FULL PAPER

Self-Assembled Metallocycles with Two Interactive Binding Domains

Sung-Youn Chang, Hye-Young Jang, and Kyu-Sung Jeong*[a]

Dedicated to Professor Julius Rebek, Jr. on the occasion of his 60th birthday

Abstract: Five metallocycles **1a–e** have been self-assembled from S-shaped bis-pyridyl ligands **2a–e** and a palladium complex, [Pd(dppp)(OTf)$_2$] (dppp = 1,3-bis(diphenylphosphanyl)propane), and have been characterized by elemental analysis and various spectroscopic methods including ^{1}H NMR spectroscopy and electrospray ionization (ESI) mass spectrometry. These metallocycles all are monocyclic compounds, but can fold to generate two binding domains bearing hydrogen-bonding sites based on pyridine-2,6-dicarboxamide units. The binding properties of the metallocycles with *N,N,N′,N′*-tetramethylterephthalamide (**G**) have been probed by means of ESI mass spectrometry and ^{1}H NMR spectroscopy. The results both in the gas phase and in solution are consistent with the fact that the metallocycles accommodate two molecules of the guest **G**. Thus, the ESI mass spectra clearly show fragments corresponding to the 1:2 complexes in all cases. ^{1}H NMR studies on **1a** and **G** support the formation of a 1:2 complex in solution; the titration curves are nicely fitted to a 1:2 binding isotherm, but not to a 1:1 binding isotherm. In addition, a Job plot also suggests a 1:2 binding mode between **1a** and **G**, showing maximum complexation at ~0.33 mol fraction of the metallocycle **1a** in CDCl$_3$. The binding constants K_1 and K_2 are calculated to be 1600 and 1400 M^{-1} ($\pm 10\%$), respectively, at 25 °C in CDCl$_3$, indicative of positively cooperative binding. This positive cooperativity was confirmed by the Hill equation, affording a Hill coefficient of $n = 1.6$. Owing to insufficient solubility in CDCl$_3$, for comparison purposes the binding properties of the metallocycles **1b–e** were investigated in a more polar medium, 3% CD$_3$CN/CDCl$_3$. ^{1}H NMR titrations revealed that the metallocycles all bind two molecules of the guest **G** with Hill coefficients ranging from 1.4 to 1.8. This positive cooperativity may be attributed to a structural reorganization of the second binding cavity when the first guest binds to either one of the subcavities present in the metallocycles.

Keywords: allosterism · cooperative binding · hydrogen bonds · metallocycles · self-assembly

Introduction

Metal-coordination-driven self-assembly has been successfully used for the construction of two- and three-dimensional supramolecular entities with diverse structures and topologies. A large variety of such examples, including metallocycles, cages, polyhedra, and interlocked species, have been reported over the past decade,[1] and their sizes and shapes have been conveniently controlled by modification of the ligand as well as by the selection of metallic units with appropriate geometries.

In particular, two-dimensional metallocycles, such as triangles, squares, and higher polygons, have been mostly self-assembled with rigid bidendate ligands. These macrocycles possess a well-defined, internal cavity with nearly identical shape to that of the macrocycle itself, but only a few of them serve as artificial receptors for organic guests in solution.[2] This is attributed to weak intermolecular interactions between the nonpolar surfaces of the internal cavity and the guest in organic solvents, thus yielding a kinetically and thermodynamically unstable complex. One way of increasing the stability is to incorporate polar binding units inside the cavity. For example, Stang et al. attached silver ions, Ag^I, to the diagonal corners of a metallocycle for coordination of the heterocyclic guests pyrazine and phenazine.[3] Hunter's group[4] and our group[5] have utilized hydrogen-bonding interactions to enhance the binding affinity between a metallocycle and a dicarbonyl guest. Much effort is still needed for development of functional metallocycles that can serve as artificial receptors and bio-inspired models, beyond simple curiosity about their structures and shapes.

We report herein on the self-assembly and binding properties of the metallocycles **1a–e**, which are monocyclic but

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have two separate binding domains, and are thus capable of binding two molecules of a guest in a cooperative manner (Scheme 1).[6] The metallocycles have been self-assembled from S-shaped bispyridyl ligands **2a–e** with different linking units and a palladium complex, [Pd(dppp)(OTf)$_2$] (dppp =
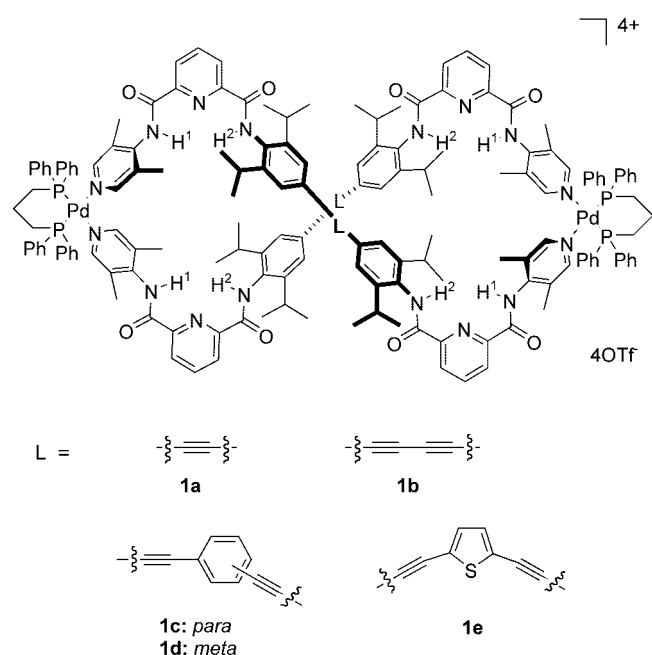

Scheme 1. The molecular formulae of metallocycles **1a, 1b, 1c, 1d**, and **1e**.

1,3-bis(diphenylphosphanyl)propane).[7] ^{1}H NMR spectroscopic and electrospray ionization (ESI) mass spectrometric results have proved that these metallocycles bind two molecules of a diamide guest, N,N,N',N'-tetramethylterephthalamide through the formation of intermolecular hydrogen bonds. The degree of cooperativity, as well as the magnitude of the binding constants, depends on the nature of the linker between the two binding domains. Although a variety of artificial allosteric models have been developed to date,[8, 9] this is the first example based on self-assembled metallocycles (Scheme 1).

Results and Discussion

Design principle and synthesis of ligands 2a–e: The ligands **2a–e** are composed of three functional parts (Scheme 2): a metal-coordination site at each end, a hydrogen-binding site at each corner, and a linker in the middle. The hydrogen-bonding site consists of a pyridine-2,6-dicarboxamide unit, both amide hydrogens of which are directed inwards by virtue of internal N–H(amide)···N(pyridine) hydrogen bonds,[10] as a result of which they are capable of being simultaneously involved in intermolecular hydrogen bonds. The methyl and isopropyl substituents on the aryl rings are introduced to increase the solubility of the ligands **2a–e**, and ultimately of the metallocycles **1a–e**, in organic solvents. The two hydrogen-binding sites are connected with flat link-
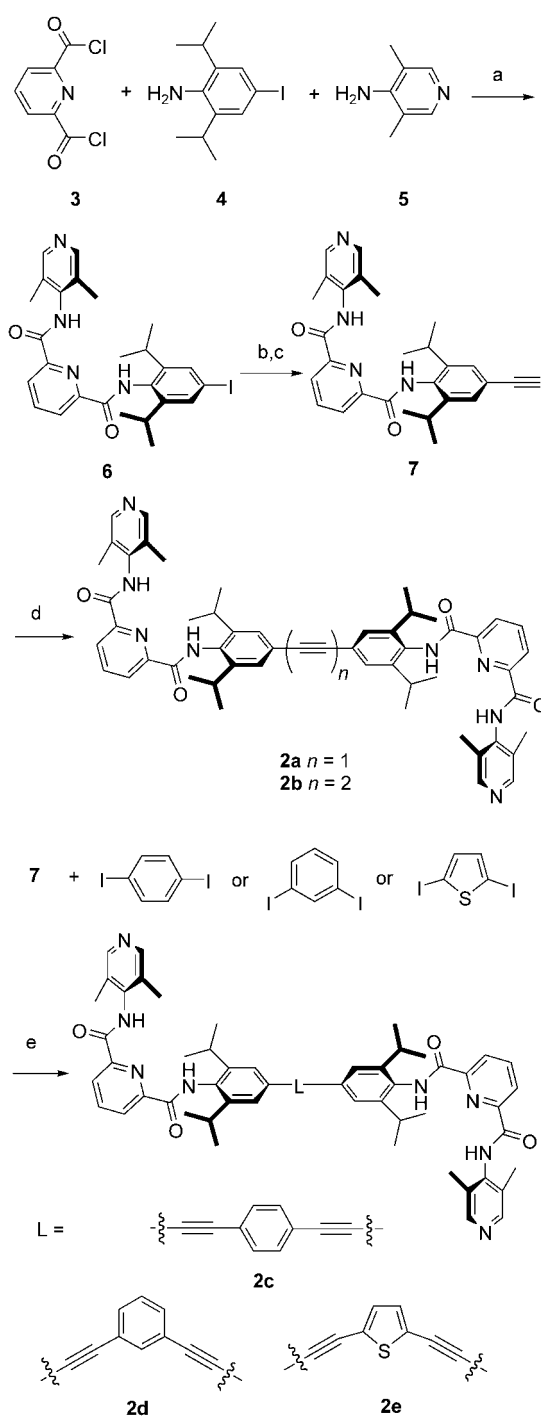
Scheme 2. Synthesis of ligands **2a–e**. Reagents, conditions, and yields: a) diisopropylethylamine, CH$_2$Cl$_2$, 0 °C to RT, 75 %; b) triisopropylsilyl-ethyne, [Pd(PPh$_3$)$_2$Cl$_2$], CuI, THF, Et$_3$N, 60–65 °C, 72 %; c) Bu$_4$NF, THF, H$_2$O, 60–70 °C, 91 %; d) **6**, [Pd(PPh$_3$)$_4$], CuI, Et$_2$NH, DMF, 60–65 °C, 60 % for **2a**, Cu(OAc)$_2$·H$_2$O, pyridine, 60–65 °C, 46 % for **2b**; e) [Pd(dba)$_2$], PPh$_3$, CuI, THF, Et$_3$N, 60–65 °C, 35–76 %.

ers such as ethynyl, phenylene, and thiophene, these units being expected to minimize steric crowding around the crossing point of the two ligand strands upon assembly of the metallocycle. Moreover, the rigidity of these linkers prevents the formation of mononuclear metallocycles by 1:1 (ligand/metal) assembly.

The syntheses of the ligands **2a–e** are outlined in Scheme 2. Stepwise coupling of pyridine-2,6-dicarbonyl dichloride (**3**) with 4-iodo-2,6-diisopropylaniline (**4**),[11] and 4-amino-3,5-dimethylpyridine (**5**)[12] gave compound **6** in 75% yield. Palladium-catalyzed Sonogashira coupling[13] (72% yield) of **6** and triisopropylsilylethyne, followed by removal of the silyl moiety with Bu₄NF (91%), provided compound **7**. Finally, **7** was coupled with **6**, 1,4- and 1,3-diiodobenzenes, and 2,5-diiodothiophene to afford the S-shaped ligands **2a**, **2c**, **2d**, and **2e**, respectively, in 35–76% yields. On the other hand, the butadiynyl-linked ligand **2b** was obtained by Cu[II]-catalyzed dimerization of **7** in 46% yield.

Synthesis and characterization of metallocycles 1a–e: For the synthesis of **1a–e**, Stang's bisphosphinepalladium complex [Pd(dppp)(OTf)₂][7] was chosen, which has been widely used in the construction of supramolecular squares soluble in organic solvents.[1h,q] The self-assembly of **1a–e** was conducted at room temperature by simple mixing of the ligands **2a–e** with [Pd(dppp)(OTf)₂] in a 1:1 molar ratio in CH₂Cl₂ containing a small amount of dimethyl sulfoxide or acetonitrile. In the case of ligand **2a**, which is sparingly soluble, the initial suspension became a clear solution as the reaction proceeded. All the reactions proceeded quantitatively, but the isolated yields were 76–98%.

Elemental analyses and spectroscopic data of the products were all consistent with the structures of the metallocycles **1a–e** shown in Scheme 1. The ¹H NMR signals for the pyridyl C-H protons of **1a–e** are shifted downfield ($\Delta\delta$ = 0.3–0.4 ppm) compared to those of the free ligands **2a–e**, as expected for coordination of the pyridyl nitrogen atom to the Pd[II] center. Elemental analyses and ¹H NMR integrals supported a 1:1 ratio of the ligand and metal components. ESI mass spectrometry provided clear evidence for the formation of dinuclear metallocycles **1a–e** as a result of 2:2 (ligand/metal) assembly. For instance, the mass spectrum of **1a** in CHCl₃ clearly shows the fragments [**1a**−2OTf]²⁺ (*m/z* 1549, 3%), [**1a**−3OTf]³⁺ (*m/z* 983, 14%), and [**1a**−4OTf]⁴⁺ (*m/z* 700, 7%), along with fragments corresponding to the complexes (which are discussed further below) in the presence of *N,N,N′,N′*-tetramethylterephthalamide (**G**) as a guest (Figure 1). Moreover, the observed isotopic distributions of these peaks are in accordance with theoretical ones based on the dinuclear metallocycle **1a** (Figure 2).

The ESI mass spectra of **1b–e** are all consistent with dinuclear structures resulting from 2:2 ligand/metal assembly.[14] For **1b**, characteristic peaks due to [**1b**−2OTf]²⁺, [**1b**−3OTf]³⁺, and [**1b**−4OTf]⁴⁺ appear at *m/z* 1574 (100%), 1000 (65%), and 712 (70%), respectively, in 50% CHCl₃/CH₃CN. Likewise, the other metallocycles **1c**, **1d**, and **1e** show the mass fragments [*M*−3OTf]³⁺ and [*M*−4OTf]⁴⁺ with reasonable intensities under the same conditions. No signal attributable to higher aggregates such as a 3:3 (ligand/metal) complex is seen in any case (see Supporting Information).

Conformations and binding properties of 1a–e: As shown schematically in Figure 3, S- and C-shaped conformations are possible for the free ligands **2a–e**. Consequently, when two molecules of each ligand and two metal ions are assem-
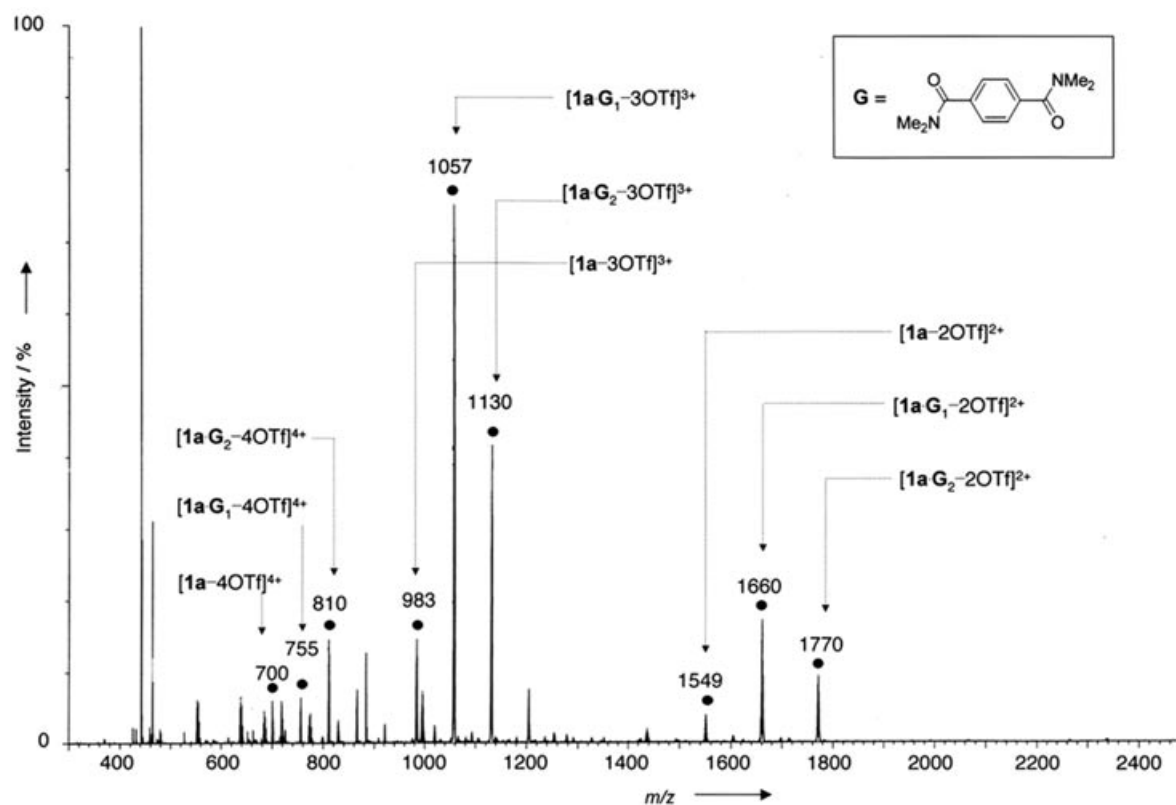

Figure 1. Electrospray ionization (ESI) mass spectrum of **1a** and excess **G** in CHCl₃.
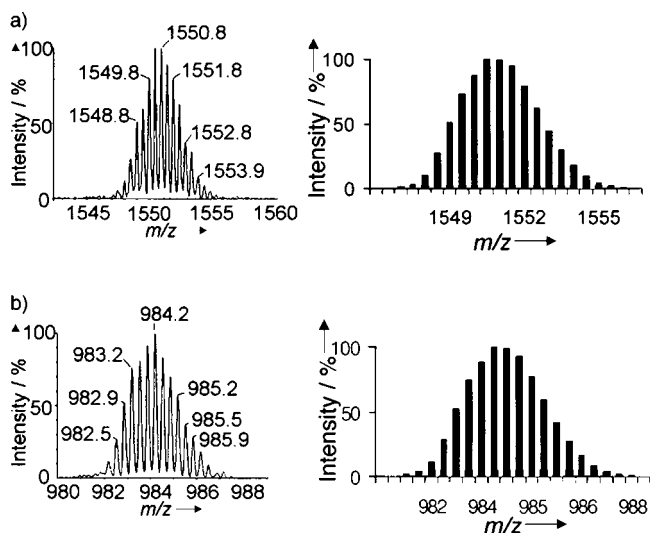
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Figure 2. Observed (left) and theoretical (right) isotopic distributions for the fragments a) $[\mathbf{1a}-2\,OTf]^{2+}$ and b) $[\mathbf{1a}-3\,OTf]^{3+}$.

Figure 4. a) Top and b) side views of energy-minimized structure of metallocycle **1a**. Hydrogen atoms have been omitted for clarity.
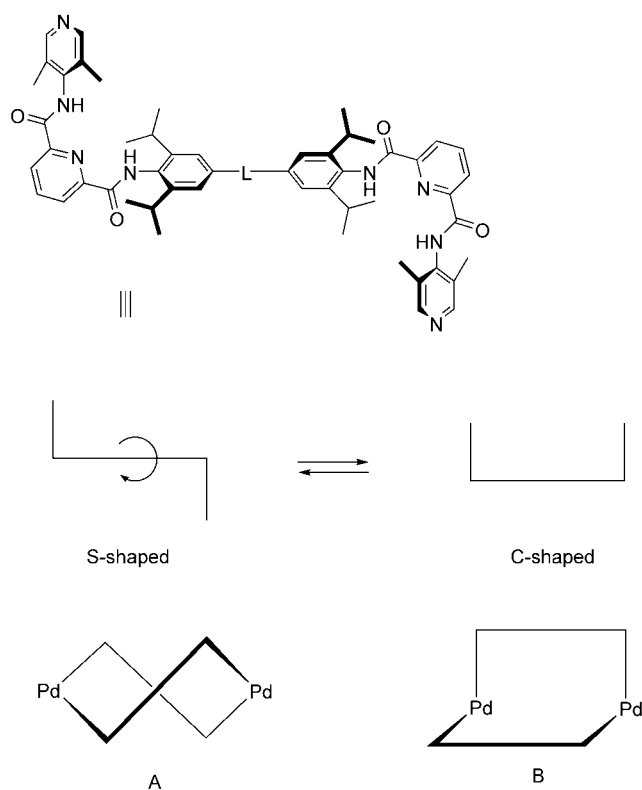

Figure 3. Two plausible conformers of ligands **2a–e** and metallocycles **1a–e**.

bled to form the dinuclear metallocycles **1a–e**, two different conformers, **A** and **B**, can be envisaged. Both of them are monocyclic structures, but the side views of the conformers are different. Computer modeling using the MacroModel program[15] with the MM3* force field afforded conformer **A** as the energy-minimized structure, which resembles the Arabic number '8' (Figure 4).[16] Unfortunately, no single crystals of **1a–e** suitable for X-ray crystallographic analysis
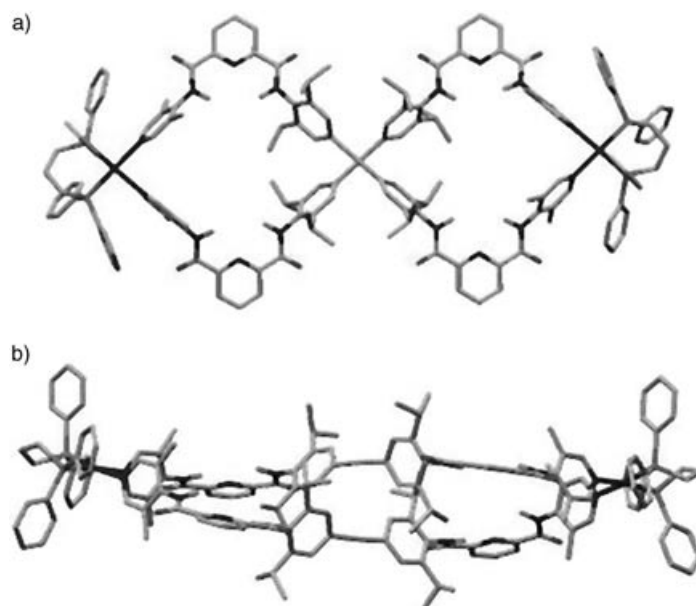
could be obtained, despite a large number of attempts under various conditions. However, the binding properties of the metallocycles described below are consistent with the energy-minimized structure, which has two symmetrical subcavities to allow the binding of two molecules of a guest, one to each subcavity.

For binding studies, *N,N,N′,N′*-tetramethylterephthalamide (**G**; Scheme 3) was chosen as a guest because computer modeling showed that it can be nicely fitted into each cavity. The binding properties of the the metallocycles with the guest **G** were first examined by ESI mass spectrometry. Mass spectra were recorded from a mixture of each metallocycle and excess **G** (~10 equiv) in pure $CHCl_3$ or in 3% $CH_3CN/CHCl_3$. A representative example is shown in Figure 1, which is the ESI mass spectrum obtained from a solution of **1a** and excess **G** (~10 equiv) in $CHCl_3$. Evidently, fragments corresponding to a 1:2 complex $\mathbf{1a\cdot G_2}$ can be seen at m/z 1770 ($[\mathbf{1a\cdot G_2}-2\,OTf]^{2+}$, 9%), m/z 1130 ($[\mathbf{1a\cdot G_2}-3\,OTf]^{3+}$, 45%), and m/z 810 ($[\mathbf{1a\cdot G_2}-4\,OTf]^{4+}$, 14%). In addition, the mass spectrum also shows peaks corresponding to the 1:1 complex $\mathbf{1a\cdot G_1}$ and the metallocycle **1a** itself.

Next, the binding interactions between **1a** and **G** in solution were probed by ${}^1H$ NMR titrations. When a small portion of the guest **G** was added to a solution of **1a** in $CDCl_3$ at 25°C, the two NH resonances of **1a** were gradually shifted from $\delta = 9.26$ and 8.92 ppm to $\delta = 10.36$ and 10.27 ppm, respectively, as a result of hydrogen-bonding interactions (Figure 5b). Meanwhile, the signal due to the aromatic protons of **G** was significantly upfield-shifted ($\Delta\delta \approx 1.0$ ppm) upon complexation, implying that **G** is located within a cavity surrounded by the aromatic surfaces of the pyridine moieties. These observations closely match those obtained in our previous studies[17] on a molecular square **8** that possesses a single binding cavity, implying that the environment of each cavity in **1a** is similar to that in **8**.
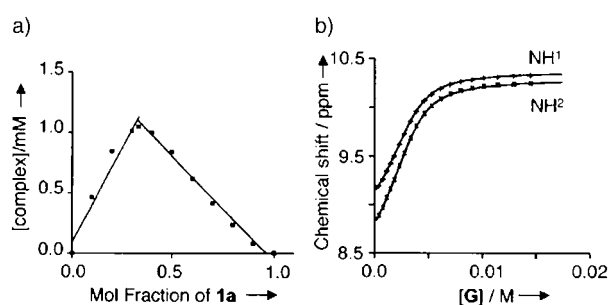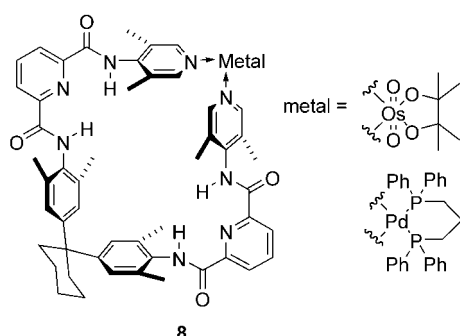
Figure 5. a) Job plot for the binding between metallocycle **1a** (NH[1]) and guest **G**, and b) ^{1}H NMR titration curves for **1a** and **G** in CDCl$_3$ at 25 °C. Solid lines are theoretical ones, obtained from the 1:2 binding isotherm of the HOSTEST program.

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The binding constants were first evaluated by nonlinear least-squares fitting using the HOSTEST program developed by Wilcox.[18] The titration curves were poorly fitted to a 1:1 binding isotherm, but nicely fitted to a 1:2 binding isotherm (Figure 5b). Job plots[19] also support a 1:2 binding mode, showing the highest concentration of the complex at ~0.33 mol fraction of **1a** in CDCl$_3$ (Figure 5a). The binding constants ($\pm$10 %) K_1 (= [**1a·G**$_1$]/[**1a**][**G**]) and K_2 (= [**1a·G**$_2$]/[**1a·G**$_1$][**G**]) were found to be 1600 and 1400 M^{-1}, respectively. Considering the relationship $K_2 = \frac{1}{4}K_1$ for non-cooperative binding, these values reflect positively cooperative binding of two molecules of the guest. This cooperative binding between **1a** and **G** was confirmed by the Hill equation[19] (see below for details), affording values of $n = 1.6$ and $\log K = 4.9$.

The metallocycles **1b–e**, which have different kinds of linkers, are poorly soluble in CDCl$_3$ alone, but all proved to be sufficiently soluble in 3 % CD$_3$CN/CDCl$_3$ to allow binding studies to be conducted. The ESI mass spectral pattern of a mixture of **1a** and **G** in 3 % CH$_3$CN/CHCl$_3$ is the same as that in CHCl$_3$ (Figure 1) except for the relative intensities

of the fragments (see Supporting Information). Similarly, the ESI mass spectra of metallocycles **1b–e** in the presence of **G** showed fragments corresponding to the 1:2 complexes, along with those corresponding to the 1:1 complexes and the free macrocycles. The results are summarized in Table 1 (see also the Supporting Information).

The ^{1}H NMR titration experiments were duplicated and performed at 23 $\pm$ 1 °C by gradually increasing the mole fraction of the guest **G** at a constant concentration of the metallocycle (0.5 mM in 3 % CD$_3$CN/CDCl$_3$). During the titrations, the amide NH signals of the metallocycle were shifted downfield ($\Delta\delta \approx 1$ ppm). The data were analyzed by using the Hill equation, which is based on the assumption of a single equilibrium process as depicted in Equation (1)[19]

$$H + 2G \rightleftharpoons HG_2 \qquad (1)$$

where

$$K = \frac{[HG_2]}{[H][G]^2}.$$

This equation can be transformed into $\log(y/(1-y)) = n\log[G] + \log K$, where n and K are the Hill coefficient and the binding constant, respectively, and $y = K/([G]^{-n} + K)$. The magnitudes of n and $\log K$ can then be obtained from the slope and the intercept of a linear plot of $\log(y/(1-y))$ versus $\log[G]$.

Table 1. ESI mass spectral data of metallocycles **1a–e** in the presence of excess guest **G** in 3 % CH$_3$CN/CHCl$_3$.

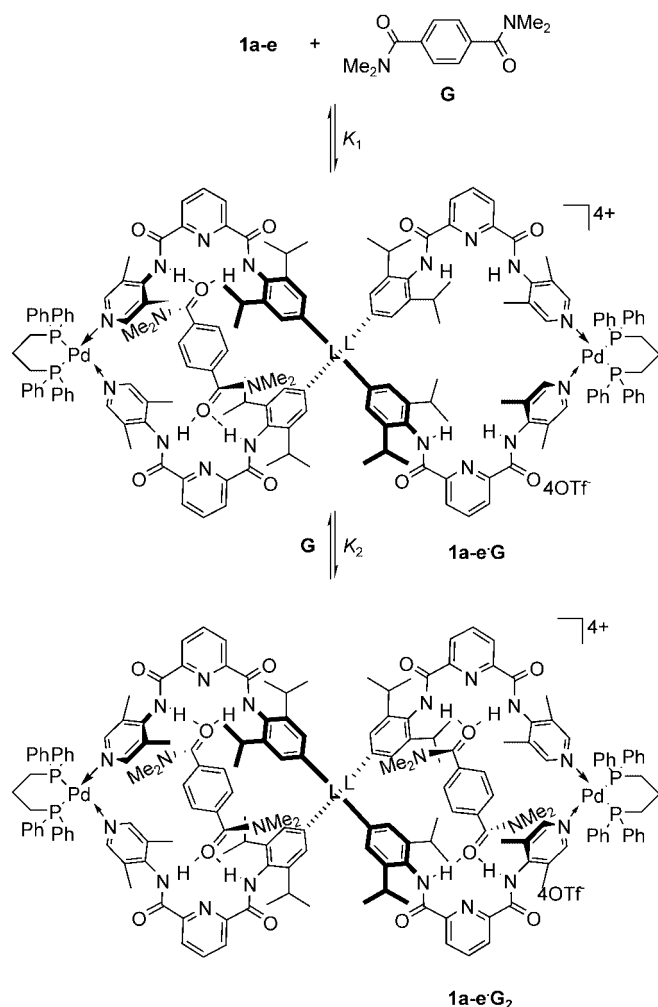|	Metallocycle		1:1 Complex		1:2 Complex	
	ion	m/z (intensity, %)	ion	m/z (intensity, %)	ion	m/z (intensity, %)
1a	[**1a**–2OTf]$^{2+}$	1549(3)	[**1a·G**$_1$–2OTf]$^{2+}$	1660(16)	[**1a·G**$_2$–2OTf]$^{2+}$	1770(9)
	[**1a**–3OTf]$^{3+}$	983(14)	[**1a·G**$_1$–3OTf]$^{3+}$	1057(76)	[**1a·G**$_2$–3OTf]$^{3+}$	1130(55)
	[**1a**–4OTf]$^{4+}$	700(17)	[**1a·G**$_1$–4OTf]$^{4+}$	755(7)	[**1a·G**$_2$–4OTf]$^{4+}$	810(40)
1b	[**1b**–2OTf]$^{2+}$	1574(3)	[**1b·G**$_1$–2OTf]$^{2+}$	1684(7)	[**1b·G**$_2$–2OTf]$^{2+}$	1794(7)
	[**1b**–3OTf]$^{3+}$	1000(13)	[**1b·G**$_1$–3OTf]$^{3+}$	1073(38)	[**1b·G**$_2$–3OTf]$^{3+}$	1146(25)
	[**1b**–4OTf]$^{4+}$	712(80)	[**1b·G**$_1$–4OTf]$^{4+}$	768(4)	[**1b·G**$_2$–4OTf]$^{4+}$	823(32)
1c	[**1c**–2OTf]$^{2+}$	1651(2)	[**1c·G**$_1$–2OTf]$^{2+}$	1761(6)	[**1c·G**$_2$–2OTf]$^{2+}$	1871(8)
	[**1c**–3OTf]$^{3+}$	1051(36)	[**1c·G**$_1$–3OTf]$^{3+}$	1124(80)	[**1c·G**$_2$–3OTf]$^{3+}$	1197(100)
	[**1c**–4OTf]$^{4+}$	751(35)	[**1c·G**$_1$–4OTf]$^{4+}$	806(27)	[**1c·G**$_2$–4OTf]$^{4+}$	861(68)
1d	[**1d**–2OTf]$^{2+}$	1651(1)	[**1d·G**$_1$–2OTf]$^{2+}$	1761(2)	[**1d·G**$_2$–2OTf]$^{2+}$	1871(10)
	[**1d**–3OTf]$^{3+}$	1051(27)	[**1d·G**$_1$–3OTf]$^{3+}$	1124(84)	[**1d·G**$_2$–3OTf]$^{3+}$	1197(100)
	[**1d**–4OTf]$^{4+}$	751(24)	[**1d·G**$_1$–4OTf]$^{4+}$	806(35)	[**1d·G**$_2$–4OTf]$^{4+}$	861(84)
1e	[**1e**–2OTf]$^{2+}$	1656(1)	[**1e·G**$_1$–2OTf]$^{2+}$	1766(5)	[**1e·G**$_2$–2OTf]$^{2+}$	1876(10)
	[**1e**–3OTf]$^{3+}$	1055(50)	[**1e·G**$_1$–3OTf]$^{3+}$	1128(52)	[**1e·G**$_2$–3OTf]$^{3+}$	1201(100)
	[**1e**–4OTf]$^{4+}$	754(67)	[**1e·G**$_1$–4OTf]$^{4+}$	809(30)	[**1e·G**$_2$–4OTf]$^{4+}$	864(85)

The results are summarized in Table 2. Here, the Hill coefficient n reflects the degree of cooperativity and should be between 1 and 2 for positive cooperativity in this system with two binding sites. When the medium is changed from CDCl$_3$ to 3 % CD$_3$CN/CDCl$_3$, the Hill coefficient n (= 1.6) for **1a** remains constant, but the overall binding affinity $\log K$ considerably decreases from 4.9 to 2.8 as expected. All of the metallocycles **1a–e** show a positive cooperativity with Hill coefficients ranging from 1.4 to 1.8.[20] Among them, the metallocycle **1b**, which has a butadiynyl linker, shows the highest cooperativity as well as the strongest binding affini-

Conclusion

We have described the self-assembly of metallocycles that fold to create two symmetrical binding cavities possessing hydrogen-bonding sites. Two molecules of a diamide guest, one to each cavity, have been shown to bind in a positively cooperative manner to the metallocycles through hydrogen-bonding interactions. These metallocycles therefore belong to a new type of positive homotropic allosteric models, which have been rarely reported to date. As illustrated in this study, the design and self-assembly of an artificial supramolecular entity that functions at least partly as seen in natural macromolecules is one of the most important goals in supramolecular chemistry.

Experimental Section

General methods: Unless otherwise noted, all reagents were used as received. Dichloromethane, chloroform, and acetonitrile were distilled under nitrogen from CaH_2, tetrahydrofuran from Na/benzophenone, and N,N-diisopropylethylamine and Et_3N from KOH. DMF was dried over anhydrous $MgSO_4$ and distilled under reduced pressure. Melting points were determined using a Mel-Temp II capillary melting point apparatus and are uncorrected. Infrared spectra were obtained on a Nicolet Impact 410 FT-IR spectrometer. All NMR spectra were recorded on a DRX-500 spectrometer and chemical shifts are reported in ppm downfield from TMS ($\delta = 0$), relative to the residual protonated solvent peaks (CHCl$_3$: $\delta = 7.26$ ppm for ^{1}H NMR, $\delta = 77$ ppm for ^{13}C NMR). ESI mass spectra were obtained with a QUATTRO LC triple-quadrupole tandem mass spectrometer (Micromass, UK). Column chromatography was performed on silica gel (230–400 mesh).

N-(4-Iodo-2,6-diisopropylphenyl)-N-(3,5-dimethylpyridin-4-yl)pyridine-2,6-dicarboxamide (6): A solution of 4-iodo-2,6-diisopropylaniline (4)[11] (1.2 g, 4.0 mmol) and N,N-diisopropylethylamine (3.0 mL, 16 mmol) in CH$_2$Cl$_2$ (10 mL) was slowly added over 2 h by means of a syringe pump to a solution of 2,6-pyridinedicarbonyl dichloride (3) (0.81 g, 4.0 mmol) in CH$_2$Cl$_2$ (30 mL) at 0 °C (iced-water bath). The mixture was stirred for 3 h at room temperature, and then 4-amino-3,5-dimethylpyridine (5)[12] (0.48 g, 4.0 mmol) was added. After stirring at room temperature for an additional 2 h, the solution was washed with saturated NaHCO$_3$ solution and brine, and dried over anhydrous MgSO$_4$. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (acetone/CHCl$_3$, 1:1) to give 6 as a white solid (1.7 g, 75%); m.p. 270–271 °C; ^{1}H NMR (500 MHz, CDCl$_3$, 25 °C): $\delta = 9.54$ (s, 1H; NH), 9.05 (s, 1H; NH), 8.57 (d, ^3J(H,H) = 7.8 Hz, 1H; Ar-H), 8.51 (d, ^3J(H,H) = 7.8 Hz, 1H; Ar-H), 8.27 (s, 2H; Ar-H), 8.19 (t, ^3J(H,H) = 7.8 Hz, 1H; Ar-H), 7.53 (s, 2H; Ar-H), 3.12 (m, 2H; CH(CH$_3$)$_2$), 2.21 (s, 6H; Ar-CH$_3$), 1.21 ppm (d, ^3J(H,H) = 6.8 Hz, 12H; CH(CH_3)$_2$); ^{13}C NMR (126 MHz, CDCl$_3$, 25 °C): $\delta = 162.9$, 161.0, 149.5, 149.2, 148.8, 148.2, 141.6, 139.9, 133.3, 131.1, 130.0, 126.7, 126.0, 95.2, 29.1, 23.7, 15.7 ppm; IR (KBr): $\tilde{\nu} = 3287$ (NH), 1693 cm^{-1} (C=O); elemental analysis calcd (%) for C$_{26}$H$_{29}$IN$_4$O$_2$ (556.44): C 56.12, H 5.25, N 10.07; found: C 56.50, H 5.28, N 9.96.

N-(4-Ethynyl-2,6-diisopropylphenyl)-N-(3,5-dimethylpyridin-4-yl)pyridine-2,6-dicarboxamide (7): Compound 6 (2.9 g, 5.2 mmol), CuI (40 mg, 0.21 mmol), and [Pd(PPh$_3$)$_2$Cl$_2$] (76 mg, 0.11 mmol) were placed in a Schlenk tube, and the tube was evacuated and back-filled with nitrogen three times. Tetrahydrofuran (THF, 60 mL), triethylamine (Et$_3$N, 3.0 mL), and triisopropylsilylacetylene (1.8 mL, 8.0 mmol, 1.5 equiv) were added, and the solution was stirred at 60–65 °C for 17 h. The reaction mixture was then filtered through Celite, the filtrate was washed with saturated NaHCO$_3$ solution and brine, and dried over anhydrous MgSO$_4$. After concentration, the residue was purified by column chromatography (acetone/CHCl$_3$, 1:1) to give an intermediate en route to 7, bearing a triisopropylsilanylethynyl substituent, as a white solid (2.3 g, 72%); m.p. 264–265 °C; ^{1}H NMR (500 MHz, CDCl$_3$, 25 °C): $\delta = 9.67$ (s, 1H; NH),

Table 2. Comparison of Hill coefficient (n) and log K of metallocycles **1a–e** in 3% CD$_3$CN/CDCl$_3$ at 23 ± 1 °C.[a]

Metallocycle	n	log K
1a	1.6	2.8
1b	1.8	4.2
1c	1.5	3.2
1d	1.5	3.5
1e	1.4	3.0

[a] Errors in the magnitudes of n and log K are less than 15% in all cases.

ty. Although the degree of cooperativity observed here is modest owing to the rigid skeleton of the metallocycle, the positive cooperativity dictates the structural organization of the second binding cavity when a guest binds to either one of the subcavities. That is, the distance between two hydrogen-bonding sites in the subcavity may be favorably changed for the second guest to form stronger hydrogen bonds in a bridged manner (Scheme 3), thus enhancing the second binding affinity.

Scheme 3. Proposed structures of 1:1 and 1:2 complexes between metallocycles **1a–e** and guest **G**.

9.06 (s, 1H; NH), 8.57 (d, ^3J(H,H) = 7.7 Hz, 1H; Ar-H), 8.50 (d, ^3J(H,H) = 7.7 Hz, 1H; Ar-H), 8.26 (s, 2H; Ar-H), 8.18 (t, ^3J(H,H) = 7.7 Hz, 1H; Ar-H), 7.31 (s, 2H; Ar-H), 3.17 (m, 2H; CH(CH$_3$)$_2$), 2.19 (s, 6H; Ar-CH$_3$), 1.23 (d, ^3J(H,H) = 6.8 Hz, 12H; CH(CH_3)$_2$), 1.15 ppm (s, 21H; SiCH(CH$_3$)$_2$); ^{13}C NMR (126 MHz, CDCl$_3$): δ = 162.9, 161.0, 149.5, 149.3, 148.2, 146.4, 141.7, 139.8, 131.5, 130.0, 127.7, 126.6, 125.8, 123.9, 107.5, 90.5, 29.2, 23.7, 18.9, 15.6, 11.5 ppm; IR (KBr): $\tilde{\nu}$ = 3346 (NH), 2159 (C≡C), 1684 cm^{-1} (C=O); elemental analysis calcd (%) for C$_{37}$H$_{50}$N$_4$O$_2$Si (610.90): C 72.74, H 8.25, N 9.17; found: C 72.76, H 8.41, N 9.03.

The aforementioned intermediate bearing a triisopropylsilanylethynyl substituent (2.3 g, 3.7 mmol) was taken up in THF (60 mL) containing H$_2$O (1.0 mL), and Bu$_4$NF (5.6 mL of 1.0 M THF solution, 1.5 equiv) was added. The solution was stirred at 60–70 °C for 14 h, and then iced water (40 mL) was added. The resulting mixture was extracted with CHCl$_3$ (3 × 30 mL), and the combined organic layers were washed with brine and dried over anhydrous MgSO$_4$. After concentration, the residue was purified by column chromatography (acetone/CHCl$_3$, 1:2) to give **7** as a white solid (1.5 g, 91%); m.p. 268–269 °C (dec.); ^{1}H NMR (500 MHz, CDCl$_3$, 25 °C): δ = 9.57 (s, 1H; NH), 9.06 (s, 1H; NH; Ar-H), 8.57 (d, ^3J(H,H) = 7.7 Hz, 1H; Ar-H), 8.51 (d, ^3J(H,H) = 7.7 Hz, 1H; Ar-H), 8.28 (s, 2H; Ar-H), 8.19 (t, ^3J(H,H) = 7.7 Hz, 1H; Ar-H), 7.37 (s, 2H; Ar-H), 3.17 (m, 2H; CH(CH$_3$)$_2$), 3.09 (s, 1H; C≡CH), 2.20 (s, 6H; Ar-CH$_3$), 1.23 ppm (d, ^3J(H,H) = 6.8 Hz, 12H; CH(CH_3)$_2$); ^{13}C NMR (126 MHz, CDCl$_3$, 25 °C): δ = 162.9, 161.0, 149.6, 149.2, 148.2, 146.7, 141.6, 139.9, 131.9, 130.0, 127.9, 126.6, 126.0, 122.4, 84.0, 29.2, 23.7, 15.7 ppm; IR (KBr): $\tilde{\nu}$ = 3334 (NH), 1696 cm^{-1} (C=O); elemental analysis calcd (%) for C$_{28}$H$_{30}$N$_4$O$_2$ (454.56): C 73.98, H 6.65, N 12.33; found: C 73.64, H 6.72, N 12.17.

Ligand 2a: Compound **6** (0.61 g, 1.1 mmol), **7** (0.50 g, 1.1 mmol), CuI (21 mg, 0.11 mmol, 0.1 equiv), and [Pd(PPh$_3$)$_4$] (64 mg, 0.055 mmol, 0.05 equiv) were placed in a Schlenk tube, and then the tube was degassed and back-filled with nitrogen three times. Degassed N,N-dimethylformamide (DMF, 30 mL) and diethylamine (Et$_2$NH, 5 mL) were added, and the solution was stirred at 60–65 °C for 25 h. Thereafter, the reaction mixture was filtered and the filter cake was collected and dissolved in CHCl$_3$ containing dimethyl sulfoxide (DMSO). After the removal of insoluble particles, n-hexane was added to the solution and the product was precipitated out. The precipitate was washed with CHCl$_3$ and dried to give a white solid (0.58 g, 60%); m.p. >270 °C; ^{1}H NMR (500 MHz, 95:5 CDCl$_3$/[D$_6$]DMSO, 25 °C): δ = 10.76 (s, 2H; NH), 10.64 (s, 2H; NH), 8.49–8.46 (m, 4H; Ar-H), 8.39 (s, 4H; Ar-H), 8.15 (t, ^3J(H,H) = 7.6 Hz, 2H; Ar-H), 7.44 (s, 4H; Ar-H), 3.25–3.22 (m, 4H; CH(CH$_3$)$_2$), 2.33 (s, 12H; Ar-CH$_3$), 1.26 ppm (d, ^3J(H,H) = 6.4 Hz, 24H; CH(CH_3)$_2$); ^{13}C NMR (125 MHz, 95:5 CDCl$_3$/[D$_6$]DMSO, 25 °C): δ = 163.7, 162.3, 149.7, 149.3, 148.7, 147.4, 143.1, 139.4, 133.1, 131.3, 127.2, 125.9, 125.6, 123.2, 89.8, 29.1, 24.0, 15.7 ppm; IR (KBr): $\tilde{\nu}$ = 3347 (NH), 1690 cm^{-1} (C=O); elemental analysis calcd (%) for C$_{54}$H$_{58}$N$_8$O$_4$ (883.09): C 73.44, H 6.62, N 12.69; found: C 73.61, H 6.84, N 12.77.

Ligand 2b: Compound **7** (2.9 g, 6.3 mmol) was dissolved in pyridine (60 mL) and Cu(OAc)$_2$·H$_2$O (2.5 g, 13 mmol, 2.0 equiv) was added. The solution was stirred at 60–65 °C for 20 h and then iced-water (100 mL) was added. The resulting mixture was extracted with CHCl$_3$ (2 × 30 mL), and the combined organic layers were washed first with 25% acetic acid (100 mL) and then with 25% NaHCO$_3$ solution (120 mL). After concentration, the residue was purified by column chromatography (MeOH/CHCl$_3$/EtOAc, 1:10:10) to give ligand **2b** as a white solid (1.3 g, 46%); m.p. >270 °C; ^{1}H NMR (500 MHz, 3% CD$_3$CN/CDCl$_3$, 25 °C): δ = 9.66 (s, 2H; NH), 9.59 (s, 2H; NH), 8.52 (m, 4H; Ar-H), 8.38 (s, 4H; Ar-H), 8.19 (t, ^3J(H,H) = 7.7 Hz, 2H; Ar-H), 7.42 (s, 4H; Ar-H), 3.17 (m, 4H; CH(CH$_3$)$_2$), 2.30 (s, 12H; Ar-CH$_3$), 1.22 ppm (d, ^3J(H,H) = 6.6 Hz, 24H; CH(CH_3)$_2$); ^{13}C NMR (125 MHz, 3% CD$_3$CN/CDCl$_3$, 25 °C): δ = 162.7, 161.2, 149.3, 148.5, 148.1, 147.1, 141.7, 139.4, 132.5, 130.1, 127.8, 125.8, 125.6, 121.6, 81.8, 73.7, 28.8, 23.3, 15.2 ppm; IR (KBr): $\tilde{\nu}$ = 3288 (NH), 1696 cm^{-1} (C=O); MALDI-MS (m/z): [M+H]$^+$ calcd for C$_{56}$H$_{58}$N$_8$O$_4$: 907.46; found: 907.46.

Ligand 2c: 1,4-Diiodobenzene (0.15 g, 0.44 mmol, 1 equiv), **7** (0.40 g, 0.88 mmol, 2 equiv), [Pd(dba)$_2$] (21 mg, 0.036 mmol, 0.08 equiv; dba = *trans,trans*-dibenzylideneacetone), PPh$_3$ (46 mg, 0.18 mmol, 0.4 equiv), and CuI (8.0 mg, 0.042 mmol, 0.1 equiv) were placed in a Schlenk tube, and then the tube was degassed and back-filled with nitrogen three times.

Degassed THF (10 mL) and Et$_3$N (1.5 mL) were added to the tube and the mixture was heated at 60–65 °C for 19 h. After the mixture was cooled to room temperature, CHCl$_3$ (20 mL) and MeOH (10 mL) were added to dissolve the organic suspension. The mixture was filtered through Celite, and the filtrate was concentrated. The residue was redissolved in CHCl$_3$ (50 mL) and washed with saturated NaHCO$_3$ solution and brine. After concentration, the residue was purified by column chromatography (CHCl$_3$/MeOH, 10:1) to give **2c** as a pale yellow solid (0.25 g, 57%); m.p. 200 °C; ^{1}H NMR (500 MHz, 3% CD$_3$CN/CDCl$_3$, 25 °C): δ = 9.60 (2H; NH), 9.48 (2H; NH), 8.52–8.49 (m, 4H; Ar-H), 8.36 (s, 4H; Ar-H), 8.17 (t, ^3J(H,H) = 7.7 Hz, 2H; Ar-H), 7.53 (s, 4H; Ar-H), 7.40 (s, 4H; Ar-H), 3.16 (m, 4H; CH(CH$_3$)$_2$), 2.29 (s, 12H; Ar-CH$_3$), 1.23 ppm (d, ^3J(H,H) = 6.6 Hz, 24H; CH(CH_3)$_2$); ^{13}C NMR (125 MHz, 3% CD$_3$CN/CDCl$_3$, 25 °C): δ = 162.7, 161.2, 149.4, 148.7, 148.2, 146.9, 141.7, 139.5, 131.6, 131.5, 130.1, 127.0, 125.9, 125.6, 123.0, 116.4, 91.4, 88.9, 28.9, 23.4, 15.3 ppm; IR (KBr): $\tilde{\nu}$ = 3340 (NH), 1689 cm^{-1} (C=O); elemental analysis calcd (%) for C$_{62}$H$_{62}$N$_8$O$_4$ (983.21): C 75.74, H 6.36, N 11.40; found: C 75.75, H 6.42, N 11.23.

Ligand 2d: Compound **2d** was synthesized according to the procedure described for the synthesis of **2c**, except that 1,3-diiodobenzene was used instead of 1,4-diiodobenzene. The product was obtained as a pale yellow solid (35%); m.p. 204–206 °C; ^{1}H NMR (500 MHz, 3% CD$_3$CN/CDCl$_3$, 25 °C): δ = 9.61 (2H; NH), 9.50 (2H; NH), 8.52–8.49 (m, 4H; Ar-H), 8.36 (s, 4H; Ar-H), 8.16 (t, ^3J(H,H) = 7.8 Hz, 2H; Ar-H), 7.76 (s, 1H; Ar-H), 7.50 (d, ^3J(H,H) = 7.7 Hz, 2H; Ar-H), 7.40 (s, 4H; Ar-H), 7.35 (t, ^3J(H,H) = 7.7 Hz, 1H; Ar-H), 3.16 (m, 4H; CH(CH$_3$)$_2$), 2.28 (s, 12H; Ar-CH$_3$), 1.23 ppm (d, ^3J(H,H) = 6.7 Hz, 26H; CH(CH$_3$)$_2$); ^{13}C NMR (125 MHz, 3% CD$_3$CN/CDCl$_3$, 25 °C): δ = 162.7, 161.2, 149.4, 148.6, 148.2, 146.9, 141.7, 139.4, 131.6, 131.2, 130.1, 128.5, 127.0, 125.9, 125.6, 123.5, 122.9, 116.3, 90.1, 88.3, 28.8, 23.4, 15.3 ppm; IR (KBr): $\tilde{\nu}$ = 3373 (NH), 1686 cm^{-1} (C=O); elemental analysis calcd (%) for C$_{62}$H$_{62}$N$_8$O$_4$ (983.21): C 75.74, H 6.36, N 11.40; found: C 75.75, H 6.46, N 11.40.

Ligand 2e: Compound **2e** was synthesized according to the procedure described for the synthesis of **2c**, but using 2,5-diiodothiophene. The product was obtained as a yellow solid (76%); m.p. 208–210 °C; ^{1}H NMR (500 MHz, 3% CD$_3$CN/CDCl$_3$, 25 °C): δ = 9.58 (2H; NH), 9.50 (2H; NH), 8.52–8.49 (m, 4H; Ar-H), 8.35 (s, 4H; Ar-H), 8.17 (t, ^3J(H,H) = 7.7 Hz, 2H; Ar-H), 7.39 (s, 4H; Ar-H), 7.18 (s, 2H; Ar-H), 3.15 (m, 4H; CH(CH$_3$)$_2$), 2.28 (s, 12H; Ar-CH$_3$), 1.22 ppm (d, ^3J(H,H) = 6.7 Hz, 24H; CH(CH_3)$_2$); ^{13}C NMR (125 MHz, 3% CD$_3$CN/CDCl$_3$, 25 °C): δ = 162.7, 161.2, 149.3, 148.7, 148.1, 146.9, 141.7, 139.4, 131.9, 130.2, 126.8, 125.9, 125.6, 124.5, 122.5, 116.4, 94.2, 82.1, 28.9, 23.4, 15.2 ppm; IR (KBr): $\tilde{\nu}$ = 3373 (NH), 1693 cm^{-1} (C=O); elemental analysis calcd (%) for C$_{60}$H$_{60}$N$_8$O$_4$S (989.24): C 72.85, H 6.11, N 11.33, S 3.24; found: C 72.89, H 11.46, N 6.14, S 3.15.

Metallocycle 1a: Ligand **2a** (0.21 g, 0.23 mmol) and [Pd(dppp)(OTf)$_2$]$^{[7]}$ (0.19 g, 0.23 mmol) were added to CH$_2$Cl$_2$ (200 mL) containing DMSO (0.5 mL). The suspension was stirred at room temperature under argon for 32 h, during which time it became a clear solution. Upon addition of n-hexane (250 mL) to the solution, the product precipitated out. The precipitate was collected, washed with n-hexane, and dried to give **1a** as a pale yellow solid (0.35 g, 91%); m.p. >250 °C; ^{1}H NMR (500 MHz, CDCl$_3$, 25 °C): δ = 8.98 (s, 4H; NH), 8.67 (s, 4H; NH), 8.62 (s, 8H; Ar-H), 8.50 (d, ^3J(H,H) = 7.6 Hz, 4H; Ar-H), 8.44 (d, ^3J(H,H) = 7.6 Hz, 4H; Ar-H), 8.14 (t, ^3J(H,H) = 7.7 Hz, 4H; Ar-H), 7.65 (brs, 16H; Ar-H), 7.60 (s, 8H; Ar-H), 7.44 (brs, 24H; Ar-H), 3.19 (brs, 8H; PCH$_2$), 2.90 (m, 8H; CH(CH$_3$)$_3$), 2.25 (m, 4H; PCH$_2$CH_2), 2.02 (s, 24H; Ar-CH$_3$), 1.04 ppm (brs, 48H; CH(CH_3)$_2$); ^{13}C NMR (126 MHz, CDCl$_3$, 25 °C): δ = 162.6, 160.9, 149.2, 148.3, 147.6, 146.5, 145.2, 139.3, 134.2, 132.7, 130.9, 129.6, 127.1, 126.3, 125.4, 125.2, 125.0, 124.8, 122.0, 119.4, 90.2, 28.8, 23.3, 17.6, 15.5 ppm; IR (KBr): $\tilde{\nu}$ = 3479 (NH), 1685 (C=O), 1251 (OTf), 1162 (OTf), 1030 cm^{-1} (OTf); elemental analysis calcd (%) for C$_{166}$H$_{168}$F$_{12}$N$_{16}$O$_{20}$P$_4$Pd$_2$S$_4$ (3400.19): C 58.64, H 4.98, N 6.59, S 3.77; found: C 58.67, H 4.64, N 6.58, S 4.04.

Metallocycle 1b: A solution of ligand **2b** (0.70 g, 0.77 mmol) and [Pd(dppp)(OTf)$_2$] (0.63 g, 0.77 mmol, 1 equiv) in CH$_2$Cl$_2$ (10 mL) was stirred at room temperature for 4 h under argon, and then n-hexane was added to precipitate out **1b**. The precipitate was collected, washed with n-hexane, and dried to give **1b** as a pale yellow solid (1.3 g, 98%); m.p. 263–264 °C; ^{1}H NMR (500 MHz, 3% CD$_3$CN/CDCl$_3$, 25 °C): δ = 9.44 (s, 4H; NH), 9.31 (s, 4H; NH), 8.71 (s, 8H; Ar-H), 8.47 (d, ^3J(H,H) =

7.7 Hz, 4H; Ar-H), 8.41 (d, ^3J(H,H) = 7.7 Hz, 4H; Ar-H), 8.14 (t, ^3J(H,H) = 7.7 Hz, 4H; Ar-H), 7.63 (br s, 16H; Ar-H), 7.44–7.29 (m, 32H; Ar-H), 3.14 (br s, 8H; PCH$_2$), 2.98 (m, 8H; CH(CH$_3$)$_3$), 2.22 (m, 4H; PCH$_2$CH$_2$), 2.02 (s, 24H; Ar-CH$_3$), 1.09 ppm (br s, 48H; CH(CH$_3$)$_2$); ^{13}C NMR (125 MHz, 3% CD$_3$CN/CDCl$_3$, 25°C): δ = 162.7, 160.6, 149.1, 148.7, 147.6, 145.1, 139.6, 133.9, 132.5, 129.6, 128.0, 126.3, 125.6, 125.2, 125.0, 124.6, 122.1, 116.5, 81.8, 74.6, 28.8, 23.4, 21.6, 17.5, 15.4 ppm; IR (KBr): $\tilde{\nu}$ = 3265 (NH), 1684 (C=O), 1158 (OTf), 1099 (OTf), 1025 cm^{-1} (OTf); elemental analysis calcd (%) for C$_{170}$H$_{168}$F$_{12}$N$_{16}$O$_{20}$P$_4$Pd$_2$S$_4$·4H$_2$O (3520.29): C 58.00, H 5.04, N 6.37, S 3.64; found: C 57.78, H 5.07, N 6.27, S 3.61; ESI-MS: m/z (%): 1574 (100) $[M-2\,CF_3SO_3]^{2+}$, 1000 (65) $[M-3\,CF_3SO_3]^{3+}$, 712 (70) $[M-4\,CF_3SO_3]^{4+}$.

Metallocycle 1c: [Pd(dppp)(OTf)$_2$] (50 mg, 0.061 mmol) was added to a solution of **2c** (60 mg, 0.061 mmol) in CH$_3$CN/CHCl$_3$ (1:10, 11 mL) and the resulting mixture was stirred at room temperature for 2 h under nitrogen. The solution obtained was concentrated to a volume of approximately 1 mL, and then *n*-hexane (10 mL) was added to precipitate out **1c**. After washing with *n*-hexane, the product **1c** was obtained as a pale yellow solid (99 mg, 91%); m.p. >250°C; ^{1}H NMR (500 MHz, 3% CD$_3$CN/CDCl$_3$, 25°C): δ = 9.37 (4H; NH), 9.28 (4H; NH), 8.74 (s, 8H; Ar-H), 8.47 (d, ^3J(H,H) = 7.7 Hz, 4H; Ar-H), 8.42 (d, ^3J(H,H) = 7.7 Hz, 4H; Ar-H), 8.13 (t, ^3J(H,H) = 7.7 Hz, 4H; Ar-H), 7.62 (br s, 16H; Ar-H), 7.48 (s, 8H; Ar-H), 7.42 (s, 24H; Ar-H), 7.39 (s, 8H; Ar-H), 3.09 (br s, 8H; PCH$_2$), 3.00 (m, 8H; CH(CH$_3$)$_2$), 2.17 (br s, 4H; PCH$_2$CH$_2$), 2.02 (s, 24H; Ar-CH$_3$), 1.09 ppm (br s, 48H; CH(CH$_3$)$_2$); ^{13}C NMR (125 MHz, 3% CD$_3$CN/CDCl$_3$, 25°C): δ = 162.6, 160.4, 149.0, 148.6, 147.5, 146.9, 144.9, 139.3, 133.7, 132.6, 132.2, 131.4, 129.5, 127.0, 126.1, 125.6, 125.1, 123.0, 122.8, 116.4, 91.6, 89.2, 28.6, 23.2, 21.6, 17.3, 15.3 ppm; IR (KBr): $\tilde{\nu}$ = 3483 (NH), 1682 (C=O), 1250 (OTf), 1162 (OTf), 1030 cm^{-1} (OTf); ESI-MS: m/z (%): 751 (100) $[M-4\,CF_3SO_3]^{4+}$, 1051 (7) $[M-3\,CF_3SO_3]^{3+}$; elemental analysis calcd (%) for C$_{182}$H$_{176}$F$_{12}$N$_{16}$O$_{20}$P$_4$Pd$_2$S$_4$ (3600.42): C 60.71, H 4.93, N 6.22, S 3.56; found: C 60.80, H 4.79, N 6.16, S 3.82.

Host 1d: Compound **1d** was synthesized from ligand **2d** by the same method as used for the synthesis of **1c**. The product was obtained as a pale yellow solid (76%); m.p. >250°C; ^{1}H NMR (500 MHz, 3% CD$_3$CN/CDCl$_3$, 25°C): δ = 9.31 (4H; NH), 9.15 (4H; NH), 8.74 (s, 8H; Ar-H), 8.45 (d, ^3J(H,H) = 7.7 Hz, 4H; Ar-H), 8.39 (d, ^3J(H,H) = 7.7 Hz, 4H; Ar-H), 8.25 (s, 2H; Ar-H), 8.11 (t, ^3J(H,H) = 7.7 Hz, 4H; Ar-H), 7.63 (br s, 16H; Ar-H), 7.55 (d, ^3J(H,H) = 7.6 Hz, 4H; Ar-H), 7.42–7.35 (m, 34H; Ar-H), 3.13 (br s, 8H; PCH$_2$), 2.94 (m, 8H; CH(CH$_3$)$_2$), 2.16 (br s, 4H; PCH$_2$CH$_2$), 2.00 (s, 24H; Ar-CH$_3$), 1.10 ppm (s, 48H; CH(CH$_3$)$_2$); ^{13}C NMR (125 MHz, 3% CD$_3$CN/CDCl$_3$, 25°C): δ = 162.4, 160.5, 148.8, 148.4, 147.2, 146.7, 145.0, 139.4, 134.0, 132.6, 132.3, 131.2, 130.9, 129.4, 128.7, 127.1, 126.0, 125.4, 124.9, 124.7, 123.5, 122.9, 116.6, 90.5, 88.7, 28.5, 23.2, 21.4, 17.3, 15.2 ppm; IR (KBr): $\tilde{\nu}$ = 3473 (NH), 1686 (C=O), 1249 (OTf), 1161 (OTf), 1030 cm^{-1} (OTf); ESI-MS: m/z (%): 751 (100) $[M-4\,CF_3SO_3]^{4+}$, 1051 (23) $[M-3\,CF_3SO_3]^{3+}$; elemental analysis calcd (%) for C$_{182}$H$_{176}$F$_{12}$N$_{16}$O$_{20}$P$_4$Pd$_2$S$_4$ (3600.42): C 60.71, H 4.93, N 6.22, S 3.56; found: C 60.74, H 5.00, N 6.14, S 3.43.

Host 1e: Compound **1e** was synthesized from ligand **2e** by the same method as used for the synthesis of **1c**. The product was obtained as a pale yellow solid (83%); m.p. >250°C; ^{1}H NMR (500 MHz, 3% CD$_3$CN/CDCl$_3$, 25°C): δ = 9.32 (4H; NH), 9.23 (4H; NH), 8.76 (s, 8H; Ar-H), 8.47 (d, ^3J(H,H) = 7.6 Hz, 4H; Ar-H), 8.42 (d, ^3J(H,H) = 7.6 Hz, 4H; Ar-H), 8.13 (t, ^3J(H,H) = 7.6 Hz, 4H; Ar-H), 7.62 (br s, 16H; Ar-H), 7.41 (s, 24H; Ar-H), 7.24 (s, 4H; Ar-H), 3.10 (br s, 8H; PCH$_2$), 3.00 (m, 8H; CH(CH$_3$)$_2$), 2.18 (br s, 4H; PCH$_2$CH$_2$), 2.02 (s, 24H; Ar-CH$_3$), 1.09 ppm (br s, 48H; CH(CH$_3$)$_2$); ^{13}C NMR (125 MHz, 3% CD$_3$CN/CDCl$_3$, 25°C): δ = 162.5, 160.4, 149.1, 148.7, 147.6, 147.0, 144.9, 139.4, 133.7, 132.7, 132.3, 132.1, 131.6, 129.6, 126.9, 126.2, 125.7, 124.6, 122.6, 116.4, 94.5, 82.7, 28.7, 23.3, 22.4, 17.4, 15.4 ppm; IR (KBr): $\tilde{\nu}$ = 3473 (NH), 1686 (C=O), 1248 (OTf), 1160 (OTf), 1029 cm^{-1} (OTf); ESI-MS: m/z (%): 754 (100) $[M-4\,CF_3SO_3]^{4+}$, 1055 (62) $[M-3\,CF_3SO_3]^{3+}$; elemental analysis calcd (%) for C$_{178}$H$_{172}$F$_{12}$N$_{16}$O$_{20}$P$_4$Pd$_2$S$_6$ (3612.48): C 59.18, H 4.80, N 6.20, S 5.33; found: C 59.20, H 4.94, N 6.17, S 5.54.

^{1}H NMR titrations: Chloroform was stored over 4 Å molecular sieves, and filtered through basic alumina prior to use. A 0.5 mM solution of each metallocycle in 97:3 CDCl$_3$/CD$_3$CN (4–4.5 mL) was prepared at 23±1°C. By using this solution of the macrocycle as a solvent, a solution of the guest **G** (50–80 mM) was prepared. A 500 μL aliquot of the metal-

locycle solution was transferred to an NMR tube, and an initial NMR spectrum was taken to determine the initial chemical shift (δ_{free}) of the free metallocycle. Aliquots of the guest solution (10 μL initially, then 80–100 μL, and finally 600–800 μL) were added to the metallocycle solution. A spectrum was recorded after each addition and 15–20 data points were obtained. As described in detail earlier, the binding parameters were calculated either by nonlinear curve fitting with the aid of the HOSTEST program,[18] or by means of the Hill equation.[19]

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