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Templated Synthesis of Cyclic [4]Rotaxanes Consisting of Two Stiff Rods Threaded through Two Bis-macrocycles with a Large and Rigid Central Plate as Spacer

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Abstract: Two related cyclic [4]rotaxanes consisting of double macrocycles and rigid rods incorporating two bidentate chelates have each been prepared in high yield. The first step is a multigathering and threading reaction driven by coordination of two different bidentate chelates (part of either the rings or the rods) to each copper(I) center so as to afford the desired precursor. In both cases, the assembly step is done under very mild conditions, and it is quantitative. The second key reaction is the stopper-attaching reaction, based on click chemistry. Even if the quadruple stoppering reaction is not quantitative, it is relatively high-yielding (60% and 95%), and the copper-driven assembly process is carried out at room temperature without any aggressive reagent. The final copper-complexed [4]rotaxanes obtained contain two aromatic plates roughly parallel to one another located at the center of each bis-macrocycle. In the most promising case in terms of host–guest properties, the plates are zinc(II) porphyrins of the tetra-aryl series. The compounds have been fully characterized by various spectroscopic techniques (¹H NMR, mass spectrometry, and electronic absorption spectroscopy). Unexpectedly, the copper-complexed porphyrinic [4]rotaxane could be crystallized as its 4PF_6^- salt to afford X-ray quality crystals. The structure obtained is in perfect agreement with the postulated chemical structure of the compound. It is particularly attractive in terms of symmetry and molecular aesthetics. The distance between the zinc atoms of the two porphyrins is 8.673 Å, which is sufficient to allow insertion between the two porphyrinic plates of small ditopic basic substrates able to interact with the central porphyrinic Zn atoms. This prediction has been confirmed by absorption spectroscopy measurements in the presence of various organic substrates. However, large substrates cannot be introduced in the corresponding recognition site and are thus complexed mostly in an exo fashion, being located outside the receptor cavity. Noteworthy, the stability constants of the 1:1 host–guest complexes are high (10^7 M^{-1}).

Introduction

Topologically nontrivial species are nowadays relatively accessible thanks to the introduction of various efficient template strategies.¹ In particular, interlocking ring systems and, to a lesser extent, knotted rings are accessible species, which find more and more applications in several areas (electron and energy

transfer,² controlled motions and mechanical properties,^{3–10} and new “intelligent” materials^{11–18}).

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[§] X-ray crystallography.

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Within the vast family of catenanes and rotaxanes^{4,19–31} synthesized since the first directed synthesis of a [2]catenane in 1964,³² multirotaxanes are particularly promising as molecular machines³³ able to perform complex chemical functions. Particularly significant examples include molecular “muscles”, able to contract or stretch under the action of a chemical,³⁴

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electrochemical,^{17,35} or photochemical³⁶ signal and consisting of a doubly threaded species incorporating two ring-and-string conjugates and thus belonging to the family of molecules named “daisy chain”.³⁷ Switchable rotaxanes attached to inorganic porous materials and able to act as molecular “valves” are also particularly noteworthy.³⁸ Another type of threaded system, based on a [3]rotaxane, has been reported to behave as an adjustable host for guests of various sizes. This last system consists of two porphyrinic plates bearing macrocycles threaded on the same axis.³⁹ In order to gain control over the geometry of the system and, in particular, to have an accurate knowledge of the distance between the two plates of the receptor, it was anticipated that a cyclic [4]rotaxane should be preferable to a [3]rotaxane. The assembly principle was recently described in preliminary communications for the non-porphyrinic compound⁴⁰ and for the most complex system consisting of porphyrin nuclei connecting the rings of the bis-macrocycles.⁴¹ In these two papers, we reported the copper(I)-induced quantitative formation of [4]pseudorotaxanes from two rods and two bis-macrocycles. We would now like to describe the synthesis of two cyclic [4]rotaxanes (i.e., stoppered species), a porphyrin-containing one and a non-porphyrinic system. The 4-fold stopper-attaching reaction is based on click chemistry. It turned out to be very efficient for a quadruple reaction, and thus relatively large quantities of each copper-complexed rotaxane could be obtained. In addition, the ability of the two-porphyrin compound to act as a receptor for various substrates was investigated and compared to that of the less constrained [3]rotaxane described last year.³⁹ This cyclic [4]rotaxane is a large molecule, which could be crystallized and studied by X-ray diffraction. The crystallographic study reveals a beautiful centrosymmetric molecular structure in the solid state. Because of the higher rigidity of the two-porphyrin [4]rotaxane described in the present paper compared to that of a related [3]rotaxane³⁹ (cf Figure 1), the association constants are generally higher and the selectivity of complexation is more pronounced.

Results and Discussion

1. Design of the System. The construction of the two final [4]rotaxanes described in the present report involves two critical

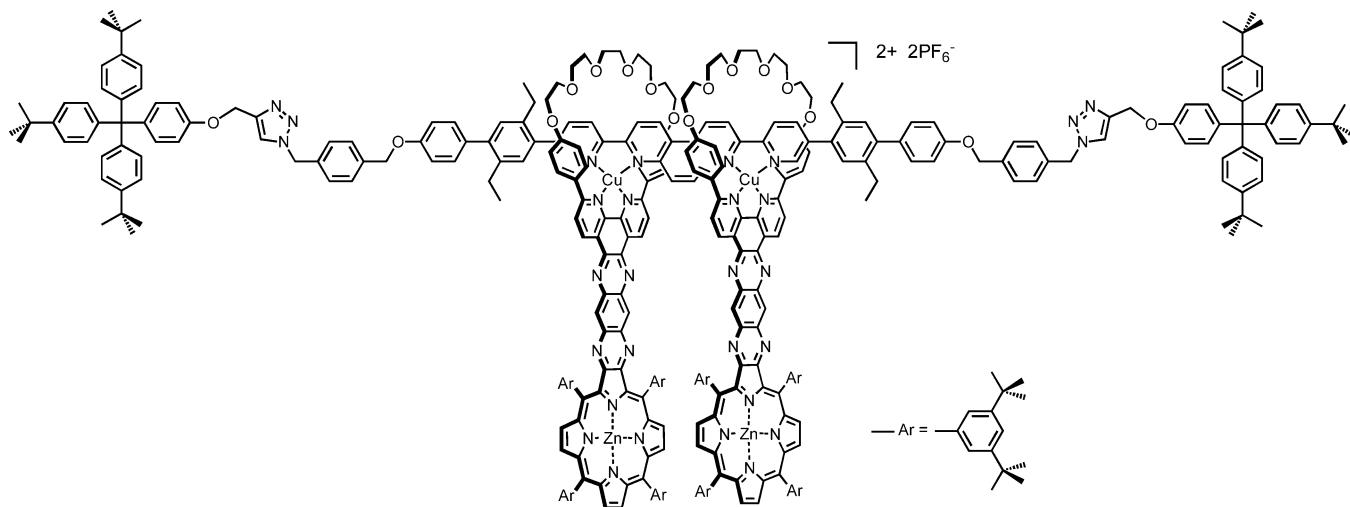
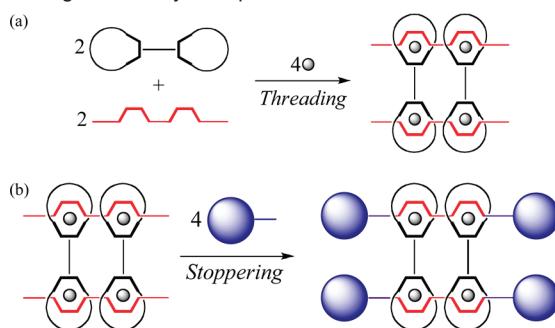


Figure 1. Chemical structure of the previously published porphyrinic [3]rotaxane.³⁹

Scheme 1. (a) Copper(I)-Driven Formation of a Cyclic [4]Pseudorotaxane;^a (b) “Real” [4]Rotaxane Obtained by Connecting Four Bulky Groups to the Ends of the Threads



^a The metal center is represented by a grey dot, and the chelating groups are indicated by a black or red U-shaped symbol.

steps: (i) the copper(I)-driven threading of two coordinating “filaments” through the rings of two bis-macrocycles followed by (ii) the attachment of bulky stoppers at the ends of the threaded fragments.

The principle of the first step has already been described in previous reports.^{40,41} It is based on the thermodynamics of the reaction, the threaded species of Scheme 1a representing the most stable situation among all the other possibilities, as explained below. Mixing 2 equiv of bis-ring, 4 equiv of copper(I), and 2 equiv of an acyclic ligand will lead to multiply threaded species if the complexation reaction is done under thermodynamic control. With this 2:4:2 stoichiometry (thread/copper(I)/bis-macrocycle = 2:4:2), the complex depicted in Scheme 1a represents the only situation in which neither ligands nor metal centers are “frustrated”. In other words, any other state will involve uncoordinated ligands and/or coordinatively unsaturated metal centers. The multiple threading reaction of Scheme 1 is thus expected to be quantitative provided the design of bis-macrocycle and thread is appropriate (1:2:1 cannot be realized) and the reaction stoichiometry is respected accurately. This principle was applied very long ago by our group for making singly threaded species from a 1,10-phenanthroline-containing ring, copper(I), and another phenanthroline-type ligand.^{1a,19} The second step, namely, the stoppering reaction, is relatively classical since it has been used in most cases for making rotaxanes. In the present examples, the reaction of choice turned out to be the copper(I)-catalyzed formation of triazoles

from a terminal acetylene and an azide, a particularly selective Huisgen reaction⁴² recently developed simultaneously by Meldal and Sharpless,⁴³ known as a “click chemistry” reaction.

The two target compounds are represented in Figure 2.

By analogy with our recent work on [3]rotaxanes used as adjustable receptors³⁹ it is obvious that compound **2**⁴⁺ could also act as a host for various ditopic guests bearing pyridyl groups or amines as terminal functions. The higher degree of geometrical control is expected to lead to a better selectivity of recognition and a higher stability constant than with [3]rotaxanes, which was the main rationale for elaborating such complex structures as **1**⁴⁺ and **2**⁴⁺ in addition to the synthetic challenge.

2. Synthesis of the Non-porphyrinic Copper-Complexed Rotaxane **1⁴⁺.** To the best of our knowledge, there are just two examples of cyclic [4]rotaxane in the literature,⁴⁴ but the synthesis strategy was different from that used for making the present compounds.

The [4]pseudorotaxane **6**⁴⁺ (see Figure 3) was obtained by mixing acetylenic thread **3**, bis-macrocycle **4**, and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ in a mixture of $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ (4:1) and stirring under argon during 3 days. Acetylenic thread **3** and bis-macrocycle **4** were synthesized according to literature procedures.⁴⁵ The poor solubility of both ligands in this mixture of solvents did not allow for the “classical” threading procedure that consists in (i) complexing Cu(I) with the macrocycle and then (ii) adding the thread. Nevertheless, the desired compound was obtained in quantitative yield. This result confirms the power of translational entropy for these pseudorotaxanes, as described in previous papers.⁴⁰

The stoppering reaction was performed with azide stopper **5**,^{45a} $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ as catalyst, and Na_2CO_3 as a base in a $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ (4:1) mixture following classical “click chemistry” conditions.⁴³ The desired [4]rotaxane **1**⁴⁺ was

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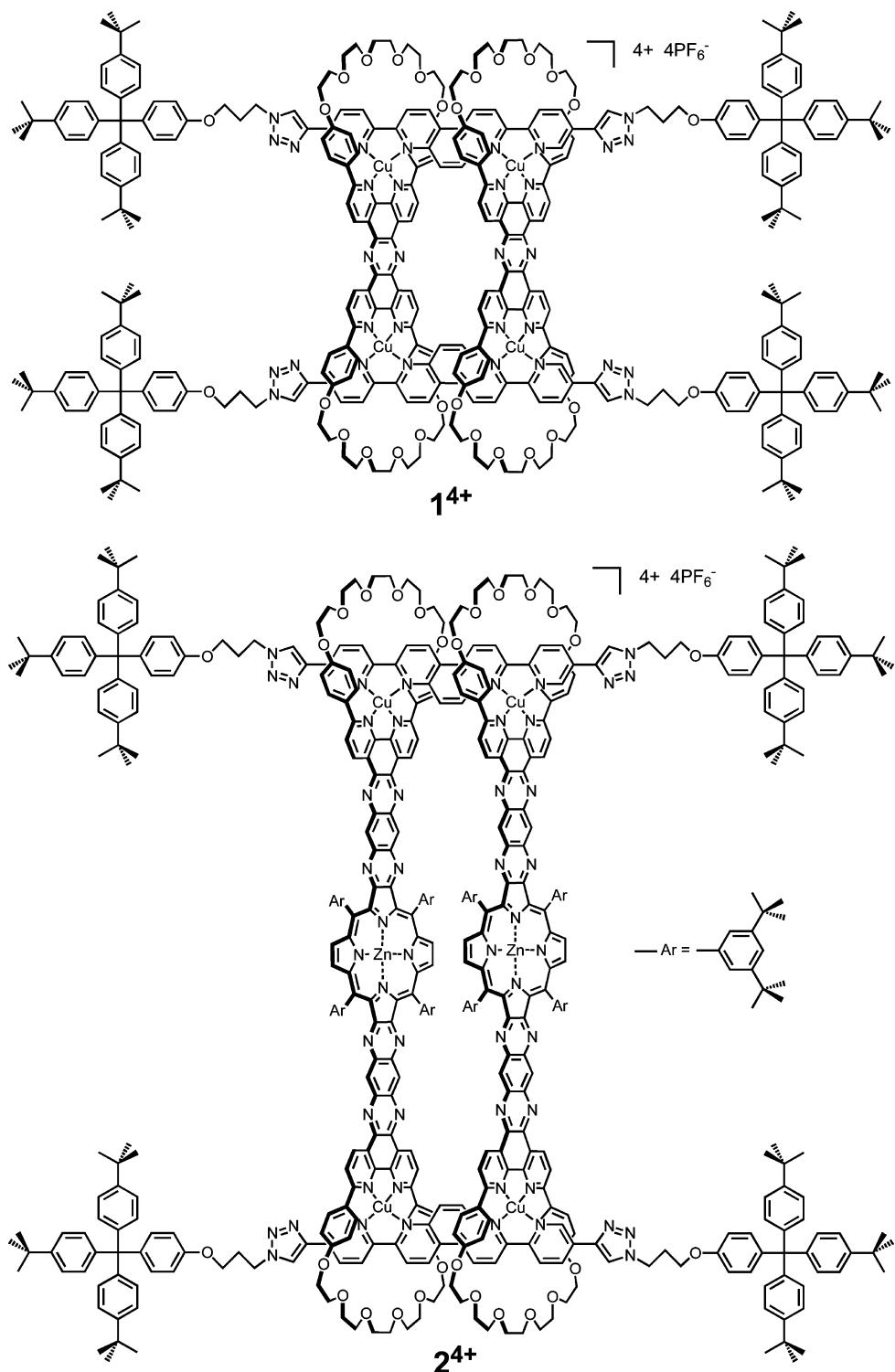


Figure 2. Target rotaxanes **1⁴⁺** and **2⁴⁺**.

obtained with a very satisfactory yield of 60%. This remarkably high yield for a tetra-stoppering reaction (88% yield per function) can be explained by the high stability of the precursor. The fact that the bis-macrocycle is threaded twice and that, in order to dissociate the system, several unthreading reactions would have to be involved, stabilizes very significantly the whole structure toward dethreading of the axle.

Compound **1⁴⁺** was characterized by NMR spectroscopy (1D, COSY, ROESY, and DOSY) as well as high resolution mass spectrometry (ES-MS). The DOSY spectrum of the rotaxane

1⁴⁺ is represented in the Supporting Information (Figure SI6). It shows that only one species was formed, characterized by a diffusion coefficient of $263 \pm 3 \mu\text{m}^2 \text{s}^{-1}$.

The threaded nature of compound **1⁴⁺** was confirmed by the very strong upfield chemical shifts observed for the aromatic protons of the phenyl groups of the macrocycles as well as the various interfragment interactions that are observed by NOESY NMR experiments. Particularly noteworthy is, for instance, the correlations between aromatic protons of the chelating part of

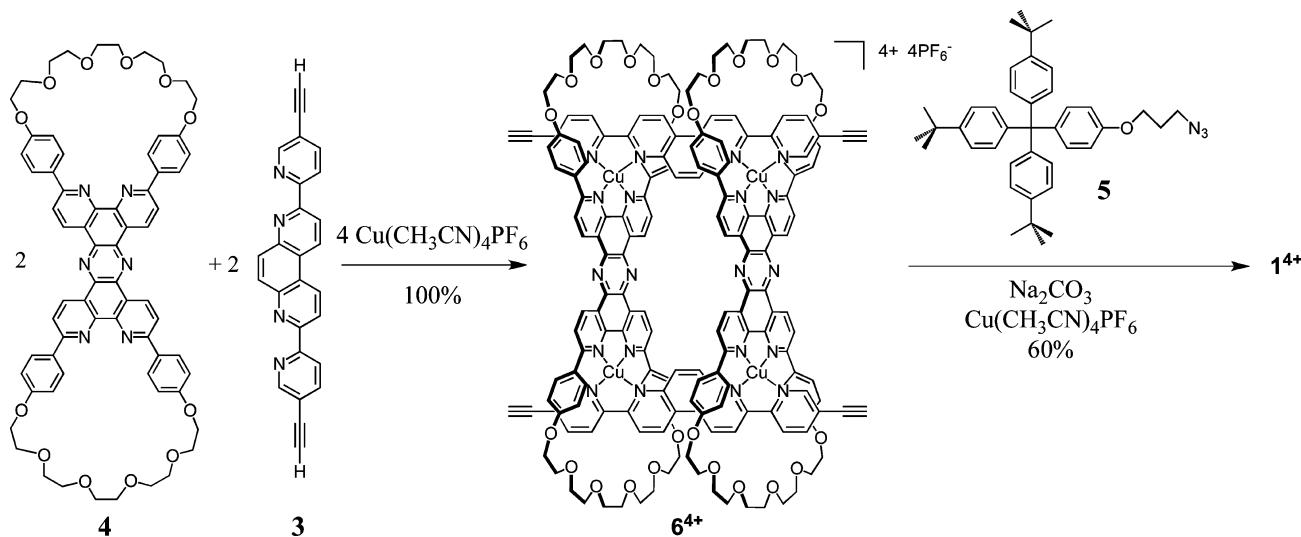


Figure 3. Synthesis of rotaxane 1^{4+} .

the thread and protons of the poly(ethylene glycol) chain of the bis-macrocycle.

3. Synthesis of Porphyrinic Copper-Complexed Rotaxane 2^{4+} . **3.1. Synthesis of Zinc(II) Porphyrinic Bis-macrocycle 11.** The synthetic procedure started with the porphyrin α -tetraone **8** developed in the group of Crossley to make linear extended porphyrin conjugates.^{46,47} In our case, it was synthesized in several steps starting from the β -nitro Cu(II) porphyrin as precursor as described in the literature by two groups.^{47,48} We followed the procedure described by Crossley et al. Preparation of **7** has already been reported in the literature.^{45b}

Condensation of **7** and **8** on a 1,2,4,5-benzenetetramine **9** was realized using a stepwise procedure. Porphyrin α -tetraone **8** and benzenetetramine tetrahydrochloride (2.4 equiv) were reacted in pyridine at 60 °C for 6 h, then macrocycle **7** (3 equiv) was added, and the reaction was prolonged under the same conditions for 18 h. Compound **10** was obtained as a brown solid in 45% yield and was fully characterized by ^1H NMR and high resolution ES-MS.

Metalation of the porphyrinic site of **10** was carried out in a mixture of chloroform and methanol by adding an excess of $\text{Zn}(\text{OAc})_2$ (20 equiv) to a refluxing solution of **10**. A further treatment with an EDTA solution to remove Zn(II) from the phenanthroline chelates made it possible to obtain **11** quantitatively from **10**. Bis-macrocycle **11** has already been used in a preliminary study.⁴¹

3.2. Synthesis of Porphyrinic Cu(I) Cyclic [4]Pseudorotaxane 12^{4+} and of Porphyrinic Copper-Complexed Rotaxane 2^{4+} . As described in the first paragraph, threading two porphyrinic bis-macrocycles with a two-chelate rod relies on a thermodynamically controlled reaction using Cu(I) as gathering and threading metal center. The kinetically relatively labile copper–nitrogen bonds allows for self-repair, and therefore formation of the most thermodynamically stable compound is expected.

The reaction is depicted in Figure 5. In a typical procedure, stoichiometric amounts of **11** in CHCl_3 and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$

in CH_3CN were first mixed, to afford the desired copper(I) complex after 30 min at room temperature. Subsequently, a stoichiometric amount of **3** in CHCl_3 was added, and the solution was stirred for further 7 days, leading to the desired [4]pseudorotaxane **12⁴⁺** in quantitative yield after solvent evaporation.⁴¹

The stoppering reaction was performed in exactly the same way as that described previously for rotaxane 1^{4+} . The desired [4]rotaxane 2^{4+} was also obtained with an excellent yield of 95%, even higher than for 1^{4+} . This unexpected high yield can be explained by the same reasons as those exposed for rotaxane 1^{4+} , namely, high stability of the threaded precursor.

Rotaxane 2^{4+} was fully characterized by UV–vis spectroscopy, high resolution mass spectrometry (ES-MS), and ^1H NMR (1D, COSY, ROESY and DOSY). The aromatic region of the ^1H NMR spectrum of [4]rotaxane 2^{4+} is represented in Figure 6.

The protons that are labeled by “op” (cf. Figure 6 for labeling) correspond to two different signals. This is because the di-*tert*-butylphenyl units attached to the porphyrin moiety are disposed approximately orthogonally to the porphyrin itself, and steric interactions between bulky ‘Bu groups belonging to two face-to-face bis-macrocycles hinder free rotation. Therefore, one op proton points “into” the space between the two porphyrins and one “outside”. Thus, they correspond to two different peaks on the NMR spectrum.

Also particularly noteworthy is the very strong upfield shift observed for the protons of the phenyl groups of the macrocycles labeled by “m”. This upfield shift is typical of the threaded nature of this family of compound. It originates from the spatial proximity of an aromatic ring (a pyridyl group) that has a strong ring current effect on the “m” protons. Moreover, various interfragment interactions are observed by ROESY NMR experiments, which clearly prove the threaded nature of compound 2^{4+} (see Supporting Information).

The DOSY spectrum of rotaxane 2^{4+} in CD_2Cl_2 is represented in the Supporting Information (Figure S111). It shows that only one species was formed, characterized by a diffusion coefficient of $230 \pm 3 \mu\text{m}^2 \text{s}^{-1}$. As expected, rotaxane 2^{4+} , which has an overall volume higher than that of 1^{4+} , has a lower diffusion coefficient.

4. X-ray Crystal Structural Analysis. After several and time-consuming crystallizations from several solvent mixtures, our

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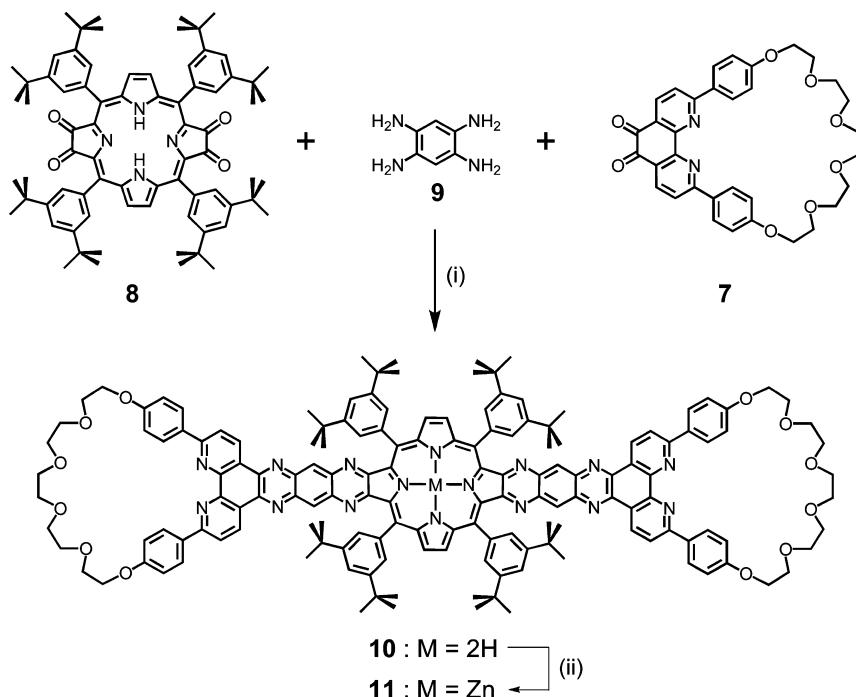


Figure 4. Synthesis of porphyrinic bis-macrocycles **10** and **11**: (i) (1) **8**, **9** (2.4 equiv), pyridine, 60 °C, 5 h; (2) **7** (3.0 equiv), pyridine, 60 °C, 18 h (45%); (ii) (1) $\text{Zn}(\text{OAc})_2$, $\text{CHCl}_3/\text{MeOH}$, reflux, 24 h; (2) EDTA, $\text{CHCl}_3/\text{MeOH}/\text{H}_2\text{O}$, rt, 24 h (quant).

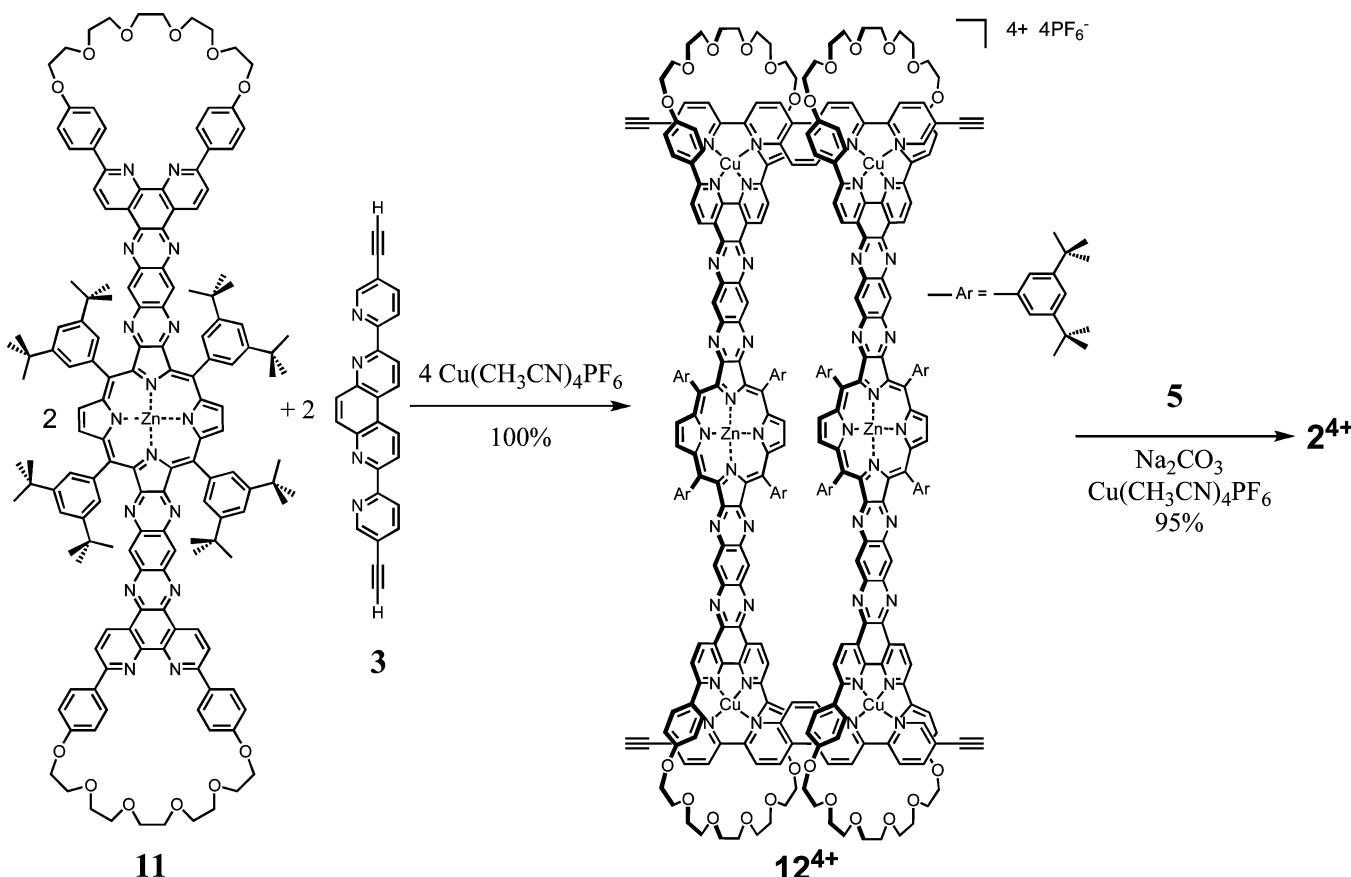


Figure 5. Synthesis of the porphyrinic rotaxane **2⁴⁺**.

attempts were finally rewarded by very fragile brown prismatic plate-like crystals. The X-ray structure⁴⁹ of the rotaxane **2⁴⁺** confirmed the [4]rotaxane structure (Figure 7).

The [4]rotaxane **2⁴⁺** represents the largest rotaxane molecule ($\text{MW} \approx 8700$) the X-ray structure of which has been determined so far, being a true nanosize single molecule. To the best of

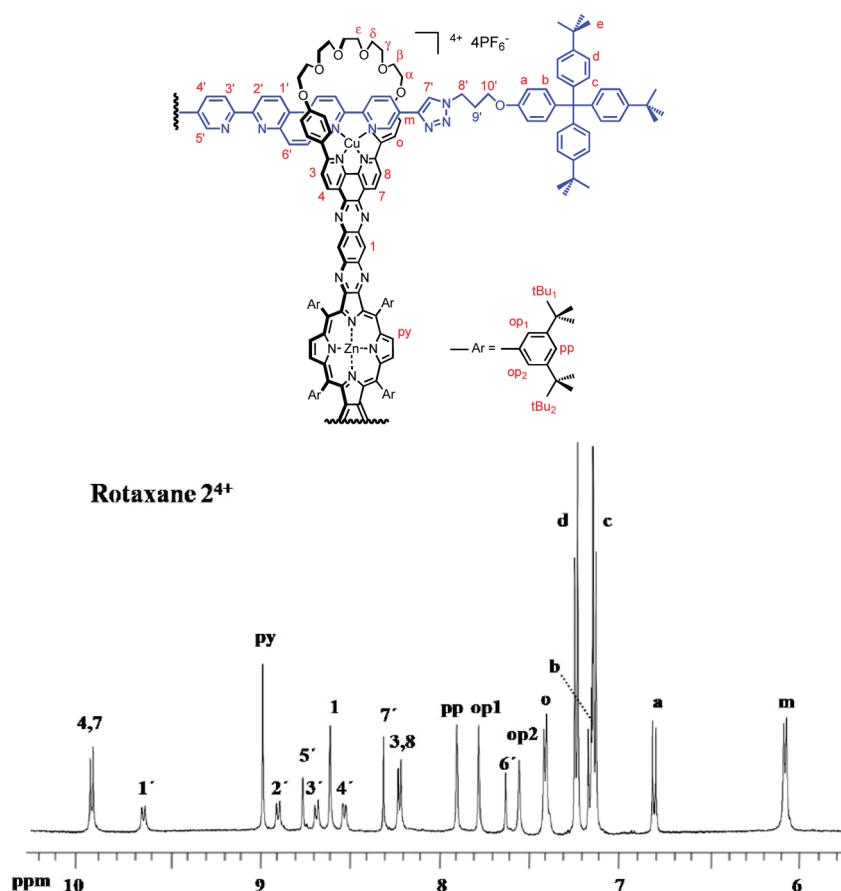


Figure 6. ^1H NMR spectrum of rotaxane 2^{4+} displaying the peaks in the 6–10 ppm range. Part of rotaxane 2^{4+} is represented above for complete atom numbering.

our knowledge, the former largest rotaxane whose X-ray structure was solved was synthesized by Leigh's group (MW ≈ 8000).^{22c} The overall dimensions of 2^{4+} are ca. 5 nm \times 3.5 nm \times 2 nm (width \times height \times thickness). In the crystalline state 2^{4+} has a symmetry element (center of inversion) located between the two porphyrins of the molecule. As a result of some steric mismatches and spatial requirements, the molecule shows severe bending and twisting of the central porphyrinic bis-macrocycles **11**. The two very bulky porphyrin moieties cannot stack exactly on top of each other, showing a slight offset stacking. The X-ray data revealed a high electron density peak inside the cavity formed by the porphyrin moieties and close to (ca. 2.3 Å) the Zn atoms and was assigned to a coordinated water molecule (H-atoms could not be located). The intramolecular distance of these water molecules inside the cavity is 5.36 Å, and the corresponding Zn...Zn distance is 8.68 Å. As the Cu...Cu distance in the axle is 7.75 Å, the Zn-porphyrinic bis-macrocycles **11** have to bend to compensate the sterical demand of their central Zn-porphyrin moieties. Indeed the bending is manifested in the angle Cu...Zn...Cu, which is 171.66°, where the two Cu are coordinated to two different rods. However the bending is not symmetrical; careful inspection of the structure of **11** reveals that two-thirds of it is nearly planar and the remaining one-third is bent, resulting in a shallow J-shape for **11** as a part of the rotaxane 2^{4+} . This J-shape bending can be visualized by calculating a plane through the planar part of the Zn-porphyrinic bis-macrocycle **11** (viz. the plane through the central Zn-porphyrin and the Cu-complexing phenanthroline moieties and Cu-atom) and measuring the off-plane distance of the second Cu-atom. In **11**, this off-plane distance is 2.39 Å,

which corresponds well to the Cu...Zn...Cu bending angle of ca. 171.5° of the 5 nm (50 Å) long **11**. In addition to the bending the off-plane part is twisted in respect to planar part of **11**; the twist angle between the planar part (as defined above) and the bent Cu-complexing moiety is 56.2°. The observed bending and twisting of the Zn-porphyrinic bis-macrocycles **11** is obviously not severe enough to prevent the formation of 2^{4+} . In addition the twisting of the Zn-porphyrinic bis-macrocycles **11** results in a twisting of the whole [4]rotaxane. The di-tris-phenyl-phenanthroline axles are twisted 40.6° with respect to each other (the torsion angle defined as C(di-'Bu-Ph)₃...Cu...Cu...C(di-'Bu-Ph)₃). In the absence of π - π interactions the slant angle of 58° between the axle and the two nearly parallel polyoxaethylene macrocycles of **11** in 2^{4+} is comparable to that of other Cu-containing [2] and [3]rotaxanes.⁵⁰ The hexafluorophosphate anions are nesting in the space between the two Zn-porphyrins and macrocycle parts of **11** and in the "armpits" between the axle and **11** (Figure 8).

5. Electronic Spectroscopy Titration of Porphyrinic [4]Rotaxane 2^{4+} with Various Ditopic Ligands. The stability constants between the receptor [4]rotaxane 2^{4+} and various guests were

(49) Crystal data for $2(\text{PF}_6)_4$: brown prism, $0.10 \times 0.30 \times 0.30 \text{ mm}^3$, $M = 9004.82$, $C_{524}\text{H}_{534}\text{N}_{52}\text{O}_{30}\text{P}_4\text{F}_{24}\text{Cu}_2\text{Zn}_2$, triclinic, space group $P-1$, $a = 15.9812(19)$ Å, $b = 27.908(4)$ Å, $c = 34.355(4)$ Å, $\alpha = 70.843(5)$ °, $\beta = 79.695(6)$ °, $\gamma = 73.704(6)$ °, $V = 13829(3)$ Å³, $Z = 1$, $D_c = 1.081 \text{ g/cm}^3$, 2695 parameters, 4153 restraints, $R = 0.122$ [$I_o > 2\sigma(I_c)$], $wR = 0.357$ (all reflections).

(50) Sleiman, H.; Baxter, P. N. W.; Lehn, J.-M.; Rissanen, K. *J. Chem. Soc., Chem. Commun.* **1995**, 715–717.

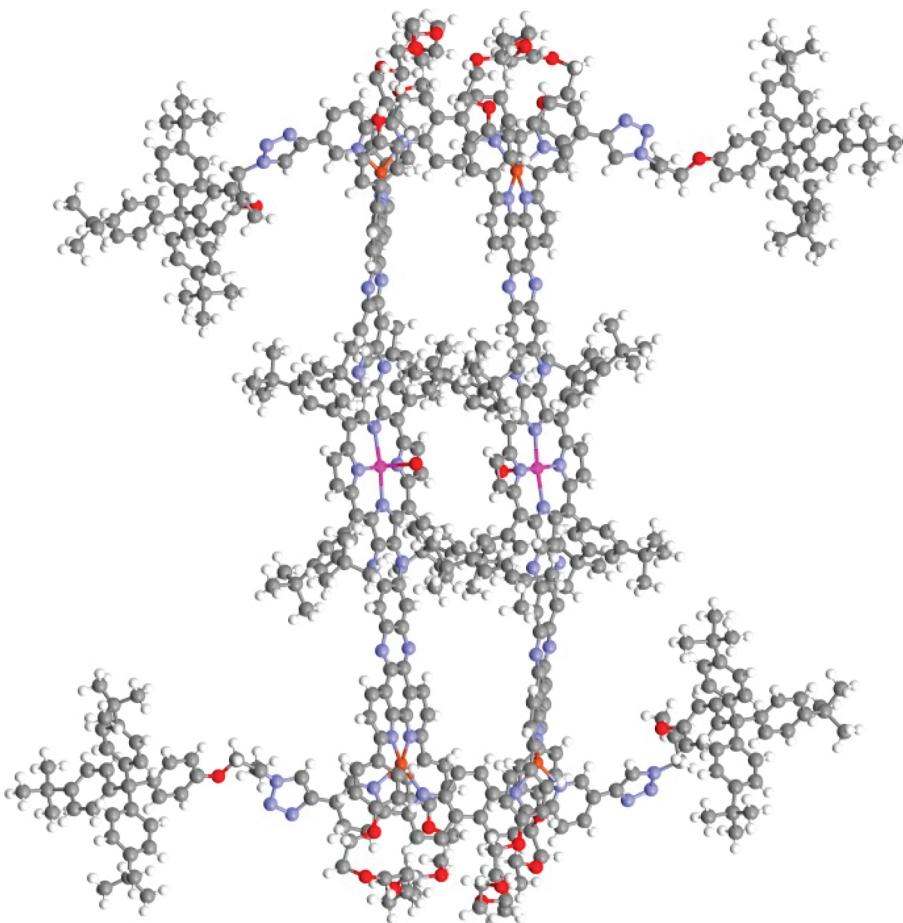


Figure 7. Ball-and-stick presentation of the X-ray structure of 2^{4+} . The PF_6^- anions are excluded for clarity.

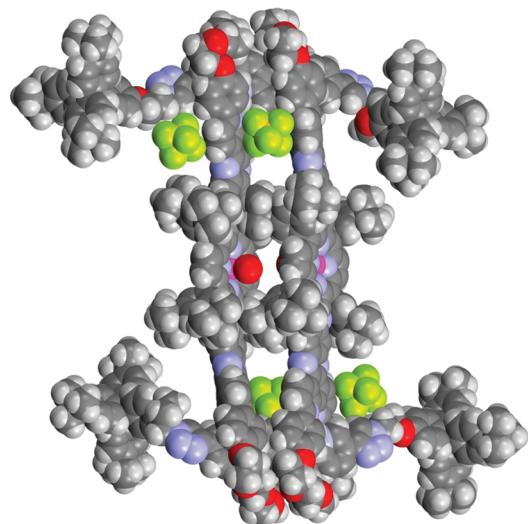


Figure 8. VDW presentation of the X-ray structure of 2^{4+} .

determined by UV-vis spectroscopy titrations. The guests used, **G1** to **G5**, are represented in Figure 9.

The bidentate ligand **G1** is the shortest one with a distance of 2.8 Å between the nitrogen atoms. It has been used previously in conjunction with various porphyrinic assemblies.^{39,51} Guests **G2** to **G5** are constituted by two 4-pyridyl units connected by rigid spacers (0, 1, or 2 phenyl groups) or by a flexible C_{10} aliphatic chain. The Soret band of the Zn-porphyrins is an excellent probe to monitor the complexation reaction between

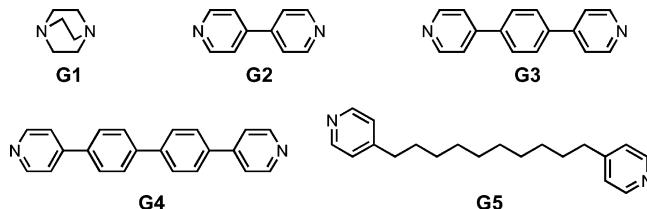


Figure 9. Chemical structures of guests **G1**–**G5**.

host 2^{4+} and the various guests. By adding gradual amounts of the bidentate substrate **G1** to **G5** to a toluene solution of 2^{4+} , significant bathochromic shifts of the Soret band (3 to 9 nm) were observed, in accordance with previous observations.⁵²

A clear isosbestic point was obtained for the titration of 2^{4+} with **G2**. Figure 10 shows the spectra, in the range of the Soret band, obtained by titration of rotaxane 2^{4+} by guest **G2**. This behavior constitutes a good indication that only one equilibrium is to be considered; the association equilibrium takes place between only two species (Figure 10). In addition, the 1:1 stoichiometry (H:G) is corroborated by a mathematical treatment of the spectroscopic data by Specfit 32 software since the best fit is obtained for the 1:1 model. This mathematical treatment

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- (52) Nappa, M.; Valentine, J. S. *J. Am. Chem. Soc.* **1978**, *100*, 5075–5080.

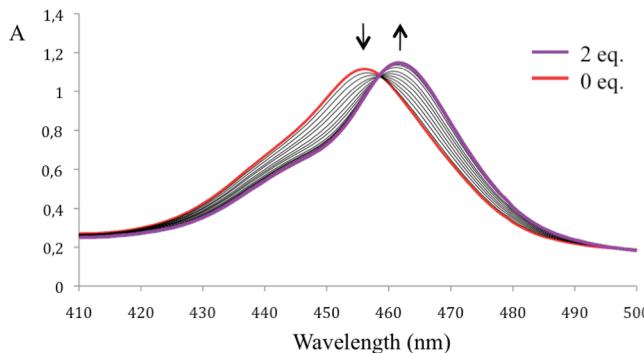


Figure 10. UV-vis titration spectra in toluene (Soret band) of rotaxane 2^{4+} (1.5×10^{-6} M) with substrate **G2** (4.5×10^{-5} M) from 0 (red curve) to 2 equiv (blue curve). Arrows show changes of the host spectrum with increasing guest **G2** concentration.

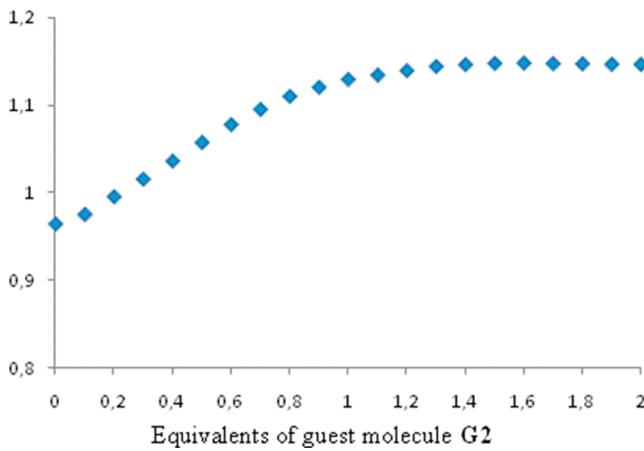


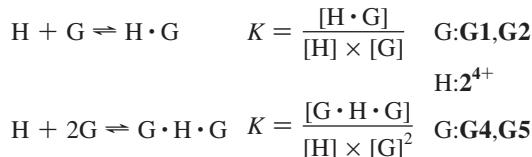
Figure 11. UV-vis titration of rotaxane 2^{4+} with substrate **G2** in toluene. Absorbance plotted against the added substrate equivalents at $\lambda_{\text{max}} = 462$ nm.

of the spectroscopic data for the titration of **G1** is also in accordance with the 1:1 model.

In the cases of **G4** and **G5**, no isosbestic point was observed, only a decrease of the absorbance of the Soret band. With these guests, the formation of 1:1 complexes is clearly not the main complexation process. On the contrary, the 1:2 stoichiometry of these complexes was corroborated by the mathematical treatment.

For **G3**, no isosbestic point was observed, and the mathematical treatment of this behavior did not clearly corroborate any stoichiometry (1:1, 1:2, or 2:1). Since formation of a specific complex did not account for the titration curves obtained, it can be concluded that we are in an intermediate situation with several coexisting complexes in a large concentration range. This guest must have a critical size that does not allow any selectivity with rotaxane 2^{4+} .

The stability constants for the complexes corresponding to the following equilibria have been determined:



Their values are reported in Table 1.

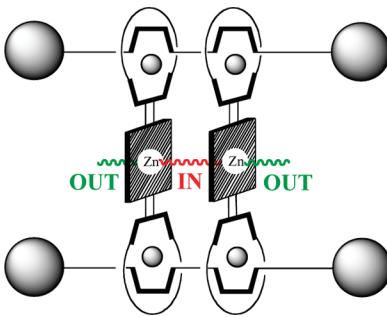


Figure 12. Various coordination modes of ligands **G1** to **G5** to rotaxane 2^{4+} : “IN” for **G1** to **G2** and “OUT” for **G4** and **G5**. As far as **G3** is concerned, both IN and OUT complexes should be considered.

All of these values are in accordance with the compatibility of N–N distance of the guest and the distance between the parallel porphyrinic units (the Zn–Zn distance is about 8.7 Å according to the crystallographic data presented above). For **G1** and **G2**, the complexes are formed by guest inclusion (internal complexes, IN), whereas for guests **G4** and **G5**, external complexes (OUT) are formed (Figure 12). This assessment is corroborated by the association constant values. Indeed, for **G1** and **G2**, such values cannot be envisaged if no cooperative effect with the coordination of two nitrogen atoms is considered (the order of magnitude of the association constant between a simple pyridyl ligand and a zinc porphyrin is about 10^3 mol⁻¹ L). This is the reason why for **G1** and **G2** there is no other possibility than having an internal coordination mode with the 1:1 stoichiometry. On the contrary, the 1:2 stoichiometry calculated for **G4** and **G5** tends to indicate an external coordination mode that can be explained by the size of these ligands, which are too long to be included between the two porphyrinic units without breaking the system (Figure 12).

All of these results are in accordance with studies realized with the previously reported bis-porphyrin [3]rotaxane.³⁹ As expected, the more pronounced rigidity of [4]rotaxane 2^{4+} is favorable to the formation of more stable complexes for **G1** and **G2** than those previously obtained with the [3]rotaxane. Moreover, this rigidity inhibits the possibility for **G4** and **G5** to be coordinated between the porphyrins, which is the main difference observed with this new generation of receptors compared to the previous system based on a [3]rotaxane.

6. ¹H NMR and ES-MS Characterization of (2⁴⁺:G1). In order to confirm the hypothesis of a 1:1 stoichiometry with ligands **G1** and **G2**, we characterized one of these complexes, the (2⁴⁺:**G1**) complex, by other techniques than UV-vis spectroscopy.

The first technique used was electrospray mass spectrometry (ES-MS). The fact that the 1:1 system could be detected reflects its relatively high stability.

The second technique used was ¹H NMR spectroscopy. After mixing 1 equiv of rotaxane 2^{4+} with 1 equiv of **G1** in CD₂Cl₂, we obtained a system whose ¹H NMR spectrum is significantly different from the one of the sole 2^{4+} rotaxane in the same solvent. As expected, the chemical shifts of the porphyrinic protons (py, pp, op) underwent the main changes for rotaxane 2^{4+} . For instance, the “py” protons underwent an upfield shift of 0.12 ppm. However, the main change concerns **G1**; indeed, a drastic change of the -CH₂- chemical shift is observed from 2.65 to -3.27 ppm. Such a strong upfield chemical shift has already been observed when DABCO **G1** was complexed in

Table 1. Stability Constants in Toluene for the Complexes Formed with Rotaxane **2⁴⁺** and Bridging Ligands **G1–G5**

	1:1 stoichiometry		1:2 stoichiometry		
	G1	G2	G3	G4	G5
bridging ligand N–N distance in Å, extended conformation (from CPK model)	2.6	7.2	11.6	15.9	18
log <i>K</i>	7.4 ± 0.1	7.3 ± 0.2	see text	13.6 ± 0.4	11.9 ± 0.2

between two zinc porphyrins,⁵³ which corroborates once more the IN coordination mode of **G1** in rotaxane **2⁴⁺**.

Conclusion

In conclusion, two different cyclic [4]rotaxanes consisting of two stoppered rod-like fragments threaded through the four rings of two bis-macrocyclic components could be prepared in good yields. The general strategy, combining (i) a copper-driven gathering and threading step and, subsequently, (ii) a click-chemistry-based stopper-attaching reaction, is remarkably efficient in terms of simplicity of the experimental conditions (reactions carried out at room temperature) and synthesis overall yield. This is particularly true for the porphyrin-incorporating compound **2⁴⁺**, which was obtained from the various organic fragments in more than 90% after the multithreading and quadruple stoppering processes, despite a very large separation between the bis-macrocycle coordinating units used in the complexation reaction with copper(I). In addition, this porphyrin-containing [4]rotaxane is an interesting receptor for various ditopic guests, as shown by complexation studies. Compared to a related porphyrin-containing [3]rotaxane that also behaves as a receptor, the present system seems to be significantly more selective in the way that long substrates, whose overall length in their extended conformation exceeds 15 Å (such as **G4** and **G5**), do not form stable 1:1 complexes with **2⁴⁺**, whereas the smaller guests (**G1** and **G2**) do form stable 1:1 complexes. In subsequent work, the corresponding metal-free rotaxanes will also be prepared and studied, in particular for the porphyrin-incorporating compound, in relation to their host–guest properties.

Experimental Section

General Methods. Dry CH₂Cl₂ and CHCl₃ were distilled from CaH₂ as drying agent, and dry CH₃CN was purchased from Aldrich. Preparative column chromatography was carried out using silica gel (Merck Kieselgel, silica gel 60, 0.063–0.200 mm).

NMR spectra for ¹H were acquired on Bruker AVANCE 500 or 300 spectrometers. The spectra were referenced to residual proton-solvent references (¹H, CD₂Cl₂ at 5.32 ppm, CDCl₃ at 7.26 ppm). In the assignments, the chemical shift (in ppm) is given first, followed in brackets by the multiplicity of the signal (s, singlet; d, doublet; t, triplet; dd, doublet of doublets; m, multiplet), the value of the coupling constants in Hz if applicable, the number of protons implied, and finally the assignment.

Mass spectra were obtained by using a Bruker MicroTOF spectrometer (ES-MS).

Starting Materials. All commercially available chemicals were used without further purification. DABCO and 4,4'-bipyridine were purchased from Aldrich. The guests **G3**, **G4**, and **G5** were prepared according to published procedures.^{39b,54}

Spectral and Equilibrium Constant Measurements. UV-vis spectra were recorded with a Kontron Instruments UVIKON 860 spectrometer at 25 °C with a 1 cm path cell. All measurements were made in toluene solutions. UV-vis spectrophotometric titrations were analyzed by fitting the series of spectra at 1 nm

intervals by using the SPECFIT/32 3.0 (Spectrum Software Associates), which takes into account the changes in volume during the titration.⁵⁵

[4]Pseudorotaxane 6⁴⁺. To a suspension of bis-macrocycle **4** (23 mg, 19.9 μmol) and acetylenic thread **3** (7 mg, 18.3 μmol) in 20 mL of dry and degassed CH₂Cl₂ was added a solution of [Cu(CH₃CN)₄](PF₆) (15 mg, 40.2 μmol) in 5 mL of degassed CH₃CN under argon via canula. The mixture turned black and homogeneous in few seconds and was reacted during 3 days. After evaporation of the solvents, the crude product was redissolved in CH₃CN and filtered in order to eliminate the possible excess of organic ligands. The CH₃CN was evaporated to give the [4]pseudorotaxane **6⁴⁺** in quantitative yield (35 mg, 8.94 μmol). ¹H NMR (300 MHz, CD₂Cl₂, 298 K): δ 9.97 (d, ³J = 8.1 Hz, 8H, H-4,7), 9.53 (d, ³J = 8.8 Hz, 4H, H-1'), 8.75 (d, ³J = 8.9 Hz, 4H, H-2'), 8.56 (d, ³J = 8.5 Hz, 4H, H-3'), 8.24 (dd, ³J = 8.4 Hz, ⁴J = 1.6 Hz, 4H, H-4'), 8.21 (d, ³J = 8.4 Hz, 8H, H-3,8), 8.11 (s, ⁴J = 1.3 Hz, 4H, H-5'), 7.46 (s, 4H, H-6'), 7.29 (d, ³J = 8.5 Hz, 16H, H-o), 6.13 (d, ³J = 8.6 Hz, 16H, H-m), 4.05–3.80 (m, 80H, H-α, H-β, H-γ, H-δ, H-ε), 3.70 (s, 4H, H-7') ppm. MS (ES): *m/z* (%) = 833.2252 (100) [M – 4PF₆]⁴⁺/4 (calcd 833.2201 for [C₁₈₈H₁₅₆Cu₄N₂₀O₂₄]⁴⁺/4).

[4]Rotaxane 1⁴⁺. [4]Pseudorotaxane **6⁴⁺** (90 mg, 23.0 μmol), azide stopper **5** (87 mg, 148 μmol), [Cu(CH₃CN)₄](PF₆) (8.7 mg, 23.3 μmol), Na₂CO₃ (3 mg, 28.3 μmol), and sodium ascorbate (2 mg, 10.1 μmol) were diluted in 6 mL of dry and degassed CH₂Cl₂ and 1.5 mL of dry and degassed CH₃CN. The solution was stirred under argon during 6 days. The solvents were then evaporated, and the resulting deep green residue was purified by silica chromatography. A gradient of elution from CH₂Cl₂/MeOH 100/0 to 97/3 gave 86 mg (13.7 μmol) of rotaxane (60%). ¹H NMR (300 MHz, CD₂Cl₂, 298 K): δ 9.97 (d, ³J = 8.2 Hz, 8H, H-4,7), 9.53 (d, ³J = 9.0 Hz, 4H, H-1'), 8.76 (d, ³J = 8.8 Hz, 4H, H-2'), 8.63 (d, ³J = 8.5 Hz, 4H, H-3'), 8.56 (d, ⁴J = 1.5 Hz, 4H, H-5'), 8.53 (dd, ³J = 8.4 Hz, ⁴J = 1.7 Hz, H-4'), 8.20 (s, 4H, H-7'), 8.18 (d, ³J = 8.4 Hz, 8H, H-3,8), 7.48 (s, 4H, H-6'), 7.31 (d, ³J = 8.4 Hz, 16H, H-o), 7.22 (d, ³J = 8.6 Hz, 24H, H-d), 7.16 (d, ³J = 9.0 Hz, 8H, H-b), 7.12 (d, ³J = 8.7 Hz, 24H, H-c), 6.80 (d, ³J = 9.0 Hz, 8H, H-a), 6.05 (d, ³J = 8.5 Hz, 16H, H-m), 4.68 (t, ³J = 6.6 Hz, 8H, H-8'), 4.10–3.70 (m, 88H, H-α, H-β, H-γ, H-δ, H-ε, H-10'), 2.46 (q, ³J = 6.1 Hz, 8H, H-9'), 1.26 (s, 108H, H-^tBu) ppm. MS (ES): *m/z* (%) = 1421.1104 (100) [M – 4PF₆]⁴⁺/4 (calcd 1421.1091 for [C₃₄₈H₃₅₂Cu₄N₃₂O₂₈]⁴⁺/4).

Porphyrinic Bis-macrocycle 10. Avoiding light exposure, porphyrin- α -tetraone **8** (50 mg, 44.5 μmol) and benzene tetramine tetrahydrochloride **9** (30.3 mg, 107 μmol) were mixed, degassed, and dissolved in freshly distilled pyridine (20 mL). The mixture was heated to 60 °C under argon, and after stirring during 6 h, macrocycle **7** (79.8 mg, 134 μmol, 3.0 equiv) was added under a stream of argon. The solution was reacted for further 18 h at 60 °C. After removal of the solvent, the product was partitioned in CHCl₃ (50 mL) and water (50 mL). The organic layers were separated and evaporated. The crude product (147 mg) was subjected to chromatography (80 g of silica, prepared in CH₂Cl₂, gradient elution from CH₂Cl₂/MeOH 100/0 to 99/1) and then recrystallized from CH₂Cl₂/MeOH, giving compound **10** as a brown

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solid (49 mg, 45%). ¹H NMR (CD_2Cl_2 , 300 MHz, 298 K): δ 9.74 (d, $^3J = 8.4$ Hz, 4H, H-4,7), 9.09 (d, $^3J = 1.3$ Hz, 4H, H-py), 8.96 (s, 4H, H-1), 8.55 (m, $^3J = 8.8$ Hz, 8H, H-o), 8.31 (d, $^3J = 8.5$ Hz, 4H, H-3,8), 8.15–8.11 (m, 12H, H-op + H-pp), 7.28 (m, $^3J = 8.8$ Hz, 8H, H-m), 4.39 (t, $^3J = 5.9$ Hz, 8H, H- α), 3.88 (t, $^3J = 5.9$ Hz, 8H, H- β), 3.78–3.63 (m, 24H, H- γ + H- δ + H- \square), 1.59 (s, 72H, H- $'\text{Bu}$), -2.16 (bs, 2H, H-NH) ppm. ES-MS: m/z 1225.1185 [$\text{M} - 2e^-$] calcd 1225.1211 for $[\text{C}_{156}\text{H}_{158}\text{N}_{16}\text{O}_{12} - 2e^-]^+$. UV-vis (CH_2Cl_2): λ_{\max} (log ϵ) = 449(5.41), 662(4.20), 718(3.94) nm.

Bis-macrocycle 11. Free base compound **10** (40 mg, 20.4 μmol) was dissolved in CHCl_3 (30 mL), degassed with argon, and heated to reflux. Then a degassed solution of Zn(OAc)_2 (91 mg, 410 μmol) in MeOH (15 mL) was added, and the mixture was stirred for 24 h. Then a solution of EDTA (0.1 M, pH ~ 4 –5, 40 mL) was mixed, and the solution was vigorously stirred for further 24 h at room temperature. Organic layers were separated, washed several times with water, and evaporated under reduced pressure giving **11** in quantitative yield (40 mg). ¹H NMR (CDCl_3 , 300 MHz, 298 K): δ 9.98 (d, $^3J = 8.3$ Hz, 4H, H-4,7), 9.05 (s, 4H, H-py), 8.95 (s, 4H, H-1), 8.41 (m, $^3J = 8.6$ Hz, 8H, H-o), 8.18 (d, $^3J = 8.4$ Hz, 4H, H-3,8), 8.06 (s, 12H, H-op + H-pp), 7.12 (m, $^3J = 8.6$ Hz, 8H, H-m), 4.21 (t, $^3J = 4.5$ Hz, 8H, H- α), 3.67 (t, $^3J = 4.4$ Hz, 8H, H- β), 3.57–3.44 (m, 24H, H- γ + H- δ + H- ε), 1.57 (s, 72H, H- $'\text{Bu}$) ppm. ES-MS: m/z 1262.5926 [$\text{M} - e + \text{Li}]^{2+}$ + [$\text{M} + 2\text{Li}]^{2+}$, calcd 1260.0862 for $[\text{LiC}_{156}\text{H}_{158}\text{N}_{16}\text{O}_{12}\text{Zn} - e]^{2+}$ and 1263.0945 for and $[\text{Li}_2\text{C}_{156}\text{H}_{158}\text{N}_{16}\text{O}_{12}\text{Zn}]^{2+}$. UV-vis (CH_2Cl_2): λ_{\max} (log ϵ) = 450 (5.36), 522 (5.17), 706 (4.25) nm.

[4]Pseudorotaxane 12⁴⁺. To a degassed solution of porphyrinic bis-macrocycle **11** (106 mg, 42.2 μmol) in dry and degassed CHCl_3 (25 mL) was added a solution of $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (31.5 mg, 84.5 μmol) in degassed CH_3CN (25 mL), and the mixture was stirred at room temperature during 30 min under argon. This solution is then added to a degassed suspension of acetylenic thread **3** (16.2 mg, 42.4 μmol) in dry and degassed CHCl_3 (25 mL), and the mixture was stirred at room temperature during 7 days. After evaporation of the solvents, 139 mg (21.0 μmol) of [4]pseudorotaxane was obtained with a quantitative yield. ¹H NMR (CD_2Cl_2 , 500 MHz, 298 K): δ 9.95 (d, $^3J = 7.8$ Hz, 8H, H-4,7), 9.67 (d, $^3J = 8.6$ Hz, 4H, H-1'), 8.97 (s, 8H, H-py), 8.89 (d, $^3J = 8.4$ Hz, 4H, H-2'), 8.64 (d, $^3J = 8.8$ Hz, 4H, H-3'), 8.61 (s, 8H, H-1), 8.26 (d, $^3J = 7.3$ Hz, 8H, H-3,8), 8.24 (s, 4H, H-5'), 8.21 (d, $^3J = 8.8$ Hz, 4H, H-4'), 7.90 (s, 8H, H-pp), 7.76 (s, 8H, H-op₁), 7.66 (s, 4H, H-6'), 7.56 (bs, 8H, H-op₂), 7.42 (d, $^3J = 7.1$ Hz, 16H, H-o), 6.12 (d, $^3J = 7.4$ Hz, 16H, H-m), 4.03–3.73 (m, 80H, H- α + H- β + H- γ + H- δ + H- ε), 3.55 (s, 4H, H-7'), 1.40 (s, 72H, H- $'\text{Bu}_1$), 1.06 (s, 72H, H- $'\text{Bu}_2$) ppm. MS (ES): m/z (%) = 1510.8145 (100) [$\text{M} + 3\text{MeOH} - 4\text{PF}_6]$ ⁴⁺/4 (calcd 1510.8304 for $[\text{C}_{356}\text{H}_{340}\text{N}_{40}\text{O}_{24}\text{Zn}_2\text{Cu}_4\text{-}(\text{CH}_3\text{OH})_3]^{4+}$ /4).

[4]Rotaxane 2⁴⁺. [4]Pseudorotaxane **12⁴⁺** (134 mg, 20.2 μmol), azide stopper **5** (72 mg, 122 μmol), $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (8 mg, 21.4 μmol) and Na_2CO_3 (3 mg, 28.3 μmol) were diluted in 3 mL of dry and degassed CH_2Cl_2 and 1 mL of dry and degassed CH_3CN . The solution was stirred under argon during 5 days. The solvents

were then evaporated, and the resulting residue was redissolved in CH_2Cl_2 . This organic layer was washed with water and the two layers were separated. The aqueous layer was extracted with CH_2Cl_2 , and the organic layers were collected and evaporated to dryness. The crude product was then purified by silica chromatography. A gradient of elution $\text{CH}_2\text{Cl}_2/\text{MeOH}$ 97/3 to 92/8 gave 172 mg (19.2 μmol) of [4]rotaxane **2⁴⁺** (95%). ¹H NMR (CD_2Cl_2 , 500 MHz, 298 K): δ 9.93 (d, $^3J = 7.8$ Hz, 8H, H-4,7), 9.64 (d, $^3J = 8.6$ Hz, 4H, H-1'), 8.98 (s, 8H, H-py), 8.89 (d, $^3J = 8.9$ Hz, 4H, H-2'), 8.75 (s, 4H, H-5'), 8.68 (d, $^3J = 8.8$ Hz, 4H, H-3'), 8.60 (s, 8H, H-1), 8.52 (d, $^3J = 8.5$ Hz, 4H, H-4'), 8.31 (s, 4H, H-7'), 8.21 (d, $^3J = 8.8$ Hz, 8H, H-3,8), 7.90 (s, 8H, H-pp), 7.77 (s, 8H, H-op₁), 7.62 (s, 4H, H-6'), 7.55 (s, 8H, H-op₂), 7.41 (d, $^3J = 7.9$ Hz, 16H, H-o), 7.23 (d, $^3J = 8.6$ Hz, 24H, H-d), 7.16 (d, $^3J = 8.8$ Hz, 8H, H-b), 7.13 (d, $^3J = 8.6$ Hz, 24H, H-c), 6.80 (d, $^3J = 8.8$ Hz, 8H, H-a), 6.07 (d, $^3J = 8.0$ Hz, 16H, H-m), 4.68 (t, $^3J = 6.9$ Hz, 8H, H-8'), 4.03 (t, $^3J = 5.6$ Hz, 8H, H-10'), 4.02–3.75 (m, 80H, H- α , H- β , H- γ , H- δ , H- ε), 2.47 (q, $^3J = 6.3$ Hz, 8H, H-9'), 1.40 (s, 72H, H- $'\text{Bu}_1$), 1.23 (s, 108H, H-e), 1.05 (s, 72H, H- $'\text{Bu}_2$) ppm. MS (ES): m/z (%) = 2098.6690 (100) [$\text{M} - 4\text{PF}_6]$ ⁴⁺/4 (calcd 2098.6997 for $[\text{C}_{524}\text{H}_{536}\text{Cu}_4\text{N}_{52}\text{O}_{28}\text{Zn}_2]^{4+}$ /4). UV-vis (CH_2Cl_2): λ_{\max} (log ϵ) = 344 (5.23), 458 (5.50), 533 (5.16) nm.

Complex (2⁴⁺:G1). ¹H NMR (CD_2Cl_2 , 500 MHz, 298 K): δ 9.88 (d, $^3J = 7.2$ Hz, 8H, H-4,7), 9.59 (d, $^3J = 8.6$ Hz, 4H, H-1'), 8.86 (s, 8H, H-py), 8.84 (d, $^3J = 8.6$ Hz, 4H, H-2'), 8.66 (s, 4H, H-5'), 8.68 (d, $^3J = 8.6$ Hz, 4H, H-3'), 8.64 (s, 8H, H-1), 8.55 (d, $^3J = 8.6$, $^4J = 1.1$ Hz, 4H, H-4'), 8.34 (s, 4H, H-7'), 8.21 (d, $^3J = 7.3$ Hz, 8H, H-3,8), 7.94 (s, 8H, H-op), 7.92 (s, 8H, H-pp), 7.47 (s, 4H, H-6'), 7.38 (m, 24H, H-o, H-op), 7.23 (d, $^3J = 8.6$ Hz, 24H, H-d), 7.17 (d, $^3J = 8.9$ Hz, 8H, H-b), 7.13 (d, $^3J = 8.6$ Hz, 24H, H-c), 6.81 (d, $^3J = 8.9$ Hz, 8H, H-a), 6.05 (d, $^3J = 7.6$ Hz, 16H, H-m), 4.73 (t, $^3J = 6.0$ Hz, 8H, H-8'), 4.10–3.70 (m, 88H, H-10', H- α , H- β , H- γ , H- δ , H- ε), 2.50 (q, $^3J = 6.0$ Hz, 8H, H-9'), 1.65 (s, 72H, H- $'\text{Bu}_1$), 1.23 (s, 108H, H-e), 1.17 (s, 72H, H- $'\text{Bu}_2$), -3.27 (s, 12H, H-DABCO) ppm. MS (ES): m/z (%) = 2126.458 (100) [$\text{M} - 4\text{PF}_6]$ ⁴⁺/4 (calcd 2126.475 for $[\text{C}_{530}\text{H}_{548}\text{Cu}_4\text{N}_{54}\text{O}_{28}\text{Zn}_2]^{4+}$ /4).

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Supporting Information Available: ¹H NMR and ES-MS spectra of compounds **6⁴⁺**, **1⁴⁺**, **12⁴⁺**, and **2⁴⁺**; NOESY or ROESY spectra and DOSY spectra of compounds **1⁴⁺** and **2⁴⁺**; X-ray crystallography of compound **2⁴⁺**; UV-vis spectra of titration of compound **2⁴⁺** with guests **G1**, **G3**, **G4**, and **G5**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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