JOC Article

Recognition through Self-Assembly. A Quadruply-Hydrogen-Bonded, Strapped Porphyrin Cleft That Binds Dipyridyl Molecules and a [2]Rotaxane

Xue-Bin Shao,[†] Xi-Kui Jiang,[†] Xin Zhao,[†] Cheng-Xue Zhao,[‡] Yan Chen,[‡] and Zhan-Ting Li*,[†]

Shanghai Institute of Organic Chemistry (SIOC), Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China, and Department of Chemistry, Shanghai Jiaotong University, 800 Dongchuan Lu, Shanghai 200240, China

ztli@mail.sioc.ac.cn

Received August 12, 2003

Quadruply-hydrogen-bonded porphyrin homodimer **Zn1·Zn1** has been designed, assembled, and evaluated as a supramolecular cleft-featured receptor for its ability to bind dipyridyl guests in chloroform-*d*. Monomer **Zn1** consists of a 2-ureidopyrimidin-4(1*H*)-one unit, which was initially reported by Meijer et al., and a zinc porphyrin unit. The zinc porphyrin is strapped with an additional aliphatic chain for controlling the atropisomerization of porphyrin. The 2-ureidopyrimidin-4(1*H*)-one unit dimerizes exclusively in chloroform even at the dilute concentration of 10^{-4} M, while the two "strapped" zinc porphyrin units of the homodimer provide additional binding sites for selective guest recognition. ^{1}H NMR studies indicate that the new homodimer **Zn1·Zn1** adopts an S-type conformation due to strong donor−acceptor interaction between the electron-rich porphyrin units and the electron-deficient 2-ureidopyrimidin-4(1*H*)-one unit. ^{1}H NMR, UV−vis, and vapor pressure osmometry investigations reveal that **Zn1·Zn1** could function as a new generation of assembled supramolecular cleft, to be able to not only efficiently bind linear dipyridyl molecules **14**−**17**, resulting in the formation of stable termolecular complexes, with K_{aasoc} values ranging from 3.8×10^6 to 8.9×10^7 M^{-1}, but also strongly complex a hydrogen-bond-assembled [2]rotaxane, **18**, which consists of a rigid fumaramide thread and a pyridine-incorporated tetraamide cyclophane, with $K_{aasoc} = 1.2 \times 10^4$ M^{-1}. ^{1}H NMR competition experiments reveal that complexation to the dipyriyl guests also promotes the stability of the quadruply-hydrogen-bonded dimeric receptor.

Introduction

An ongoing enterprise in supramolecular chemistry is the design, synthesis, and investigation of unnatural receptors with convergent recognition functionality.[1] Although studies of molecular recognitions based on unicomponent receptors have always been vigorously performed,[2] in the past decade a significant amount of multicomponent supramolecular systems have been developed as a new generation of artificial receptors. A large number of supramolecular capsules have been engineered and self-assembled by utilizing hydrogen bonds[3] or metal−ligand coordination[4] as the driving force. At present, these new supramolecular species have been used as novel "tools of physical organic chemistry" [3e] for controllable guest encapsulation and release,[5] for recognition sensing,[6] and as microreactors.[7] Metal−ligand

[†] Chinese Academy of Sciences.
[‡] Shanghai Jiaotong University.

(1) (a) Vögtle, F. *Supramolecular Chemistry*; Wiley & Sons: Chichester, U.K., 1991. (b) Lehn, J.-M. *Supramolecular Chemistry*; VCH: Weinheim, Germany, 1995. (c) Atwood, J. L., Davies, J. E. D., Macnicol, D. D., Vögtle, F., Lehn, J.-M., Eds. *Comprehensive Supramolecular Chemistry*; Pergamon: Oxford, 1996; Vols. 1−9. (d) Sauvage, J.-P., Dietrich-Buchecker, C., Eds.; *Molecular Catenanes, Rotaxanes and Knots*; Wiley-VCH: Weinheim, Germany, 1999. (e) Steed, J. W., Atwood, J. L., Eds. *Supramolecular Chemistry*; Wiley-VCH: Weinheim, Germany, 1999. (f) Schneider, H.-J.; Yatsimirski, A. *Principles and Methods in Supramolecular Chemistry*; Wiley: Somerset, MA, 2000. (g) Lindoy, L. F.; Atkinson, I. M. *Self-assembly in Supramolecular Systems*; Royal Society of Chemistry: London, 2000.

(2) For recent reviews, see (a) Beer, P. D.; Gale, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 486. (b) Lavigne, J. J.; Anslyn, E. V. *Angew. Chem., Int. Ed.* **2001**, *40*, 3118. (c) Dervan, P. B. *Bioorg. Med. Chem.* **2001**, *9*, 2215. (d) Hill, D. J.; Mio, M. J.; Prince, R. B.; Hughes, T.; Moore, J. S. *Chem. Rev.* **2001**, *101*, 3893. (e) Gokel, G. W.; Barbour, L. J.; Ferdani, R.; Hu, J. *Acc. Chem. Res.* **2002**, *35*, 878. (f) Zhao, D.; Moore, J. S. *Chem. Commun.* **2003**, 807.

(3) (a) Böhmer, V. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 713. (b) De Mendoza, J. *Chem.—Eur. J.* **1998**, *4*, 1373. (c) Rebek, J., Jr. *Acc. Chem. Res.* **1999**, *32*, 278. (d) Hof, F.; Rebek, J., Jr. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4775. (e) Hof, F.; Craig, S. L.; Nuckolls, C.; Rebek, J., Jr. *Angew. Chem., Int. Ed.* **2002**, *41*, 1488.

(4) (a) MacGillivray, L. R.; Atwood, J. L. *Angew. Chem., Int. Ed.* **1999**, *38*, 1018. (b) Fujita, M.; Umemoto, K.; Yoshizawa, M.; Fujita, N.; Kusukawa, T.; Biradha, K. *Chem. Commun.* **2001**, 509. (c) Seidel, S. R.; Stang, P. J. *Acc. Chem. Res.* **2002**, *35*, 972. (d) Davis, A. V.; Yeh, R. M.; Raymond, K. N. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4793.

(5) For recent examples, see: (a) Mogck, O.; Pons, M.; Böhmer, V.; Vogt, W. *J. Am. Chem. Soc.* **1997**, *119*, 5706. (b) O'Leary, B. M.; Grotzfeld, R. M.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1997**, *119*, 11701. (c) Chapman, R. G.; Sherman, J. C. *J. Org. Chem.* **2000**, *65*, 513. (d) Kusukawa, T.; Yoshizawa, M.; Fujita, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 1879. (e) Ikeda, A.; Udzu, H.; Zhong, Z.; Shinkai, S. *J. Am. Chem. Soc.* **2001**, *123*, 3872. (f) Caulder, D. L.; Brückner, C.; Powers, R. E.; König, S.; Parac, T. N.; Raymond, K. N. *J. Am. Chem. Soc.* **2001**, *123*, 8923.

(6) Castellano, R. K.; Rudkevich, D. M.; Rebek, J., Jr. *J. Am. Chem. Soc.* **2000**, *122*, 7876.

(7) For recent examples, see: (a) Kang, J.; Rebek, J., Jr. *Nature* **1997**, *385*, 50. (b) Ziegler, M.; Brumaghim, J. L.; Raymond, K. N. *Angew. Chem., Int. Ed.* **2000**, *39*, 4119. (c) Yoshizawa, M.; Takeyama, Y.; Kusukawa, T.; Fujita, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 1347.

10.1021/jo0351872 CCC: $27.50
Published on Web 01/10/2004

coordination-driven supramolecular squares[8] and macrocyclic ensembles[9] and hydrogen-bond-induced rosettes[10] and heterodimers[11] have also been reported for discrete guest recognition, transport, or catalysis. Nevertheless, compared with classic covalent counterparts, investigation of supramolecular receptors for multimolecular recognition is still in its infancy. The challenge remains for the construction of new types of assemblies for achieving selective recognitions and exploring new binding modules.

Due to their extraordinary coordination, electronic, and geometrical properties, porphyrins are ideal building blocks for constructing artificial receptors. In the past decade, a large number of covalently bonded porphyrin receptors have been reported which recognize a variety of ions and organic molecules.[12] Coordination-bond-driven porphyrin squares have also been extensively investigated.[8,13] However, hydrogen-bond-assembled porphyrin systems for molecular or supramolecular recognition have been much less investigated; there are yet only a very few hydrogen-bond-assembled porphyrin rosette receptors in the literature which bind tripyridyl or a sugar derivative.[10]

One of the major obstacles for generating self-assembled porphyrin receptors is atropisomerization of the attached functional units, which substantially reduces or even makes impossible selective guest recognition.[14] To overcome this obstacle, we have developed a new efficient method to prepare strapped porphyrin precursors for further incorporation of a specific functional moiety.[15,16] The additional strap, which links two oppositely located phenyl groups, can prevent the atropisomerization of the corresponding *meso*-phenyl groups. It also ensures that any ligand can approach the porphyrin metal ion only from the strap-free side, consequently facilitating selective self-assembly or molecular recognition. Moreover, it also raises the chances of making the two porphyrins arrange in a cofacial orientation. Here we describe (1) the self-assembly and characterization of the first cleft-featured porphyrin dimeric receptor **Zn1·Zn1** by utilizing Meijer's versatile quadruply-hydrogen-bonded dimeric module[17−20] and (2) ^{1}H NMR, UV−vis, and vapor pressure osmometry (VPO) studies of the highly efficient recognition of the new supramolecular receptor for dipyridyl molecules **14**−**17** and also [2]rotaxane **18**, which has been self-assembled by using Leigh's hydrogen-bond-templating principle.[21,22]

Results and Discussion

The synthesis of compounds $\mathbf{H_21}$ and **Zn1** is outlined in Scheme 1. Acid **2** was first transformed into ester **3** with benzyl chloride. Treatment of **3** with **4** with potassium carbonate as base resulted in the formation of dialdehyde **5** in high yield. Porphyrin **7** was then prepared in 15% yield from a trifluoroacetic acid-catalyzed reaction of **5** with **6**. Selective deprotection of **7** with $MeSO_3H$ in anisole gave the key intermediate **8** in 85% yield.[23] It was found that this debenzylation reaction could be achieved by the normal Pd−C-catalyzed hydrogenation reaction, which led to the formation of insoluble materials. Another intermediate, **12**, was prepared from the Pd-catalyzed hydrogenation of **11**. The latter could be obtained in good yield from the reaction of **9** and **10** in hot pyridine. Then, treatment of **8** with **12** in CH_2Cl_2 in the presence of DCC afforded porphyrin $\mathbf{H_21}$ in 47% yield. Porphyrin $\mathbf{H_21}$ was then quantitatively transformed into **Zn1** with zinc acetate. The octyl ester and nonyl groups in $\mathbf{H_21}$ and **Zn1** provide them good solubility in organic solvents such as chloroform, dichloromethane, and toluene.

Before it was utilized as a bimolecular supramolecular receptor, **Zn1** had to be proved to exist exclusively as a homodimer in nonpolar solvents. Therefore, a systematic ^{1}H NMR study was first performed in $CDCl_3$.[24] Partial ^{1}H NMR spectra of $\mathbf{H_21}$, **Zn1**, and **13** (for comparison) are presented in Figure 1. The large downfield shifts for the NH signals of **13** as a simple homodimer are well expected. The AADD binding mode for dimer **13·13** could be easily established by comparison with reported sys-

(8) (a) Czaplewski, K. F.; Hupp, J. T.; Snurr, R. Q. *Adv. Mater.* **2001**, *13*, 1895. (b) Mines, G. A.; Tzeng, B.; Stevenson, K. J.; Li, J.; Hupp, J. T. *Angew. Chem., Int. Ed.* **2002**, *41*, 154.

(9) (a) Sommer, R. D.; Rheingold, A. L.; Goshe, A. J.; Bosnich, B. *J. Am. Chem. Soc.* **2001**, *123*, 3940. (b) Goshe, A. J.; Steele, I. M.; Ceccarelli, C.; Rheingold, A. L.; Bosnich, B. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4823.

(10) (a) Calama, M. C.; Timmerman, P.; Reinhoudt, D. N. *Angew. Chem.* **2000**, *112*, 771; *Angew. Chem., Int. Ed.* **2000**, *39*, 755. (b) Ishi, T.; Mateos-Timoneda, M. A.; Timmerman, P.; Crego-Calama, M.; Reinhoudt, D. N.; Shinkai, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 2300.

(11) Mertz, E.; Mattei, S.; Zimmerman, S. C. *Org. Lett.* **2000**, *2*, 2931.

(12) For recent examples, see: (a) Sirish, M.; Chertkov, V. A.; Schneider, H.-J. *Chem.—Eur. J.* **2002**, *8*, 1181. (b) D'Souza, F.; Deviprasad, G. R. *J. Org. Chem.* **2001**, *66*, 4601. (c) Sanders, J. K. M. *Pure Appl. Chem.* **2000**, *72*, 2265. (d) Sessler, J. L.; Andrievsky, A. *Chem.—Eur. J.* **1998**, *4*, 159.

(13) (a) Stang, P. J.; Olenyuk, B. *Acc. Chem. Res.* **1997**, *30*, 502. (b) Dinolfo, P. H.; Hupp, J. T. *Chem. Mater.* **2001**, *13*, 3113.

(14) Ogoshi, H. Mizutani, T. *Acc. Chem. Res.* **1998**, *31*, 81.

(15) Shao, X.-B.; Jiang, X.-K.; Wang, X.-Z.; Li, Z.-T.; Zhu, S.-Z. *Tetrahedron* **2003**, *59*, 4881.

(16) The length of this chain is suitable for the porphyrin unit to keep its planarity; see: (a) Bag, N.; Grogan, T. M.; Magde, D.; Slebodnick, C.; Johnson, M. R.; Ibers, A. J. *J. Am. Chem. Soc.* **1994**, *116*, 11833. (b) Osuka, A.; Kabayashi, F.; Maruyama, K. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1213.

(17) (a) Rebek, J., Jr. *Science* **1987**, *235*, 1478. (b) Zimmerman, S. C.; Wu, W. *J. Am. Chem. Soc.* **1989**, *111*, 8054.

(18) Beijer, F. H.; Sijbesma, R. P.; Kooijman, H.; Spek, A. L.; Meijer, E. W. *J. Am. Chem. Soc.* **1998**, *120*, 6761.

(19) For recent reviews concerning this binding module, see: (a) Brunsveld, L.; Folmer, B. J. B.; Meijer, E. W.; Sijbesma, R. P. *Chem. Rev.* **2001**, *101*, 4071. (b) Schmuck, C.; Wienand, W. *Angew. Chem., Int. Ed.* **2001**, *40*, 4363.

(20) For recent examples of other types of quadruply-hydrogen-bonded systems, see: (a) Beijer, F. H.; Sijbesma, R. P.; Kooijman, H.; Spek, A. L.; Meijer, E. W. *J. Am. Chem. Soc.* **1998**, *120*, 6761. (b) Sessler, J. L.; Wang, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 1726. (c) Lüning, U.; Kühl, C. *Tetrahedron Lett.* **1998**, *38*, 5735. (d) Corbin, P. S.; Zimmerman, S. C. *J. Am. Chem. Soc.* **1998**, *120*, 9710. (e) Gong, B.; Yang, Y.; Zeng, H.; Skrzypczak-Jankunn, E.; Kim, Y. W.; Zhu, J.; Ickes, H. *J. Am. Chem. Soc.* **1999**, *121*, 5607. (f) Corbin, P. S.; Zimmerman, S. C.; Thiessen, P. A.; Hawryluk, N. A.; Murray, T. J. *J. Am. Chem. Soc.* **2001**, *123*, 10475.

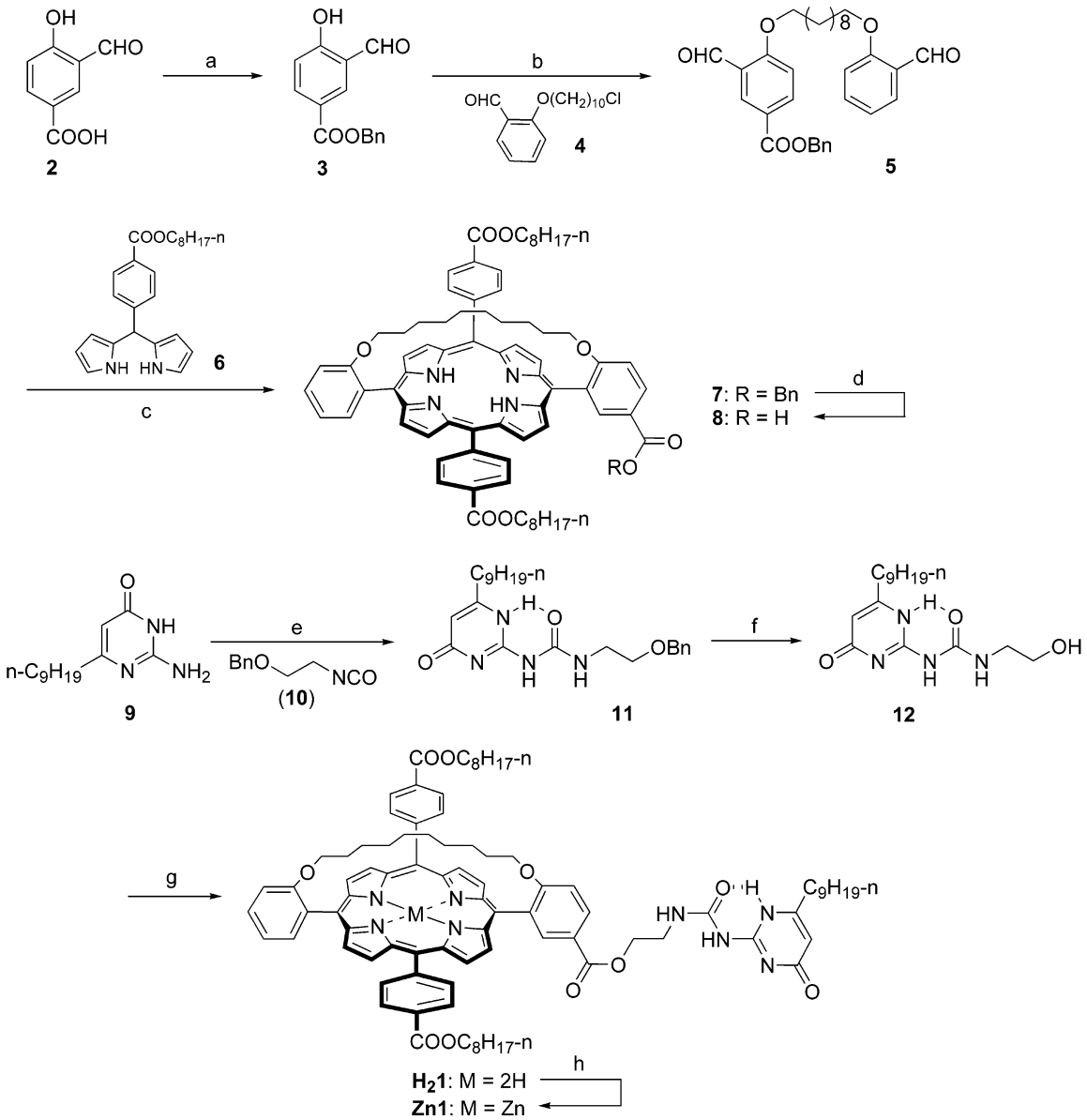
(21) (a) Lane, A. S.; Leigh, D. A.; Murphy, A. *J. Am. Chem. Soc.* **1997**, *119*, 11092. (b) Leigh, D. A.; Murphy, A.; Smart, J. P.; Slawin, A. M. Z. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 728.

(22) For examples of other types of hydrogen-bonded [2]rotaxanes, see: (a) Vögtle, F.; Händel, M.; Meier, S.; Ottens-Hildebrandt, S.; Ott, F.; Schmidt, T. *Liebigs Ann.* **1995**, 739. (b) Vögtle, F.; Jäger, R.; Händel, M.; Ottens-Hildebrandt, S.; Schmidt, W. *Synthesis* **1996**, 353.

(23) Nakayama, Y.; Senokuchi, K.; Sakaki, K.; Kato, M.; Maruyama, T.; Miyazaki, T.; Ito, H.; Nakai, H.; Kawamura, M. *Bioorg. Med. Chem.* **1997**, *5*, 971.

(24) No useful information could be provided from their ^{13}C NMR spectra due to important overlaps.

SCHEME 1[a]



[a] Reagents and conditions: (a) BnCl, KF, DMF, 80 °C, 4 h, 67%, (b) K_2CO_3, $Bu_4N^+I^-$, FMD, 80 °C, 3 h, 91%, (c) (i) TFA, CH_2Cl_2, rt, 2 h, (ii) 4-chloranil, THF, 15%, (d) $MeSO_3H$, PhOMe, rt, 85%, (e) pyridine, 90 °C, 5 h, 71%, (f) HCO_2NH_4, Pd−C (catalytic), MeOH, reflux, 1.5 h, 84%, (g) **8**, DCC, DMAP (cat.), CH_2Cl_2, rt, 3 days, 47%, (h) $Zn(OAc)_2$, CH_2Cl_2/MeOH, reflux, 12 h, 100%.

tems[18,25] and also from a 2D NOESY study. Unexpectedly, substantial upfield shifts were exhibited for the NH protons of both **$H_2$1** and **Zn1**. The very large upfield shifts of H-1 (−2.93 ppm), H-2 (−2.53 ppm), H-3 (−4.10 ppm), and H-4 (−2.93 ppm) of **Zn1**, relative to those of reference molecule **13**, initially led us to propose a folded conformation for **Zn1**, in which one ureidopyrimidone nitrogen was coordinated to the central porphyrin zinc ion. However, molecular modeling revealed that substantial twisting of the porphyrin skeleton is required for such an intramolecular coordination to occur. In addition, VPO experiments gave an average molecular mass of 2850 ± 300 u in chloroform/toluene (1:1 v/v, 30 °C), which strongly suggests a dimeric structure (calculated molecular mass 3016 u). The UV−vis spectrum of **Zn1** in $CHCl_3$ between 350 and 650 nm is also very similar to that of the zinc(II) complex of porphyrin **7** both in shape and intensity, excluding the existence of significant intra- or intermolecular coordination. All the NH signals of **Zn1** and **$H_2$1** in the ^{1}H NMR spectra in $CDCl_3$ did not shift upon dilution (up to 10^{-5} M) but shifted downfield remarkably when the temperature was increased. Adding 1.0 equiv of **13** to the solution of **Zn1** in $CDCl_3$ led to the generation of a new set of (six) signals for the NH protons (Figure 1d, indicated by the arrows), which could be reasonably ascribed to the new heterodimer **Zn1·13**, whereas the signals produced by **Zn1** and **13** themselves were weakened remarkably but did not disappear.[26] The new set of signals were intensified when another 1.0 equiv of **13** was added (Figure 1e). The chemical shifts of the amide C═O

(25) Söntjens, S. H. M.; Sijbesma, R. P.; van Genderen, M. H. P.; Meijer, E. W. *J. Am. Chem. Soc.* **2000**, *122*, 7487.

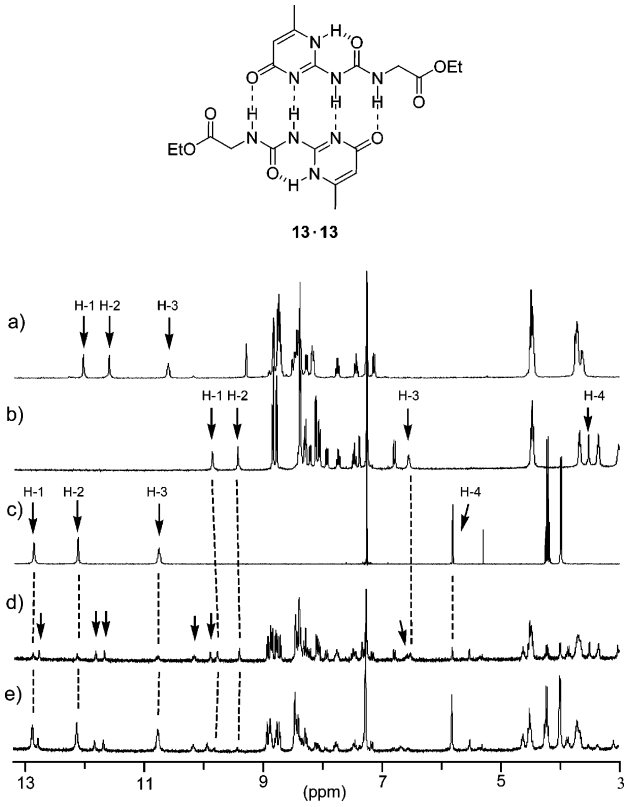


FIGURE 1. Partial ^{1}H NMR spectra (400 MHz) in $CDCl_3$ at 25 °C: (a) **H$_2$1** (20 mM), (b) **Zn1** (20 mM), (c) **13** (20 mM), (d) **Zn1** (20 mM) + **13** (1:1), and (e) **Zn1** (20 mM) + **13** (1:2).

carbon and pyrimidin-4(1*H*)-one CH carbon of **Zn1** (171.17, 103.55 ppm) and **H$_2$1** (172.39, 104.38 ppm) in the ^{13}C NMR spectra also notably moved upfield compared to those of **13** (172.92, 105.71 ppm) as a result of the shielding effect of the porphyrin unit. All these results indicate that both **Zn1** and **H$_2$1** exist as stable homodimers **Zn1·Zn1** and **H$_2$1·H$_2$1** in $CDCl_3$. What is different from dimer **13·13** is that the hydrogen-bonding moiety of **Zn1·Zn1** and **H$_2$1·H$_2$1** is shielded by the two peripheral porphyrin units. In other words, both dimers **Zn1·Zn1** and **H$_2$1·H$_2$1** adopt an "S" conformation in $CDCl_3$, as shown (Figure 2), which may be attributed to the donor−acceptor interaction between an electron-rich porphyrin unit and an electron-deficient pyrimidone unit. The much more stronger shielding effect observed for **Zn1** should reflect the increased electron-donating ability of the zinc porphyrin unit relative to the metal-free porphyrin in **1**. The AADD binding pattern of dimer **Zn1·Zn1** in $CDCl_3$ had been established with 2D NOESY experiments. In principle, an additional group such as methyl introduced to the carbon of the benzene between the porphyrin and ester moieties of **Zn1** should prevent the folding conformation. Nevertheless, it would also generate potential steric repelling to any guest molecule in the complexes.

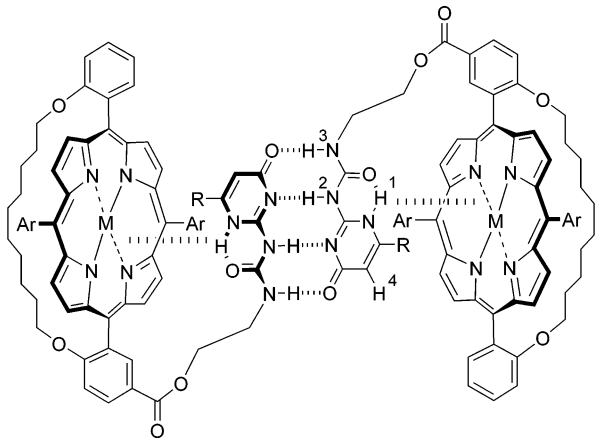
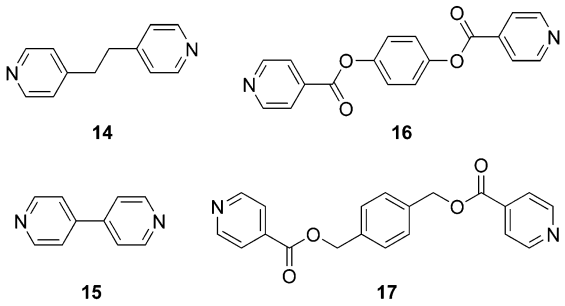


FIGURE 2. Proposed S conformation of homodimers **1·1** and **Zn1·Zn1** in chloroform-*d* as a result of strong intramolecular donor−acceptor interaction.

The UV−vis absorption spectra of **Zn1** did not change in shape over the concentration range of 1.0−0.01 mM. This observation, together with the above ^{1}H NMR dilution experiment, suggests a very high binding constant for homodimer **Zn1·Zn1** ($\geq 10^7$ M^{-1}).[25,27,28] These results well allow homodimer **Zn1·Zn1** to be treated as a single component at [**Zn1**] ≥ 0.01 mM.[11] Therefore, the binding behaviors of dimer **Zn1·Zn1** to linear dipyridyl molecules **14**−**17** were then investigated.



Mixing **14** with 2.0 equiv of **Zn1** in $CDCl_3$ led to the signals of **14** in the ^{1}H NMR spectrum to shift upfield substantially, as shown in Figure 3. The large upfield shift (−6.39 ppm) exhibited by the α-H suggests that the pyridine unit is fully bonded to the porphyrin zinc.[29] Strong binding of the pyridine units to the zinc porphyrins also led to weakening of the shielding effect of the zinc porphyrin unit on the hydrogen-bonding moiety in dimer **Zn1·Zn1**. Consequently, the NH signals of **Zn1** shift back greatly to the "normal" downfield positions.[18,25] The signals of guest **14** and the signals of the NH protons of **Zn1** in Figure 3b have been assigned by changing their ratios and comparing the spectra with those of pure samples. The 2:1 binding stoichiometry (**Zn1·Zn1**)·**14** has been proved by a ^{1}H NMR investigation of Job's plot, in

(26) These results were used to support the dimeric structure but not the possible folded state, since, if it exists, the folded state should be obviously more stable than the dimeric structure. If 1 equiv of **13** were added to the solution of **Zn1** in $CDCl_3$, such a folded conformation of **Zn1** would not be broken to the extent as shown in Figure 1d. However, it is reasonable to assume that the stability of three possible dimers, **Zn1·Zn1**, **Zn1·13**, and **13·13**, are comparable and formed in comparable yields.

(27) Attempts to determine the K_{assoc} of dimer **Zn1·Zn1** with UV−vis or the fluorescent dilution method (ref 25) did not succeed, possibly due to the $\pi\angle\pi$ stacking between the porphyrin units and the hydrogen-binding moiety.

(28) A K_{dim} of 5.7×10^7 M^{-1} has been determined in chloroform for similar homodimers; see ref 25.

(29) (a) Ikeda, A.; Ayabe, M.; Shinkai, S.; Sakamoto, S.; Yamaguchi, K. *Org. Lett.* **2000**, *2*, 3707. (b) Hunter, C. A.; Hyde, R. K. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1936.

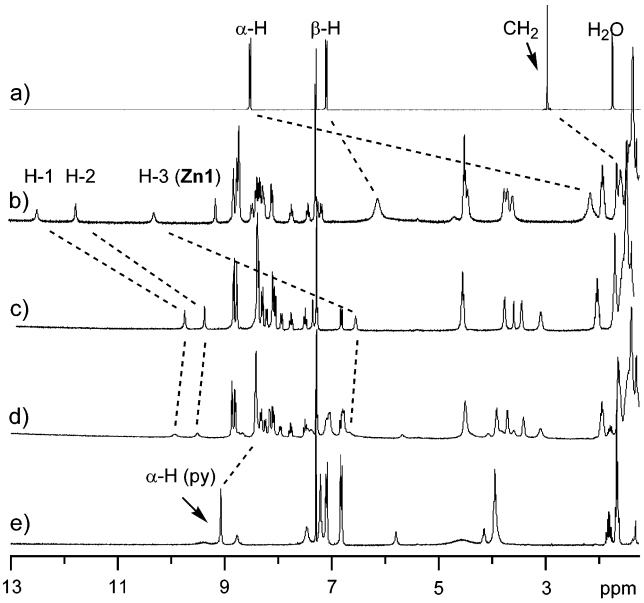


FIGURE 3. Partial ^{1}H NMR spectra (400 MHz) in $CDCl_3$ at 25 °C: (a) **14** (5.0 mM), (b) **Zn1** (10.0 mM) + **14** (2:1), (c) **Zn1** (10.0 mM), (d) **Zn1** (10.0 mM) + **18** (2:1), and (e) **18** (5.0 mM).

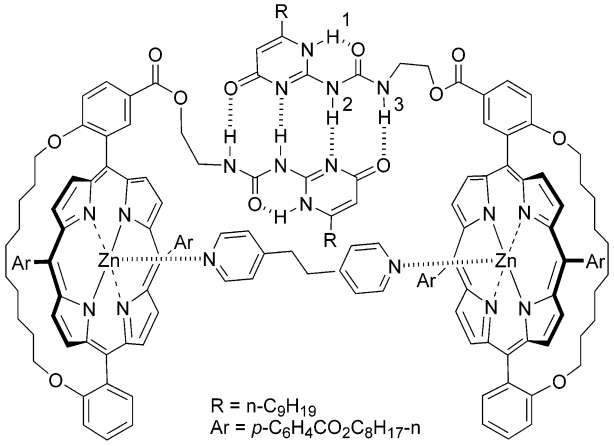


FIGURE 4. Proposed structure of termolecular complex (**Zn1**·**Zn1**)·**14**.

which the maximum signal change for the α-H of **14** was observed at the 2:1 mole fraction.[30] Therefore, a stable tercomponent complex is formed, as shown in Figure 4.

Upon mixing **Zn1** with 0.5 equiv of **15**, **16**, or **17** in $CDCl_3$, large downfield shifts (−5.65, −6.09, and −6.04 ppm) were also displayed for the pyridine α-H signals, indicating that strong binding also occurs between dimeric receptor **Zn1**·**Zn1** and these dipyridyl guests, resulting in the formation of the corresponding tercomponent complexes similar to (**Zn1**·**Zn1**)·**14**.[31]

Quantitative binding studies were first attempted by using the ^{1}H NMR dilution or titration method, which did not afford reliable results due to the lowered resolution of the pyridine α-H probes at low concentration.

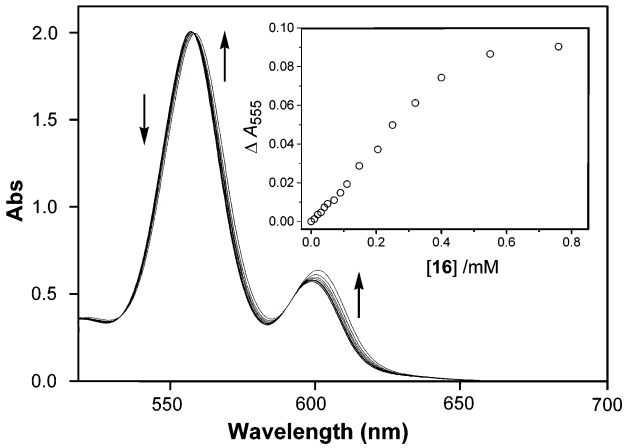


FIGURE 5. Absorption spectral change in **Zn1** ([**Zn1**] = 1.0 × 10^{-4} M) in $CHCl_3$ at 25 °C: [**16**] = 1.0 × 10^{-6} to 7.3 × 10^{-4} M. Inset: ΔA_{555} vs [**16**].

Therefore, UV−vis titration experiments of **Zn1**·**Zn1** with the dipyridine guests were performed in chloroform. Figure 5 shows the influence of added **16** on the absorbance spectral change of **Zn1**. It can be seen that a pronounced red shift was exhibited for the Q-band of the porphyrin unit with a clear isosbestic point at 558 nm.[29,32] This result indicates that the two pyridine units in guest **16** simultaneously coordinate to Zn(II) in dimer **Zn1**·**Zn1**.[29a] A plot of the absorbance intensity change of the porphyrin unit ([**Zn1**] = 1.0 × 10^{-4} M) at 555 nm vs [**16**] (inserted in Figure 5) was then fit to a nonlinear 1:1 binding model,[33,34] which afforded an association constant K_{assoc} = (4.7 ± 0.6) × 10^6 M^{-1} for the termolecular complex (**Zn1**·**Zn1**)·**16**. By using the same principle, K_{assoc} values for termolecular complexes (**Zn1**·**Zn1**)·**14**, (**Zn1**·**Zn1**)·**15**, and (**Zn1**·**Zn1**)·**17** in chloroform were determined to be (8.9 ± 1.4) × 10^7, (9.8 ± 1.4) × 10^6, and (3.8 ± 0.5) × 10^6 M^{-1}, respectively. The largest K_{assoc} exhibited by **14** might reflect its strongest coordination ability relative to **15**−**17**. The binding constants are comparable to those of the covalently bonded diporphyrin receptors for dipyridyl guests.[35]

The extremely strong binding affinity exhibited by homodimer **Zn1**·**Zn1** to the linear pyridine guests suggests that **Zn1**·**Zn1** may recognize more complicated molecular or even supramolecular species. To explore this possibility, [2]rotaxane **18**, with a neutral cyclic component bearing two pyridine units, was designed. The fumaramide thread **23** was chosen as template, since previous studies by Vögtle and Leigh et al. had shown that the rigid fumaramide unit could induce the generation of the hydrogen-bond-assembled [2]rotaxanes of similar structures in higher yields,[36] whereas the pentyl groups were introduced to **23** to improve the solubility of the resulting [2]rotaxane in common organic solvents.

(30) Job, P. *Ann. Chim. Ser. 10* **1928**, *9*, 113.

(31) Addition of even 10 equiv of pyridine to the solution of **Zn1**·**Zn1** (5.0 mM) in $CDCl_3$ induced a ca. 1.8 ppm downshifting for the H-1 signal of **Zn1**, indicating that a significant corporative effect exists for the formation of the complexes between dimeric receptor **Zn1**·**Zn1** and dipyridyl molecules **14**−**17**.

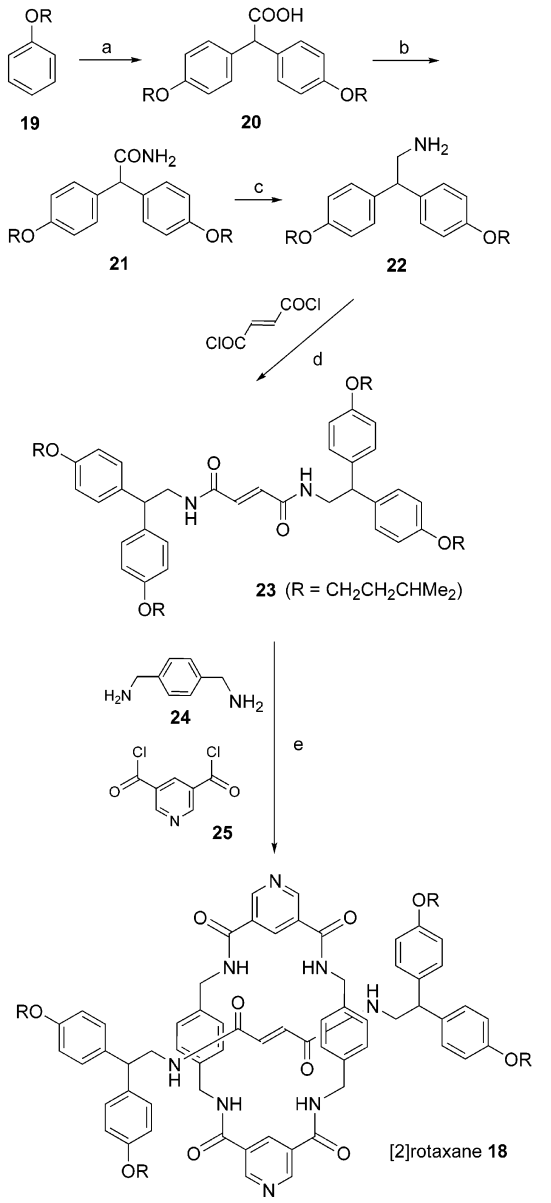
(32) Takeuchi, M.; Shioya, T.; Swager, T. M. *Angew. Chem., Int. Ed.* **2001**, *40*, 3372.

(33) Assuming a lower limit of K_{assoc} = 1.0 × 10^7 M^{-1} for dimer **Zn1**·**Zn1** in chloroform at room temperature, ca. 97.8% of **Zn1** exists as dimers at [**Zn1**] = 1.0 × 10^4 M^{-1}.

(34) (a) Conners, K. A. *Binding Constants: The Measurement of Molecular Complex Stability*; Wiley: New York, 1987. (b) Wilcox, C. S. In *Frontiers in Supramolecular Organic Chemistry and Photochemistry*; Schneider, H.-J., Dürr, H., Eds.; VCH: New York, 1991; p 123.

(35) Anderson, H. L.; Anderson, S.; Sanders, J. K. M. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2231.

SCHEME 2[a]



[a] Reagents and conditions: (a) CHOCOOH, H_2SO_4 (catalytic), HOAc, 40 °C, 12 h, 68%, (b) NH_3(g), DCC, HOBt, CH_2Cl_2, rt, 12 h, 94%, (c) $NaBH_4$, BF_3·OEt_2, THF, reflux, 8 h, 90%, (d) NEt_3, CH_2Cl_2, rt, 12 h, 78%, (e) NEt_3, $CHCl_3$, MeCN, rt, 2 h, 57%.

The synthesis of [2]rotaxane **18** is outlined in Scheme 2. Ether **19** was first converted into acid **20** according to the condensation method reported by Baarschers.[37] **20** was then treated with ammonia in the presence of DCC, to afford amide **21** in high yield. The latter was reduced with sodium borohydride in the presence of boron trifluoride to amine **22** in good yield. **22** was then treated with but-2-enedioyl dichloride, to generate the linear template **23**. Treatment of diamine **24** with 1 equiv of compound **25** in the presence of excess **23** led to the formation of [2]rotaxane **18** in 57% yield.

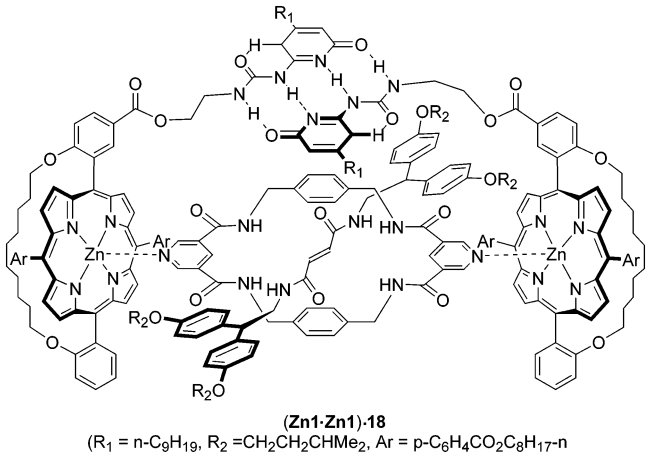


FIGURE 6. Proposed structure of tetramolecular complex (**Zn1**·**Zn1**)·**18**.

The [2]rotaxane has a good solubility in nonpolar solvents such as chloroform and toluene at room temperature, and has been characterized by (2D NOESY) ^{1}H NMR, ESI-MS, and elemental analysis. Adding 2.0 equiv of **Zn1** to the solution of [2]rotaxane **18** (5.0 mM) in $CDCl_3$ caused a significant upfield shift (−0.67 ppm) (Figure 3d) for the pyridine α-H signal in [2]rotaxane **18**, indicative of significant coordination between the porphyrin zinc ion of **Zn1** and the pyridine nitrogen of [2]rotaxane **18**. A Job plot study of the ^{1}H NMR results, with the pyridine α-H as a probe, supported a 2:1 binding stoichiometry. Compared to those of the tercomponent systems of **Zn1** and **14**−**17**, similar UV−vis absorbance spectral patterns were also displayed when **18** was added to the solution of **Zn1** in chloroform. A VPO investigation afforded an average molecular mass of 3900 ± 400 u in toluene at 30 °C (calculated value for the species **Zn1**/**Zn1**/**18**, 4368 u).[38] All these results support the formation of the novel tetramolecular complex (**Zn1**·**Zn1**)·**18**, as shown in Figure 6. Quantitative binding studies were then carried out. A ^{1}H NMR dilution investigation[15,39] of the 2:1 solution of **Zn1** and **18** ([**18**] = 8.0−0.1 mM) in $CDCl_3$ afforded a K_{assoc} of 1.0×10^4 M^{-1} for (**Zn1**·**Zn1**)·**18**. A UV−vis titration study of **Zn1**·**Zn1** ([**Zn1**] = 0.3 mM) at 555 nm with **18** ([**18**] = 0.020−5.0 mM) was also performed, which gave a comparable $K_{assoc} = (1.2 \pm 0.2) \times 10^4$ M^{-1} for (**Zn1**·**Zn1**)·**18**. Although the value is significantly lower than those of the above termolecular complexes, it is still very impressive considering that steric hindrance between **Zn1**·**Zn1** and **18** should be substantially larger than those in the termolecular systems, and the coordination ability of the pyridines in **18** is expected to be reduced due to the existence of two electron-withdrawing amide groups at its β-positions.

A variable-temperature ^{1}H NMR study reveals significant temperature dependence of all the new supramolecular complexes. All the pyridine protons of the guests and the NH protons of **Zn1** shifted upfield

(36) (a) Jäger, R.; Baumann, S.; Fischer, M.; Safarowsky, O.; Nieger, M.; Vögtle, F. *Liebigs Ann./Recl.* **1997**, 2269. (b) Parham, A. H.; Windisch, B.; Vögtle, F. *Eur. J. Org. Chem.* **1999**, *1233*, 3. (c) Gatti, F. G.; Leigh, D. A.; Nepogodiev, S. A.; Slawin, A. M. Z.; Teat, S. J. T.; Wong, J. K. Y. *J. Am. Chem. Soc.* **2001**, 123, 5983.

(37) Baarschers, W. H.; Vukmanich, J. P. *Can. J. Chem.* **1986**, *64*, 932.

(38) The VPO investigations for the termolecular species (**Zn1**·**Zn1**)·**14**−**17** did not provide useful information because of the small change of their average molecular masses relative to that of dimer **Zn1**·**Zn1**.

(39) Corbin, P. S.; Zimmerman, S. C.; Thiessen, P. A.; Hawryluk, N. A.; Murray, T. J. *J. Am. Chem. Soc.* **2001**, *123*, 10475.

remarkably with the increase of the temperature, indicative of the weakening of the complexes and decreased shielding effect at higher temperature. At lowered temperature, these proton signals shifted downfield, and new sets of signals were generated for the **Zn1** NH protons of the termolecular complexes. This observation can be reasonably attributed to the formation of a new type of more complicated complexes. Unfortunately, quantitative investigations of the new sets of signals could not be performed due to the reduced resolution of the spectra at lower temperature. An attempt to investigate the influence of the complexation of [2]rotaxane **18** by dimeric receptor **Zn1·Zn1** on the dynamic behavior of the [2]rotaxane was also proved impossible as a result of the reduced solubility of the [2]rotaxane at reduced pressure.

Addition of excess **13** (20.0 mM) to the solution of complex (**Zn1·Zn1**)·**14** (5.0 mM) caused ca. 30% (based on the ^{1}H NMR integrating intensity of H-1 of **Zn1**) of the hydrogen-bond-assembled dimer **Zn1·Zn1** to dissociate and induced the formation of the new heterodimer **Zn1·13**, indicating that the **Zn1·Zn1** moiety in complex (**Zn1·Zn1**)·**14** is more stable than dimer **Zn1·Zn1**, which does not involve a complexing process.

Conclusion

We have demonstrated that quadruply-hydrogen-bonded strapped porphyrin homodimer **Zn1·Zn1** is a novel efficient bimolecular receptor for recognizing dipyridyl molecules and a supramolecular species. In the past decade, interlocked systems such as catenanes and rotaxanes have been important kinds of self-assembling targets in supramolecular chemistry. The efficient binding of [2]rotaxane **18** by dimeric receptor **Zn1·Zn1**, the first example of its kind, demonstrates that selective recognition between discrete supramolecular species can be achieved by rational molecular design. Further study along this line may lead to development of new supramolecular principles for controlling dynamic properties of specifically designed interlocked assemblies. By introducing chiral groups to assembled receptors and/or guests, new chemistries of chiral recognition[40] or receptor amplification[41] are also expected. Efforts in these directions will be reported in due course.

Experimental Section

General Methods. Melting points are uncorrected. All reactions were performed under an atmosphere of dry nitrogen. The ^{1}H NMR spectra were recorded on a 600, 400, or 300 MHz spectrometer in the indicated solvents. Chemical shifts are expressed in parts per million (δ) using residual solvent protons as internal standards. Chloroform (δ 7.26 ppm) was used as an internal standard for chloroform-*d*. Elemental analysis was carried out at the SIOC analytical center. Unless otherwise indicated, all starting materials were obtained from commercial suppliers and were used without further purification. All solvents were dried before use following standard procedures.

3-Formyl-4-hydroxybenzoic Acid Benzyl Ester (3). A mixture of compound **2**[42] (10.5 g, 63.0 mmol) and anhydrous KF (3.70 g, 63.0 mmol) was stirred at 80 °C for 30 min. Then benzyl chloride (8.70 mL, 75.6 mmol) was added in one portion. The mixture was stirred at 80 °C for 4 h and then cooled to room temperature. The mixture was triturated with ether (1000 mL). The organic phase was then washed with water (100 mL × 3) and saturated brine solution (150 mL) and dried over Na_2SO_4. After evaporation of the solvent, the resulting residue was recrystallized from ethanol, to afford pure compound **3** (10.4 g, 67%) as a white solid. Mp: 106−106.5 °C. ^{1}H NMR ($CDCl_3$): δ = 5.34 (s, 2H), 7.01 (d, J = 9.17 Hz, 1H), 7.35−7.45 (m, 5H), 8.20 (d, J = 9.16 Hz, 1H), 8.31 (s, 1H), 9.92 (s, 1H), 11.39 (s, 1H). MS (EI): m/z 256 (M^+). Anal. Calcd for $C_{15}H_{12}O_4$: C, 70.30; H, 4.72. Found: C, 70.40; H, 4.74.

2-(10-Chlorodecyloxy)benzaldehyde (4). To a stirred suspension of salicyaldehyde (10.5 mL, 0.10 mol) and K_2CO_3 (30.0 g, 0.22 mol) in DMF (100 mL) was added 1, 10-dichlorodecane (32.0 mL, 0.15 mol). The mixture was stirred at 80 °C for 3 h, and the solvent was evaporated under reduced pressure. The resulting residue was triturated with ether (1000 mL), and the organic phase was washed with dilute NaOH solution (200 mL × 2), water (150 mL), and saturated brine solution (150 mL) and dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by column chromatography (petroleum ether/ethyl acetate, 20:1), to afford compound **4** (16.2 g, 54%) as an oil. ^{1}H NMR ($CDCl_3$): δ = 1.31−1.49 (m, 12H), 1.71−1.87 (m, 4H), 3.53 (t, J = 6.8 Hz, 2H), 4.07 (t, J = 6.3 Hz, 2H), 6.96−7.03 (m, 2H), 7.53 (t, d, J = 7.7 and 2.1 Hz, 1H), 7.83 (d, d, J = 7.8 and 2.6 Hz, 1H). MS (EI): m/z 296 (M^+). Anal. Calcd for $C_{17}H_{25}ClO_2$: C, 68.79; H, 8.49. Found: C, 68.77; H, 8.61.

3-Formyl-4-[10-(2-formylphenoxy)decyloxy]benzoic Acid Benzyl Ester (5). To a stirred solution of compounds **3** (5.12 g, 20.0 mmol) and **4** (5.94 g, 20.0 mmol) in dry DMF (100 mL) were added K_2CO_3 (5.50 g, 40.0 mmol) and $Bu_4N^+I^-$ (0.74 g, 2.0 mmol) at room temperature. The mixture was then stirred at 80 °C for 4 h. The solid was filtered off, and the solvent was distilled under reduced pressure. The resulting residue was triturated with dichloromethane (300 mL). The organic phase was washed with dilute NaOH solution (1 N) (60 mL × 2), water (60 mL), and saturated brine solution (60 mL) and dried over Na_2SO_4. After evaporation of the solvent, the residue was subjected to column chromatography (chloroform/ethyl acetate, 80:1). Pure compound **5** (9.36 g) was obtained as a white solid in 91% yield. Mp: 55−56 °C. ^{1}H NMR ($CDCl_3$): δ = 1.35−1.62 (m, 12H), 1.82−1.90 (m, 4H), 4.08 (t, J = 6.6 Hz, 2H), 4.15 (t, J = 6.5 Hz, 2H), 5.35 (s, 2H), 6.96−7.04 (m, 3H), 7.36−7.53 (m, 6H), 7.83 (d, d, J = 7.5 Hz, 1.8 Hz, 1H), 8.25 (d, d, J = 8.7 Hz, 2.4 Hz, 1H), 8.53 (d, J = 2.4 Hz, 1H), 10.48 (s, 1H), 10.52 (s, 1H). MS (EI): m/z 516 (M^+). Anal. Calcd. for $C_{32}H_{36}O_6$: C, 74.40; H, 7.02. Found: C, 74.03; H, 6.71.

4-[Bis(1*H*-pyrrol-2-yl)methyl]benzoic Acid Octyl Ester (6). A solution of 4-formylbenzoic acid octyl ester[43] (8.70 g, 33.2 mmol) and pyrrole (23.0 mL, 0.33 mol) in toluene (250 mL) was degassed by a stream of nitrogen for 30 min. Then, 1 mL of saturated tosyl acid in hot toluene solution (at ca. 100°) was added in one portion. The solution was heated under reflux for 1.5 h and cooled to room temperature. The solution was washed with aqueous K_2CO_3 solution (2 N, 40 mL) and water (40 mL × 2) and dried over sodium sulfate. Evaporation of the solvent gave a brown oil, which was subjected to flash chromatography ($CHCl_3$) and further purified by recrystallization (chloroform/hexane), to give 8.11 g of pure product **4** in 65% yield as a white solid. Mp: 84−85 °C. ^{1}H NMR ($CDCl_3$): δ = 0.89 (t, J = 6.7 Hz, 3 H), 1.27−1.44 (m, 10 H), 1.71−1.78 (m, 2 H), 4.30 (t, J = 6.6 Hz, 2 H), 5.53 (s, 1 H), 5.90 (s, 2 H), 6.15−6.18 (m, 2 H), 6.70−6.73 (m, 2 H), 7.24−7.30 (m, 2 H), 7.97 (s, 2 H), 8.00 (s, 2 H). MS (EI): m/z 378 $[M]^+$. Anal. Calcd for $C_{24}H_{30}N_2O_2$: C, 76.16; H, 7.99; N, 7.40. Found: C, 76.25; H, 7.99; N, 7.29.

(40) (a) Huang, X.; Fujioka, N.; Pescitelli, G.; Koehn, F. E.; Williamson, R. T.; Nakanishi, K.; Berova, N. *J. Am. Chem. Soc.* **2002**, *124*, 10320. (b) Borovkov, V. V.; Lintuluoto, J. M.; Sugeta, H.; Fujiki, M.; Arakawa, R.; Inoue, Y. *J. Am. Chem. Soc.* **2002**, *124*, 2993.

(41) Prins, L. J.; Reinhoudt, D. N.; Timmerman, P. *Angew. Chem., Int. Ed.* **2001**, *40*, 2382.

(42) Cheng, C.-C.; Lu, Y.-L. *J. Chin. Chem. Soc.* **1998**, *45*, 611.

(43) Barry, J.; Bram, G.; Decodts, G.; Loupy, A.; Orange, C.; Petit, A.; Sansoulet, J. *Synthesis* **1985**, 40.

Porphyrin 7. Compounds **5** (2.07 g, 4.00 mmol) and **6** (1.52 g, 4.00 mmol) were dissolved in dichloromethane (850 mL). The solution was degassed for 30 min with nitrogen at room temperature, and then trifluoroacetic acid (1 mL) was added in one portion. The solution was stirred at room temperature overnight. Then a solution of 4-chloranil (2.93 g, 12.0 mmol) in THF (100 mL) was added. The mixture was stirred at room temperature for another 2 h and then washed with saturated aqueous $NaHCO_3$ solution (100 mL × 3), water (100 mL), and saturated brine solution (100 mL) and dried over sodium sulfate. The solvent was evaporated, and the resulting residue was subjected to column chromatography (dichloromethane), to afford the crude product **7**, which was unstable in the air and used directly for the next step.

Porphyrin 8. To a solution of the above compound **7** in anisole (10 mL) was added methanesulfonic acid (2 mL). The solution was stirred at room temperature for 2 h. Then dichloromethane (100 mL) was added. The organic solution was washed with saturated $NaHCO_3$ solution (30 mL × 3), water (30 mL), and saturated brine solution (30 mL) and dried over sodium sulfate. After solvent removal, the resulting residue was purified by column chromatography (dichloromethane/ethyl acetate/triethylamine/methanol, 40:4:4:1), to afford compound **8** (0.36 g, 7.9% for two steps) as a purple solid. Mp: 130−132 °C. ^{1}H NMR ($CDCl_3$): $\delta = -2.65$ (s, 1H), −1.27−1.22 (m, 2H), −1.02−0.88 (m, 4H), −0.60−0.45 (m, 6H), 0.61−0.71 (m, 4H), 0.91 (t, $J = 6.8$ Hz, 6H), 1.33−1.60 (m, 20H), 1.86−1.96 (m, 4H), 3.69 (t, $J = 5.3$ Hz, 2H), 3.84 (t, $J = 4.8$ Hz, 2H), 4.50 (t, $J = 6.8$ Hz, 4H), 7.24−7.28 (m, 2H), 7.45 (t, $J = 7.4$ Hz, 1H), 7.75 (t, d, $J = 8.0$ Hz, 1.7 Hz, 1H), 8.15 (d, $J = 7.8$ Hz, 2H), 8.31−8.57 (m, 8H), 8.76−8.85 (m, 8H), 9.10 (d, $J = 2.1$ Hz, 1H). MS (ESI): m/z 1142 (M^+). Anal. Calcd for $C_{73}H_{80}N_4O_8$: C, 76.81; H, 7.06; N, 4.91. Found: C, 76.81; H, 7.07; N, 4.88.

1-(2-Benzyloxyethyl)-3-(6-nonyl-4-oxo-1,4-dihydropyrimidin-2-yl)urea (11). To a stirred biphasic mixture of dichloromethane (280 mL) and saturated aqueous $NaHCO_3$ solution (280 mL) was added $BnOCH_2CH_2NH_2 \cdot HCl$[44] (2.25 g, 14.0 mmol) at room temperature. The mixture was cooled to 0 °C while being stirred for ca. 10 min. Stirring was stopped, and the layers were allowed to separate. A solution of triphosgene (2.80 g) in dichloromethane (30 mL) was added in a single portion via syringe to the organic phase. Stirring was resumed immediately for 0.5 h. The layers were then separated, the aqueous phase was extracted with CH_2Cl_2 (100 mL × 2), and the combined organic phases were dried over Na_2SO_4 and concentrated to give crude isocyanate **10**. The isocyanate was dissolved in dry pyridine (50 mL), and then compound **9**[45] (3.32 g, 14.0 mmol) was added. After the solution was heated under reflux for 4 h, the solvent was removed under reduced pressure, and the resulting residue was washed completely with ether and then subjected to column chromatography (dichloromethane/methanol, 30:1), to afford compound **11** (4.13 g, 71%) as a white solid. Mp: 98 °C. ^{1}H NMR ($CDCl_3$): $\delta = 0.88$ (t, $J = 6.75$ Hz, 3H), 1.24−1.32 (m, 12H), 1.64 (p, $J = 7.5$ Hz, 2H), 2.46 (t, $J = 7.5$ Hz, 2H), 3.49−3.55 (q, $J = 5.6$ Hz, 2H), 3.65 (t, $J = 5.6$ Hz, 2H), 4.57 (s, 1H), 5.81 (s, 1H), 7.24−7.37 (m, 5H), 10.36 (s, 1H), 11.97 (s, 1H), 13.09 (s, 1H). MS (EI): m/z 414 (M^+). Anal. Calcd for $C_{23}H_{34}N_4O_3$: C, 66.64; H, 8.27; N, 13.52. Found: C, 66.61; H, 8.06; N, 13.52.

1-(2-Hydroxyethyl)-3-(6-nonyl-4-oxo-1,4-dihydropyrimidin-2-yl)urea (12). To a mixture of compound **11** (2.07 g, 5.00 mmol) and NH_4HCO_3 (7.0 g) in methanol (150 mL) was added 10% Pd−C (0.3 g) at room temperature. The mixture was then stirred under reflux for 1.5 h and then filtered to remove the catalyst. The solvent was evaporated, and the resulting residue was subjected to a flash column. The crude was then purified by recrystallization from methanol/acetone (1:1). Pure compound **12** was obtained as a white solid (1.37 g, 84%). Mp: 136−138 °C. ^{1}H NMR ($CDCl_3$): $\delta = 0.88$ (t, $J = 6.8$ Hz, 3H), 1.31−1.33 (m, 12H), 1.64 (q, $J = 7.7$ Hz, 2H), 2.47 (t, $J = 7.7$ Hz, 2H), 3.44 (t, $J = 4.5$ Hz, 2H), 3.72 (br, 1H), 3.79−3.83 (m, 2H), 5.82 (s, 1H), 10.29 (s, 1H), 11.81 (s, 1H), 13.06 (s, 1H). MS (EI): m/z 293 ($M^+ - CH_3O$). Anal. Calcd for $C_{16}H_{28}N_4O_3$: C, 59.23; H, 8.70; N, 17.27. Found: C, 59.29; H, 8.55; N, 17.01.

Porphyrin $H_2$1. To a stirred solution of compound **8** (0.32 g, 0.28 mmol), compound **12** (0.18 g, 0.56 mmol), and DMAP (30 mg) in dry dichloromethane (10 mL) was added DCC (0.11 g, 0.56 mmol) at room temperature. The solution was stirred at room temperature for 3 days and then washed with water (2 mL × 3) and brine (2 mL) and dried over sodium sulfate. After evaporation of the solvent, the residue was purified by column chromatography (dichloromethane/methanol, 40:1), to give porphyrin **$H_2$1** as a purple solid (0.19 g, 47%). Mp: 148−150 °C. ^{1}H NMR ($CDCl_3$): $\delta = -2.71$ (s, 2H), −1.13 (br, 4H), −0.78 (br, 4H), −0.52 (br, 4H), −0.33−0.16 (m, 4H), 0.35−0.44 (m, 2H), 0.57−1.58 (m, 49H), 1.85−1.95 (m, 4H), 3.58−3.75 (m, 6H), 4.41−4.51 (m, 5H), 7.14 (d, $J = 8.4$ Hz, 1H), 7.28 (br, 1H), 7.44 (t, d, $J = 7.3$ Hz, 1H), 7.75 (t, $J = 7.3$ Hz, 1H), 8.17 (d, $J = 7.5$ Hz, 2H), 8.26−8.52 (m, 8H), 8.71−8.84 (m, 8H), 9.29 (d, $J = 2.4$ Hz, 1H), 10.61 (br, 1H), 11.60 (s, 1H), 12.04 (s, 1H). ^{13}C NMR ($CDCl_3$): $\delta = 14.12$, 14.19, 22.70, 22.67, 24.98, 25.16, 25.77, 26.22, 27.34, 27.54, 27.61, 28.35, 28.57, 28.75, 28.95, 29.05, 29.32, 29.40, 29.78, 30.61, 31.76, 31.91, 38.83, 63.86, 65.55, 69.40, 69.82, 104.38, 111.53, 113.40, 115.37, 116.96, 118.44, 119.93, 121.75, 127.97, 129.89, 130.10, 130.66, 131.35, 131.94, 132.71, 134.50, 134.70, 134.94, 135.36, 146.84, 151.06, 153.79, 156.65, 159.77, 163.43, 166.96, 172.39. MS (MALDI-TOF): m/z 1448 ($M^+ + H$). Anal. Calcd for $C_{89}H_{106}N_8O_{10}$: C, 73.83; H, 7.38; N, 7.74. Found: C, 73.73; H, 7.31; N, 7.53.

Porphyrin Zn1. The free base porphyrin **$H_2$1** (0.15 g, 0.10 mmol) was dissolved in dichloromethane/methanol (3:1, 60 mL), and zinc acetate (0.12 g, 1.00 mmol) was added with stirring. The mixture was stirred under reflux overnight. The solvent was removed in vacuo, and the product was subjected to column chromatography (dichloromethane/methanol, 40:1), to afford porphyrin **Zn1** as a purple solid in quantitative yield. Mp: >260 °C. ^{1}H NMR ($CDCl_3$): $\delta = -1.55$ (t, $J = 6.2$ Hz, 2H), −1.37 (br, 2H), −1.24 (br, 2H), −0.81 (br, 6H), −0.31 (br, 2H), 0.60 (br, 2H), 0.92−1.55 (m, 47H), 1.88−1.93 (m, 4H), 3.03 (s, 2H), 3.36 (s, 2H), 3.53 (s, 1H), 3.67 (s, 2H), 4.48 (br, 4H), 6.58 (s, 1H), 6.80 (d, $J = 8.8$ Hz, 1H), 7.26 (br, 1H), 7.41−7.50 (m, 2H), 7.74 (t, $J = 7.5$ Hz, 1H), 7.94 (d, $J = 7.5$ Hz, 1H), 8.05−8.39 (m, 13H), 8.78−8.86 (m, 4H), 9.45 (s, 1H), 9.91 (s, 1H). ^{13}C NMR ($CDCl_3$): $\delta = 14.13$, 14.17, 22.71, 2430, 24.92, 26.02, 26.18, 26.89, 27.17, 28.00, 28.38, 28.85, 28.93, 29.28, 29.38, 29.59, 31.38, 31.88, 31.95, 36.53, 59.56, 65.42, 68.80, 69.74, 103.76, 111.30, 113.32, 114.65, 114.70, 117.86, 118.86, 119.85, 121.06, 121.11, 127.50, 127.55, 129.22, 129.67, 130.64, 130.72, 131.55, 131.76, 132.17, 132.41, 132.95, 134.76, 135.06, 147.90, 149.09, 149.63, 149.88, 150.69, 151.12, 151.44, 154.60, 159.47, 163.22, 165.60, 166.84, 171.17. MS (MALDI-TOF): m/z 1509 ($M^+ + H$). Anal. Calcd for $C_{89}H_{104}N_8O_{10}Zn$: C, 70.73; H, 6.94; N, 7.41. Found: C, 70.43; H, 6.65; N, 7.50.

[3-(6-Methyl-4-oxo-1,4-dihydropyrimidin-2-yl)ureido]-acetic Acid Ethyl Ester (13). A mixture of 2-amino-4-hydroxy-6-methylpyrimidine (0.50 g, 4.00 mmol) and ethyl 2-isocyanoglycinate (0.50 g, 3.91 mmol) in dried pyridine (20 mL) was stirred under reflux for 3 h. The solvent was removed under reduced pressure, and the residue was washed with ether completely and then subjected to flash chromatography (CH_2Cl_2/MeOH, 10:1), to give compound **13** as a white solid (0.77 g, 78%). Mp: 197.5−199 °C. ^{1}H NMR ($CDCl_3$): $\delta = 1.25-1.30$ (t, $J = 5.6$ Hz, 3H), 2.22 (s, 3H), 3.99 (d, $J = 5.6$ Hz, 2H), 4.12−4.25 (m, 2H), 5.82 (s, 1H), 10.76 (s, 1H), 12.13 (s, 1H), 12.87 (s, 1H). ^{13}C NMR ($CDCl_3$): $\delta = 13.62$, 24.46, 48.21, 60.12, 105.71, 152.22, 154.43, 156.72, 172.92. MS (EI): m/z 254 $[M]^+$.

(44) Hu, X. E.; Cassady, J. M. *Synth. Commun.* **1995**, *25*, 907.
(45) González, J. J.; Prados, P.; de Mendoza, J. *Angew. Chem., Int. Ed.* **1999**, *38*, 525.

Anal. Calcd for $C_{10}H_{14}N_4O_4$: C, 47.24; H, 5.55; N, 22.03. Found: C, 47.17; H, 5.50; N, 22.26.

Diisonicotinic Acid 1,4-Phenylene Diester (16). To a stirred suspension of isonicotinoyl chloride hydrochloride (0.77 g, 6.88 mmol) and 1,4-benzenediol (0.18 g, 1.64 mmol) in dry dichloromethane (15 mL) was added dropwise triethylamine (1 mL) at room temperature. The clean solution was then refluxed for 2 h. After workup, the crude product was purified by column chromatography (dichloromethane/acetone, 8:1), to give compound **16** (0.39 g, 73%). Mp: 222 °C. ^{1}H NMR ($CDCl_3$): δ = 7.33 (s, 4H), 8.03 (d, J = 5.9 Hz, 4H), 8.89 (d, J = 5.9 Hz, 4H). MS (EI): m/z 320 (M^+). Anal. Calcd for $C_{18}H_{12}N_2O_4$: C, 67.50; H, 3.78; N, 8.75. Found: C, 67.36; H, 3.93; N, 8.18.

Diisonicotinic Acid 1,4-Xylylene Diester (17). This compound was prepared on the basis of the method described for **16** as a white solid. Mp: 117−118 °C. ^{1}H NMR ($CDCl_3$): δ = 5.41 (s, 4H), 7.49 (s, 4H), 7.87 (d, J = 6.3 Hz, 4H), 8.79 (d, J = 6.3 Hz, 4H). MS (EI): m/z 348 (M^+). Anal. Calcd for $C_{20}H_{16}N_2O_4$: C, 68.96; H, 4.63; N, 8.04. Found: C, 68.58; H, 4.65; N, 7.76.

Bis[4-(3-methylbutoxy)phenyl]acetic Acid (20). A solution of glyoxylic acid (5.85 g, 79.0 mmol) and compound **19**[46] (25.6 g, 0.16 mol) in acetic acid (80 mL) was cooled in an ice bath. Concentrated sulfuric acid (3 mL) was added dropwise under stirring. The solution was then stirred at 40 °C overnight. After most solvent was removed under reduced pressure, the residue was triturated with dichloromethane (200 mL). The solution was washed with aqueous sodium carbonate solution to pH 6, water, and brine and dried over Na_2SO_4. After evaporation of the solvent, the residue was recrystallized from 2-propanol. Compound **20** (16.7 g, 68%) was obtained as a white solid. Mp: 97.5−98 °C. ^{1}H NMR ($CDCl_3$): δ = 0.94 (d, J = 6.6 Hz, 12H), 1.65 (q, J = 6.6 Hz, 4H), 1.77−1.86 (m, 2H), 3.95 (t, J = 6.6 Hz, 4H), 4.92 (s, 1H), 6.84 (d, J = 8.9 Hz, 4H), 7.24 (d, J = 8.9 Hz, 4H). MS (EI): m/z 384 (M^+). Anal. Calcd for $C_{24}H_{32}O_8$: C, 74.98; H, 8.39. Found: C, 74.98; H, 8.65.

2,2-Bis[4-(3-methylbutoxy)phenyl]acetamide (21). To a stirred suspension of compound **20** (7.70 g, 20.0 mmol) and HOBt·H_2O (3.10 g, 20.0 mmol) in dichloromethane (50 mL) was added DCC (5.20 g, 25.0 mmol). The mixture was stirred at room temperature for 1 h, and then ammonia gas was bubbled into the solution under stirring for 10 min. The mixture was stirred overnight under NH_3 atmosphere. The precipitate was filtered off and washed with dichloromethane (50 mL). The combined organic phase was worked up. After the solvent was removed, the resulting residue was subjected to column chromatography (dichloromethane/ethyl acetate, 20:1). Compound **21** (7.21 g) was obtained as a white solid in 94% yield. Mp: 124−125 °C. ^{1}H NMR ($CDCl_3$): δ = 0.93 (d, J = 6.0 Hz, 12H), 1.65 (q, J = 6.8 Hz, 4H), 1.78−1.87 (m, 2H), 3.95 (t, J = 6.8 Hz, 4H), 4.92 (s, 2H), 6.84 (d, J = 9.0 Hz, 4H), 7.21 (d, J = 9.0 Hz, 4H). MS (EI): m/z 340 ($M^+ - CONH_2$). Anal. Calcd for $C_{24}H_{33}NO_3$: C, 75.14; H, 8.67; N, 3.65. Found: C, 75.11; H, 8.40; N, 3.55.

2,2-Bis[4-(3-methylbutoxy)phenyl]ethylamine (22). Compound **21** (0.38 g, 1.00 mmol) and $NaBH_4$ (0.19 g, 5.00 mmol) were added to THF (15 mL). To the stirred suspension was added a solution of BF_3·Et_2O (0.82 mL, 6.50 mmol) in THF (5 mL) over a period of 3.5 h. Then the mixture was refluxed for 8 h and then cooled to room temperature. Diluted hydrochloride solution was added dropwise until the solid was dissolved. Most solvent was removed, and diluted sodium hydroxide solution was added to pH 7. The mixture was extracted with dichloromethane (100 mL). After normal workup, the resulting residue was purified by column chromatography (dichloromethane/ethyl acetate, 20:1), to afford compound **22** (0.33 g, 90%) as a white solid. Mp: 57−58 °C. ^{1}H NMR ($CDCl_3$): δ = 0.94 (d, J = 7.2 Hz, 12H), 1.40 (br, 2H), 1.60−1.66 (m, 4H), 1.78−1.87 (m, 2H), 3.23 (d, J = 7.8 Hz, 2H), 3.86 (t, J = 7.8 Hz, 1H), 3.94 (t, J = 6.6 Hz, 4H), 6.83 (d, J = 8.7 Hz, 4H), 7.12 (d, J = 8.7 Hz, 4H). MS (EI): m/z 340 ($M^+ - CH_2NH_2$). Anal. Calcd for $C_{24}H_{35}NO_2$·H_2O: C, 74.38; H, 9.62; N, 3.61. Found: C, 74.44; H, 9.48; N, 3.47.

But-2-enedioic Acid Bis({2,2-bis[4-(3-methylbutoxy)-phenyl]ethyl}amide) (23). To a solution of **22** (4.70 g, 12.7 mmol) and triethylamine (1.8 mL) in anhydrous dichloromethane (150 mL) was added dropwise a solution of fumaryl chloride (0.70 mL) in anhydrous dichloromethane (20 mL) at room temperature within 30 min. The mixture was stirred overnight. After workup, the crude product was subjected to column chromatography (chloroform/acetone, 25:1), to afford compound **23** (4.04 g, 78%) as a white solid. Mp: 205−206 °C. ^{1}H NMR ($CDCl_3$): δ = 0.94 (d, d, J = 6.2 Hz, 3.5 Hz, 24H), 1.63−1.68 (m, 8H), 1.78−1.87 (m, 4H), 3.87 (d, d, J = 8.1 Hz, 5.7 Hz, 4H), 3.94 (t, J = 6.5 Hz, 8H), 4.06 (t, J = 8.1 Hz, 2H), 5.90 (t, J = 5.7 Hz, 2H), 6.70 (s, 2H), 6.81 (d, J = 9.0 Hz, 4H), 7.08 (d, J = 9.0 Hz, 4H). MS (EI): m/z 818 (M^+). Anal. Calcd for $C_{52}H_{70}N_2O_6$: C, 76.25; H, 8.61; N, 3.42. Found: C, 76.39; H, 8.64; N, 3.16.

[2]Rotaxane 18. Compound **23** (0.82 g, 1.00 mmol) and triethylamine (2.1 mL) were dissolved in acetonitrile/chloroform (100 mL, 1:9). The mixture was stirred vigorously while a solution of **24** (1.09 g, 8.00 mmol) in chloroform (45 mL) and a solution of compound **25** (1.62 g, 8.00 mmol) in chloroform (45 mL) were added simultaneously over a period of 2 h. The solution was then stirred for 2 h, and the precipitate was filtered off. The solution was washed with dilute hydrochloride solution, dilute sodium carbonate solution, water, and brine and dried over sodium sulfate. After the solvent was removed, the residue was subjected to column chromatography (chloroform/methanol, 20:1). [2]Rotaxane **18** (0.77 g) was obtained as a white solid in 57% yield. Mp: >300 °C. ^{1}H NMR (DMSO-d_6): δ = 0.87−0.91 (m, 12H), 1.60−1.64 (m, 8H), 1.73−1.79 (m, 4H), 3.88−3.92 (m, 12H), 4.10−4.12 (m, 2H), 4.56 (br, 8H), 5.76 (s, 2H), 6.78 (d, J = 5.4 Hz, 8H), 7.07 (d, J = 5.4 Hz, 8H), 7.18 (s, 8H), 7.43 (s, 4H), 8.74 (s, 2H), 9.05 (s, 4H), 9.37 (br, 2H). MS (ESI): m/z 1553 [M^+ + H]. Anal. Calcd for $C_{82}H_{96}N_8O_{10}$: C, 72.76; H, 7.15; N, 8.28. Found: C, 72.72; H, 7.50; N, 8.11.

Binding Studies. For UV−vis absorption titration experiments, typically a chloroform solution of **Zn1** was prepared at a [**Zn1**·**Zn1**] of about 1.0 mM. Chloroform solutions of dipyridyl guests were prepared at concentrations of 10−1000 μM. A 2.5 mL sample of the mixture solution with the fixed [**Zn1**·**Zn1**] and the changing concentration of guests was placed in a cuvette, and the UV−vis absorption spectra were sequentially recorded. The values of the absorbance at fixed wavelengths were used. Origin6.0 software was used to fit the data to a 1:1 binding isotherm: $\Delta A = (\Delta A_{max}/[\mathbf{Zn1}\cdot\mathbf{Zn1}])\{0.5[G] + 0.5([\mathbf{Zn1}\cdot\mathbf{Zn1}] + K_d) - 0.5[[G]^2 + (2[G](K_d[\mathbf{Zn1}\cdot\mathbf{Zn1}]) + (K_d + [\mathbf{Zn1}\cdot\mathbf{Zn1}])^2)^{1/2}]\}$, where [G] is the dipyridyl guest concentration and $K_d = (K_{assoc})^{-1}$. For the ^{1}H NMR dilution study, the following equation was used to fit the 1:1 binding isotherm: $\Delta\delta = \delta - \delta_0 = \Delta\delta_{max}\{1 + (0.5/K_{assoc}[\mathbf{Zn1}\cdot\mathbf{Zn1}]) - [(0.5/K_{assoc}[\mathbf{Zn1}\cdot\mathbf{Zn1}])^2 + 1/K_{assoc}[\mathbf{Zn1}\cdot\mathbf{Zn1}]]^{1/2}\}$, where δ = the chemical shift of the probe signal in the monomer/complex mixture, δ_0 = the chemical shift of the probe signal in the monomer, and [**Zn1**·**Zn1**]) = [**18**]. Association constants reported are the average values of two or three experiments.

Acknowledgment. This work is financially supported by the Ministry of Science and Technology (Grant G2000078101), the National Natural Science Foundation of China (Grant 90206005), the Chinese Academy of Sciences, and the State Laboratory of Bio-Organic and Natural Products Chemistry of China. We thank Prof. Ji-Liang Shi and Min Shi for beneficial discussions.

JO0351872

(46) Chiles, M. S.; Jackson, D. D.; Reeves, P. C. *J. Org. Chem.* **1980**, *45*, 2915.