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FULL PAPER

Positive Allosteric Control of Guests Encapsulation by Metal Binding to Covalent Porphyrin Cages

Ryan Djemili,[a] Lucas Kocher,[a] Stéphanie Durot,[a] Anssi Peuronen,[b] Kari Rissanen,*[c] and Valérie Heitz*[a]

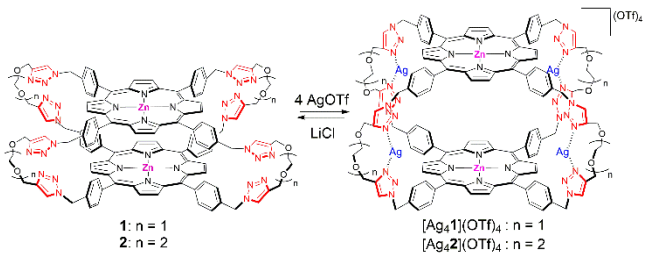
Abstract: The allosteric control of the receptor property of two flexible covalent cages is reported. These receptors consist of two zinc(II) porphyrins connected by four linkers of two different sizes, each incorporating two 1,2,3-triazolyl ligands. Silver(I) ions act as an effector, responsible for an on/off encapsulation mechanism of neutral guest molecules. Binding silver(I) ions to the triazoles opens the cages and triggers the coordination of pyrazine or the encapsulation of N,N'-dibutyl-1,4,5,8-naphthalene diimide. The X-ray structure of the silver(I)-complexed receptor with short connectors is reported, revealing the hollow structure with a cavity well-defined by two eclipsed porphyrins. Rather unexpectedly, the crystallographic structure of this receptor with pyrazine as guest shows that the cavity is occupied with two pyrazines, each binding to the zinc(II) porphyrin in a monotopic fashion.

Introduction

Allostery is one of the most important regulatory mechanism of protein activity. It is associated to a great diversity of cellular processes and involves a binding event at a specific site to trigger an action at a remote site.[1] Hemoglobin is a tetrameric protein considered as the allosteric protein archetype displaying a cooperative homotropic binding of four dioxygen molecules. Many more complex multidomain regulatory proteins and biological machines that integrate multiple signaling events and long-range coupled conformational modifications through homotropic or heterotropic binding events have shown to proceed also through allosteric mechanisms.[2,3] Whereas the design of 3D hollow structures has led to selective receptors for guest encapsulation and promising molecular nanoreactors,[4–24] their development as biomimetic allosteric receptors able to control guest complexation through large conformational changes remains a significant challenge.[25–32] Such control implies to integrate in the framework of the structure several components with defined regulation and guest binding functions. Moreover, the structure must ensure the preorganization of the active components, the flexibility for conformational rearrangements and should prevent direct interactions between the recognition and regulation sites.

Promising allosteric modulation of the receptor activity of multi-component 3D containers has been obtained using chemical,[33–48] redox,[49–51] or photoinduced reactions.[52–58] Most of such structures are self-assembled using hydrogen or metal-ligand bonds, but covalent structures remain interesting for their high chemical stability and their ability to respond to various signaling events. Porphyrins are attractive as active components for artificial allosteric systems due to their involvements in many biological processes through their binding, redox or photophysical properties. Especially, structures incorporating metalloporphyrins with a defined binding pocket have shown molecular recognition properties and catalytic activity.[11,59–75]

Our previous work has focused on the synthesis of coordination[76] and covalent architectures incorporating metalloporphyrins.[77–79] In particular, flexible covalent cages incorporating orthogonal binding sites, metalloporphyrins and 1,2,3-triazoles, were obtained using a DABCO-templated copper(I)-catalyzed alkyne-azide reaction (DABCO: 1,4-diazabicyclo[2.2.2]octane). This templated synthesis enabled to perform simultaneously the macrocyclization reaction as well as the synthesis of four out of eight triazole ligands of the structure, limiting therefore the synthetic effort to obtain these molecules.[78,79] Protonation of both the porphyrins and the triazoles in the cages with two free-base porphyrins was shown to inflate the structures.[79] Moreover, a controlled-breathing of the cage with reversible binding of silver(I) ions to the peripheral triazoles was shown to operate with both the free-base and zinc(II)-metalated porphyrins (Scheme 1).



Scheme 1. Breathing motion of flexible zinc(II) porphyrin cages by reversible binding of silver(I) ions to the peripheral triazoles.

Herein, the allosteric control of the receptor properties of the molecular structures **1** and **2** is investigated. It is shown that silver(I) ions act as a chemical effector that triggers upon binding to the cages, the encapsulation of neutral guest molecules.

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Thanks to the chemical nature of the zinc(II) porphyrins, the allosteric mechanism is shown to operate both for a ditopic ligand, pyrazine, and for a flat aromatic guest, N,N'-dibutyl-1,4,5,8-naphthalene diimide (NDI). The X-ray structural analyses confirmed the open structure of silver(I)-complexed cage **1** as well as the encapsulation of pyrazine in this receptor

Results and Discussion

X-ray structure of $[Ag_4\mathbf{1}](BArF)_4$

To assess the ability of the cage to act as an allosteric receptor, guest molecules that can be trapped by coordination to the zinc(II) porphyrins or stabilized in between their large π-electron rich core were considered. It must be noticed that cages **1** and **2** adopt a flattened conformation in a DCM /10% MeOH solution or even in solvents of higher polarity (DMSO, DMF).[78,79] This compact form stabilized by π-π interactions between the zinc(II) porphyrins was confirmed in the solid state with an X-ray crystallographic structure of cage **2**.[78] Complexes $[Ag_4\mathbf{X}](BArF)_4$ (**X** = **1** or **2**, $BArF^-$: tetrakis[3,5-bis(trifluoromethyl)phenyl]borate)), soluble in DCM, were obtained quantitatively as reported.[79] To characterize the cavity of the silver(I)-complexed cages several attempts of crystallization were made before single crystals suitable for X-ray analysis were obtained, by diffusion of cyclohexane into a solution of $[Ag_4\mathbf{1}](BArF)_4$ in 1,2-dichloroethane. The X-ray structure revealed the cage structure with ca. two types of rectangular windows, sized ca. 4.5 x 15 Å and 6 x 8 Å, resulting from the *syn-anti-syn-anti* disposition of the four silver(I)-triazolyl connectors in which each of the silver(I) ions lie in a coordination pocket formed by two triazolyl groups and a diethoxyethane linker (Figure 1).

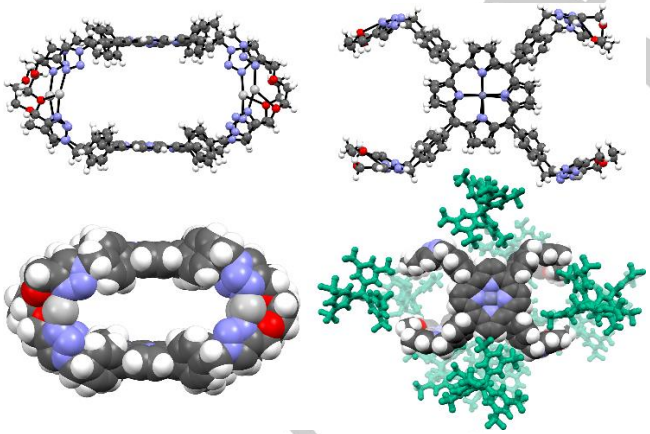

Figure 1. Crystal structure of the cage $[Ag_4\mathbf{1}](BArF)_4$, ball-and-stick (top) and VDW (below) representations. The $BArF^-$ anions and the located solvent cyclohexanes are excluded for clarity for all except for the bottom right illustration which demonstrates the packing of the anions and solvent molecules (shown in green) at close proximities to the host cavity openings.

The Ag^I–N bond lengths are similar to those observed in analogous silver(I) complexes[80] whereas the distances of the Ag^I–O bonds are longer on average. This can be attributed to the inability of the diethoxyethane O-atoms to adopt optimal position around the silver(I) ion due to steric effects. The silver(I) ion complexation brings the two zinc(II) porphyrins in an eclipsed cofacial position with intramolecular Zn···Zn distance of 9.5 Å. Such arrangement leads to a well-defined cavity between the zinc(II) porphyrin moieties, with an approximate volume of 230 $Å^3$ (Figure 1 bottom, see SI for further discussion on the cavity volume).

Allosteric control of pyrazine encapsulation

The encapsulation of pyrazine in molecular cages **1** and **2** was studied at millimolar concentration by NMR spectroscopy. The reaction performed with 1 equivalent of pyrazine did not show evidence of encapsulation of this ligand in various solvents (CH_2Cl_2, $CHCl_3$, DMF or DMSO) even after sonication or prolonged heating. In apolar solvent, external binding of the ligand to the zinc(II) porphyrins led to insoluble oligomers (Figure S11). This result contrasts with the one obtained with DABCO that was encapsulated quantitatively in cages **1** and **2**, in CH_2Cl_2 and CH_2Cl_2/10% MeOH, respectively.[78,79]

The complexation of pyrazine was therefore tested on silver(I)-complexed cages $[Ag_4\mathbf{X}](BArF)4$ (**X** = **1** or **2**) in DCM. When 1 equivalent of pyrazine was added to the solution of the complex $[Ag_4\mathbf{1}](BArF)_4$ in CD_2Cl_2, the singlet that accounts for its four protons experienced a huge upfield shift of 7.54 ppm attributed to its inward coordination to the zinc(II) porphyrins (Figure 2). A NOESY spectrum showed cross-peaks of the pyrazine protons with the pyrrolic protons (H_{pyr}) of the porphyrins and with the protons of the phenyl rings that point inside the cavity ($H_{o\ in}$) (Figure S4). These correlations attested the internal binding mode of the pyrazine to the silver(I)-complexed cage $[Ag_4\mathbf{1}](BArF)_4$. Since the Zn···Zn distance 9.5 Å is larger than the distance for a ditopic binding (ca. 7 Å), the guest was expected to be in fast exchange between the two zinc(II)-porphyrin coordination sites on the NMR timescale. A variable-temperature ^1H NMR experiment showed a sharpening and an upfield shift of the pyrazine signal upon lowering the temperature, in accordance with this hypothesis (Figure S12). ^1H DOSY spectrum supported the quantitative encapsulation of the pyrazine since the host and guest molecules had the same diffusion coefficient 330 $\mu m^2.s^{-1}$ (Figure S8). UV-vis titration gave the best fit for the 1:1 binding model with an association constant log K_a = 6.65 ± 0.03 (Figure S14). The pyrazine@$[Ag_4\mathbf{1}](BArF)_4$ complex was also detected at m/z = 2293.7599 by cold-spray ionization mass-spectrometry (Figure S9). NMR experiments showed also evidence of the encapsulation of pyrazine in $[Ag_4\mathbf{2}](BArF)_4$ (Figure S35-38). In this case, the diffusion coefficient of the pyrazine, 346 $\mu m^2.s^{-1}$ and the one of the cage, 328 $\mu m^2.s^{-1}$ were within the experimental errors of 5%.

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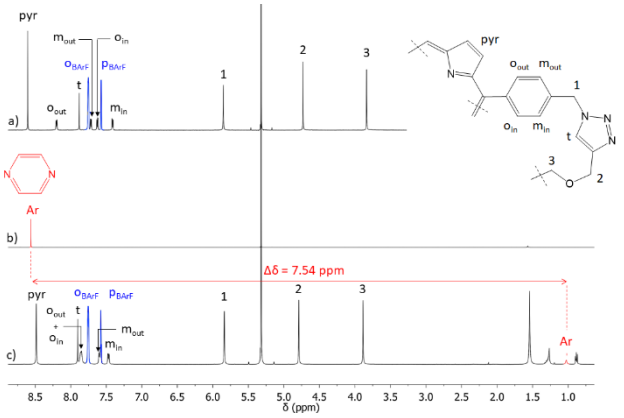

Figure 2. ^{1}H NMR (400 MHz, CD_2Cl_2, 298 K) a) [Ag_4**1**](BArF)$_4$, b) pyrazine and c) [Ag_4**1**](BArF)$_4$ with 1 equivalent pyrazine..

Binding silver(I) ions opens the structures of **1** and **2** and leads to C_4-symmetric complexes in solution with a face-to-face disposition of the porphyrins. Such preorganization enables the pyrazine to be readily inserted in the silver(I)-complexed hosts whereas pyrazine coordination does not overcome the π-stacking energy between the porphyrins in cages **1** and **2**, and the entropic penalty of its inclusion. Indeed, pyrazine is a much weaker ligand (pK_{a1} = -5.8 and pK_{a2} = 0.7)[81] than DABCO (pK_{a1} = 2.9 and pK_{a2} = 8.6)[82] despite their similar sizes, 2.8 Å and 2.7 Å, respectively. This explains why DABCO, as a stronger ligand, opens the cages upon binding without the help of the effector, silver(I) ion. Silver(I) ions can be decoordinated using photons[64] or chemically with a chloride salt. Upon addition of NBu_4Cl to a solution of cage [Ag_4**1**](BArF)$_4$ including pyrazine, the cage and pyrazine signals became broad and progressively disappeared in accordance with the ejection of the ligand from the cage upon removal of silver(I) ions (Figure S10). The formation of insoluble oligomers by external binding of pyrazine to the cage was also observed when the binding was tested on the cage **1** (vide supra and Figure S11). This result shows that the positive allosteric guest binding triggered by silver(I) ions is a reversible on/off process.

Single crystals were grown by diffusion of cyclohexane into a 1,2-dichloroethane solution the 1:1 host-guest pyrazine-[Ag_4**1**](BArF)$_4$ complex. The X-ray structure reveals a large conformational change of the silver(I)-triazolyl connectors from a *syn-anti-syn-anti* conformation observed for the guest free [Ag_4**1**](BArF)$_4$ to a *syn-syn-syn-syn* conformation and the presence of two pyrazines encapsulated in its cavity, each binding in a monotopic fashion to one zinc(II) porphyrin (Figure 3). The complexation of the two pyrazines into the cavity and the orientation of the Ag-triazolyl connectors modulate the conformation of the whole cage so that the Zn-atoms are no longer on top of each other, since the two porphyrin planes show a ca. 2 Å offset with respect to each other (Figure 3, top left). However, the distance between the porphyrin planes does not change more than 0.5 Å, which results in a slight reduction in the cavity size to ca. 200 – 210 Å^3. The volume of the pyrazine is 86 Å^3 and thus the Rebek[83] packing coefficient is 2 x 86/205 x 100 = 84%, i.e. substantially higher than the 55% for a non-coordinated guest. The encapsulation of two pyrazines contrasts with the encapsulation of one guest only in solution (vide supra). Upon addition of a second equivalent of pyrazine to a solution of pyrazine@[Ag_4**1**](BArF)$_4$, the variable temperature NMR data showed intermediate exchange binding at 273 K and slow exchange of the encapsulated guest with the free guest at 193 K (Figure S13). Clearly, in the solid state, the large size of the cavity, the Zn-to-N binding energies and the steric fit (high packing coefficient) are the driving force for the "double" pyrazine complexation. This is supported by the fact that the two pyrazine guests will fill up the cavity fully with interplanar distance of 3.48 Å, indicating π-π interactions between the pyrazine guests. This result was reproducible, since the X-ray analysis of another crystal obtained from another crystallization tube grown in the same crystallization conditions gave the same result.

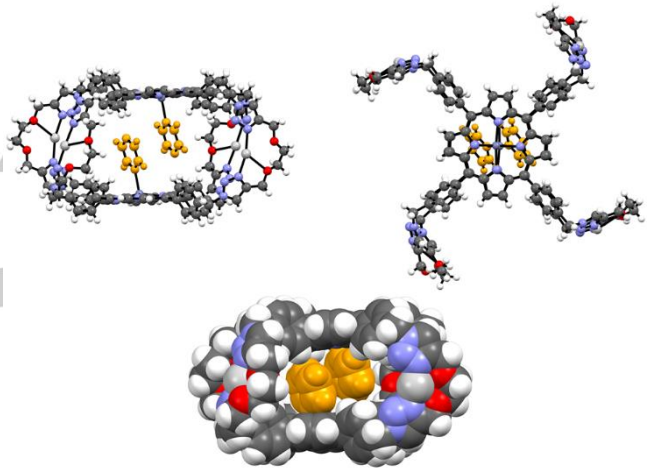

Figure 3. The crystal structure of (pyrazine)$_2$@[Ag_4**1**](BArF)$_4$, ball-and-stick (top) and VDW (below) representations. The pyrazines are shown in orange color, the BArF$^-$ anions and disordered atoms are excluded for clarity.

Allosteric control of NDI encapsulation

The affinity of a π-acceptor NDI guest for the cages was also studied. This guest was not encapsulated in the flattened molecular cages **1** and **2** in DCM or DMF even upon prolonged heating. The ability of silver(I) ions to trigger its encapsulation was then investigated. When 1 equivalent of NDI was added to a solution of [Ag_4**1**](BArF)$_4$ in DCM, all the guest protons were upfield shifted as seen on the ^{1}H NMR spectra (Figure 4). The most pronounced shifts were observed for the NDI aromatic protons (0.54 ppm) in accordance with its stabilization between the two porphyrins. NOESY NMR spectrum (Figure S18) showed cross-peaks between the CH_2 (H_α) of the NDI and both the pyrrolic protons (H_{pyr}) and phenyl protons ($H_{o\,in}$) of the cages in agreement with the close proximity of the guest enclosed in the cage. ^{1}H DOSY experiments in DCM or DMF showed also the affinity of NDI for silver(I)-complexed cages. In both solvents, NDI had a lower diffusion coefficient than free NDI. ^{1}H NMR titration of [Ag_4**1**](BArF)$_4$ with NDI was performed in DCM to evaluate the strength of this interaction (Figure S24). Data were fitted to a 1:1

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stoichiometry and gave a binding constant K_a = (95 ± 20) M^{-1}. This encapsulation process is also reversible since upon addition of NBu_4Cl and precipitation of AgCl, the guest was quantitatively expelled from the cage (Figure S25).

The complexation of NDI with $[Ag_4\mathbf{1}](BArF)_4$ and $[Ag_4\mathbf{2}](BArF)_4$ was also detected using high resolution ESI mass-spectrometry (Figure S23, S45).

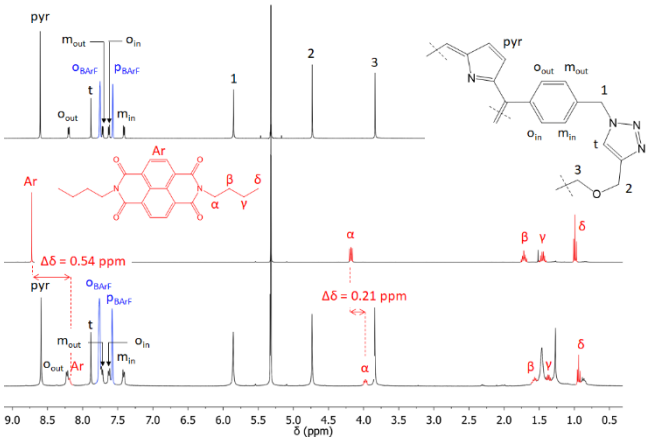

Figure 4. ^{1}H NMR (400 MHz, CD_2Cl_2, 298 K) a) $[Ag_4\mathbf{1}](BArF)_4$, b) NDI and c) $[Ag_4\mathbf{1}](BArF)_4$ with 1 equivalent of NDI.

Conclusions

The flexible cages **1** and **2** equipped with peripheral triazoles behave as on/off allosteric receptors as represented in Figure 5.

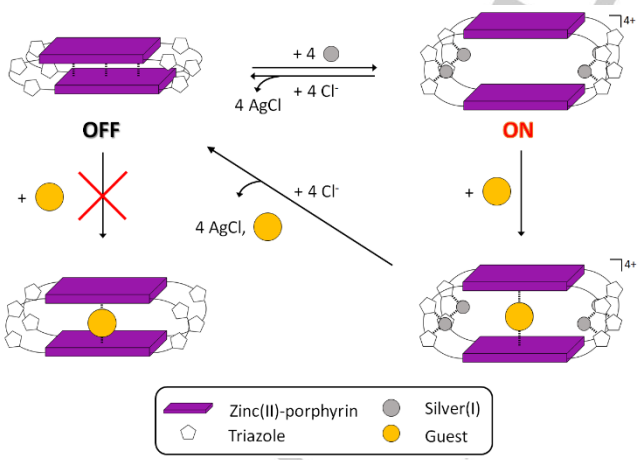

Figure 5. Schematic representation of the allosteric control of guest binding in flexible molecular cage receptors.

Guest binding inside these receptors is controlled by the reversible coordination/decoordination of an effector, silver(I) ions. Upon binding, silver(I) ions trigger a large conformational change of the cages that opens the cavity, as shown on the crystallographic structure obtained for the silver(I)-complexed cage **1**. Such modification activates the receptors that are able to bind in their open form two different kinds of guest molecules inside the cavity, a pyrazine ligand or a π-acceptor NDI molecule. This reversible on/off control of guest binding inside such structures opens the way to develop highly selective molecular sensors but also stimuli-responsive nanoreactors able to fine-tune the reactivity performed in their hollow structures upon addition of a suitable effector.

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Conflicts of interest

The authors declare no competing financial interest.

Keywords: supramolecular chemistry • allosteric control • host-guest systems • cage compounds • porphyrin

[1] J.-P. Changeux, A. Christopoulos, *Cell* **2016**, *166*, 1084–1102.
[2] P. Tompa, *Chem. Rev.* **2014**, *114*, 6715–6732.
[3] A. Peracchi, A. Mozzarelli, *Biochim. Biophys. Acta BBA - Proteins Proteomics* **2011**, *1814*, 922–933.
[4] J. H. Jordan, B. C. Gibb, *Chem. Soc. Rev.* **2015**, *44*, 547–585.
[5] J. Rebek Jr, *Acc. Chem. Res.* **2009**, *42*, 1660–1668.
[6] R. Chakrabarty, P. S. Mukherjee, P. J. Stang, *Chem. Rev.* **2011**, *111*, 6810–6918.
[7] K. Harris, D. Fujita, M. Fujita, *Chem. Commun.* **2013**, *49*, 6703–6712.
[8] S. Mukherjee, P. S. Mukherjee, *Chem Commun* **2014**, *50*, 2239–2248.
[9] D. Fiedler, D. H. Leung, R. G. Bergman, K. N. Raymond, *Acc. Chem. Res.* **2005**, *38*, 349–358.
[10] M. Yoshizawa, J. K. Klosterman, M. Fujita, *Angew. Chem. Int. Ed.* **2009**, *48*, 3418–3438.
[11] S. H. A. M. Leenders, R. Gramage-Doria, B. de Bruin, J. N. H. Reek, *Chem. Soc. Rev.* **2015**, *44*, 433–448.
[12] J.-N. Rebilly, B. Colasson, O. Bistri, D. Over, O. Reinaud, *Chem. Soc. Rev.* **2015**, *44*, 467–489.
[13] S. Zarra, D. M. Wood, D. A. Roberts, J. R. Nitschke, *Chem. Soc. Rev.* **2015**, *44*, 419–432.
[14] D. S. Kim, J. L. Sessler, *Chem. Soc. Rev.* **2015**, *44*, 532–546.
[15] K. I. Assaf, W. M. Nau, *Chem. Soc. Rev.* **2015**, *44*, 394–418.
[16] M. Otte, *ACS Catal.* **2016**, *6*, 6491–6510.
[17] M. Raynal, P. Ballester, A. Vidal-Ferran, P. W. N. M. van Leeuwen, *Chem. Soc. Rev.* **2014**, *43*, 1734–1787.
[18] T. S. Koblenz, J. Wassenaar, J. N. H. Reek, *Chem. Soc. Rev.* **2008**, *37*, 247–262.
[19] C. J. Brown, F. D. Toste, R. G. Bergman, K. N. Raymond, *Chem. Rev.* **2015**, *115*, 3012–3035.
[20] Y. Ueda, H. Ito, D. Fujita, M. Fujita, *J. Am. Chem. Soc.* **2017**, *139*, 6090–6093.

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[21] T. M. Bräuer, Q. Zhang, K. Tiefenbacher, *J. Am. Chem. Soc.* **2017**, *139*, 17500–17507.
[22] P. Zhang, J. Meijide Suárez, T. Driant, E. Derat, Y. Zhang, M. Ménand, S. Roland, M. Sollogoub, *Angew. Chem.* **2017**, *129*, 10961–10965.
[23] J. Jiao, C. Tan, Z. Li, Y. Liu, X. Han, Y. Cui, *J. Am. Chem. Soc.* **2018**, *140*, 2251–2259.
[24] L. Zhao, X. Jing, X. Li, X. Guo, L. Zeng, C. He, C. Duan, *Coord. Chem. Rev.* **2017**.
[25] H.-J. Schneider, *Org. Biomol. Chem.* **2016**, *14*, 7994–8001.
[26] L. Kovbasyuk, R. Krämer, *Chem. Rev.* **2004**, *104*, 3161–3188.
[27] C. Kremer, A. Lützen, *Chem. – Eur. J.* **2013**, *19*, 6162–6196.
[28] S. Shinkai, M. Ikeda, A. Sugasaki, M. Takeuchi, *Acc. Chem. Res.* **2001**, *34*, 494–503.
[29] A. M. Lifschitz, M. S. Rosen, C. M. McGuirk, C. A. Mirkin, *J. Am. Chem. Soc.* **2015**, *137*, 7252–7261.
[30] M. J. Wiester, P. A. Ulmann, C. A. Mirkin, *Angew. Chem. Int. Ed.* **2011**, *50*, 114–137.
[31] L. Yang, X. Jing, B. An, C. He, Y. Yang, C. Duan, *Chem. Sci.* **2018**, *9*, 1050–1057.
[32] X. Chen, T. M. Gerger, C. Räuber, G. Raabe, C. Göb, I. M. Oppel, M. Albrecht, *Angew. Chem. Int. Ed.* **2018**, *57*, 11817–11820.
[33] N. Branda, R. M. Grotzfeld, C. Valdes, J. J. Rebek Jr, *J. Am. Chem. Soc.* **1995**, *117*, 85–88.
[34] S. Löffler, J. Lübben, L. Krause, D. Stalke, B. Dittrich, G. H. Clever, *J. Am. Chem. Soc.* **2015**, *137*, 1060–1063.
[35] J. Mendez-Arroyo, J. Barroso-Flores, A. M. Lifschitz, A. A. Sarjeant, C. L. Stern, C. A. Mirkin, *J. Am. Chem. Soc.* **2014**, *136*, 10340–10348.
[36] S. Rieth, B.-Y. Wang, X. Bao, J. D. Badjić, *Org. Lett.* **2009**, *11*, 2495–2498.
[37] D. Preston, A. Fox-Charles, W. K. C. Lo, J. D. Crowley, *Chem. Commun.* **2015**, *51*, 9042–9045.
[38] N. Kishi, M. Akita, M. Yoshizawa, *Angew. Chem. Int. Ed.* **2014**, *53*, 3604–3607.
[39] D. Ajami, J. Rebek Jr, *J. Am. Chem. Soc.* **2006**, *128*, 15038–15039.
[40] T. Gottschalk, B. Jaun, F. Diederich, *Angew. Chem. Int. Ed.* **2007**, *46*, 260–264.
[41] S. Hiraoka, K. Harano, M. Shiro, M. Shionoya, *Angew. Chem. Int. Ed.* **2005**, *44*, 2727–2731.
[42] W. J. Ramsay, J. R. Nitschke, *J. Am. Chem. Soc.* **2014**, *136*, 7038–7043.
[43] C. M. Davis, J. M. Lim, K. R. Larsen, D. S. Kim, Y. M. Sung, D. M. Lyons, V. M. Lynch, K. A. Nielsen, J. O. Jeppesen, D. Kim, et al., *J. Am. Chem. Soc.* **2014**, *136*, 10410–10417.
[44] S. Akine, M. Miyashita, T. Nabeshima, *J. Am. Chem. Soc.* **2017**, *139*, 4631–4634.
[45] Y.-L. Ma, H. Ke, A. Valkonen, K. Rissanen, W. Jiang, *Angew. Chem. Int. Ed.* **2018**, *57*, 709–713.
[46] D. Zhang, J. R. Cochrane, S. Di Pietro, L. Guy, H. Gornitzka, J.-P. Dutasta, A. Martinez, *Chem. – Eur. J.* **2017**, *23*, 6495–6498.
[47] V. Marcos, A. J. Stephens, J. Jaramillo-Garcia, A. L. Nussbaumer, S. L. Woltering, A. Valero, J.-F. Lemonnier, I. J. Vitorica-Yrezabal, D. A. Leigh, *Science* **2016**, *352*, 1555–1559.
[48] P. Thordarson, E. J. A. Bijsterveld, J. A. A. W. Elemans, P. Kasák, R. J. M. Nolte, A. E. Rowan, *J. Am. Chem. Soc.* **2003**, *125*, 1186–1187.
[49] V. Croué, S. Goeb, G. Szalóki, M. Allain, M. Sallé, *Angew. Chem. Int. Ed.* **2016**, *55*, 1746–1750.
[50] S. Stojanović, D. A. Turner, A. I. Share, A. H. Flood, C. M. Hadad, J. D. Badjić, *Chem. Commun.* **2012**, *48*, 4429–4431.
[51] I. Pochorovski, F. Diederich, *Acc. Chem. Res.* **2014**, *47*, 2096–2105.
[52] M. Han, R. Michel, B. He, Y.-S. Chen, D. Stalke, M. John, G. H. Clever, *Angew. Chem. Int. Ed.* **2013**, *52*, 1319–1323.
[53] F. Corbellini, R. M. A. Knegtel, P. D. J. Grootenhuis, M. Crego-Calama, D. N. Reinhoudt, *Chem. – Eur. J.* **2005**, *11*, 298–307.
[54] E. Busseron, J. Lux, M. Degardin, J. Rebek Jr, *Chem. Commun.* **2013**, *49*, 4842–4844.
[55] O. B. Berryman, A. C. Sather, A. Lledó, J. Rebek Jr, *Angew. Chem. Int. Ed.* **2011**, *50*, 9400–9403.
[56] M. Liu, X. Yan, M. Hu, X. Chen, M. Zhang, B. Zheng, X. Hu, S. Shao, F. Huang, *Org. Lett.* **2010**, *12*, 2558–2561.
[57] R. S. Stoll, S. Hecht, *Angew. Chem. Int. Ed.* **2010**, *49*, 5054–5075.
[58] N. Kishi, M. Akita, M. Kamiya, S. Hayashi, H.-F. Hsu, M. Yoshizawa, *J. Am. Chem. Soc.* **2013**, *135*, 12976–12979.
[59] S. Durot, J. Taesch, V. Heitz, *Chem. Rev.* **2014**, *114*, 8542–8578.
[60] C. García-Simón, R. Gramage-Doria, S. Raoufmoghaddam, T. Parella, M. Costas, X. Ribas, J. N. H. Reek, *J. Am. Chem. Soc.* **2015**, *137*, 2680–2687.
[61] P. F. Kuijpers, M. Otte, M. Dürr, I. Ivanović-Burmazović, J. N. H. Reek, B. de Bruin, *ACS Catal.* **2016**, *6*, 3106–3112.
[62] C. Colomban, C. Fuertes-Espinosa, S. Goeb, M. Sallé, M. Costas, L. Blancafort, X. Ribas, *Chem. – Eur. J.* **2018**, *24*, 1–12.
[63] W. Brenner, T. K. Ronson, J. R. Nitschke, *J. Am. Chem. Soc.* **2017**, *139*, 75–78.
[64] H. Sato, K. Tashiro, H. Shinmori, A. Osuka, Y. Murata, K. Komatsu, T. Aida, *J. Am. Chem. Soc.* **2005**, *127*, 13086–13087.
[65] N. P. E. Barry, O. Zava, P. J. Dyson, B. Therrien, *Aust. J. Chem.* **2010**, *63*, 1529–1537.
[66] A. N. Oldacre, A. E. Friedman, T. R. Cook, *J. Am. Chem. Soc.* **2017**, *139*, 1424–1427.
[67] S. K. Samanta, A. Rana, M. Schmittel, *Angew. Chem. Int. Ed.* **2016**, *55*, 2267–2272.
[68] P. T. Smith, B. P. Benke, Z. Cao, Y. Kim, E. M. Nichols, K. Kim, C. J. Chang, *Angew. Chem. Int. Ed.* **2018**, *57*, 9684–9688.
[69] C. Zhang, Q. Wang, H. Long, W. Zhang, *J. Am. Chem. Soc.* **2011**, *133*, 20995–21001.
[70] F. Hajjaj, K. Tashiro, H. Nikawa, N. Mizorogi, T. Akasaka, S. Nagase, K. Furukawa, T. Kato, T. Aida, *J. Am. Chem. Soc.* **2011**, *133*, 9290–9292.
[71] J. Zhang, X. Zheng, R. Jiang, Y. Yu, Y. Li, H. Liu, Q. Li, Z. Shuai, Y. Li, *RSC Adv.* **2014**, *4*, 27389–27392.
[72] B. Zhu, H. Chen, W. Lin, Y. Ye, J. Wu, S. Li, *J. Am. Chem. Soc.* **2014**, *136*, 15126–15129.
[73] S. K. Samanta, M. Schmittel, *Org. Biomol. Chem.* **2013**, *11*, 3108–3115.
[74] F. J. Rizzuto, W. J. Ramsay, J. R. Nitschke, *J. Am. Chem. Soc.* **2018**, *140*, 11502–11509.
[75] Y. Shi, K. Cai, H. Xiao, Z. Liu, J. Zhou, D. Shen, Y. Qiu, Q.-H. Guo, C. Stern, M. R. Wasielewski, et al., *J. Am. Chem. Soc.* **2018**, *140*, 13835–13842.
[76] P. Ballester, M. Claudel, S. Durot, L. Kocher, L. Schoepff, V. Heitz, *Chem. – Eur. J.* **2015**, *21*, 15339–15348.
[77] J. Taesch, V. Heitz, F. Topić, K. Rissanen, *Chem. Commun.* **2012**, *48*, 5118–5120.
[78] L. Kocher, S. Durot, V. Heitz, *Chem. Commun.* **2015**, *51*, 13181–13184.
[79] L. Schoepff, L. Kocher, S. Durot, V. Heitz, *J. Org. Chem.* **2017**, *82*, 5845–5851.
[80] M. L. Gower, J. D. Crowley, *Dalton Trans.* **2010**, *39*, 2371–2378.
[81] A. S. Chia, R. F. J. Trimble, *J. Phys. Chem.* **1961**, *65*, 863–866.
[82] J. Rumble, *CRC Handbook of Chemistry and Physics*, Taylor & Francis Group, **2018**.
[83] S. Mecozzi, J. Rebek Jr, *Chem. – Eur. J.* **1998**, *4*, 1016–1022.

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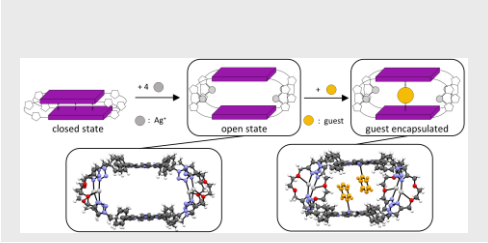

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Page No. – Page No.

Positive Allosteric Control of Guests Encapsulation by Metal Binding to Covalent Porphyrin Cages

Allosteric receptor: two flexible covalent cages have shown an on/off encapsulation mechanism triggered by significant conformational changes upon silver(I) coordination to the peripheral binding sites. In addition, the X-ray structure of the silver(I)-bound receptor and the one with pyrazine as guest confirmed the large cavity size of the receptor.

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