfO⁻⁶⁰ ions are omitted for clarity. Zn^{II} and Cd^{II} ions are illustrated with the space filling model, Zn^{II}-porphyrin core skeletons with the bold stick model, and the other atoms with the stick model. Colours are coded according to the CPK colouring. Only a $\Delta\Delta\Delta\Delta\Delta\Delta$ isomer is shown here.

64 Violet crystals of L1-Zn₁₁ and L1-Cd₁₁ suitable for XRD 65 analysis were obtained by vapor diffusion of Et₂O into a 66 solution of L1-Zn₁₁ or L1-Cd₁₁ in CDCl₃/CD₃OD/D₂O = 67 10:10:1 (v/v/v), respectively. As shown in Figure 3, both $[Zn_{11}(L1 \cdot CH_3OH)_6(H_2O)_{18}]^{22+}$ 68 and [Cd₁₁(L1·CH₃OH)₆(H₂O)₁₈]²²⁺ moieties contain six ligands 69 70 L1 and eleven Zn^{II} or Cd^{II} ions. For their counter anions, only 71 six TfO⁻ ions were solved and the remaining sixteen TfO⁻ ion 72 were not due to their high disorder. L1-Zn₁₁ has three distinct

Zn^{II} centers, that is, one Zn^{II}(bpy)₃ (Zn1) and two 1 2 Zn^{II}(bpy)₂(H₂O)₂ (Zn2, Zn3). L1-Cd₁₁ has a similar structural 3 framework with three distinct Cd^{II} centers, one Cd^{II}(bpy)₃ 4 (Cd1) and two Cd^{II}(bpy)₂ (H₂O)₂ (Cd2, Cd3). Each racemic 5 crystal with a space group R-3c (No. 167) contains two 6 enantiomers with $\Delta \Delta \Delta \Delta \Delta$ and $\Delta \Delta \Delta \Delta \Lambda$ configurations at the metal centers bound by bpy as shown in Figure 3. Notably, in 7 8 both L1-Zn₁₁ and L1-Cd₁₁, one CH₃OH molecule 9 coordinates to each Zn^{II}-porphyrin center at the axial position 10 from inside the cavity, whereas, in the previously reported L0-Zn11, one H₂O molecule coordinates from outside the 11 12 cavity in the crystal state (Figure 4).





¹³

14 Figure 4. Comparison between L0-Zn11, L1-Zn11, and L1-Cd11 in the 15 crystal structures: X-ray crystal structures (left: side view, right: top 16 view) and the positions of the axial ligands on the Zn^{II}-porphyrins. a) X-17 ray crystal structures of L0-Zn₁₁ with six H₂O molecules as the axial 18 ligands bound to the Zn^{II}-porphyrin from outside. b) X-ray crystal 19 structures of L1-Zn11 and L1-Cd11, each with six CH3OH molecules as 20 the axial ligands bound to the Zn^{II}-porphyrin from *inside*. The core 21 22 structures with Zn^{II} porphyrins and the axial ligands are shown in bold stick, and the other moieties in line.

23 The most attractive, common feature of these two cage 24 complexes, L1-Zn₁₁ and L1-Cd₁₁, is the presence of six inner 25 molecular coordination sites in their crystal structure, which could enable the direct binding of included coordinating 26 27 guest molecules to Zn^{II}-porphyrin. Indeed, the inner space of 28 each cage complex has two sets of three adjacent CH₃OH 29 molecules bound to each Zn^{II}-porphyrin center, which are 30 distantly positioned with a distance of 11~12 Å. By the introduction of methyl groups onto the 5'-positions of bpy 31 moieties of methyl-free ligand L0, the space group R32 for 32

the crystal of L0-Zn₁₁ was changed into the space group R-33 34 3c (#167) for those of L1-Zn₁₁ and L1-Cd₁₁. More 35 specifically, one bpy group of an $L1-Zn_{11}$ (or $L1-Cd_{11}$) 36 complex gets close to the porphyrin ring of adjacent L1-Zn₁₁ 37 (or $L1-Cd_{11}$) in the crystal packing, and therefore the 38 coordination of axial CH₃OH ligands from inside should be 39 more favorable with L1-Zn₁₁ and L1-Cd₁₁.

40 The structural frameworks of L1-Zn₁₁ and L1-Cd₁₁ 41 appear to be maintained in solution as confirmed by NMR 42 and ESI-MS analyses. However, the possibility of flip-out of 43 the axial positions on the square-pyramidal Zn^{II}-porphyrins 44 of L1-Zn₁₁ and L1-Cd₁₁ in solution remain unclear due to the 45 fast axial ligand exchange in solution.

46 Figure 5 compares L1-Zn₁₁ and L1-Cd₁₁ (Figure 5a and 47 5b, respectively) for the distances between two metal centers 48 bound by bpy: for L1-Zn₁₁, Zn1-Zn1 = 27.455 Å, Zn1-Zn2 = 49 12.331 Å, and Zn2-Zn3 = 11.860 Å and 12.581 Å, and for 50 $L1-Cd_{11}$, Cd1-Cd1 = 27.745 Å, Cd1-Cd2 = 12.678 Å, and 51 Cd2-Cd3 = 11.867 Å and 12.473 Å.



53 Figure 5. Structural comparison between L1-Zn₁₁ (a) and L1-Cd₁₁ (b) 54 for the distances (Å) between two metal centers bound by bpy when seen 55 from the C_2 and C_3 axes.

56 The angles between three metal centers were also calculated; 57 for L1-Zn₁₁, \angle Zn2-Zn3-Zn2 = 64.33°, \angle Zn4-Zn3-Zn4 = 58 98.31°, and for L1-Cd₁₁, \angle Cd2-Cd3-Cd2 = 61.60°, \angle Cd3-59 $Cd2-Cd3 = 100.07^{\circ}$ (Figures S34 and S35). These results indicate that the whole structure of $L1-Cd_{11}$ is elongated 60 61 along C_3 -axis compared with L1-Zn₁₁ mainly due to the larger ionic radius of Cd^{II}. Regardless of this structural 62 63 change, the inner volume of L1-Cd₁₁, 509 Å³, was almost the 64 same as that of L1-Zn₁₁, 511 Å³ (4.0 Å Connolly radius was 65 used as a prove).

66 Guest encapsulation of L1-Zn₁₁ and L1-Cd₁₁ in 67 $CDCl_3/CD_3OD/D_2O = 10:10:1 (v/v/v)$ was then preliminarily 68 examined with 2,7-dinitro-9-fluorenone as a guest molecule 69 (Figures S25–S30). However, the quantitative analysis was 70 practically difficult due to the low solubility of 2,7-dinitro-9fluorenone in the solvent.

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In conclusion, we have newly synthesized two 1 2 isostructural M₁₁L₆ complexes, L1-Zn₁₁ and L1-Cd₁₁, from 3 4-fold-symmetric Zn^{II}-porphyrin-centered tetrakis-meso-(5'-4 methyl-2,2'-bipyridyl) ligands (L1) and metal ions. The self-5 assembled cage structures were characterized by NMR, ESI-6 MS, and XRD analyses. A common feature of these 7 isostructural L1-Zn₁₁ and L1-Cd₁₁ complexes is the presence 8 of their inner molecular coordination sites on the Zn^{II}-9 porphyrin centers in the nano-sized cage structures. Such an 10 approach would develop metallo-porphyrins that work as 11 catalysts in a confined space.

12

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15 16

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20 **References and Notes**

- Present address: Division of Chemistry, Faculty of Pure and Applied Science, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki 305-8571, Japan.
- 1 Supramolecular Chemistry, 2nd ed., ed. by J. W. Steed, J. L. Atwood, Wiley-VCH, New York, 2009.
- 2 a) R. Chakrabarty, P. S. Mukherjee, P. J. Stang, Chem. Rev. 2011, 111, 6810. b) P. J. Stang, J. Am. Chem. Soc. 2012, 134, 11829. c) T. R. Cook, P. J. Stang, Chem. Rev. 2015, 115, 7001.
- Z. Laughreya, B. C. Gibb, Chem. Soc. Rev. 2011, 40, 363 3
- 4 S. Zarra, D. M. Wood, D. A. Roberts, J. R. Nitschke, Chem. Soc. Rev. 2015, 44, 419.
- 5 Y. Fang, J. A. Powell, E. Li, Q. Wang, Z. Perry, A. Kirchon, X. Yang, Z. Xiao, C. Zhu, L. Zhang, F. Huang, H.-C. Zhou, Chem. Soc. Rev. 2019, 48, 4707.
- A. Galana, P. Ballester, Chem. Soc. Rev. 2016, 45, 1720. 6
- L.-J. Chen, H.-B. Yang, M. Shionoya, Chem. Soc. Rev. 2017, 46, 7 2555
- 8 J. A. Wytko, R. Ruppert, C. Jeandon, J. Weiss, Chem. Commun. 2018, 54, 1550.
- 9 S. Durot, J. Taesch, V. Heitz, Chem. Rev. 2014, 114, 8542.
- $\begin{array}{c} 21223456789012223456789012333335678900\\ 3333333333344423445678901\\ 512334555555600 \end{array}$ a) W. Meng, B. Breiner, K. Rissanen, J. D. Thoburn, J. K. Clegg, 10 J. R. Nitschke, Angew. Chem. Int. Ed. 2011, 50, 3479. b) J. Mosquera, B. Szyszko, S. K. Y. Ho, J. R. Nitschke, Nat. Commun. 2017, 8, 14882. c) W. Brenner, T. K. Ronson, J. R. Nitschke, J. Am. Chem. Soc. 2017, 139, 75. d) E. G. Percástegui, J. Mosquera, J. R. Nitschke, Angew. Chem. Int. Ed. 2017, 56, 9136.
- a) M. Otte, P. F. Kuijpers, O. Troeppner, I. Ivanović-Burmazović, 11 J. N. H. Reek, B. de Bruin, Chem. Eur. J. 2013, 19, 10170. b) M. Otte, P. F. Kuijpers, O. Troeppner, I. Ivanović -Burmazović, J. N. H. Reek, B. de Bruin, Chem. Eur. J. 2014, 20, 4880.
- 12 N. Struch, C. Bannwarth, T. K. Ronson, Y. Lorenz, B. Mienert, N. Wagner, M. Engeser, E. Bill, R. Puttreddy, K. Rissanen, J. Beck, S. Grimme, J. R. Nitschke, A. Lützen, Angew. Chem. Int. Ed. 2017, 56, 4930.
- 13 C. S. Wood, C. Browne, D. M. Wood, J. R. Nitschke, ACS Cent. Sci. 2015, 1, 504.
- 14 a) S. P. Black, D. M. Wood, F. B. Schwarz, T. K. Ronson, J. J. Holstein, A. R. Stefankiewicz, C. A. Schalley, J. K. M. Sanders, J. R. Nitschke, Chem. Sci. 2016, 7, 2614. b) D. M. Wood, W. Meng, T. K. Ronson, A. R. Stefankiewicz, J. K. M. Sanders, J. R. 61 Nitschke, Angew. Chem. Int. Ed. 2015, 54, 3988. c) F. J. Rizzuto, D. M. Wood, T. K. Ronson, J. R. Nitschke, J. Am. Chem. Soc. 62 63 2017, 139, 11008.

- 64 15 a) F. J. Rizzuto, J. R. Nitschke, Nat. Chem. 2017, 9, 903. b) F. J. 65 Rizzuto, W. J. Ramsay, J. R. Nitschke, J. Am. Chem. Soc. 2018, 66 140 11502
- 67 16 G. Jayamurugan, D. A. Roberts, T. K. Ronson, J. R. Nitschke, 68 Angew. Chem. Int. Ed. 2015, 54, 7539
 - 17 a) T. Nakamura, H. Ube, M. Shiro, M. Shionoya, Angew. Chem. Int. Ed. 2013, 52, 720. b) T. Nakamura, H. Ube, M. Shionoya, Chem. Lett. 2013, 42, 328.
 - 18 T. Nakamura, H. Ube, R. Miyake, M. Shionoya, J. Am. Chem. Soc. 2013, 135, 18790.
 - 19 H. Ube, K. Endo, H. Sato, M. Shionoya, J. Am. Chem. Soc. 2019, 141, 10384.
- 69 70 71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 20 (a) D. Fujita, Y. Ueda, S. Sato, N. Mizuno, T. Kumasaka, M. Fujita, Nature 2016, 540, 563. (b) D. Fujita, Y. Ueda, S. Sato, H. Yokoyama, N. Mizuno, T. Kumasama, M. Fujita, Chem 2016, 1, 91. (c) A. J. Metherell, M. D. Ward Chem. Sci., 2016, 7, 910. (d) S. P. Argent, H. Adams, T. Riis-Johannessen, J. C. Jeffery, L. P. Harding, M. D. Ward. J. Am. Chem. Soc. 2006, 128, 72.
 - 21 CRC Handbook of Chemistry and Physics 98th Ed., ed. by John R. Rumble, CRC press, Boca Raton, 2017.
 - Critical Stability Constants vol. 2, ed. by R. M. Smith, A. E. 22 Martell, Plenum Press, New York, 1975.
- 23 CCDC 1967765 (L1-Cd11), and 1967766 (L1-Zn11) contain the supplementary crystallographic data for this paper. These data are 88 provided free of charge by the Cambridge Crystallographic Data 89 Centre: https://www.ccdc.cam.ac.uk/.