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Chemically-induced breathing of flexible porphyrinic covalent cages

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ABSTRACT: The synthesis of two flexible bis-porphyrin cages **3** and **4**, incorporating respectively Zn(II) porphyrins and free-base porphyrins is reported. In both cages, the four covalent linkers that bind the two porphyrins are functionalized with two 1,2,3-triazolyl ligands. These cages were characterized by NMR and HRMS and for cage **3** incorporating 1,4-diazabicyclo[2.2.2]octane (DABCO), an X-ray crystallographic structure was obtained. Chemically-induced conformational changes are studied and compared to the ones of two related cages with longer flexible linkers. Binding of four silver(I) ions to the peripheral ligands opens the flattened structures in solution and locks the two porphyrins in a face-to-face disposition. Addition of an excess of acid fully expand the cages due to electrostatic repulsion between the positively charged sites. These two reversible processes allow for a chemically-induced breathing of the flexible structures.

INTRODUCTION

The construction of molecular containers, capsules or cage-like compounds represents an active field of research and many chemical tools, in terms of bond formation (covalent, coordination and hydrogen bonds) and synthesis pathway (self-assembly, templated synthesis, dynamic combinatorial chemistry) have been exploited, leading to 3D architectures of high diversity.¹ As anticipated, these hollow structures were able to stabilize guest molecules according to their size, shape and affinity for the host. Isolated from the bulk solvent, the encapsulated guest modifies sometimes to a large extent its physical and chemical properties. Therefore, molecular encapsulation enables to stabilise reactive molecules or to perform chemical reactions inside molecular containers that behave as nanoreactors.² One way to control the binding and delivery of the guest molecule or the release of the reaction product is to incorporate constituents in the nanocontainer structure that respond to an external stimulus by triggering a large conformational change that modifies the host encapsulation properties. Some results in this area were obtained with multicomponent structures using photonic,³ chemical⁴ or redox signal.⁵

In the large variety of molecular containers conceivable, the synthesis of covalent hollow structures incorporating several metalated or free-base porphyrins is attractive for the high chemical stability expected with covalent structures and for the aptitude of porphyrins to interact with various types of guest molecules through π - π interactions or coordination bonds.⁶ Several improved synthetic procedures were recently reported to afford such compounds.⁷ Our aim was to synthesize covalent porphyrinic cages with additional active components in their structures. We have developed the synthesis of covalent cages consisting of two porphyrins connected by four flexible diethyleneglycol linkers **1-2**, each incorporating two 1,2,3-triazolyl ligands (Scheme 1a).⁸ In such structures, silver(I) was used as a chemical stimulus to control the cavity size. Herein, the DABCO-templated Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction leading to molecular cage **3**, characterized by shorter covalent linkers between the zinc(II) porphyrins is reported. The synthesis of cage **4**, incorporating two free-base porphyrins is also described. The chemical induced conformational changes triggered by silver(I) coordination to the peripheral triazoles or by protonation of the free-base porphyrins and the triazoles are investigated and compared to the ones occurring in cages **1-2** with longer spacers. Addition of an acid allows for a greater expansion of cages **2** and **3** as compared to silver(I) complexation, due to the numerous repulsive protonated sites. The NMR and DOSY experiments provide evidence of the large size modifications of the flexible covalent structures associated to these reversible chemical processes.

Scheme 1. a) Cages **1-2** already reported.⁸ b) Cages **3-4** of the present study in which shorter linkers connect the porphyrins.

RESULTS AND DISCUSSION

The synthesis of cage **3** relies on a DABCO-templated CuAAC reaction from two porphyrinic precursors **5** and **6** (Scheme 2 a). The CuAAC reaction enables to introduce one triazolyl ligand in each of the four bis-porphyrin linkers while proceeding to the cyclisation reaction between the tetraazide-functionalized porphyrin **5** and the tetraalkyne-functionalized porphyrin **6**. The two porphyrin precursors **5**⁹ and **6** were prepared without difficulty at the hundred mg scale. A first CuAAC reaction performed in DMF on the azide-functionalized Zn(II) porphyrin **5** in presence of the triisopropylsilyl (TIPS)-monoprotected alkyne **7** and using CuSO₄ as catalyst led to porphyrin **8** in 89% yield (Scheme 2 b). Classical removal of the TIPS protecting groups from porphyrin **8** using tetrabutylammonium fluoride (TBAF) afforded **6** in 80% yield. A mixture of three **DABCO**•porphyrin dimers was obtained upon addition of 1 equiv of DABCO to a millimolar solution of **5** and **6** in CH₂Cl₂ (Scheme 2 c). The four intramolecular CuAAC click reactions proceed only from the **5**•**DABCO**•**6** hetero dimer, with [Cu(tren')]Br as catalyst¹⁰ to avoid the decoordination of DABCO. After 2 days of reaction, the crude was submitted to column chromatographies to remove polymers and partially cyclized by-products. The cage including DABCO, **3**•**DABCO**, was isolated as a purple solid in 46% yield. In another attempt to isolate **3**, the crude was treated with HCl to demetallate the porphyrins. Column chromatographies afforded cage **4** in 58% yield and subsequent metalation of the free-base porphyrins with 2 equiv of Zn(OAc)₂•2H₂O gave **3** quantitatively.

Scheme 2. a) DABCO-templated CuAAC strategy to obtain cage **3•DABCO**. b) Synthesis of precursor **6**. c) Synthesis of cages **3•DABCO**, **4** and **3**.

The DABCO-templated cyclisation reaction reported for cage **1** was performed in analogous conditions but afforded **1** in lower yield, 25%.⁸ The DABCO-preorganisation of the two porphyrin precursors is more effective in the present synthesis, due to the shorter linkers of precursor **6**. Furthermore, DABCO is more stable in cage **3** and was not partially removed during purification by column chromatography, making the purification of **3•DABCO** easier to handle.

Single crystals of **3•DABCO** were obtained by slow diffusion of pentane into a chloroform solution of the **3•DABCO** complex (Figure 1). The already mentioned X-ray crystal structure of **4** (300 MHz).⁸ The two structures **3•DABCO** and **1•DABCO** are similar, with two eclipsed Zn(II) porphyrins. The shorter linkers of **3** ensure enough flexibility to accommodate DABCO inside the cavity without distortion of the porphyrins and the Zn-N bond length, 2.19 Å, is typical for this kind of complex. The mean planes of the porphyrins are separated by 7.53 Å, a distance close to the one measured in cage **1•DABCO** (7.44 Å).

Figure 1. ORTEP representation of the molecular structure of the complex **3•DABCO**. a) Top view and b) side view. ORTEP ellipsoids are set at 30% probability. H atoms and solvent molecules are omitted for clarity (Color code for the atoms: C grey, N blue, O red, Zn purple, DABCO green).

In solution, the ¹H NMR spectrum of **3•DABCO** is also consistent with an eclipsed disposition of the porphyrins and an average structure of *C*₄ symmetry (Figure 2). DABCO coordinated to the zinc(II) porphyrins inside the cavity is affected by the strong ring current of the two porphyrins resulting in a high upfield shifted signal at -4.67 ppm for its twelve protons.

Figure 2. ¹H NMR spectra in DMF-*d*₇ (298 K) of a) **3•DABCO** (400 MHz), b) cage **3** (DMF-*d*₇ + 2% pyridine-*d*₅, 500 MHz), and c) cage **3** (300 MHz). * Residual solvents.

After removal of DABCO with an excess of pyridine, cage **3** was soluble in polar coordinating solvents like DMSO, DMF/pyridine 2% or in a mixture of CHCl₃/MeOH/pyridine (9:1:0.5). In the ¹H NMR spectra recorded in either of these deuterated solvents, important upfield shifts of the aromatic protons *o*_{in} and *m*_{in}, pointing inside the cavity and less pronounced upfield shifts of protons H1, H2 and H3 of the linkers were noticed (Figure 2). They demonstrate a conformational change of the cage leading to a closer proximity of the porphyrins favoured by stabilizing π - π interactions. Cage **4** incorporating free-base porphyrins displays chemical shifts close to the

ones of cage **3** (Figure 2c), supporting a related flattened conformation for both cages as previously observed in solution for cages **1** and **2** and in the solid state for **1**.⁸

The modifications of the shape and position of the Soret absorption band of the zinc(II) porphyrins in cage **3** upon inclusion of the guest illustrated also the cage rearrangement. The initial very broad Soret band is consistent with electronic interactions between close porphyrins in the conformational free structure of **3** in solution (Figure 3). Upon DABCO binding, the porphyrins move away from each other in agreement with a thinning and bathochromic shift of the Soret band (Figure 3). The 1:1 binding constants K of cages **1**•DABCO and **3**•DABCO were obtained by performing UV-visible titrations in CHCl₃/MeOH (9:1) since they were too high to be determined in CHCl₃. The obtained association constant K $\square$ $1.3 \times 10^7 \text{ M}^{-1}$ for **3**•DABCO is 67% higher than the one of **1**•DABCO, $K = 7.8 \times 10^6 \text{ M}^{-1}$ (SI Figures S85-86 and Table S2). This increased binding affinity can be attributed to the shorter linkers of cage **3** which insure a better preorganisation of the host structure for the guest molecule.

Figure 3. UV-vis titration of **3** with DABCO in CHCl₃/MeOH (9:1). The concentration of **3** was maintained constant at 1.2 μM . Number of equiv added: 0, 0.1, 0.2, 0.4, 0.6, 0.7, 1.0, 1.4 and 2.7.

In order to control the cage conformation using a chemical stimulus, a solution of **3** or **4** in a mixture of CH₂Cl₂/CHCl₃/MeOH (5:5:1) was reacted with four equiv of AgOTf. The red solid that precipitated readily was dissolved in DMF and fully characterized by ¹H (COSY, NOESY, DOSY) and ¹³C NMR as well as HR-mass spectrometry. The high-resolution mass spectrum attested the formation of the complex with a 4:1 silver/cage stoichiometry, with the detected [Ag₄•**3**]⁴⁺/4 peak at $m/z = 693.0854$ whose isotopic profile was in accordance with the experimental ones. Another peak resulting from the loss of one silver ion in the ESI experiment was also detected. Whereas silver(I) coordination did not modify the number of proton signals in agreement with a structure of high symmetry, some important chemical shifts were observed on the ¹H NMR spectrum in DMF-*d*₇ (Figure 4). The downfield shift of 0.47 ppm of the triazole protons attested silver(I) binding to the triazolyl ligands. The large downfield shifts of the aromatic protons *o*_{in} ($\Delta\delta = 0.58 \text{ ppm}$) and *m*_{in} ($\Delta\delta = 0.67 \text{ ppm}$), as compared to the ones of *o*_{out} ($\Delta\delta = 0.01 \text{ ppm}$) and *m*_{out} ($\Delta\delta = 0.20 \text{ ppm}$) brings them at chemical shifts close to the ones observed for **3**•DABCO (Figure 4c) where the zinc(II) porphyrins are about 7 Å apart. These shifts indicate that silver(I) binding to the peripheral triazoles opens the flattened cage **3** (Figure 4).

Figure 4. ¹H NMR spectra (500 MHz, 298 K) in DMF-*d*₇ of a) Cage **3**, b) Cage [Ag₄•**3**](OTf)₄ and c) Cage **3**•DABCO. * Residual solvents.

The DOSY experiment corroborated this interpretation. The diffusion coefficient of **3** in DMF-*d*₇ decreased from $2.14 \times 10^{-10} \text{ m}^2 \cdot \text{s}^{-1}$ to $1.89 \times 10^{-10} \text{ m}^2 \cdot \text{s}^{-1}$ upon silver(I) coordination, which corresponds in a spherical model¹¹ to an increase of the hydrodynamic radius associated to the cage from 11.3 Å to 12.8 Å. Cage **1** in its collapse conformation has a similar hydrodynamic radius of 10.9 Å, that also increases upon silver binding to 13.4 Å for [Ag₄•**1**](OTf)₄ (Table S1). It must be noticed that silver complexes [Ag₄•**1**](OTf)₄ and [Ag₄•**3**](OTf)₄ are very stable in presence of an excess of silver(I) since no noticeable change occurred on the ¹H and DOSY NMR spectra from 4 to 200 equiv of added silver(I) ion (SI Figures S44-46). Solubilizing the silver cage [Ag₄•**1**]⁴⁺ or [Ag₄•**3**]⁴⁺ in a solvent of low polarity as DCM was possible by exchanging triflate with BARF⁻ (BARF⁻: tetrakis[3,5-bis(trifluoromethyl)phenyl]borate anions. With BARF⁻ as counter ion, the hydrodynamic radii of [Ag₄•**1**](BARF)₄ and [Ag₄•**3**](BARF)₄ were almost identical, 13.9 Å and 13.8 Å respectively. These results show that silver(I) coordination fixes the conformation of the flexible cages **1** and **3** with a co-facial disposition of the porphyrins leading to very close hydrodynamic radii. The same conclusions could be drawn from the DOSY results obtained when binding of silver(I) was performed on cages **2** and **4**, which incorporate free-base porphyrins (SI Table S1). Such metal-induced conformational changes are reversible and switching from the open silver-complexed cages back to the flattened conformations could be easily achieved by removal of the silver(I) in presence of an excess of chloride anions (SI Figure S47).

In order to enlarge the cavity size further than by coordinating silver(I) to the peripheral binding sites, protonation of the various basic sites was considered. Protonation of the eight triazoles and of the two free-base porphyrins of cages **2** and **4**, could lead to twelve positively charged species. Thanks to the flexible linkers, expansion of both cages is expected in response to strong electro-

static repulsion. Cage **4** gave a green solution in CD_2Cl_2 upon addition of deuterated trifluoroacetic acid (TFA-d). Its ^1H NMR spectrum (Figure 5) attested that the two porphyrins are moving away from each other by the progressive downfield chemical shifts of the o_{in} and m_{in} aromatic protons. After addition of 24 equiv of TFA-d (Figure 5b), all the signals are large, indicating slow exchange between partially protonated cages. In presence of a large excess of acid, the chemical shifts of the o_{in} and m_{in} protons were downfield shifted and closer to those of protons o_{out} and m_{out} (Figure 5d). The use of an excess of TFA ensured a fully protonated and soluble cage.

Figure 5. ^1H NMR spectra (300 MHz, 298 K) in CD_2Cl_2 of a) cage **4**, b) cage **4** after addition of 24 equiv TFA-d , c) cage **4** after addition of 1200 equiv TFA-d and d) protonated cage **4** after neutralization with Et_3N . *Residual solvents.

The DOSY experiment confirmed an increased volume for the protonated cage **4** with a hydrodynamic radius of 15.6 Å (SI Figure S76), consistent with the repulsion of the numerous positively charged sites. The open form could be shrunk back to its flattened conformation by addition of a base (Figure 5d). The same protonation reaction performed with cage **2** gave as expected based on the longer chemical linkers, a molecule of larger size with a hydrodynamic radius of 16.2 Å (SI Figure S84). Despite several attempts, no crystal suitable for X-ray diffraction analysis of cages in their expanded states, either by protonation or silver(I) coordination, could be obtained.

Molecular models (PM6, Spartan '16) of the twelve-time protonated cages **4** (Figure 6a) and **2** (Figure 6c) gave structures that fit well in spheres with hydrodynamic radii deduced from the DOSY experiments. From these models, the estimated mean plane distances between the porphyrins in the protonated cages **2** and **4** are substantial, respectively 20 and 16 Å (Figure 6 d, b). Whereas in cage **1**, the flattened porphyrins are separated by 3.81 Å in the compact conformation according to the X-ray structure,⁸ protonation fully expands the cage and increases this distance in solution to around 20 Å.

Figure 6. Energy-minimized structures (PM6, Spartan'16) of protonated cages **4** a), b) and **2** c), d). The hydrodynamic radii obtained from DOSY experiments of the spheres including **4** or **2** are 15.6 Å (a) and 16.2 Å (c) respectively. The mean plane distances between the porphyrins in the protonated cages **4** and **2** are indicated in b) and d) respectively.

CONCLUSION

The DABCO-templated CuAAC reaction was effective to afford in 46% yield a bis-Zn(II)porphyrin cage **3•DABCO** assembled with four flexible covalent linkers each incorporating two triazolyl ligands. Demetalation afforded quantitatively cage **4** incorporating two free-base porphyrins. The compact conformation that **3** adopts in solution expands by coordination of DABCO to the Zn-porphyrins. The flexibility of the linkers as well as the two types of constituents (porphyrin and triazole) incorporated in cages **3** and **4** and in the related cages **1** and **2** enables a chemically-induced breathing of the structure, based on reversible complexation or protonation reaction. The distance between the porphyrins can thus be increased by silver(I) coordination to the peripheral triazoles and maximized by protonation of the basic sites of cages **2** and **4**. These results demonstrated two ways of controlling large and reversible chemically-induced conformational changes in 3D structures that are particularly promising for the development of switchable receptors, sensors or reactors.

EXPERIMENTAL SECTION

General methods. All chemicals were of the best commercially available grade and used without further purification. CH_2Cl_2 and CHCl_3 were distilled over CaH_2 before use. THF was dried using dry-station GT S100 or distilled over sodium before use. Column chromatography was carried out using silica gel (Merck, silica gel 60, 63-200 or 40-63 μm). Mass spectra were obtained by using a Bruker MicroTOF spectrometer in electrospray mode (ES-MS). Nuclear Magnetic Resonance (NMR) spectra for ^1H , ^{13}C were acquired on Bruker AVANCE 300, 400, 500 spectrometers. The ^1H and ^{13}C spectra were referenced to residual solvent peaks. (CDCl_3 , 7.24 and 77.16; CD_2Cl_2 , 5.32 and 53.84; DMSO, 2.50 and 39.52; DMF, 8.03 and 163.15) Measures of self-diffusion coefficients were performed on a BRUKER 600 MHz spectrometer - Avance III, equipped with a DOTY (high strength z gradient probe DOTY Scientific, developing a pulse field gradient of 50 G/cm/A) or a BBI probe (Bruker BBI probe developing a pulse field gradient of 5 G/cm/A). The sample was

thermostated at 298 K. Diffusion NMR data were acquired using CH₂Cl₂ and the combined organic phases were dried over a Stimulated Echo pulse sequence with bipolar z gradients. Lim-Na₂SO₄, filtered and evaporated to dryness. The crude was purified by Eddy current Delay was fixed to 5 ms. The diffusion time fixed by column chromatography on silica gel (CH₂Cl₂/MeOH) and the duration of the gradients were optimized for each sample. from 100/0 to 97/3) to afford **6** as a purple solid (258 mg, 80% A recycling delay of 3 s was respected between scans. DOSY yield). ¹H NMR (300 MHz, CDCl₃ + pyridine-d₅): δ (ppm) 8.76 (8H, s, H_{py}), 8.12 (8H, d, ³J = 7.9 Hz, H_o), 7.77 (4H, s, H_i), 7.53 (8H, d, ³J = 7.9 Hz, H_m), 5.79 (8H, s, H₁), 4.74 (8H, s, H₂), 4.17 (4H, t, ³J = 2.4 Hz, H₅), 3.76-3.71 (16H, m, H₃₋₄), 2.39 (4H, t, ³J = 2.4 Hz, H_{alkyne}); ¹³C{¹H} NMR (126 MHz, CDCl₃ pyridine-d₅): δ (ppm) 149.9 (C₂), 145.7 (C₁₀), 143.9 (C₄), 135.1 (C₅), 133.7 (C₇), 131.7 (C₁), 126.0 (C₆), 122.9 (C₉), 119.8 (C₃), 79.6 (C₁₅), 74.8 (C₁₆), 69.7 (C₁₂), 69.1 (C₁₃), 64.9 (C₁₁), 58.5 (C₁₄), 54.2 (C₈); HRMS (ESI) m/z: [M+H]⁺ calcd for C₈₀H₇₃N₁₆O₈Zn 1449.5083, found 1449.5062 (100); mp > 360°C.

Monoprotected dialkyne 7. A solution of lithium bis(trimethylsilyl)amide (1 M in THF, 11 mmol, 11 mL, 1.5 equiv) was added to a stirred solution of α,ω-bis(O-CH₂CH₂Cl) (1 mL, 141 μmol, 16.0 mg, 1 equiv) was added to a propargyl)ethyleneglycol¹² (7.29 mmol, 1 g, 1 equiv) in dry THF stirred solution of **6** (141 μmol, 206 mg, 1 equiv) and zinc (600 mL) at room temperature under argon. After 10 min, TIP- [5,10,15,20-tetrakis(p-(azidomethyl)phenyl)porphyrin] **5** (141 μmol, 127 mg, 1 equiv) in dry and degassed CH₂Cl₂ (140 mL, 1 mixture. After 25 min, aqueous KOH (1 M, 200 mL) was added. mM). The reaction mixture, protected from light, was stirred at room temperature under argon for 1 hour. [Cu(tren')]Br (172 μmol, 310 mg, 1.2 equiv) and Na₂CO₃ (670 μmol, 70 mg, 4.8 equiv) were added, and the reaction mixture was refluxed under dryness. The crude was purified by column chromatography on argon for 2 days. The mixture was cooled down to room temperature, washed with water (3 x 150 mL) and brine (150 mL), dried over Na₂SO₄, filtered and evaporated to dryness. The crude product was purified by column chromatography on alumina (petroleum ether/AcOEt 9:1) to afford **7** as a colorless ture, washed with water (3 x 150 mL) and brine (150 mL), dried oil (724 mg, 36% yield). ¹H NMR (400 MHz, CDCl₃): δ (ppm) 8.50 (16H, s, H_o), 8.43 (8H, s, H_{py}), 7.99 (8H, d, ³J = 7.6 Hz, H_o out), 7.85 (8H, d, ³J = 7.6 Hz, H_o in), 7.73 (8H, d, ³J = 7.6 Hz, H_o in), 7.56 (8H, d, ³J = 7.6 Hz, H_o in), 6.05 (16H, s, H₁), 4.83 (16H, s, H₂), 3.87 (16H, s, H₃), -4.67 (12H, s, H_{DABCO}); ¹³C{¹H} NMR (126 MHz, CDCl₃/methanol-d₄ 9:1): δ (ppm) 149.5 (C₂), 145.7 (C₁₂), 143.1 (C₄), 134.8 (C₅), 134.8 (C₇), 133.9 (C₉), 131.4 (C₁), 126.7 (C₆), 125.7 (C₈), 123.4 (C₁₁), 119.5 (C₃), 70.1 (C₁₄), 64.8 (C₁₃), 54.1 (C₁₀), 38.4 (C_{DABCO}). HRMS (ESI) m/z: [M+3H]³⁺ calcd for C₁₃₄H₁₁₉N₃₄O₈Zn/3 819.9506, found 819.9511 (95); UV-vis: (CHCl₃/MeOH (9:1)) λ_{max} nm (ε M⁻¹ cm⁻¹) 424 (985 000); 560 (36 400); 601 (7 620); mp > 360°C.

TIPS-protected porphyrin 8. To a stirred solution of **7** (1.80 mmol, 608 mg) and zinc (II) [5,10,15,20-tetrakis(p-(azidomethyl)phenyl)porphyrin] **5** (0.39 mmol, 352 mg, 1 equiv) in anhydrous DMF (39 mL) were added CuSO₄•5H₂O (0.39 mmol, 98 mg, 1 equiv) and sodium ascorbate (1.36 mmol, 270 mg, 3.5 equiv). The reaction mixture was degassed (3 vacuum-argon cycles) and stirred at 50°C overnight under argon. The solvent was evaporated and the residue was dissolved in CH₂Cl₂. The organic layer was washed with water (3x200mL), dried over Na₂SO₄, filtered and evaporated to dryness. The crude was purified by column chromatography on silica gel (CH₂Cl₂/MeOH from 100/0 to 90/10) to afford **8** as a purple solid (974 mg, 89% yield). ¹H NMR (300 MHz, CDCl₃ + pyridine-d₅): δ (ppm) 8.78 (8H, s, H_{py}), 8.15 (8H, d, ³J = 7.9 Hz, H_o), 7.80 (4H, s, H_i), 7.57 (8H, d, ³J = 7.9 Hz, H_m), 5.83 (8H, s, H₁), 4.77 (8H, s, H₂), 4.24 (8H, s, H₅), 3.75-3.79 (16H, m, H₃₋₄), 1.01 (84H, s, TIPS); ¹³C{¹H} NMR (126 MHz, CDCl₃ + pyridine-d₅): δ (ppm) 149.9 (C₂), 145.8 (C₁₀), 144.0 (C₄), 135.2 (C₅), 133.7 (C₇), 131.8 (C₁), 126.0 (C₆), 123.0 (C₉), 119.8 (C₃), 103.2 (C₁₅), 87.9 (C₁₆), 69.8 (C₁₂), 68.7 (C₁₃), 64.9 (C₁₁), 59.3 (C₁₄), 54.2 (C₈), 18.7 (C₁₈), 11.2 (C₁₇). HRMS (ESI) m/z: [M]⁺ calcd for C₁₁₆H₁₅₂N₁₆O₈Si₄Zn 2075.0329 (100); UV-vis: (CH₂Cl₂) λ_{max} nm (ε M⁻¹ cm⁻¹) 423 (395 000); 552 (4 360); 597 (16 300); mp > 360°C.

Alkyne functionalized porphyrin 6. TBAF•3H₂O (998 μmol, 315 mg, 4.5 equiv) was added to a stirred solution of **8** (224 μmol, 466 mg, 1 equiv) in THF (50 mL). The reaction mixture protected from light was stirred overnight at room temperature. After removal of the solvent under reduced pressure, the residue was dissolved in CH₂Cl₂. The organic layer was washed with water, the aqueous phase was extracted several times with CH₂Cl₂. The combined organic phases were dried over Na₂SO₄, filtered and evaporated to dryness. The crude was purified by column chromatography on silica gel (CH₂Cl₂/MeOH (9:1)) to afford **6** as a purple solid. (181 mg, 58% yield) ¹H NMR (500 MHz, DMSO-d₆): δ (ppm) 8.38 (16H, s, H_{py}), 8.30 (8H, s, H_o), 8.00 (8H, d, ³J = 7.6 Hz, H_o out), 7.60 (8H, d, ³J = 7.6 Hz, H_o in), 6.81 (8H, d, ³J = 7.6 Hz, H_o in), 6.11 (8H, d, ³J = 7.6 Hz, H_o in), 5.56 (16H, s, H₁), 4.58 (16H, s, H₂), 3.66 (16H, s, H₃), -3.19 (4H, s, NH). ¹H NMR (500 MHz, DMF-d₇): δ (ppm) 8.45 (16H, s, H_{py}), 8.39 (8H, s, H_o), 8.02 (8H, d, ³J = 7.6 Hz, H_o out), 7.78 (8H, d, ³J = 7.6 Hz, H_o in), 7.04 (8H, d, ³J = 7.6 Hz, H_o in), 6.82 (8H, d, ³J = 7.6 Hz, H_o in), 5.88 (16H, s, H₁), 4.70 (16H, s, H₂), 3.76 (16H, s, H₃), -3.31 (4H, s, NH). ¹H NMR (300 MHz,

CD₂Cl₂): δ (ppm) 8.33 (16 H, s, H_{py}), 7.86 (8 H, d, $^3J = 7.6$ Hz, (8 H, s, H_l), 7.76 (32 H, m, H_o BArF), 7.72 (8 H, d, $^3J = 7.6$ Hz, H_o out), 7.76 (8H, s, H_l), 7.56 (8 H, d, $^3J = 7.6$ Hz, H_m out), 6.96 (8 H_m out), 7.62 (8 H, d, $^3J = 7.6$ Hz, H_o in), 7.58 (16 H, m, H_o BArF), H, d, $^3J = 7.6$ Hz, H_o in), 6.63 (8 H, d, $^3J = 7.6$ Hz, H_m in), 5.65 (16 7.41 (8H, d, $^3J = 7.6$ Hz, H_m in), 5.85 (16H, s, H_l), 4.73 (16H, s, H, s, H_l), 4.72 (16 H, s, H₂), 3.79 (16H, s, H₃), -3.66 (4 H, s, H₂), 3.83 (16H, s, H₃). **¹H NMR** (500 MHz, DMF-*d*₇): δ (ppm) NH); **¹³C{¹H} NMR** (126 MHz, DMSO-*d*₆): δ (ppm) 144.4 (C₁₂), 8.83 (8 H, s, H_l), 8.54 (16 H, s, H_{py}), 8.16 (8 H, d, $^3J = 7.6$ Hz, H_o 140.3 (C₄), 135.4 (C₉), 133.9 (C₅₊₇), 131.1 (C₁), 126.0 (C₆), 124.8 out), 7.97 (8 H, d, $^3J = 7.6$ Hz, H_m out), 7.81 (48 H, m, BArF), 7.78 (C₈), 124.6 (C₁₁), 119.2 (C₃), 69.0 (C₁₄), 63.6 (C₁₃), 52.2 (C₁₀); (8 H, d, $^3J = 7.6$ Hz, H_o in), 7.44 (d, $^3J = 7.6$ Hz, 8 H, H_m in), 6.21 pyrrolic ¹³C C₂ are too enlarged to be observed at 298K; **HRMS** (s, 16 H, H₁), 4.97 (s, 16 H, H₂), 4.01 (s, 16 H, H₃); **¹³C{¹H} NMR** (ESI) m/z: [M+2H]²⁺ calcd for C₁₂₈H₁₁₀N₃₂O₈/2 1111.4587, found **NMR** (126 MHz, CD₂Cl₂): δ (ppm) 162.1 (q, ¹J_{B-C} = 50 Hz, 1111.4560 (100); [M+H]⁺ calcd for C₁₂₈H₁₀₉N₃₂O₈ 2221.9101, BArF), 150.1 (C₂), 145.9 (C₁₂), 143.6 (C₄), 135.9 (C₇), 135.2 (s, found 2222.9086; **UV-vis**: (dmsol) λ_{max} nm (ϵ M⁻¹ cm⁻¹) 417 (780 BArF), 134.5 (C₅), 133.4 (C₉), 131.9 (C₁), 129.2 (q, ¹J_{C-F} = 31.5 000); 516 (34 600); 552 (16 300); 590 (10 200); 646 (8 880); Hz, BArF), 126.5 (C₆), 125.8 (C₈), 124.9 (q, ¹J_{C-F} = 272 Hz, BArF), 122.8 (C₁₁), 120.2 (C₃), 117.9 (s, BArF), 70.6 (C₁₄), 63.6

Synthesis of cage 3. Zn(OAc)₂·2H₂O (49.5 μ mol, 11 mg, 2.2 (C₁₃), 55.6 (C₁₀); **¹⁹F{¹H} NMR** (282 MHz, CD₂Cl₂): δ (ppm) - 63.89; **¹¹B NMR** (96 MHz, CD₂Cl₂): δ (ppm) -6.59; **HRMS** (ESI) m/z: [M-4BArF]⁴⁺ calcd for C₁₂₈H₁₀₄Ag₄N₃₂O₈Zn₂/4 693.0870, found 693.0881 (100); [M-4BArF-Ag]³⁺ calcd for C₁₂₈H₁₀₄Ag₃N₃₂O₈Zn₂/3 888.4811, found 888.4842 (41); [M-3BArF]³⁺ calcd for C₁₂₈H₁₀₄Ag₄BF₂₄N₃₂O₈Zn₂/3 1211.8045, Found 1211.8067 (10); mp > 360°C.

Silver(I)-complexed cage [Ag₄·4](OTf)₄. AgOTf (7.20 μ mol, 1.85 mg, 4 equiv) was added at room temperature to a stirred solution of cage 4 (1.80 μ mol, 4.00 mg, 1 equiv) in dis-4.71 (16 H, s, H₂), 3.77 (16 H, s, H₃); **¹H NMR** (500 MHz, tilted CHCl₃/CH₂Cl₂/MeOH (5:5:1, 11 mL), protected from light. DMSO-*d*₆): δ (ppm) 8.37 (16 H, s, H_{py}), 8.29 (8H, s, H_l), 8.01 (8 A purple precipitate formed immediately. After 20 minutes, the H, d, $^3J = 7.6$ Hz, H_o out), 7.59 (8 H, d, $^3J = 7.6$ Hz, H_m out), 6.97 (8 H, d, $^3J = 7.6$ Hz, H_o in), 6.26 (8 H, d, $^3J = 7.6$ Hz, H_m in), 5.61 (16 afford a purple solid (5.9 mg, quantitative yield). **¹H NMR** (500 H, s, H₁), 4.60 (16 H, s, H₂), 3.68 (16H, s, H₃); **¹³C{¹H} NMR** (126 MHz, DMF-*d*₇ + pyridine-*d*₅): δ (ppm) 150.6 (C₂), 146.2 8.25 (8 H, d, $^3J = 7.6$ Hz, H_o out), vers 8.05 (8 H, d, $^3J = 7.6$ Hz, (C₁₂), 143.7 (C₄), 136.4 (C₉), 135.8 (C₇), 135.5 (C₅), 132.4 (C₁), H_m out), 7.81 (8 H, d, $^3J = 7.6$ Hz, H_o in), 7.46 (8H, d, $^3J = 7.6$ Hz, 127.2 (C₆), 126.4 (C₈), 125.4 (C₁₁), 120.9 (C₃), 70.7 (C₁₄), 65.4 H_m in), 6.23 (16H, s, H₁), 4.96 (s, 16 H, H₂), 4.00 (16H, m, H₃), - (C₁₃), 54.0 (C₁₀); **HRMS** (ESI) m/z: [M+2H]²⁺ calcd for 3.45 (4H, s, NH); **¹³C{¹H} NMR** (126 MHz, DMF-*d*₇): δ (ppm) C₁₂₈H₁₀₆N₃₂O₈Zn₂/2 1173.3722, found 1173.3729 (100); **UV-vis**: 146.8 (C₁₂), 142.5 (C₄), 136.7 (C₉), 136.3 (C₇), 135.6 (C₅), 131.9 (dmsol) λ_{max} nm (ϵ M⁻¹ cm⁻¹) 424 (1 100 000); 560 (41 100); 601 (br, C₁), 127.9 (C₆), 126.8 (C₈), 125.6 (C₁₁), 122.6 (q, ¹J_{C-F} = 322 (19 700) (CHCl₃/MeOH (9 :1)) λ_{max} nm 420; 558; 594); mp > 360°C.

Silver(I)-complexed cage [Ag₄·3](OTf)₄. AgOTf (25.5 μ mol, 6.56 mg, 4 equiv) was added at room temperature to a stirred solution of cage 3 (6.39 μ mol, 15.0 mg, 1 equiv) in distilled CHCl₃/CH₂Cl₂/MeOH (5:5:1, 25 mL), protected from light. A purple precipitate formed immediately. The solvent was removed and the residue was dried under vacuum to afford a purple solid (21.6 mg, quantitative yield). **¹H NMR** (500 MHz, DMF-*d*₇): δ (ppm) 8.83 (8 H, s, H_l), 8.51 (16 H, s, H_{py}), 8.11 (8 H, d, $^3J = 7.6$ Hz, H_o out), 7.95 (8 H, d, $^3J = 7.6$ Hz, H_m out), 7.81 (8 H, d, $^3J = 7.6$ Hz, H_o in), 7.44 (8H, d, $^3J = 7.6$ Hz, H_m in), 6.21 (s, 16 H, H₁), 4.97 (s, 16 H, H₂), 4.01 (s, 16 H, H₃); **¹³C{¹H} NMR** (126 MHz, DMF-*d*₇): δ (ppm) 150.5 (C₂), 146.9 (C₁₂), 144.0 (C₄), 136.2 (C₇), 136.0 (C₉), 135.8 (C₅), 132.3 (C₁), 127.5 (C₆), 126.4 (C₈), 125.6 (C₁₁), 122.6 (q, ¹J_{C-F} = 320 Hz, OTf), 120.8 (C₃), 70.7 (C₁₄), 63.9 (C₁₃), 55.1 (C₁₀); **¹⁹F{¹H}NMR** (282 MHz, DMF-*d*₇): δ (ppm) - 79.63; **HRMS** (cryospray ESI) m/z: [M-4OTf]⁴⁺ calcd for C₁₂₈H₁₀₄Ag₄N₃₂O₈Zn₂/4 693.086992, found 693.085448 (10); [M-4OTf-Ag]³⁺ calcd for C₁₂₈H₁₀₄Ag₃N₃₂O₈Zn₂/3 888.481139, found 888.479004 (100); mp > 360°C.

Recovering cage 3 from [Ag₄·3](OTf)₄. An excess of LiCl (16 μ mol, 0.7 mg, 10 equiv) was added at room temperature to a stirred solution of cage [Ag₄·3](OTf)₄ (1.6 μ mol, 5.5 mg, 1 equiv) in DMF-*d*₇. A white precipitate formed immediately. After filtration, the solvent was removed and the residue was washed with methanol and centrifugated. The residue was dried under vacuum to afford a purple solid (3.5 mg, 90% yield).

ASSOCIATED CONTENT

Supporting Information.

¹H, ¹³C, 2D NMR spectra and HRMS of new compounds and crystallographic data for **1-DABCO** (CCDC 1535914) and **3-DABCO** (CCDC 1535953) (PDF).

X-ray crystallographic data for **1-DABCO** (CIF).

X-ray crystallographic data for **3-DABCO** (CIF).

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Silver(I)-complexed cage [Ag₄·3](BArF)₄. NaBArF₂₄ (25.5 μ mol, 22.6 mg, 4 equiv) was added to a stirred solution of cage [Ag₄·3](OTf)₄ (6.39 μ mol, 21.6 mg, 1 equiv) in CH₂Cl₂. After 1 hour, the compound was completely soluble. The reaction mixture was then washed with water (3x20mL), dried over Na₂SO₄ and the solvent was removed under vacuum to obtain a purple solid (39.0 mg, 98 % yield). **¹H NMR** (500 MHz, CD₂Cl₂): δ (ppm) 8.61 (16 H, s, H_{py}), 8.21 (8 H, d, $^3J = 7.6$ Hz, H_o out), 7.88

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Abstract

The synthesis of two flexible bis-porphyrin cages **3** and **4**, incorporating respectively Zn(II) porphyrins and free-base porphyrins, is reported. In both cages, the four covalent linkers that bind the two porphyrins are functionalized with two 1,2,3-triazolyl ligands. These cages were characterized by NMR and HRMS, and for cage **3** incorporating 1,4-diazabicyclo[2.2.2]octane (DABCO), an X-ray crystallographic structure was obtained. Chemically induced conformational changes are studied and compared to those of two related cages with longer flexible linkers. Binding of four silver(I) ions to the peripheral ligands opens the flattened structures in solution and locks the two porphyrins in a face-to-face disposition. Addition of an excess of acid fully expands the cages due to electrostatic repulsion between the positively charged sites. These two reversible processes allow for a chemically induced breathing of the flexible structures.