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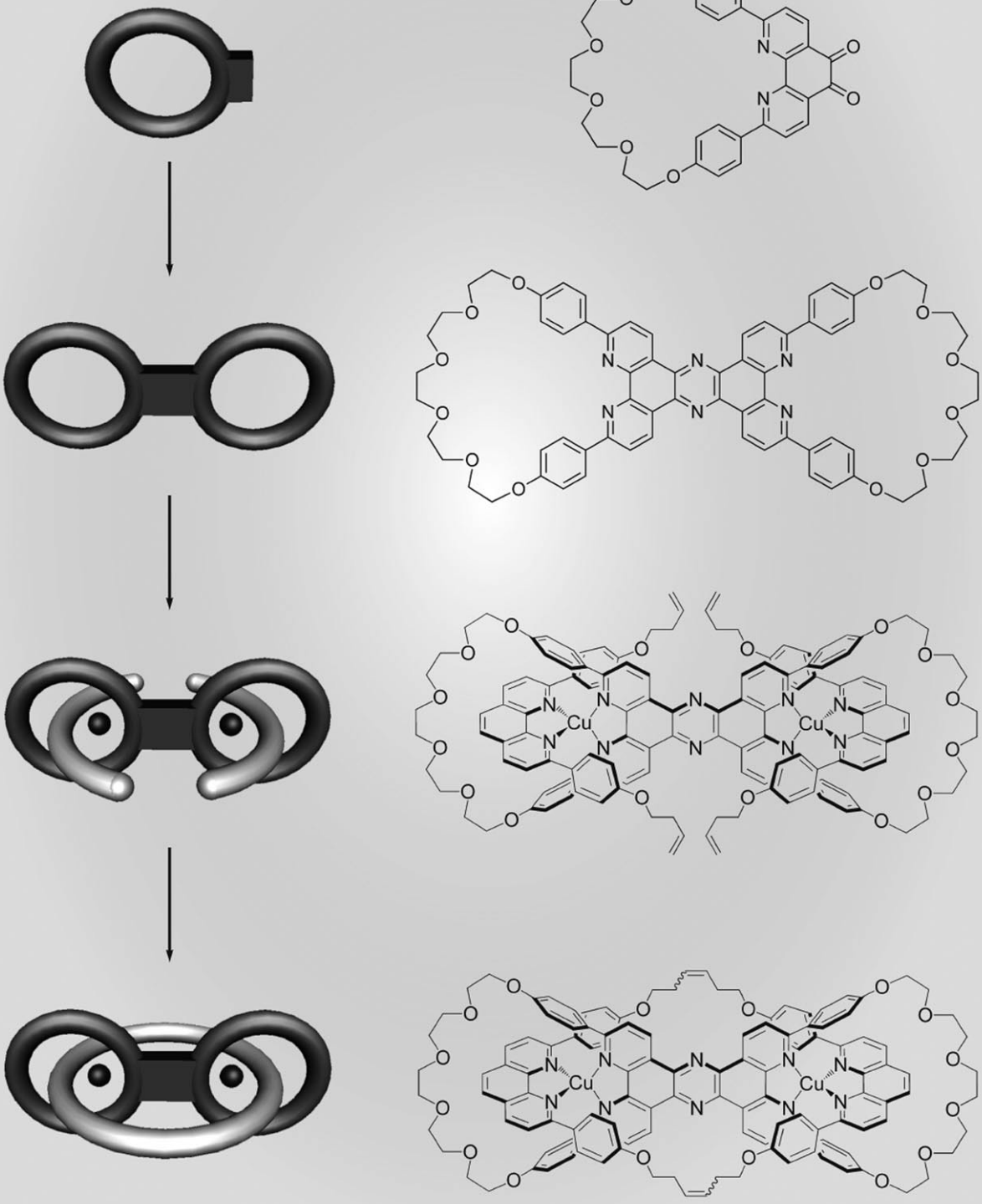

Synthesis of a Bis-macrocycle Containing Two Back-to-Back Rigidly Connected 1,10-Phenanthroline Units as a Central Core and its Incorporation in a Handcuff-Like Catenane

Julien Frey,[a] Tomáš Kraus,[b] Valérie Heitz,*[a] and Jean-Pierre Sauvage*[a]

Abstract: A bis-macrocycle containing two back-to-back connected 1,10-phenanthroline chelates has been prepared. The synthetic strategy involves the preparation of a monocyclic precursor consisting of a 1,10-phenanthroline-5,6-dione fragment incorporated in a 30-membered ring. This important intermediate has been prepared via two distinct routes, both strategies relying on the use of a ketal as a 1,2-dione protective group. A four-component condensation reaction between two molecules of the macrocyclic dione and two equivalents of ammonia (used in large excess) in the presence of a reducing agent ($Na_2S_2O_4$) leads to the desired bis-ring in good yield. The most direct synthetic route allows preparation of the bis-macrocycle in seven steps from 1,10-phenanthroline in an overall yield of 14%. Using the now well-established "gathering and threading" effect of copper(I), a doubly threaded species could be obtained in quantitative yield, in which each ring of the bis-macrocycle is threaded by a "molecular string". These fragments bear terminal allylic groups, which are used to prepare the final catenane by performing a double ring-closing metathesis reaction. This final cyclisation reaction is high yielding and affords the desired catenane consisting of a bis-macrocycle of which the two cyclic units are threaded by a large ring. The compound has been fully characterised by classical techniques. Electronic spectroscopy and electrochemical measurements suggest that the two copper complex subunits do not interact electronically, in spite of the aromatic nature of the bridging ligand between the two metal centres.

Keywords: catenanes · chelates · copper · macrocycles · templates

Introduction

Catenanes and rotaxanes[1] still represent challenging synthetic targets, especially when the number of constituent units and the topological complexity of the systems is increased from the simple two-component prototypes, [2]catenanes or [2]rotaxanes. Besides the synthetic challenge that the preparation of such molecules represents, the construction and study of ever more complex systems of the catenane and rotaxane family also holds promise in relation to their novel properties. In this respect, the field of controlled dynamic systems, generally referred to as molecular machines, is particularly active.[2]

Among the catenanes and rotaxanes described to date, either as molecular machine prototypes or simply as synthetic targets, there have been only a few examples containing bis- or multi-macrocycles. One of the most remarkable examples of such compounds is the "molecular elevator"[3] reported a few years ago, the cyclic component of which consists of a tris-cycle, that is, three connected rings.

In the present report, we describe the synthesis of a bis-macrocycle, the two coordinating rings of which are linked to one another in a highly rigid fashion, and which can be regarded as a handcuff-like compound. Such a bis-ring can be envisaged as being particularly useful for the construction of various relatively complex interlocking systems. In addition, as a further topic of the present report, the bis-macrocycle is a precursor to a catenane consisting of a large ring threaded through both cyclic units of the bis-ring.[4] Such a catenane can be prepared in good yield by means of a copper(I)-templated strategy.

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Results and Discussion

The copper(I)-assisted generation of threaded species, which involves passing a string-like molecular fragment through a ring, has been used extensively in our group to generate precursors to numerous catenanes and rotaxanes.[5] Thus far, monocyclic units have been used almost exclusively as starting compounds. The use of a bis-macrocycle has been briefly described in a preliminary communication.[6] The threading principle is indicated in Figure 1, in a very schematic fashion.

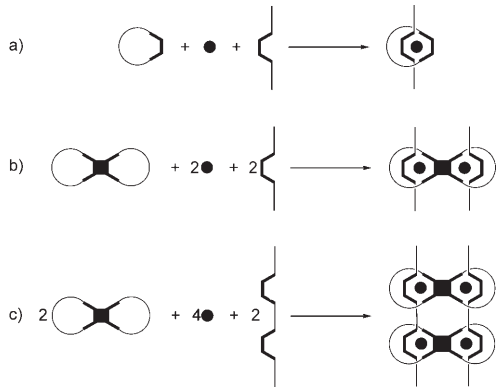


Figure 1. Principle of various threading reactions. a) The simple one-plus-one copper(I)-induced passing of a mono-chelate through a ring.[5] b) Double threading reaction: two mono-chelate units are threaded through the rings of a bis-macrocycle. In the present case, the coordinating units (U-shaped symbols) are connected back-to-back in a rigid fashion. c) Analogous reaction as in b) but using two-chelate containing molecular threads. An example of this reaction has recently been reported.[7]

Design and synthesis of the bis-macrocycle: In order to exert strict geometrical control over the system and to advantageously apply our experience in the field of 1,10-phenanthroline (phen) coordination chemistry, a system combining high rigidity and phenanthroline units was designed and subsequently synthesised. The bis-macrocycle described in the present work is depicted in Figure 2, along with its succinct retrosynthetic analysis.

The central motif consists of two back-to-back connected bidentate chelates, the ensemble being highly rigid. Related compounds have been synthesised and studied in recent years, mostly as bridging ligands between Ru and Rh centres.[8,9]

The macrocyclic dione depicted in Figure 2, precursor to bis-macrocycle **1**, could be prepared via two distinct routes,

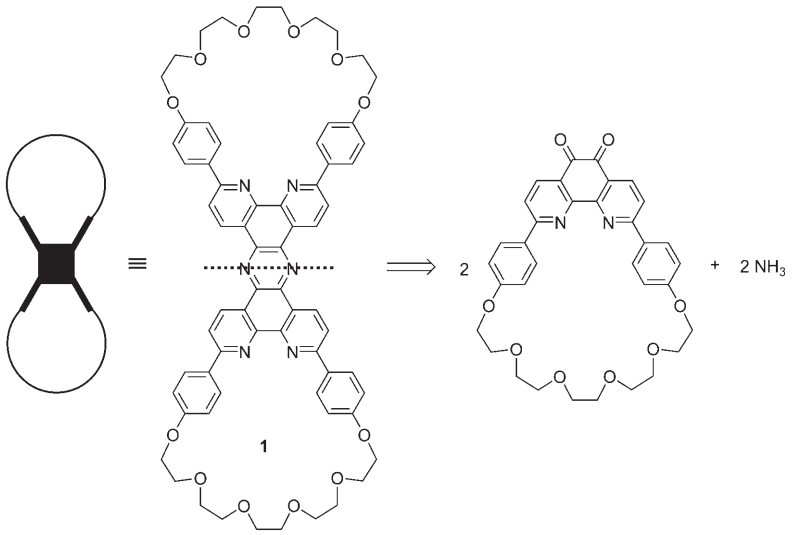


Figure 2. Bis-macrocycle **1** consists of two fused 30-membered rings. It was prepared by a homocondensation reaction between two equivalents of the macrocyclic dione and two moles of ammonia.

as depicted in Schemes 1–4. The main difference between these two routes is that, in the first, positions 2 and 9 of the phen nucleus have to be functionalised before the *p*-anisyl groups are attached at these two positions, whereas in the second, direct attachment of the *p*-anisyl groups can be carried out without prior functionalisation.

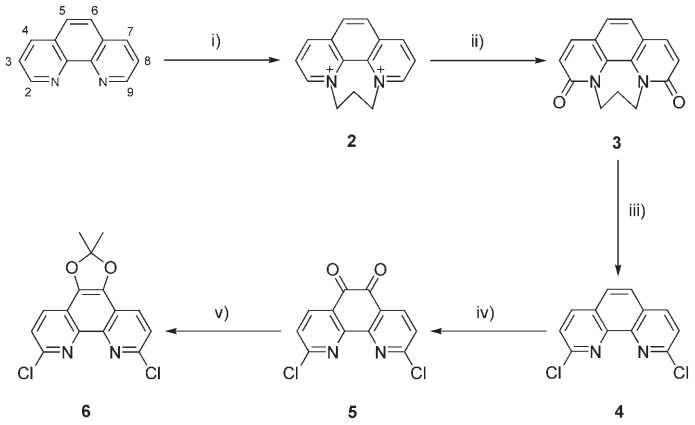
Synthesis via 2,9-dichloro-1,10-phenanthroline and Suzuki coupling: In executing the first route, several distinct phases are involved: i) functionalisation of the 2- and 9-positions of the phen nucleus, followed by ii) formation of the 5,6-dione and its protection; iii) preparation of a 2,9-diaryl-1,10-phenanthroline derivative bearing appropriate functions at the aryl groups and the protected 5,6-dione; iv) formation of the 30-membered ring and liberation of the free α-dione; v) condensation reaction leading to **1**.

Compound $\mathbf{2}^{2+}\cdot 2\,Br^-$ was obtained according to a literature account by treating 1,10-phenanthroline monohydrate with a large excess of 1,3-dibromopropane in nitrobenzene. The reaction could be carried out on a relatively large scale (10 g of 1,10-phenanthroline monohydrate afforded 16.9 g of $\mathbf{2}^{2+}\cdot 2\,Br^-$ as ochre crystals). $\mathbf{2}^{2+}\cdot 2\,Br^-$ was subsequently oxidised to the neutral species **3** using $[K_3Fe(CN)_6]$ in basic aqueous solution. In spite of the mediocre yield of this reaction, multi-gram batches of **3** could be prepared relatively easily. 2,9-Dichloro-1,10-phenanthroline (**4**) was then prepared in high yield (88%) by reacting **3** with PCl_5 and $POCl_3$ at 110°C.

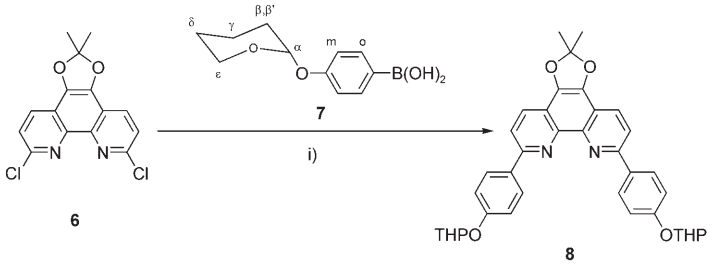
The α-dione **5** was prepared according to a literature procedure[10] by oxidising **4** with KBr and HNO_3 in concentrated sulfuric acid. After work-up and column chromatography, **5** was obtained as a yellow solid. The dione function was subsequently protected as the ketal **6** by reacting **5** with 2-nitropropane in acetonitrile under basic conditions (chromatographic purification afforded **6** in 90% yield as a bright-yellow solid).

The sequence of reactions leading to **6** from phen is indicated in Scheme 1.

The next step involved a Suzuki coupling reaction with the boronic acid **7**, as shown in Scheme 2. **7** was first obtained from 2-(4-bromophenoxy)tetrahydro-2*H*-pyran under classical conditions,[11] that is to say, reaction with *n*BuLi at −78 °C followed by addition of triisopropyl borate, B(O*i*Pr)$_3$. After chromatographic separation, an 80 % yield of **7** was obtained.



Scheme 1. Protected dione **6** obtained from 1,10-phenanthroline in five steps in an overall yield of 17 %. i) 1,3-dibromopropane, $PhNO_2$, 120 °C, 4 h (88 %); ii) $[K_3Fe(CN)_6]$, NaOH, 2–5 °C, 2 h (35 %); iii) $POCl_3$, PCl_5, 110 °C, 8 h (88 %); iv) H_2SO_4, HNO_3, KBr, 80 °C, 3 h (71 %); v) 2-nitropropane, Na_2CO_3, MeCN/H_2O 1:1, 55 °C, 5 h (90 %).



Scheme 2. Key intermediate obtained in good yield by a Suzuki coupling. i) $[Pd(PPh_3)_4]$, Na_2CO_3, PhMe/H_2O 2:1, 80 °C, 18 h (97 %).

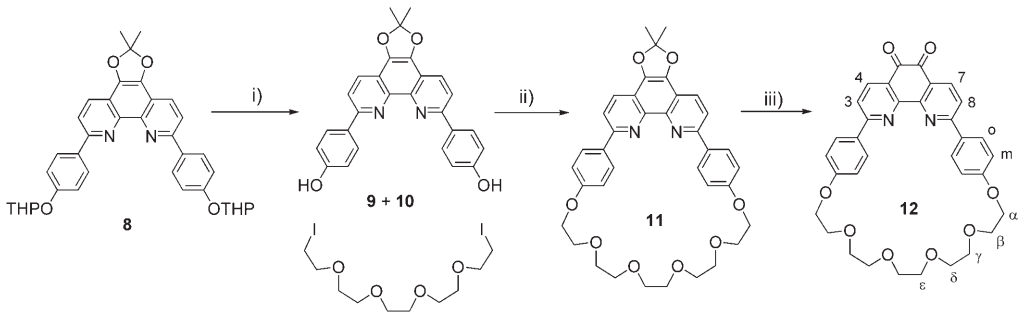
7 was subsequently reacted with **6** in toluene and aqueous Na_2CO_3, with $Pd(PPh_3)_4$ as catalyst (10 % per chloro substituent). **8** was obtained in almost quantitative yield (97 %) after column chromatography.

The following sequence of reactions is depicted in Scheme 3: i) deprotection of the phenol groups, ii) cyclisation, and iii) deprotection of the dione. The most important feature of this sequence is that the first deprotection reaction (**8**→**9**), which provides the free diphenol **9** in very high yield (96 %), can be carried out under experimental conditions (HCl in dry Et_2O/methanol at room temperature) that do not affect the ketal protective group of the α-dione. The macrocyclic compound **11** was then prepared from **9** and the diiodo derivative of pentaethylene glycol, I-CH_2-$(CH_2OCH_2)_4$-CH_2-I (**10**),[12] following a well-established procedure. A mixture of **9** and **10** was slowly added to a vigorously stirred suspension of Cs_2CO_3 in DMF at 60 °C. An excellent yield of 59 % was obtained for this ring-forming reaction, without loss of the dione protective group. Compound **11** was obtained as a yellow-orange oil.

Finally, the dione function was liberated from its ketal protective group. By heating a solution of **11** in water and F_3CCOOH at 50 °C in the presence of air, followed by work-up and chromatography on silica, **12** was obtained as an orange crystalline solid.

Compound **12** is a 30-membered ring, which could be crystallised to afford single crystals. The structure of **12** was solved by X-ray diffraction analysis and is shown in Figure 3. As expected, **12** can be seen to be an essentially planar compound. The C5−C6 bond is clearly a single bond (d = 1.540 Å), the dione being a real, non-delocalised one, with C=O bond lengths of 1.208 and 1.217 Å. The two phenyl rings borne by the phen-dione nucleus form an angle that is significantly smaller than 120°: the N1-C2-C1′ and N10-C9-C1″ angles are 115.2 and 113.9°, respectively, which may be ascribed to the "pinching" effect of the ring.

Synthesis by direct arylation of a protected phen-dione (Dietrich-Buchecker reaction): Compound **8**, used in the previous strategy (Schemes 2 and 3), can alternatively be prepared via a more direct route. The sequence of reactions leading to **8** without functionalisation of the 2- and 9-positions prior to the attachment of the aryl groups at these two positions is indicated in Scheme 4.



Scheme 3. Synthesis of the macrocyclic dione **12**. i) HCl in Et_2O, MeOH, RT, 2 h (96 %); ii) high dilution, Cs_2CO_3, DMF, 60 °C, 4 d (59 %); iii) TFA/H_2O, 50 °C, 5 h (94 %).

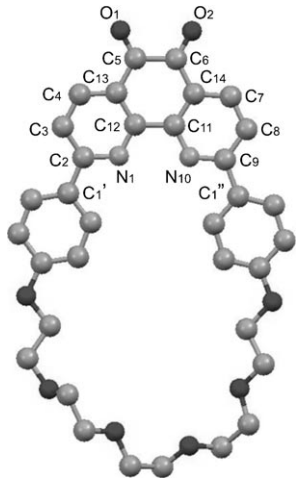
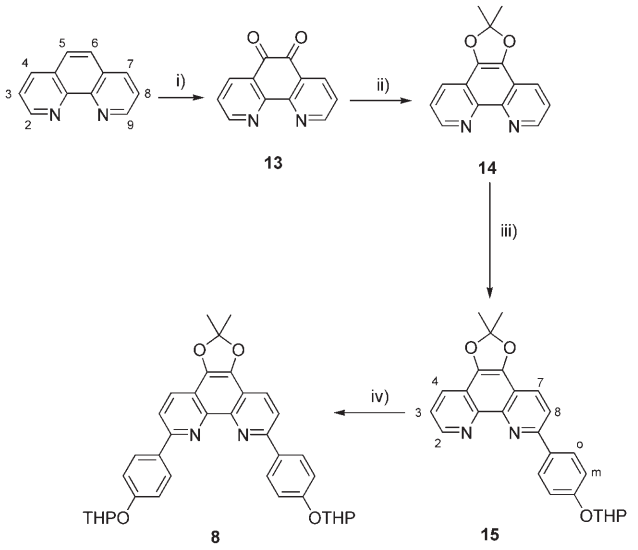


Figure 3. Ball-and-stick representation of the crystal structure of macrocycle **12**.



Scheme 4. Double nucleophilic addition/aromatisation reaction leading to **8**. i) H_2SO_4, HNO_3, KBr, 100 °C, 4 h (55 %); ii) 2-nitropropane, Na_2CO_3, MeCN/H_2O 1:1, reflux, 8 h (66 %); iii) 1) 2-(4-bromophenoxy)tetrahydro-2*H*-pyran, *n*BuLi, THF, −78 °C, 2 h; 2) MnO_2, CH_2Cl_2/PhMe 1:1, RT, 12 h (84 %); iv) 1) 2-(4-bromophenoxy)tetrahydro-2*H*-pyran, *n*BuLi, THF, from −78 °C to RT, overnight; 2) MnO_2, CH_2Cl_2, RT, 2 h (95 %).

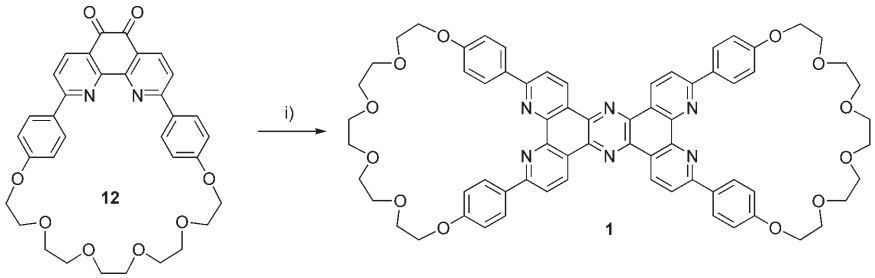
Oxidation of 1,10-phenanthroline to its 5,6-dione (compound **13**) was carried out in a similar way as that of compound **5** (KBr, HNO_3, H_2SO_4),[13] to afford **13** in a moderate yield (55 %) as a yellow crystalline solid. Protection of the dione **13**[14] using 2-nitropropane in CH_3CN/H_2O afforded **14** (66 % yield) as a brownish-yellow amorphous solid. The two aryl groups at the 2- and 9-positions of **14** were introduced under very similar experimental conditions to those used previously by Dietrich-Buchecker et al.[15] The two-step procedure (**14**→**15**→**8**) was preferred to the double arylation reaction (**14**→**8**) on the grounds that mono-arylation reactions are generally high yielding. This turned out to be true in the present case.

Compound **14** was first reacted with the in situ generated lithium derivative obtained from *n*BuLi and THP-protected 4-bromophenol at −78 °C, after which the intermediate was hydrolysed and rearomatised using MnO_2. **15** was obtained as a yellow crystalline powder in 84 % yield. Using exactly the same procedure as for the preparation of **15**, but now starting from this compound, *n*BuLi, and protected 4-bromophenol, **8** was obtained as a yellow solid in 95 % yield. Samples of **8** obtained via this second route (Scheme 4) were, of course, identical to those prepared using the first strategy (Scheme 2). They could be used in the same way to complete the synthesis of the cyclic compound **12** (Scheme 3).

Comparison of the two routes for the synthesis of macrocyclic dione 12: The first route, via 2,9-dichloro-1,10-phenanthroline (**4**), consists of nine steps (excluding the preparations of the boronic acid **7** and the diiodo derivative **10**). The overall yield is 8 %. The strong point of this strategy is the almost quantitative yield of the double Suzuki coupling reaction that furnishes **8**. The second route comprises only seven steps, which is an obvious advantage over the nine-step route discussed previously. The overall yield of 14 % is significantly higher than that of the first route. The comparison is thus clearly in favour of the second strategy, although some steps are relatively delicate, such as the conversion of **14** to **8**.

Synthesis of the bis-macrocycle 1: The ultimate organic target, bis-macrocycle **1**, was obtained in good yield utilising a condensation reaction that has been used in previous work by others[8a] in the construction of bridging acyclic ligands. It is depicted in Scheme 5.

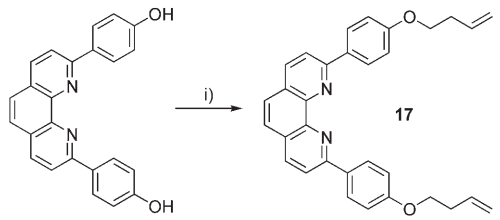
Compound **12** was reacted in a melt obtained by fusing solid $Na_2S_2O_3$ (0.2 equivalents) and a large excess of NH_4OAc at 180 °C under an inert atmosphere. After work-



Scheme 5. Preparation of bis-macrocycle **1** from dione **12**. i) NH_4OAc, $Na_2S_2O_4$, molten salt at 180 °C, 2 h (70 %).

up and chromatography, a 70% yield of **1** was obtained as a poorly soluble yellow solid.

Preparation of the ancillary ligand to be used in the threading step: As shown in Scheme 6, the 1,10-phenanthroline-based ligand **17** was prepared in moderate yield (48%) from 2,9-di(*p*-hydroxyphenyl)-1,10-phenanthroline and 1-bromo-3-butenyl in DMF in the presence of K_2CO_3. The two terminal alkene functions of **17** are suitably predisposed for use at a later stage to prepare a macrocycle by ring-closing olefin metathesis (Grubbs methodology[16]).



Scheme 6. Synthesis of the ancillary ligand **17**. i) 1-Bromo-3-butenyl, K_2CO_3, DMF, 60°C, 24 h (48%).

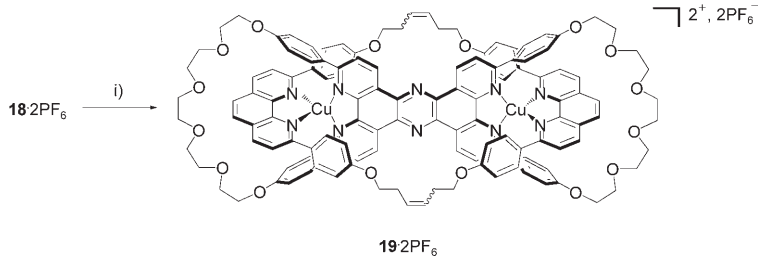
Synthesis of the handcuff-containing catenane: By taking advantage of the very powerful "gathering and threading" effect of copper(I) with appropriate ligands, the precursor to the catenane was prepared quantitatively, as depicted in Scheme 7.

Compound **1** and $[Cu(CH_3CN)_4]\cdot PF_6$ were mixed in a 1:2 stoichiometry in CH_2Cl_2/CH_3CN under argon, affording a yellowish suspension. The "thread" **17** was subsequently added, causing a spectacular colour change to yield an intense brown suspension, which was allowed to stand at room temperature for some time prior to work-up. **18**·2 PF_6 was obtained in pure form and did not require further chromatographic separation.

As depicted in Scheme 8, the target catenane **19**·2 PF_6 was prepared by subjecting **18**·2 PF_6 in CH_2Cl_2 to a ring-closing metathesis reaction analogous to those previously used for making phenanthroline-based copper(I) catenanes.[17] **18**·2 PF_6 and Grubbs first-generation catalyst $[RuCl_2(PCy_3)_2(CHPh)]$ (PCy_3: tricyclohexylphosphine) were allowed to react at room temperature for a long period of time. Work-up and chromatographic purification furnished **19**·2 PF_6 in good yield (80%) as a red-brown solid. Compound $\mathbf{19}^{2+}$ consists of a mixture of isomers (*E*/*Z* alkene units).

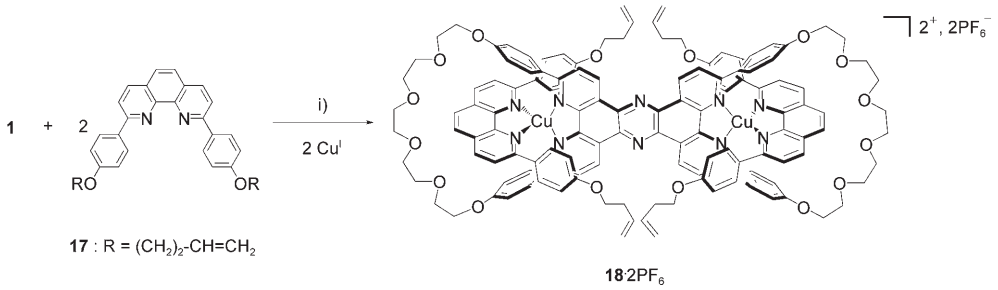
The double cyclisation reaction could be easily monitored by ^{1}H NMR. After about 10 days of reaction, it was complete. It was noted that this reaction, as well as related catenane formation reactions,[18] require a long reaction time at room temperature, in spite of the high proportion of "catalyst" ($\approx$0.25 equivalents per double bond to be formed).

The ^{1}H NMR spectra of the catenane and its precursor are depicted in Figure 4. The ^{1}H NMR spectrum of $\mathbf{18}^{2+}$ is consistent with the symmetrical structure of the compound. In spite of the presence of three diastereomers in $\mathbf{19}^{2+}$, the NMR spectrum of the catenane is almost identical to that of the open form of the precursor $\mathbf{18}^{2+}$ (Figure 4), except for the olefinic signals. The signals of protons H_d and H_e disappear, the shape of the signal due to proton H_c is modified (giving three sets of signals), and broadening of the aromatic peaks is observed. The splitting of the olefinic signals and the broadening of the aromatic peaks originate from the presence of three possible diastereoisomers, *E*–*E*, *E*–*Z*, and *Z*–*Z*. As yet, it has not been possible to determine their relative proportions.



Scheme 8. Cyclisation of the precatenane by ring-closing metathesis. i) $[RuCl_2(PCy_3)_2(CHPh)]$ in CH_2Cl_2 (10^{-3} M), RT, 10 d (80%).

The interlocked nature of $\mathbf{19}^{2+}$ was supported by 2D-ROESY ^{1}H NMR. Indeed, correlations were observed between the H atoms belonging to the -CH_2-CH_2-O- fragments of bis-macrocycle **1** (protons H-α to H-ε) and the 1,10-phenanthroline units of the large ring (protons H-4′,7′ and H-5′,6′). Similarly, interactions between protons H-a/H-b and



Scheme 7. Threading reaction using the template effect of copper(I). i) $[Cu(MeCN)_4](PF_6)$ (2 equiv), CH_2Cl_2/MeCN 2:1, RT, 3 d (quant.).

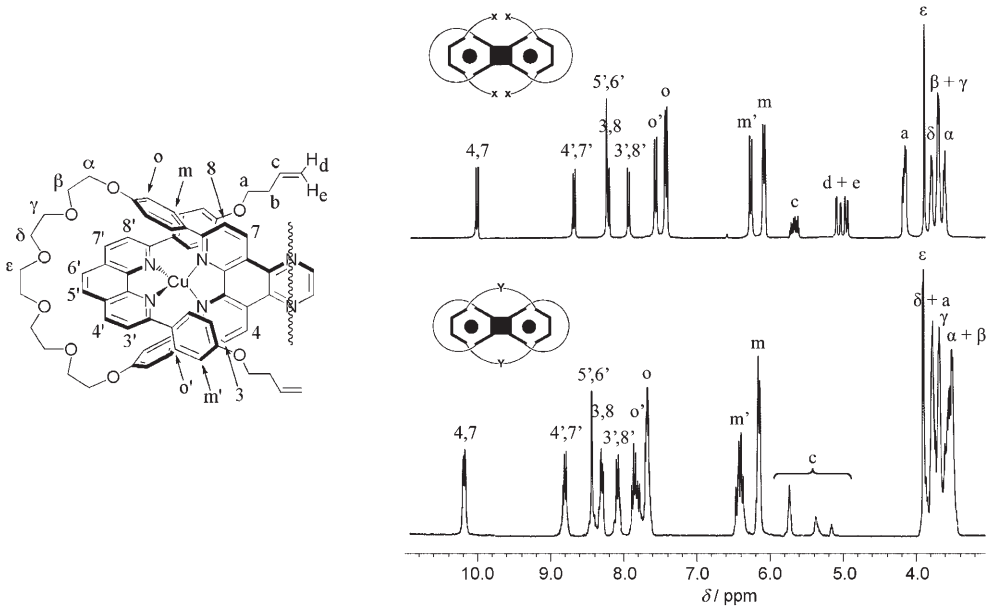


Figure 4. ^{1}H NMR ([D$_6$]acetone, 500 MHz) changes on going from precursor **18**$^{2+}$ to catenane **19**$^{2+}$.

protons H-4,7/H-3,8 confirmed the threading of the large central ring through the two cyclic components of bis-macrocycle **1**.

The high-resolution ES mass spectrum of **19**·2PF$_6$ (Figure 5) shows one peak at m/z 1086.3420, corresponding to [**19**]$^{2+}$ (calcd 1086.3433).

Compound **19**$^{2+}$ is a dicopper complex with 2,9-disubstituted phen-type ligands; these substituted derivatives lead to entwined complexes in which the metals are in tetrahedral environments, and thus strongly stabilise Cu^{I}. The electronic properties of the catenane are in perfect agreement with its structure. Relatively intense MLCT bands are observed in the visible region ($\lambda_{max} \approx 411$ nm, $\varepsilon \approx 4300\ L\,mol^{-1}\,cm^{-1}$) due to the presence of two Cu^{I} complexes, but no significant intervalence bands are apparent. Cyclic voltammetry shows that the Cu^{II}/Cu^{I} couple has a redox potential of $E^0 = 0.65$ V ($\Delta E_p \approx 92$ mV) versus SCE in acetonitrile, in accordance with previously reported values for similar systems.[19] Each reversible oxidation occurs at the same potential, confirming the absence of a strong interaction between the two metal centres.

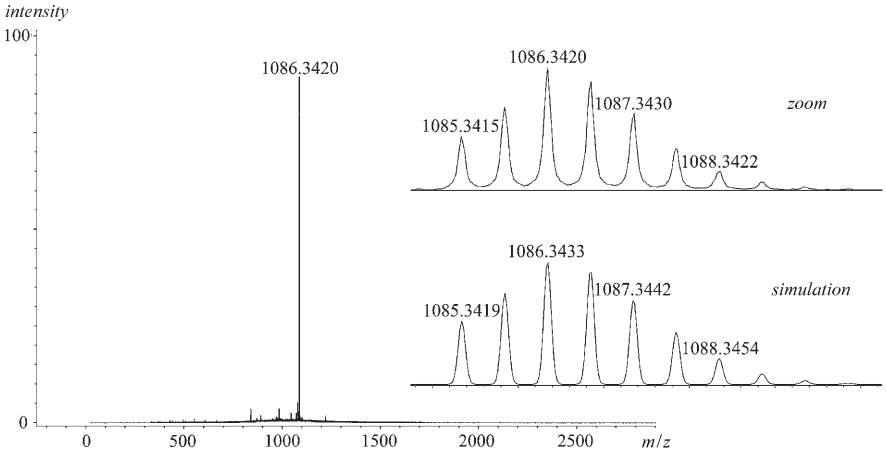


Figure 5. Electrospray mass spectrum of catenane **19**·2PF$_6$.

Conclusion

In conclusion, a novel topology has been prepared, which consists of a bis-macrocycle ("handcuff") and a large ring. The large ring passes through both rings of the handcuff-like compound. A relatively short sequence of organic reactions led to the key organic component, namely a macrocyclic dione, demonstrating the efficiency of the Dietrich-Buchecker reaction (functionalisation of the 2- and 9-positions of the 1,10-phenanthroline backbone using an alkyl- or aryl-lithium, followed by aromatisation of the hydro- intermediate). The "handcuff" was prepared in a multicomponent condensation reaction from the 1,2-dione and ammonium ions. The "gathering and threading" effect of copper(I) turned out to be particularly efficient since the formation of the threaded precursor was almost quantitative in spite of its multi-threaded nature. In the future, such a new topology will be incorporated into complex molecular machines, im-

parting novel chemical functions to the electrochemically driven dynamic systems already prepared.

Experimental Section

General: All chemicals were of the best commercially available grade and were used without further purification (except where mentioned otherwise). Dry solvents were distilled from suitable desiccants (THF from Na/benzophenone; CH_2Cl_2, DMF, and MeOH from $CaCl_2$). Thin-layer chromatography was carried out using polymer sheets pre-coated with silica gel (Macherey-Nagel, POLYGRAM, SIL G/UV_{254}). Preparative column chromatography was carried out using silica gel (Merck Kieselgel, silica gel 60, 0.063–0.200 mm). Flash column chromatography was carried out using silica gel (Merck Geduran, silica gel 60, 40–63 μm).

^1H and ^{13}C NMR spectra were recorded with a Bruker Avance 300 (300 MHz) or Avance 500 (500 MHz) spectrometer using the deuterated solvent signal as a lock. The spectra were collected at 25 °C and the chemical shifts were referenced to residual solvent proton signals as internal standards (^1H: D_2O 4.66 ppm, [D_6]acetone 2.05 ppm, CD_2Cl_2 5.32 ppm, $CDCl_3$ 7.27 ppm; ^{13}C: $CDCl_3$ 77 ppm). Attributions are displayed in the following manner: 1) chemical shifts (δ) quoted in ppm, and then in brackets 2) multiplicity of the signal, 3) coupling constant(s) quoted in Hz, 4) number of protons implied, and 5) identity of proton(s) implied. Mass spectra were obtained with a VG-BIOQ triple-quadrupole spectrometer (ES-MS).

The detailed procedures are presented below, some of which have been modified with respect to previously published accounts.

Compound 2·2Br: 1,10-Phenanthroline monohydrate (10.00 g, 50.4 mmol) was dissolved in nitrobenzene (80 mL). 1,3-Dibromopropane (≈26 mL, 253 mmol, 5 equiv) was then slowly added and the mixture was heated to 120 °C with stirring. During the reaction, a crystalline product precipitated from the reaction mixture. After 4 h, the mixture was allowed to cool to room temperature and the crystalline product was collected by filtration. The mother liquor was concentrated by evaporating the solvent under reduced pressure, producing a second crop of crystalline material. The products were combined, washed with small amounts of toluene, and dried under vacuum for 24 h. The product was then dissolved in water (ca. 50 mL), the solution obtained was warmed to 80 °C, and ethanol (ca. 300 mL) was slowly added with stirring until the precipitated material no longer dissolved in the mixture upon heating and stirring. The mixture was left to cool overnight and the crystals were collected to yield **2** (16.89 g, 88 %). ^1H NMR (300 MHz, D_2O, 25 °C): $\delta = 9.57$ (d, $^3J = 5.8$ Hz, 2H; H-2,9), 9.36 (d, $^3J = 8.5$ Hz, 2H; H-4,7), 8.49 (s, 2H; H-5,6), 8.45 (dd, $^3J = 5.8$ and 8.4 Hz, 2H; H-3,8), 5.05 (t, $^3J = 7.0$ Hz, 4H; H-a), 3.33 ppm (q, $^3J = 7.0$ Hz, 2H; H-b).

Compound 3: [$K_3Fe(CN)_6$] (123.5 g, 375 mmol, ≈10 equiv) was dissolved in water (200 mL) and NaOH (56.4 g, 1.41 mol, ≈34 equiv) was gradually added with stirring. The flask was then placed in an ice/water bath. A solution of **1** (16.0 g, 41.9 mmol) in water (25 mL) was added dropwise, maintaining the temperature in the range 2–5 °C. The mixture was allowed to react for 2 h. It was then neutralised with 4 M HCl to pH ≈ 7–8 with simultaneous cooling and concentrated under reduced pressure. The resulting brown solid was crushed and subjected to Soxhlet extraction with refluxing $CHCl_3$ (4 × 500 mL). The solvent was evaporated from the combined organic layers to give 5.71 g of a brown crude product, which was adsorbed on silica (40 g) and subjected to chromatography (440 g of silica, prepared in CH_2Cl_2). Gradient elution from CH_2Cl_2 to CH_2Cl_2/2% MeOH gave **3** (3.69 g, 35 %). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 7.72$ (d, $^3J = 9.5$ Hz, 2H; H-4,7), 7.36 (s, 2H; H-5,6), 6.80 (d, $^3J = 9.5$ Hz, 2H; H-3,8), 4.32 (t, $^3J = 6.6$ Hz, 4H; H-a), 2.46 ppm (q, $^3J = 6.6$ Hz, 2H; H-b).

Compound 4: Compound **3** (3.30 g, 13.1 mmol) was suspended in $POCl_3$ (39 mL) and PCl_5 (5.44 g, 26.1 mmol, 2 equiv) was added. The mixture was degassed and refluxed (110 °C) under argon for 8 h. The excess $POCl_3$ was then distilled off under reduced pressure and the remaining material was decomposed with ice. The resulting suspension was neutralised with aqueous ammonia solution (30 %) with simultaneous cooling. The brown precipitate was collected and dried under vacuum, and the mother liquor was extracted with CH_2Cl_2 (2 × 40 mL). The resulting crude product (4.71 g) was adsorbed on silica (30 g) and then purified by chromatography (220 g of silica, prepared in CH_2Cl_2). Elution with CH_2Cl_2 gave pure **4** (2.85 g, 88 %). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 8.22$ (d, $^3J = 8.4$ Hz, 2H; H-4,7), 7.83 (s, 2H; H-5,6), 7.65 ppm (d, $^3J = 8.4$ Hz, 2H; H-3,8).

Compound 5: Solid KBr (11.25 g, 94.5 mmol, ≈10 equiv) was placed in a two-necked flask equipped with a condenser. The flask was immersed in a large ice/water bath, and then concentrated H_2SO_4 (98 %, 16 mL) was added dropwise with stirring (evolution of gaseous bromine), followed by concentrated HNO_3 (68 %, 19 mL). Compound **4** (2.36 g, 9.47 mmol) was dissolved in concentrated H_2SO_4 (24 mL) and this solution was added dropwise to the pre-cooled mixture. The resulting mixture was stirred for 20 min at room temperature and then for 3 h at 80 °C. It was then allowed to cool to room temperature and ice (30 g) was added. After the ice had melted, the mixture was poured over further ice (300 g) in a larger flask and, with simultaneous cooling, was neutralised to pH ≈ 6 with aqueous ammonia solution (25 %, ca. 180 mL). A yellow material precipitated. CH_2Cl_2 (500 mL) was layered over the suspension and the two-phase mixture was stirred until the solid had dissolved. The organic phase was separated, washed with water (200 mL) and brine (200 mL), and concentrated to dryness. The crude product was adsorbed on silica (50 g), split into two batches, and purified by flash chromatography (2 × 230 g of fine silica prepared in CH_2Cl_2). Elution with CH_2Cl_2 gave **5** (3.22 g, 71 %). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 8.44$ (d, $^3J = 8.2$ Hz, 2H; H-4,7), 7.62 ppm (d, $^3J = 8.2$ Hz, 2H; H-3,8).

Compound 6: Compound **5** (1.00 g, 3.58 mmol) and 2-nitropropane (3.20 g, 34.8 mmol, ≈10 equiv) were dissolved in MeCN (300 mL) in a flask fitted with a condenser. A solution of Na_2CO_3 (3.04 g, 2.31 mmol) in water (300 mL) was then added. The resulting mixture was degassed and heated to 55 °C for 5 h under an argon atmosphere. It was then cooled to room temperature and the organic solvent was removed. The remaining solution was neutralised to pH ≈ 6–7 with 0.1 M aqueous HCl. CH_2Cl_2 (500 mL) was then added and the layers were separated. The aqueous layer was extracted with further CH_2Cl_2 (200 mL). The organic phases were combined and the solvent was evaporated to give a green solid (1.12 g). This material was subjected to flash chromatography (240 g of fine silica, prepared in CH_2Cl_2); elution with CH_2Cl_2 gave **6** (0.89 g, 90 %). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 8.20$ (d, $^3J = 8.6$ Hz, 2H; H-4,7), 7.61 (d, $^3J = 8.6$ Hz, 2H; H-3,8), 1.87 ppm (s, 6H; Me); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 149.49$, 140.74, 137.05, 131.13, 124.70, 121.85, 117.10, 26.25 ppm; ES-MS: m/z: calcd for $C_{15}H_{11}N_2O_2Cl_2$: 321.020; found: 321.021 $[M+H]^+$.

Compound 13: A mixture of 1,10-phenanthroline (8.00 g, 44.4 mmol) and potassium bromide (52.8 g, 444 mmol) was cooled to 0–5 °C. It was slowly dissolved in a mixture of sulfuric acid (98 %, 80 mL) and nitric acid (60 %, 40 mL), maintaining a low temperature. The mixture was then heated to 100 °C with stirring. After 4 h, it was allowed to cool to room temperature and ice (800 g) was added. The resulting solution was neutralised to pH ≈ 7 by the addition of 30 % ammonium hydroxide solution. A yellow solid precipitated from the reaction mixture. It was collected by filtration and washed several times with water. This material was dissolved in CH_2Cl_2, and the solution was dried over $MgSO_4$, filtered, and concentrated to dryness to afford pure **13** (5.13 g, 55 %). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 9.13$ (dd, $^3J = 4.8$ Hz, $^4J = 1.83$ Hz, 2H; H-2,9), 8.51 (dd, $^3J = 7.9$ Hz, $^4J = 1.83$ Hz, 2H; H-4,7), 7.60 ppm (dd, $^3J = 4.8$ and 7.9 Hz, 2H; H-3,8).

Compound 14: Compound **13** (2.00 g, 9.52 mmol) was suspended in a 1:1 mixture of MeCN and H_2O (108 mL), and 2-nitropropane (86 mL) was added. The mixture was degassed with argon and then a degassed aqueous solution of Na_2CO_3 (2 M, 4.8 mL, 1 equiv) was added via a cannula. The resulting mixture was refluxed for 8 h under an inert atmosphere. It was then cooled to room temperature and the product was extracted with CH_2Cl_2 (3 × 400 mL). The combined extracts were dried over $MgSO_4$ and concentrated, and the crude product was subjected to flash chromatography (200 g of silica, prepared in CH_2Cl_2; gradient elution from CH_2Cl_2 to CH_2Cl_2/0.5 % MeOH) to give **14** (1.54 g, 66 %). ^1H NMR (300 MHz,

$CDCl_3$, 25 °C): $\delta = 9.01$ (dd, $^3J = 4.4$ Hz, $^4J = 1.83$ Hz, 2H; H-2,9), 8.18 (dd, $^3J = 8.2$ Hz, $^4J = 1.8$ Hz, 2H; H-4,7), 7.54 (dd, $^3J = 4.4$, 8.2 Hz, 2H; H-3,8), 1.79 ppm (s, 6H; Me).

Compound 7: 2-(4-Bromophenoxy)tetrahydro-2*H*-pyran (2.51 g, 9.57 mmol) was dissolved in dry THF (50 mL) under an argon atmosphere and the solution was cooled to −78 °C. *n*-Butyllithium (8.3 mL of a 1.5 M solution in hexane, 12.44 mmol, 1.3 equiv) was then added dropwise over a period of 10 min and the mixture was allowed to react for 15 min at −78 °C. Triisopropyl borate (4.5 mL, 19.11 mmol, 2 equiv) was added in a single portion and the mixture was allowed to react for a further 1 h at −78 °C. Thereafter, it was slowly warmed to room temperature, whereupon a white precipitate formed. Water (10 mL) was slowly added to quench the reaction, then diethyl ether (500 mL) was added, followed by water (500 mL). The resulting mixture was slowly neutralised to pH ≈ 6–7 by adding aqueous HCl (0.1 M, ca. 100 mL). The layers were separated and the aqueous layer was further extracted with diethyl ether (2× 250 mL). The organic fractions were combined, concentrated to dryness, and the crude product (2.68 g) was purified by flash chromatography (230 g of fine silica, prepared in toluene/acetone 8:2). Gradient elution from toluene/acetone 8:2 to 8:3 gave **7** (1.68 g, 80 %). ^{1}H NMR (300 MHz, [D$_6$]acetone/D_2O 2:1, 25 °C): $\delta = 7.70$ (m, $^3J = 8.7$ Hz, 2H; H-*o*), 6.93 (m, $^3J = 8.7$ Hz, 2H; H-*m*), 5.41 (t, $^3J = 3.2$ Hz, 1H; H-α), 3.75 and 3.50 (2m, 2H; H-β + H-β′), 1.90–1.40 ppm (m, 6H; H-γ + H-δ + H-ε); ES-MS (negative polarity): *m*/*z*: calcd for $C_{11}H_{14}BO_4$: 221.099; found: 221.093 $[M-H]^-$.

Compound 15: *n*-Butyllithium (4.95 mL, 7.92 mmol, 2 equiv) was added dropwise over 10 min to a degassed solution of 2-(4-bromophenoxy)tetrahydro-2*H*-pyran (1.82 g, 7.92 mmol, 2 equiv) in THF (12 mL) at −78 °C. The mixture was allowed to react for 15 min, and then a solution of **14** (1.00 g, 3.96 mmol) in dry THF (8 mL) was slowly introduced by means of a cannula. The resulting mixture was stirred at −78 °C for 2 h. It was then quenched with MeOH (5 mL), allowed to warm to room temperature, and concentrated to dryness. The crude product was re-aromatised using activated MnO_2 (2.58 g) in a 1:1 mixture of CH_2Cl_2/toluene (100 mL). The reaction was complete after 12 h. The mixture was filtered through Celite, which was washed with CH_2Cl_2. The combined filtrate and washings were concentrated and the product was subjected to flash chromatography (250 g of fine silica, prepared in heptane/5 % acetone). Gradient elution from heptane/5 % acetone to heptane/20 % acetone gave pure **15** (1.42 g, 84 %). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 9.10$ (dd, $^3J = 4.4$, $^4J = 1.8$ Hz, 1H; H-2), 8.30–8.23 (m, 3H; H-4 + H-7 + H-8), 8.06 (m, $^3J = 8.8$ Hz, 2H; H-*o*), 7.60 (dd, $^3J = 4.4$, 8.2 Hz, 1H; H-3), 7.21 (m, $^3J = 8.8$ Hz, 2H; H-*m*), 5.53 (t, $^3J = 6.3$ Hz, 1H; H-α), 3.94, 3.64 (2m, 2H; H-β + H-β′), 1.95–1.55 (m, 6H; H-γ + H-δ + H-ε), 1.88 ppm (s, 6H; Me); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 158.14$, 154.91, 147.86, 142.30, 136.60, 136.55, 136.00, 133.23, 128.98, 128.66, 127.94, 122.46, 120.58, 119.90, 118.63, 116.70, 116.66, 92.26, 61.99, 30.32, 26.08, 25.22, 18.71 ppm; HR ES-MS: *m*/*z*: calcd for $C_{25}H_{25}N_2O_4$: 429.1809; found: 429.1811 $[M+H]^+$.

Compound 8: *By Suzuki coupling*: Protected phen-dione **6** (1.00 g, 3.11 mmol) and boronic acid **7** (1.80 g, 8.11 mmol, 2.6 equiv) were dissolved in toluene (70 mL) and mixed with a 2 M solution of Na_2CO_3 (6.36 g, 60.0 mmol) in water (30 mL). The solution two-phase mixture was degassed and then $Pd(PPh_3)_4$ (467 mg, 0.4 mmol) was rapidly added under a flow of argon. The mixture was heated at 80 °C with vigorous stirring for 18 h. It was then allowed to cool to room temperature and CH_2Cl_2 (600 mL) was added. The organic layer was washed with water (300 mL) and concentrated to dryness. The resulting brown solid (2.85 g) was purified by flash chromatography (230 g of fine silica, prepared in CH_2Cl_2; elution with CH_2Cl_2) to give the di-protected intermediate **8** as a mixture of diastereoisomers (1.87 g, 97 %).

By nucleophilic substitution: 2-(4-Bromophenoxy)tetrahydro-2*H*-pyran (1.03 g, 4.68 mmol, 2 equiv) was dissolved in THF (10 mL) and the solution was cooled to −78 °C under an argon atmosphere. It was then treated with *n*-butyllithium (2.91 mL of a 1.6 M solution, 4.68 mmol, 2 equiv). The mixture was allowed to react for 15 min and then a solution of compound **15** (1.00 g, 2.34 mmol) in THF (20 mL) was added by means of a cannula at −78 °C. The deep-purple reaction mixture was slowly allowed to warm to room temperature overnight, after which it was quenched with water (0.2 mL). The solution was concentrated to dryness and the residue was dried in vacuo. This material was dissolved in CH_2Cl_2 and MnO_2 was added portionwise. The progress of the oxidation was monitored by TLC and, once complete, the solid was filtered off, the filtrate was concentrated under reduced pressure, and the crude product was purified by chromatography (100 g of silica, prepared in toluene; isocratic elution with toluene) to give **8** (1.61 g, 95 %). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 8.41$ (m, $^3J = 8.9$ Hz, 4H; H-*o*), 8.29 (d, $^3J = 8.6$ Hz, 2H; H-4,7), 8.10 (d, $^3J = 8.7$ Hz, 2H; H-3,8), 6.93 (m, $^3J = 8.9$ Hz, 4H; H-*m*), 5.59 (t, $^3J = 3.0$ Hz, 2H; H-α), 4.00 (m, 2H; H-β), 3.70 (m, 2H; H-β′), 2.20–1.50 ppm (m, 18H; Me + H-γ + H-δ + H-ε); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 158.14$, 158.13, 154.00, 142.16, 136.24, 133.06, 128.67, 128.60, 120.41, 119.14, 118.63, 116.60, 96.23, 96.21, 62.03, 30.32, 26.11, 25.22, 18.72 ppm; ES-MS: *m*/*z*: calcd for $C_{37}H_{37}N_2O_6$: 605.265; found: 605.264 $[M+H]^+$.

Compound 9: Protected diphenol **8** (1.00 g, 1.65 mmol) was dissolved in dry methanol (ca. 150 mL) and a dry 2 M ethereal solution of HCl (2.5 mL, ≈3 equiv) was added. The mixture was allowed to react for 2 h at room temperature. Freshly distilled triethylamine (1.2 mL) was then added to quench the reaction. Evaporation of the solvents gave a deep-orange solid (263 mg), which was adsorbed on silica (20 g) and purified by flash chromatography (130 g of fine silica, prepared in CH_2Cl_2/2 % MeOH; gradient elution from CH_2Cl_2/2 % MeOH to CH_2Cl_2/4 % MeOH) to give **9** (0.72 g, 96 %). ^{1}H NMR (300 MHz, $CDCl_3$/[D$_6$]acetone 2:1, 25 °C): $\delta = 8.07$ (s, 2H; OH), 7.98 (m, $^3J = 8.7$ Hz, 4H; H-*o*), 7.89 (d, $^3J = 8.6$ Hz, 2H; H-4,7), 7.74 (d, $^3J = 8.7$ Hz, 2H; H-3,8), 6.67 (m, $^3J = 8.7$ Hz, 4H; H-*m*), 1.51 ppm (s, 6H; Me); ^{13}C NMR (75 MHz, $CDCl_3$/[D$_6$]acetone 2:1, 25 °C): $\delta = 158.44$, 154.74, 141.69, 136.28, 131.08, 129.12, 129.07, 120.78, 119.84, 116.79, 115.77, 26.10 ppm; ES-MS: *m*/*z*: calcd for $C_{27}H_{21}N_2O_4$: 437.150; found: 437.151 $[M+H]^+$.

Compound 10: Commercial pentaethyleneglycol ditosylate (2.00 g, 95 %) was first purified by chromatography (100 g of silica, prepared in Et_2O; elution with Et_2O/10 % EtOH). After collection of the appropriate fraction and evaporation of the solvents, the compound was dissolved in acetone (15 mL) and NaI was added until saturation. The mixture was heated to reflux for 2 h under a dry atmosphere ($CaCl_2$ guard tube). After cooling to room temperature, more NaI was added and the mixture was stirred for a further 16 h at room temperature. The white solid was then filtered off and washed with Et_2O (3×50 mL). The solvents were removed from the combined filtrate and washings under reduced pressure. The residual orange oil was partitioned between Et_2O (60 mL) and water (60 mL); the organic layer was separated and washed with an aqueous solution of $Na_2S_2O_3$ until complete disappearance of the orange color. After separation, the organic layer was washed with water (2×60 mL), dried over $MgSO_4$, filtered, and concentrated to dryness to give pure **10** (1.35 g, 96 %). ^{1}H NMR (300 MHz, [D$_6$]acetone, 25 °C): $\delta = 3.76$–3.72 (t, $^3J = 6.6$ Hz, 4H; H-β), 3.65–3.59 (d, $^3J = 8.6$ Hz, 12H; H-γ + H-δ + H-ε), 3.35–3.31 ppm (t, $^3J = 6.6$ Hz, 4H; H-α).

Compound 11: Dry Cs_2CO_3 (4.42 g, 13.57 mmol) was suspended in freshly distilled DMF (500 mL) under argon and the mixture was heated to 50 °C with vigorous stirring. A mixture of diphenol **9** (0.74 g, 1.70 mmol) and pentaethyleneglycol diiodide **10** (0.82 g, 1.78 mmol, 1.05 equiv) in DMF (100 mL) was added at a rate of one drop per minute by means of a syringe pump. After complete addition of the reagents (approx. 72 h), the mixture was allowed to react for a further 12 h. The solvent was then distilled off in vacuo and the residual solid was partitioned between water (200 mL) and CH_2Cl_2 (500 mL). The organic layer was separated and concentrated to give a brown oily material (1.87 g), which was subjected to flash chromatography (2×230 g of fine silica, prepared in CH_2Cl_2; gradient elution from CH_2Cl_2 to CH_2Cl_2/0.1 % MeOH) to yield **11** (0.64 g, 59 %). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 8.34$ (m, $^3J = 8.9$ Hz, 4H; H-*o*), 8.24 (d, $^3J = 8.6$ Hz, 2H; H-4,7), 8.03 (d, $^3J = 8.6$ Hz, 2H; H-3,8), 7.17 (m, $^3J = 8.9$ Hz, 4H; H-*m*), 4.33 (t, $^3J = 5.3$ Hz, 4H; H-α), 3.84 (t, $^3J = 5.3$ Hz, 4H; H-β), 3.75–3.67 (m, 12H; H-γ + H-δ + H-ε), 1.87 ppm (s, 6H; Me); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 159.98$, 153.94, 142.03, 136.28, 132.76, 128.79, 128.74, 120.45, 119.02, 116.79,

115.63, 71.21, 70.77, 70.57, 69.54, 68.87, 26.12 ppm; ES-MS: *m/z*: calcd for $C_{37}H_{39}N_2O_8$: 639.271; found: 639.272 $[M+H]^+$.

Compound 12: The protected macrocycle **11** (250 mg, 0.39 mmol) was dissolved in a mixture of water (5 mL) and trifluoroacetic acid (10 mL). The mixture was heated to 50 °C in the presence of oxygen. After 5 h, the solvents were evaporated under reduced pressure and the residue was partitioned between CH_2Cl_2 and a 1 M aqueous solution of $NaHCO_3$. The organic layer was washed with water, dried over $MgSO_4$, and concentrated, and the crude product was purified by flash chromatography (30 g of fine silica, prepared in CH_2Cl_2; gradient elution from CH_2Cl_2 to CH_2Cl_2/2 % MeOH) to give **12** (204 mg, 87 %). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 8.50$ (d, $^3J = 8.3$ Hz, 2H; H-4,7), 8.36 (m, $^3J = 9.0$ Hz, 4H; H-*o*), 7.93 (d, $^3J = 8.3$ Hz, 2H; H-3,8), 7.18 (m, $^3J = 9.0$ Hz, 4H; H-*m*), 4.35 (t, $^3J = 5.3$ Hz, 4H; H-α), 3.87 (t, $^3J = 5.3$ Hz, 4H; H-β), 3.85–3.68 ppm (m, 12H; H-γ + H-δ + H-ε); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 193.46$, 178.94, 162.43, 161.67, 152.96, 137.83, 130.80, 129.73, 126.22, 120.41, 115.82, 71.26, 70.83, 70.63, 69.49, 67.79 ppm; ES-MS: *m/z*: calcd for $C_{34}H_{33}N_2O_8$: 597.224; found: 597.228 $[M+H]^+$.

Monoclinic crystals of **14** suitable for X-ray analysis were obtained by slow diffusion of *n*-heptane into a solution in CH_2Cl_2.

Crystallographic data; space group $P21/n$; $Z = 4$; $\rho = 1.400\ g\,cm^{-3}$; cell constants $a = 8.7080(2)$, $b = 21.4090(5)$, $c = 17.6640(4)$ Å, $\beta = 100.8200(14)$, $V = 3234.55(13)$ Å^3; temperature of data collection 173(2) K; 8626 unique reflections ($I > 2\sigma(I)$; $R = 0.0796$; $Rw = 0.1494$.

CCDC-645 664 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

Compound 1: Compound **12** (200 mg, 16.8×10^{-5} mol) and sodium dithionite (7.0 mg, 4.0×10^{-5} mol, 0.2 equiv) were mixed with dry ammonium acetate. After degassing the flask, the mixture was slowly heated to 180 °C and the molten salt solution was allowed to react for 2 h with gentle stirring. The mixture was then cooled and water was added to induce the precipitation of a brown material. The product was collected by centrifugation, and then boiled several times in water to remove the excess ammonium salts. After collection of the solid by centrifugation, the poorly soluble material was boiled in pyridine (about 30 mL) and the solution was filtered while hot; repeating this procedure three times allowed **1** to finally be obtained as an ochre solid (137 mg, 70 %). ^{1}H NMR (300 MHz, CD_2Cl_2/10 % F_3CCO_2D, 25 °C): $\delta = 10.19$ (d, $^3J = 8.4$ Hz, 4H; H-4,7), 8.72 (d, $^3J = 8.4$ Hz, 4H; H-3,8), 8.28 (m, $^3J = 8.7$ Hz, 8H; H-*o*), 7.36 (m, $^3J = 8.6$ Hz, 8H; H-*m*), 4.44 (t, $^3J = 5.1$ Hz, 8H; H-α), 4.05 (t, 8H; H-β), 3.95–3.70 ppm (m, 24H; H-γ + H-δ + H-ε); ^{13}C NMR (75 MHz, CD_2Cl_2/10 % F_3CCO_2D, 25 °C): $\delta = 163.37$, 158.78, 158.24, 139.99, 139.35, 138.81, 129.97, 126.31, 125.54, 124.63, 116.81, 112.96, 70.53, 70.33, 70.26, 69.22, 67.74 ppm; HR ES-MS: *m/z*: calcd for $C_{68}H_{65}N_6O_{12}$ 1157.4661; found: 1157.4653 $[M+H]^+$.

Compound 17: A mixture of 2,9-di(*p*-hydroxyphenyl)-1,10-phenanthroline (200 mg, 0.55 mmol) and potassium carbonate (386 mg, 2.79 mmol, 5.1 equiv) was suspended in freshly distilled DMF (60 mL) and the suspension was heated to 60 °C under an argon atmosphere. A solution of 1-bromo-3-butenyl (747 mg, 0.57 mmol, 10 equiv) in DMF (10 mL) was then added over a period of 30 min. The vigorously stirred mixture was allowed to react for a further 24 h and then concentrated to dryness. The residue was partitioned between CH_2Cl_2 (200 mL) and water (150 mL) and the organic layer was separated. The aqueous layer was further extracted with CH_2Cl_2 (100 mL). Evaporation of the solvent from the combined organic layers gave a yellow crude product, which was purified by flash chromatography (150 g of fine silica prepared in CH_2Cl_2; elution with CH_2Cl_2) to give **17** (125 mg, 48 %). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 8.42$ (m, $^3J = 9.0$ Hz, 4H; H-*o*′), 8.26 (d, $^3J = 8.5$ Hz, 2H; H-4′,7′), 8.08 (d, $^3J = 8.5$ Hz, 2H; H-3′,8′), 7.75 (s, 2H; H-5′,6′), 7.11 (m, $^3J = 8.9$ Hz, 4H; H-*m*′), 6.03–5.89 (m, $^3J = 6.7$, 10.2, and 17.0 Hz, 2H; H-c), 5.26–5.18 (m, $^3J = 17.1$ Hz, 2H; H-d), 5.16–5.12 (m, $^3J = 10.2$ Hz, 2H; H-e), 4.15 (t, $^3J = 6.8$ Hz, 4H; H-a), 2.66–2.57 ppm (m, $^3J = 6.7$ Hz, 4H; H-b); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 160.29$, 156.36, 136.86, 134.41, 132.07, 129.00, 127.54, 125.63, 119.40, 117.16, 114.84, 67.31, 33.70 ppm; ES-MS: *m/z*: calcd for $C_{32}H_{29}N_2O_2$ 473.223; found: 473.236 $[M+H]^+$.

Compound 18·2PF$_6$: A solution of $[Cu(MeCN)_4]PF_6$ (20.4 mg, 5.47×10^{-5} mol, 2.07 equiv) in dry MeCN (10 mL) was added to a degassed solution of **1** (30.5 mg, 2.64×10^{-5} mol) in dry CH_2Cl_2 (10 mL) and the mixture was stirred at room temperature for 12 h under an inert atmosphere. A solution of bis-butenyl-phenanthroline **17** (24.9 mg, 5.27×10^{-5} mol, 2.0 equiv) in dry CH_2Cl_2 (10 mL) was then added; the mixture immediately turned brown, but was allowed to react for 2 days to ensure complete reaction. After evaporation of the solvent, the crude product was partitioned between CH_2Cl_2 (40 mL) and water (40 mL); the organic layer was separated and worked-up to give **18**·2PF$_6$ (66 mg) in quantitative yield. ^{1}H NMR (500 MHz, [D$_6$]acetone, COSY-ROESY, 25 °C): $\delta =$ 10.25 (d, $^3J = 8.4$ Hz, 4H; H-4,7), 8.87 (d, $^3J = 8.4$ Hz, 4H; H-4′,7′), 8.41 (s, 4H; H-5′,6′), 8.40 (d, $^3J = 8.4$ Hz, 4H; H-3,8), 8.12 (d, $^3J = 8.4$ Hz, 4H; H-3′,8′), 7.74 (m, $^3J = 8.7$ Hz, 8H; H-*o*′), 7.59 (m, $^3J = 8.6$ Hz, 8H; H-*o*), 6.37 (m, $^3J = 8.7$ Hz, 8H; H-*m*′), 6.20 (m, $^3J = 8.7$ Hz, 8H; H-*m*), 5.68–5.54 (m, $^3J = 5.0$, 10.2, and 17.3 Hz, 4H; H-c), 4.93–4.78 (m, $^3J = 10.2$ and 17.3 Hz, 8H; H-d + H-e), 3.88 (s, 8H; H-ε), 3.78–3.69 (m, 16H; H-δ + H-a), 3.68–3.61 (m, 16H; H-β + H-γ), 3.59–3.55 (m, 8H; H-α), 2.41–2.34 ppm (m, 8H; H-b); HR ES-MS: *m/z*: calcd for $C_{132}H_{120}N_{10}O_{16}Cu_2$: 1114.3746; found: 1114.3710 $[M]^{2+}$.

Compound 19·2PF$_6$: Compound **18**·2PF$_6$ (20 mg, 2.38×10^{-5} mol) and Grubbs first-generation catalyst $[RuCl_2(PCy_3)_2CHPh]$ (3.3 mg, 0.50 equiv) were dissolved in freshly distilled CH_2Cl_2 (so as to obtain a 10^{-3} M solution) and kept under argon. The mixture was allowed to react for 10 days at room temperature under vigorous stirring. The material was then precipitated by adding a saturated aqueous solution of KPF_6 to ensure the presence of PF_6^- as the sole counter ion. The crude product was filtered through Celite and subjected to chromatography (150 g of silica prepared in CH_2Cl_2/0.5 % MeOH; gradient elution from CH_2Cl_2/0.5 % MeOH to CH_2Cl_2/1 % MeOH) to give **19**·2PF$_6$ (16 mg, 80 %) as a mixture of three diastereomers. ^{1}H NMR (500 MHz, [D$_6$]acetone, COSY-ROESY, 25 °C): $\delta = 10.34$–10.10 (m, 4H; H-4,7), 8.91–8.80 (m, 4H; H-4′,7′), 8.37–8.31 (m, 4H; H-5′,6′), 8.16–8.07 (m, 4H; H-3,8), 7.75–7.66 (m, 4H; H-3′,8′), 7.99–7.76 (m, 8H; H-*o*′), 7.75–7.66 (m, 8H; H-*o*), 6.55–6.35 (m, 8H; H-*m*′), 6.20–6.14 (m, 8H; H-*m*), 5.74–5.16 (3m, 4H; H-c), 3.89 (s, 8H; H-ε), 3.85–3.70 (m, 16H; H-δ + H-a), 3.68–3.65 (m, 8H; H-γ), 3.60–3.46 (m, 16H; H-α + H-β), 2.40, 2.30, 2.18 ppm (3m, 8H; H-b); HR ES-MS: *m/z*: calcd for $C_{128}H_{112}N_{10}O_{16}Cu$ 1086.3425; found: 1086.3420 $[M]^{2+}$.

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