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Synthesis of new copper(I)-complexed rotaxanes via click chemistry

Stéphanie Durot, Pierre Mobian, Jean-Paul Collin, Jean-Pierre Sauvage *

Laboratoire de Chimie-Organo-Minérale, Université Louis Pasteur, Institut de Chimie, UMR 7177, 4, rue Blaise Pascal, 67070 Strasbourg Cedex, France

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ABSTRACT

The Cu(I)-catalyzed dipolar cycloaddition of azides and terminal alkynes ('click' chemistry) has been used as a mild and efficient stoppering reaction for the preparation of new copper(I)-complexed rotaxanes.

1. Introduction

One of the key steps in rotaxane synthesis is the stoppering reaction. The use of efficient templating procedures, leading to well defined multicomponent architectures as precursors to the rotaxanes, is now well documented.[1–3] The precursors, or 'pre-rotaxanes'[4] are built by taking advantage of precisely controlled non-covalent interactions such as hydrogen bonds, acceptor–donor and/or hydrophobic interactions between several organic fragments.[5–9] Alternatively, coordination chemistry has also demonstrated its power [10–16] with, in particular, the use of copper(I) as extremely efficient gathering and threading element, [17–21] able to induce the formation of pseudo-rotaxanes quantitatively. Generally speaking, such simple principles allow the preparation of rotaxane precursors in high yield and using simple experimental procedures. On the other hand, in most cases, when the final step is the introduction of one or more bulky groups, acting as stoppers, difficulties are encountered and this last step is often low-yielding and experimentally delicate.[9,21–26]

The so-called 'click chemistry' reaction,[27,28] based on a modified procedure originally described by Huisgen and co-workers[29,30] and, later on, substantially improved by Meldal[31,32] and Sharpless,[33] represents a promising possibility as stoppering reaction of the preliminarily prepared pre-rotaxane. A limited number of such reactions has been recently reported[17,18,34–39] a particularly impressive case being that of a copper-complexed rotaxane for which the copper(I) centre is used both as template and catalyst.[17,18]

In a preliminary communication, our group has recently described the synthesis of a labile copper-complexed [2]rotaxane.[39] We would now like to report additional examples as well as a complete description of the procedure for making copper(I)-based [2]rotaxanes.

2. Results and discussion

In general, in our group, two main strategies have been exploited to synthesize rotaxanes (Scheme 1). (i) The first strategy is the double-stoppering approach. After threading of a coordinating string-like fragment through a ring using a copper(I) ion as template, a double-stoppering reaction produces the desired rotaxane. Usually, this method leads to the formation of rotaxane with modest or low yield, especially if the copper(I)-complexed precursor is not very stable under the reaction conditions. (ii) To limit the unthreading reaction leading to dissociation of the precursor, a reasonably efficient strategy has been used, which consists of a stepwise approach. It comprises three steps: (1) attachment of a first stopper to the string, followed by (2) the threading reaction, and, finally, (3) fixation of the second stopper to the thread. This procedure is well adapted when the relatively harsh Williamson reaction is used to attach the stoppers, since a mono-stoppered precursor is less susceptible to unthreading than a non-stoppered one. On the other hand, the double-stoppering approach can be very efficient if 'click' chemistry is used due to the mild reaction conditions of this latter reaction, which do not cause detrimental unthreading.

Generally speaking, 'Click chemistry'[27,28,40] is a modular approach that relies on nearly perfect reactions. These reactions must

* Corresponding author. Fax: +33 3 90241368.
E-mail address: sauvage@chimie.u-strasbg.fr (J.-P. Sauvage).

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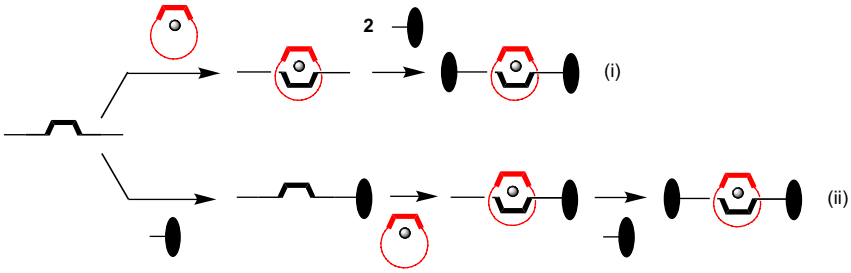
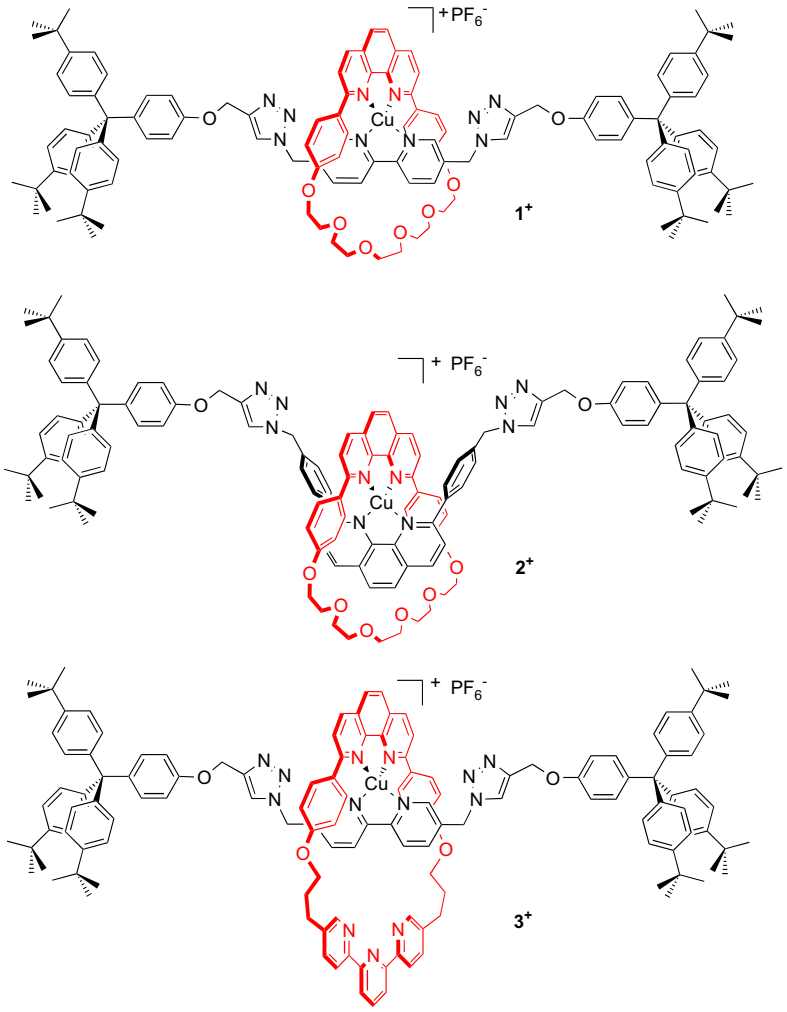


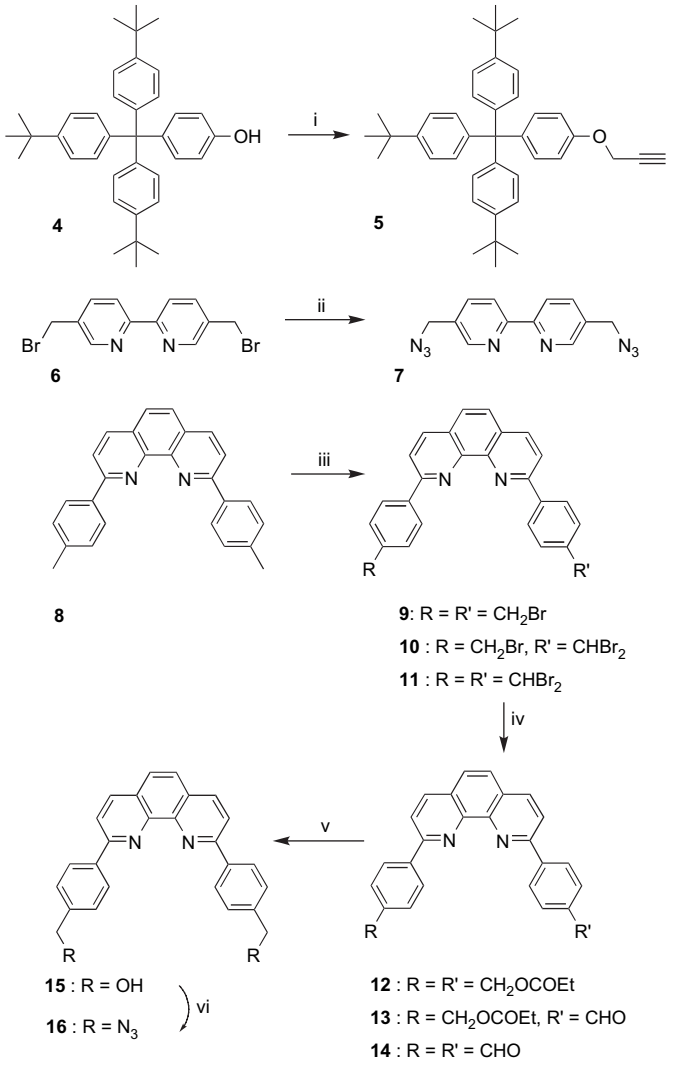
Scheme 1. Schematic representation of possible strategies to prepare rotaxanes: (i) double-stoppering approach; (ii) stepwise approach.

be wide in scope, give very high yields, proceed starting from readily available reagents, and be easy to perform (which means ideally, be insensitive to oxygen and water). They should also be selective chemical transformations, and the work-up as well as the product isolation should be simple. The prototype of a 'click' reaction is the copper(I)-catalyzed 1,3-dipolar cycloaddition of azides and alkynes, providing 1,4-disubstituted 1,2,3-triazoles.[31–33] The metallo-rotaxanes $\mathbf{1}^+$, $\mathbf{2}^+$ and $\mathbf{3}^+$ shown in Scheme 2 were all synthesized using the double-stoppering approach and click chemistry.

Compound $\mathbf{1}^+$ contains the sterically hindered 2,9-diphenyl-1,10-phenanthroline (dpp) chelate incorporated in a 30-membered ring. By contrast, the threaded fragment incorporates a sterically non-hindered chelate of the 2,2′-bipyridine family. Rotaxane $\mathbf{2}^+$ contains two dpp fragments thus leading to a better shielded metal centre than $\mathbf{1}^+$. The threaded ring of $\mathbf{3}^+$ (33-membered ring) contains two different coordinating unit: a dpp fragment and a 2,2′,6″,2″-terpyridine chelate, making this compound potentially susceptible to undergo electrochemically driven pirouetting of the ring around the axis, by analogy with related molecular machine prototypes.[41] This strategy required the preliminary synthesis of an acetylenic stopper **5** and thread-like fragments **7** and **16** bearing azide function at each end (Scheme 3). The preparation of alkyne **5** via a Williamson ether synthesis has been described recently.[18] However, we used a more straightforward procedure.[39] Compound **4**[42] was reacted with an excess of propargyl bromide to afford the



Scheme 2. Copper(I)-complexed rotaxanes synthesized by 'click chemistry'.

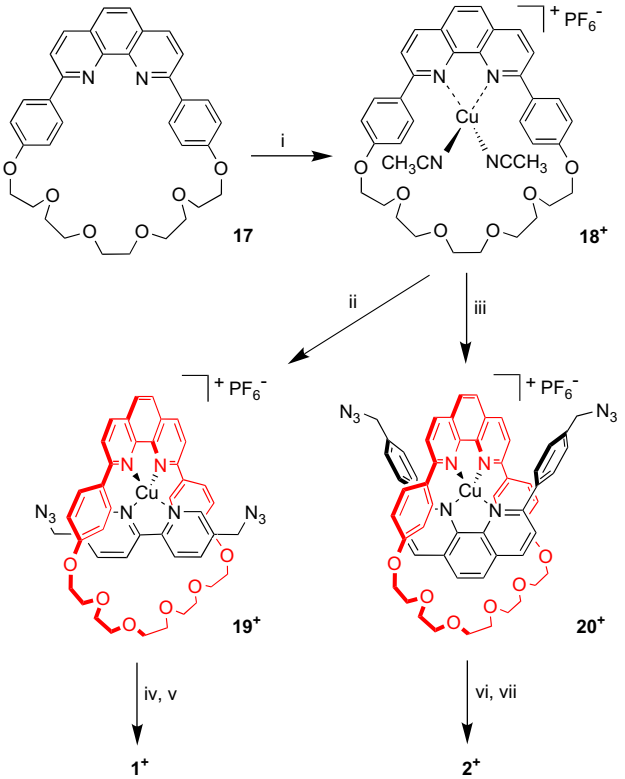


Scheme 3. Synthesis of precursors **5**, **7** and **16**. (i) NaH, propargyl bromide, THF, 45 °C, 24 h, 77%; (ii) 2.3 equiv NaN_3, DMSO/H_2O (2/1), 98%; (iii) 3.2 equiv NBS, benzoyl peroxide cat., benzene, 80 °C, 18 h; (iv) 2 equiv NaOH, propionic acid, 128 °C, 24 h; (v) 1.2 equiv $NaBH_4$, NaOH 10%, 0 °C, then rt, 66 h, 50% based on **8**; (vi) 1.2 equiv diphenyl phosphorazidate, 1.2 equiv DBU, DMF, 0 °C, then 85 °C, 15 h, 70%.

propargyl-bearing stopper **5** in 77% yield. Bipyridine **7** was prepared in excellent yield (98%) starting from the readily available compound **6**[43] in the presence of sodium azide (2.3 equiv) in a mixture of DMSO and water (2/1). Phenanthroline fragment **16** was obtained from the dialcohol **15**,[44] prepared using an improved methodology inspired by previously described functionalization of 2,9-bis(*p*-tolyl)-1,10-phenanthroline **8**.[45] The latter was subjected to 3.2 equiv of *N*-bromo succinimide in refluxing benzene using benzoyl peroxide as a radical initiator. This reaction yielded a mixture of hardly separable brominated species **9**, **10** and **11**, so that the mixture was directly engaged in the next step, treatment with sodium hydroxide in refluxing propionic acid.[46] After work-up, the crude oil contained approximately 13% of diester **12**, 75% of aldehyde-ester **13** and 12% of dialdehyde **14**. Nevertheless, the crude mixture was used directly, without further purification, since the last step consisted of one-pot reduction of the aldehyde functions with sodium borohydride and saponification of the ester groups of **12**, **13** and **14** with sodium hydroxide. 2,9-Bis(*p*-hydroxymethyl)-1,10-phenanthroline **15** was obtained in a three-step synthesis with a 50% yield from 2,9-bis(*p*-tolyl)-1,10-phenanthroline **8**. Compound **15** was converted to the diazide phenanthroline fragment **16** using modified conditions described in the literature based on diphenyl phosphorazidate and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).[47] In order to avoid contamination with Mitsunobu by-products, substoichiometric amounts of diphenyl phosphorazidate were added to a DMF solution of dialcohol **15**. To the mixture was added the same amount of DBU. After 15 h at 85 °C, the diazide **16** was isolated in 70% yield with respect to diphenyl phosphorazidate using an aqueous work-up and purification over silica gel column chromatography. Furthermore, excess of compound **15** could be recovered and recycled.

The metallo-rotaxanes $\mathbf{1}^+$ and $\mathbf{2}^+$ were then prepared from their respective precursors using click chemistry as a key step. The templated threading reactions between **7** or **16** and $\mathbf{18}^+$, the copper(I) complex of the 30-membered ring **17**, are depicted in Scheme 4, as well as the double-stoppering reaction.

In a typical procedure, the macrocycle **17** was dissolved in a degassed solution of dichloromethane and acetonitrile (1 mL, (7/3)). Upon addition of 1 equiv of $[Cu(CH_3CN)_4]PF_6$, the solution immediately turned dark orange. The threading processes between $\mathbf{18}^+$, incorporating a bidentate chelate, and the bipyridine ligand **7** or the phenanthroline one **16** occurred efficiently as shown by the instant appearance of the dark red colour characteristic of copper(I) complexes with two aromatic diimine ligands per copper. The in situ addition of acetylenic stopper **5** (2 equiv), and substoichiometric amounts of copper(I) catalyst (0.5 equiv) $[Cu(CH_3CN)_4]PF_6$ and base (0.4 equiv Na_2CO_3) to pseudo-rotaxanes $\mathbf{19}^+$ and $\mathbf{20}^+$ provided the metallo-rotaxanes $\mathbf{1}^+$ or $\mathbf{2}^+$, respectively, by double copper(I)-catalyzed 1,3-dipolar cycloaddition. The progress of the reactions was monitored by TLC analysis, which clearly showed the consumption of compound **5**. Nevertheless,



Scheme 4. Synthesis of pseudo-rotaxanes $\mathbf{19}^+$ and $\mathbf{20}^+$ and metallo-rotaxanes $\mathbf{1}^+$ and $\mathbf{2}^+$. (i) 1 equiv $[Cu(CH_3CN)_4]PF_6$, CH_2Cl_2/CH_3CN (7/3), 20 °C, 20 min; (ii) 1 equiv **7**, 1 h; (iii) 1 equiv **16**, 15 min; (iv) 2 equiv **5**, 0.5 equiv $[Cu(CH_3CN)_4]PF_6$, 0.4 equiv Na_2CO_3, 20 °C, 5 h; (v) 1 equiv **5**, 0.25 equiv $[Cu(CH_3CN)_4]PF_6$, 0.12 equiv Na_2CO_3, 20 °C, 16 h, 62%; (vi) 2 equiv **5**, 0.5 equiv $[Cu(CH_3CN)_4]PF_6$, 0.4 equiv Na_2CO_3, 20 °C, 5 h; (vii) 1 equiv **5**, 0.25 equiv $[Cu(CH_3CN)_4]PF_6$, 0.2 equiv Na_2CO_3, 20 °C, 16 h, 67%.

supplementary additions of copper(I) (0.25 equiv), stopper **5** (1 equiv), and Na_2CO_3 and stirring overnight were necessary to observe the end of the reaction. Without any work-up, the reaction mixtures were both directly purified over column chromatography on silica gel. In both cases, no by-product such as the corresponding dumbbell was observed, which is a clear indication that unthreading does not take place to a significant extent during the reaction. The compulsory use of a trace of hydrazine in degassed eluent has to be emphasized: the function of hydrazine is to inhibit formation of extremely labile copper(II) complexes, which would be detrimental and lead to lower yields (28%). The isolated yield of rotaxane $\mathbf{1}^+$ was 62%, which highlights the efficiency of the 'click' strategy that provided $\mathbf{1}^+$ via a double copper(I)-catalyzed 1,3-dipolar cycloaddition. This method proved to be at least equally efficient in the case of the [2]metallo-rotaxane $\mathbf{2}^+$ (Scheme 2), synthesized in 67% yield.

High-resolution ES-MS measurements and ^{1}H NMR spectroscopy confirmed the postulated structures of metallo-rotaxanes $\mathbf{1}^+$ and $\mathbf{2}^+$. The phenyl protons (identified as *o* and *m*, see Fig. 1) of the macrocycle component **17** undergo a strong upfield shift by copper(I)-induced threading of **16** followed by stoppering, to afford $\mathbf{2}^+$. From **16** to $\mathbf{2}^+$, this shift is equal to −1.32 ppm and −1.31 ppm for protons *o*′ and *m*′, respectively, (Fig. 1a and b). This remarkable shift results from the anisotropy cone of the phenanthroline unit of the thread. Similar upfield shifts were observed for the phenyl protons of the dpp fragment belonging to the thread (Fig. 1b and c). Furthermore, it should be noted that the order of the peaks attributed to the methylene groups (α,β,γ,δ,ε) of the ring polyoxoethylene chain was inverted in the metallo-rotaxane $\mathbf{2}^+$ by comparison to macrocycle **17** (Fig. 1a and b). The α protons of the pentaethylene glycol fragment experience the strong ring current of the phenanthroline incorporated in the axis, which explains why their chemical shift is upfield shifted ($\Delta\delta$=−0.9 ppm from **17** to $\mathbf{2}^+$). All the features are characteristic of such interlocked systems[20,48] and demonstrate that the structures of metallo-rotaxanes $\mathbf{1}^+$ and $\mathbf{2}^+$ correspond to those shown in Scheme 2.

With this efficient synthetic method in hands, we turned our attention to the formation of more elaborated rotaxanes. In particular, bistable rotaxanes are very attractive targets since interlocked architectures take a particular place in the field of artificial molecular machines and motors.[8,49–53] In our group, much effort has been devoted to develop rotaxane complexes, which undergo an electrochemically driven pirouetting motion of the ring around an axis.[54,55] In such previously described copper-based machines

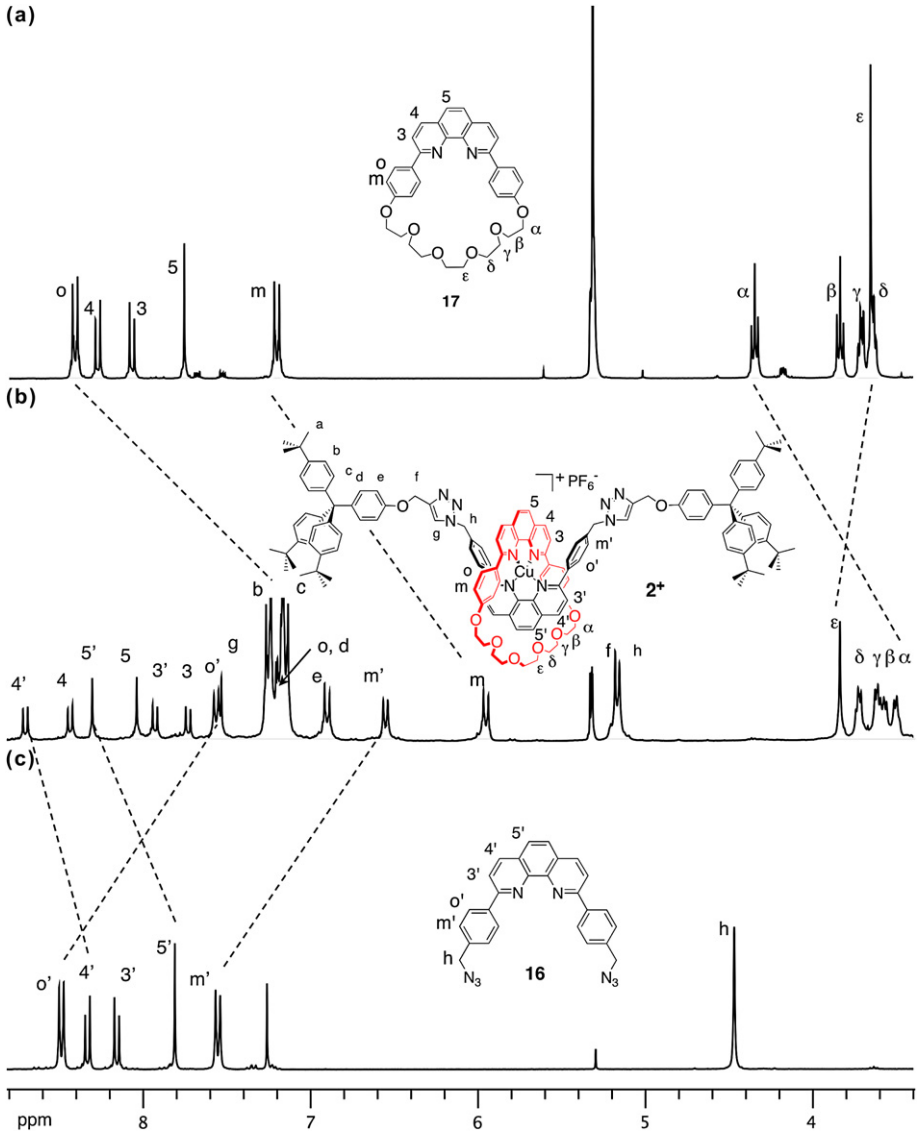
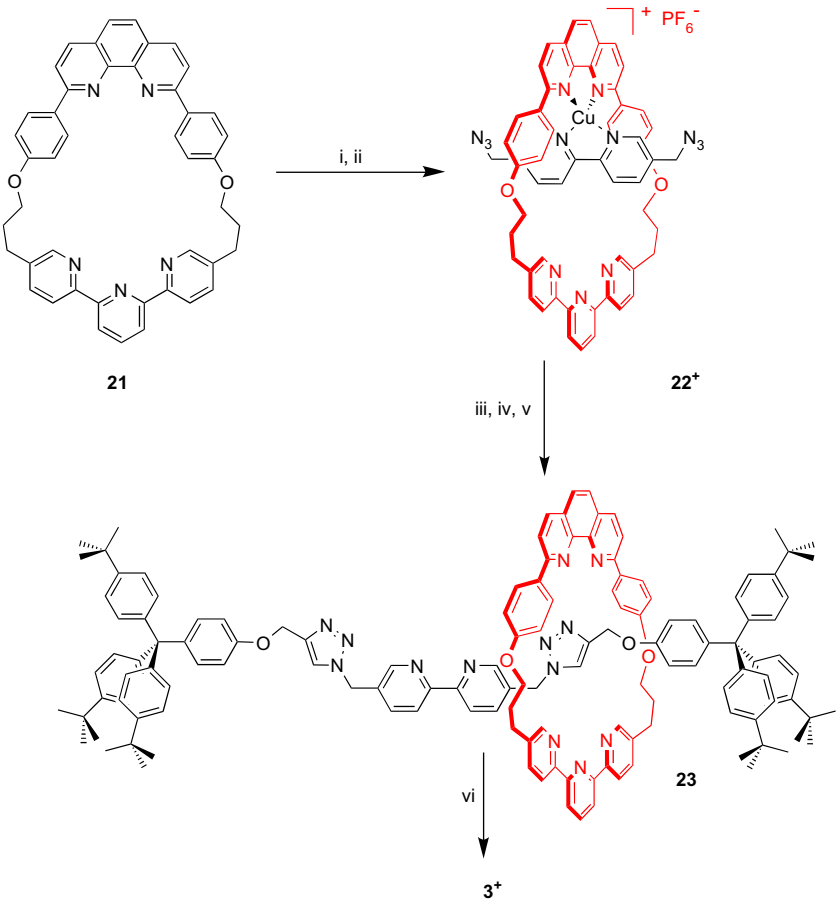


Figure 1. NMR spectra of macrocycle **17**, of metallo-rotaxane $\mathbf{2}^+$ and of thread **16**, in CD_2Cl_2, except for **16** ($CDCl_3$).

the ring incorporates both a bidentate chelate, a 1,10-phenanthroline (phen) and a tridentate fragment, a 2,2′,6″,2″-terpyridine (terpy), and the axis contains an aromatic diimine bidentate ligand.

In order to test the 'click chemistry' approach to the synthesis of a new bistable rotaxane, we thus applied a procedure close to the one described above for the synthesis of complexes $\mathbf{1}^+$ and $\mathbf{2}^+$. The synthetic pathway leading to metallo-rotaxane $\mathbf{3}^+$, as well as the two main organic precursors, ring **21** and thread-like fragment **7**, are represented in Scheme 5. The first step is similar to that employed to form complexes $\mathbf{19}^+$ and $\mathbf{20}^+$. The macrocycle was dissolved in a degassed solution of dichloromethane and acetonitrile (1:1). Upon addition of the copper salt followed by reaction with **7**, a red solution characteristic of four-coordinated copper(I) complexes of aromatic diimine ligands was obtained. It is known that the presence of the terpy moiety in the ring does not interfere with the threading step since copper(I) interacts preferably with the bidentate chelate.[48] The in situ formed intermediate complex was then subjected to 'click chemistry' conditions. An excess of copper salt, acetylenic stopper **5** and Na_2CO_3 were added twice. After 20 h, a dark red-greenish solution was obtained and the advancement of the reaction was evaluated by analytical silica gel thin layer chromatography. Unfortunately, development by elution with CH_2Cl_2/MeOH (90/10) revealed the presence of two superimposed coloured traces. In order to circumvent a difficult purification step of this mixture of complexes, we thus decided to remove the copper from the medium and then purify the organic material. Demetallation was carried out by using a method classically employed to remove copper metal ions from interlocked species.[57] To the crude product of reaction dissolved in a triphasic solution (dichloromethane/acetonitrile/water) an excess of KCN was added. The red-greenish colour of the medium disappeared rapidly, and the organic layer was isolated and purified by chromatography (Al_2O_3) using a mixture of CH_2Cl_2 and MeOH (92/8). Nevertheless, two further preparative thin layer chromatography experiments were necessary in order to isolate pure rotaxane **23**, containing the bis-chelating ring **21**, in 12% yield. The chemical integrity of compound **23** was confirmed by one- and two-dimensional ^{1}H NMR spectroscopy as well as high-resolution ES-MS measurements (m/z=2029.0956 for $[M+H]^+$, calcd 2029.0989). Remetalation was possible by adding 1 equiv of $[Cu(CH_3CN)_4]PF_6$ to a solution of **23** in a CH_2Cl_2/CH_3CN mixture. Upon addition of the copper complex, the lightly yellow coloured solution turned dark red. ^{1}H NMR confirmed that the complexation process occurred quantitatively and high-resolution ES-MS measurements (m/z=2091.0241 for $[M-PF_6]^+$, calcd 2091.0207) were in agreement with the expected structure of copper(I)-complexed rotaxane $\mathbf{3}^+$.

In this last section, we showed that the 'click chemistry' approach is also suitable for the synthesis of a rotaxane containing a ring, which incorporates both a bidentate chelate and a tridentate fragment. Furthermore, it is noteworthy that the isolated yield obtained in this case is similar to those reported for the synthesis of related bistable rotaxanes by a stepwise approach using Williamson conditions.[54–56] Nevertheless, by comparison with the formation of $\mathbf{1}^+$ and $\mathbf{2}^+$, the efficiency of the copper(I)-catalyzed Huisgen reaction in the case of the formation of $\mathbf{3}^+$ is lower even if a large amount of copper catalyst is employed. The presence of the



Scheme 5. Synthesis of pseudo-rotaxane **22**, rotaxane **23** and metallo-rotaxane $\mathbf{3}^+$. (i) 1 equiv $[Cu(CH_3CN)_4]PF_6$, CH_2Cl_2/CH_3CN (3/1), 20 °C, 30 min; (ii) 1 equiv **7**, 1 h; (iii) 2 equiv **5**, 1.5 equiv $[Cu(CH_3CN)_4]PF_6$, 0.4 equiv Na_2CO_3, 20 °C, 16 h; (iv) 0.75 equiv **5**, 0.75 equiv $[Cu(CH_3CN)_4]PF_6$, 0.4 equiv Na_2CO_3, 20 °C, 4 h; (v) excess KCN, 20 °C, 30 min, 12%; (vi) 1 equiv $[Cu(CH_3CN)_4]PF_6$, CH_2Cl_2/CH_3CN (2/1), 20 °C, 1 h, 99%.

free terpy chelate belonging to the ring, which may interfere with the copper salt catalyst might explain such a difference. Interestingly, a recent report, which describes the elegant preparation of another family of rotaxanes using 'click chemistry' is in agreement with this assumption.[57]

3. Conclusion

'Click chemistry', thanks to its mild reaction conditions and its high yields, is very well adapted to the synthesis of rotaxanes. It gives easy access to a wide range of new rotaxanes and in particular to those whose precursors might be relatively unstable and sensitive to the harsher conditions classically used for stoppering the systems. This is especially true in the case of the threaded copper(I) complex precursors to the catenanes and rotaxanes. Since such complexes are easily dissociated in presence of a base, necessary for Williamson ether synthesis and other reactions frequently used as ultimate stoppering step, unthreading is a common detrimental process. The use of 'click chemistry' represents a promising alternative when copper or other transition metal centres are used as template in the synthesis of interlocking or threaded ring compounds.

4. Experimental

4.1. General

All chemicals were of the best commercially available grade and used without further purification. Column chromatography was performed with silica gel 60 (Merck 9385, 230–400 mesh) or aluminium oxide 90 (neutral, act. II–III, Merck 1097). ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AVANCE 300 (300 MHz) spectrometer using deuterated solvent as the lock. The chemical shifts were referenced to residual solvent protons as internal standards (^{1}H: $CDCl_3$ 7.24 ppm, CD_2Cl_2 5.32 ppm, CD_3OD 3.31 ppm; ^{13}C: $CDCl_3$ 77.23 ppm, CD_2Cl_2 54.00 ppm). Mass spectra were obtained with a VG-BIOQ triple quadrupole in positive mode (ES-MS).

4.2. Synthesis

*4.2.1. 5,5′-Bis(azidomethyl)-2,2′-bipyridine (**7**)*

5,5′-Bis(bromomethyl)-2,2′-bipyridine **6** (157 mg, 0.46 mmol) was dissolved in a mixture of DMSO and water (1 mL, 2/1). To this solution was added NaN_3 (70 mg, 1.07 mmol). After 24 h at 60 °C, the reaction was quenched with water and dichloromethane was then added. The organic layer was separated, washed with water (three times) and dried over Na_2SO_4. The recovered solvent was evaporated to afford compound **7** with 98% yield.[58]

4.3. 2,9-Bis(*p*-hydroxymethylphenyl)-1,10-phenanthroline (15)

Bromination of 2,9-bis(*p*-tolyl)-1,10-phenanthroline **7** (2.00 g, 5.55 mmol) by *N*-bromo succinimide (3.20 g, 17.8 mmol, 3.2 equiv) was performed in presence of catalytic amounts of benzoyl peroxide in 100 mL of refluxing benzene, during 18 h. After cooling, filtration and benzene evaporation, the crude mixture of bromo derivatives **9**, **10** and **11** was dissolved in dichloromethane, washed with distilled water and then treated with a solution of NaOH (0.46 g, 11.5 mmol, 2 equiv, previously dissolved at 0 °C in 20 mL of propionic acid) at 128 °C during 24 h. After elimination of NaBr by filtration, a maximum of propionic acid was removed by reduced pressure evaporation and the remaining residue was dissolved in dichloromethane, neutralized by adding a saturated aqueous $NaHCO_3$ solution and washed with brine. The organic phase was dried (Na_2SO_4), and the solvent removed under reduced pressure yielded a yellow-brown oil, containing approximately 13% of diester **12**, 75% of aldehyde-ester **13** and 12% of dialdehyde **14**. The crude mixture was used directly, without further purification, since the last step consisted of one-pot reduction of the aldehyde functions and saponification of the ester groups of **12**, **13** and **14**. In that purpose, sodium borohydride (254 mg, 6.72 mmol, 1.2 equiv) was added in small portions at 0 °C to a solution (10 mL MeOH+10 mL NaOH 10%) containing **12**, **13** and **14** and stirred for 66 h at ambient temperature. Excess borohydride was destroyed by adding concentrated HCl to the reaction solution at 0 °C and solvents were evaporated to dryness. The crude mixture was dissolved in H_2O and CH_2Cl_2, the aqueous phase brought to pH=10 using Na_2CO_3: a brown solid precipitated that was separated by filtration. After drying under vacuum, the solid was dissolved in dry methanol, and insoluble salts were set aside. A yellow solid was obtained in three steps with a 50% yield starting from 2,9-bis(*p*-tolyl)-1,10-phenanthroline. ^{1}H NMR (300 MHz, CD_3OD): δ=8.48 (d, J=8.6 Hz, 2H, H-4,7), 8.18 (d, J=8.2 Hz, 4H, H-*o*), 8.18 (d, J=8.6 Hz, 2H, H-3,8), 7.86 (s, 2H, H-5,6), 7.53 (d, J=8.2 Hz, 4H, H-*m*), 4.74 ppm (s, 4H, CH_2); ^{13}C (75 MHz, CD_3OD): δ=155.83, 144.59, 139.50, 135.22, 128.17, 127.84, 127.07, 126.17, 121.74, 63.27 ppm. HR ES-MS: m/z=393.1565 $[M+H]^+$, calcd for $C_{26}H_{20}N_2O_2$=393.1598.

4.4. 2,9-Bis(*p*-azidomethylphenyl)-1,10-phenanthroline (16)

2,9-Bis(*p*-azidomethylphenyl)-1,10-phenanthroline **16** was prepared using modified conditions described in the literature.[47] Dialcohol **15** (180 mg, 0.46 mmol) was dissolved in anhydrous DMF (5 mL) under argon, cooled to 0 °C and diphenyl phosphorazidate (152 mg, 0.55 mmol, 1.2 equiv) was added dropwise through a syringe. After 20 min of stirring, neat 1,8-diazabicyclo[5.4.0]undec-7-ene (84 mg, 0.55 mmol, 1.2 equiv) was added at 0 °C. The mixture was then stirred for 15 h at 85 °C. After cooling, DMF was removed in vacuo, products were taken up with distilled water and CH_2Cl_2, then, the aqueous phase was extracted by small portions of CH_2Cl_2. The organic phase was washed with water, dried over sodium sulfate, and solvent evaporation yielded a yellow oil. Purification by column chromatography on silica gel using CH_2Cl_2 and increasing amounts of methanol as eluent gave a yellow powder (yield 85 mg, 0.19 mmol, 70% with respect to diphenyl phosphorazidate). ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.47 (d, J=8.2 Hz, 4H, H-*o*), 8.33 (d, J=8.4 Hz, 2H, H-4,7), 8.15 (d, J=8.4 Hz, 2H, H-3,8), 7.79 (s, 2H, H-5,6), 7.54 (d, J=8.2 Hz, 4H, H-*m*), 4.45 ppm (s, 4H, CH_2); ^{13}C (75 MHz, $CDCl_3$): δ=156.41, 146.28, 139.66, 137.24, 136.76, 128.89, 128.34, 128.26, 126.36, 120.26, 54.81 ppm; HR ES-MS: m/z=443.1705 $[M+H]^+$, calcd for $C_{26}H_{19}N_8$=443.1727.

*4.4.1. Metallo-rotaxane (**1**$^{+}$)*

The reaction was conducted under argon. In a typical procedure, macrocycle **17** (42.5 mg, 7.5×10^{-2} mmol) was dissolved in a degassed solution of dichloromethane and acetonitrile (1 mL, (7/3)). Upon addition of $[Cu(CH_3CN)_4]PF_6$ (28 mg, 7.5×10^{-2} mmol), the solution turned immediately to dark orange. The reaction mixture was stirred for 20 min and the bipyridine ligand **7** was then added (20 mg, 7.5×10^{-2} mmol). A dark red colour was instantaneously obtained. Stirring was continued for 1 h, and stopper **5** (81.5 mg, 15×10^{-2} mmol), Na_2CO_3 (3.2 mg, 3.0×10^{-2} mmol), and $[Cu(CH_3CN)_4]PF_6$ (14 mg, 3.75×10^{-2} mmol) were then added, and the reaction mixture was stirred for 5 h and checked by TLC (Silica, CH_2Cl_2/MeOH (90/10), R_f=0.88), which showed the consumption of the stopper. Supplementary addition of $[Cu(CH_3CN)_4]PF_6$ (7 mg, 1.87×10^{-2} mmol), Na_2CO_3 (1 mg, 0.93 mmol), stopper (40 mg, 7.4 mmol) and 16 h was necessary to observe the completion of the reaction. The reaction mixture was directly purified over silica gel chromatography eluted with a degassed eluent (CH_2Cl_2/MeOH (98.5/1.5) and a trace of hydrazine). The metallo-rotaxane was obtained as a red solid (98 mg, 62%). ^{1}H NMR (400 MHz, CD_2Cl_2):

δ=8.54 (d, J=8.3 Hz, 2H), 8.27 (d, J=8.3 Hz, 2H), 8.28–7.86 (m, 10H), 7.31 (d, 8.4 Hz, 4H), 7.24 (d, J=8.5 Hz, 12H), 7.18 (d, J=8.9 Hz, 4H), 7.13 (d, J=8.6 Hz, 12H), 6.88 (d, J=8.9 Hz, 4H), 6.17 (d, J=8.4 Hz, 4H), 5.48 (s, 4H), 5.17 (s, 4H), 3.76–3.65 (m, 20H), 1.27 (s, 54H). HR ES-MS m/z=1979.9833 $[M-PF_6]^+$, calcd for $CuC_{126}H_{136}N_{10}O_8$=1979.9833.

4.4.2. Metallo-rotaxane (**2**$^+$)

The same procedure was used as in the case of **1**$^+$. The metallo-rotaxane **2**$^+$ was obtained as a red solid (55 mg, 67%). ^{1}H NMR (300 MHz, CD_2Cl_2): δ=8.70 (d, J=8.4 Hz, 2H), 8.43 (d, J=8.3 Hz, 2H,), 8.30 (s, 2H), 8.03 (s, 2H), 7.92 (d, J=8.4 Hz, 2H), 7.73 (d, J=8.3 Hz, 2H), 7.56 (d, J=8.4 Hz, 4H), 7.52 (s, 2H), 7.25 (d, J=8.6 Hz, 12H), 7.19 (d, 4H), 7.18 (d, 4H), 7.14 (d, J=8.6 Hz, 12H), 6.90 (d, J=9.0 Hz, 4H), 6.54 (d, J=8.1 Hz, 4H), 5.95 (d, J=8.7 Hz, 4H), 5.18 (s, 4H), 5.15 (s, 4H), 3.83 (s, 4H), 3.72 (m, 4H), 3.59 (m, 8H), 3.50 (m, 4H), 1.28 ppm (s, 54H); ^{13}C (75 MHz, CD_2Cl_2): δ=159.58, 157.07, 156.86, 155.8, 149.03, 144.95, 144.79, 143.85, 143.71, 141.04, 139.42, 138.81, 137.85, 136.42, 132.67, 130.98, 129.67, 129.33, 129.10, 128.33, 128.23, 127.42, 126.75, 125.11, 124.86, 124.41, 123.59, 113.92, 113.49, 71.70, 71.32, 69.44, 67.62, 63.70, 62.50, 53.08, 34.77, 31.66, 30.26 ppm; ES-MS: m/z=2156.34 $[M-PF_6]^+$, calcd for $C_{140}H_{144}CuN_{10}O_8$ 2156.04.

4.4.3. Rotaxane (**23**)

Macrocycle **21** (50.8 mg, 7.5×10^{-2} mmol) was dissolved in a mixture of degassed dichloromethane and acetonitrile (1.3 mL, 3/1). To this solution was added $[Cu(CH_3CN)_4]PF_6$ (28 mg, 7.5×10^{-2} mmol). The mixture turned brown immediately. After 30 min of stirring under argon bipyridine **7** (20 mg, 7.5×10^{-2} mmol) was added. The colour of the reaction mixture turned instantaneously to deep red. Stirring was continued for 1 h, and stopper **5** (81.5 mg, 15×10^{-2} mmol), Na_2CO_3 (3.2 mg, 3.0×10^{-2} mmol), and $[Cu(MeCN)_4]PF_6$ (42 mg, 11.2×10^{-2} mmol), were then added, and the reaction mixture was stirred for 16 h. To observe the end of the reaction, another addition of stopper **5** (30 mg, 5.5 10^{-2} mmol), Na_2CO_3 (3.2 mg, 3.0×10^{-2} mmol), and $[Cu(CH_3CN)_4]PF_6$ (21 mg, 5.6×10^{-2} mmol) and 4 h of stirring were necessary. For the demetallation of **3**$^+$, some dichloromethane (5 mL) and water (5 mL), and KCN (40 mg, 0.6 mmol) were added. After vigorous stirring for 30 min, the phases were separated, the aqueous layer was extracted three times with 5 mL portions of dichloromethane and the combined organic layers were dried and the solvent removed under reduced pressure. The crude product was firstly purified by chromatography (Al_2O_3, CH_2Cl_2/MeOH (92/8)) followed by two preparative plate experiments (Al_2O_3, CH_2Cl_2/MeOH (99:1)). The desired rotaxane **23** was recovered in 12% yield as a yellow solid. ^{1}H NMR (400 MHz, CD_2Cl_2): δ=8.68 (d, J=8.0 Hz, 2H), 8.54 (d, J=1.5 Hz, 2H), 8.35 (d, J=7.8 Hz, 2H), 8.32 (s, 2H), 8.24 (d, J=1.5 Hz, 2H), 8.20 (d, J=8.4 Hz, 2H), 7.99 (d, J=8.2 Hz, 2H), 7.89 (t, J=7.8 Hz, 1H), 7.84–7.76 (m, 8H), 7.56 (dd, J=8.0 Hz, J=2.0 Hz, 2H), 7.36 (dd, J=8 Hz, J=2.0 Hz, 2H), 7.20 (d, J=8.6 Hz, 12H), 7.06 (d, J=8.6 Hz, 12H), 7.00 (d, J=8.8 Hz, 4H), 6.73 (d, J=8.7 Hz, 4H), 5.27 (s, 4H), 5.03 (s, 4H), 3.69 (t, 4H, J=5.9 Hz), 2.92 (m, 4H), 2.06 (m, 4H), 1.28 (s, 54H). HR ES-MS: m/z=2029.0956 $[M+H]^+$ calcd for $C_{137}H_{138}N_{13}O_4$: 2029.0989.

4.4.4. Metallo-rotaxane (**3**$^+$)

The reaction was conducted under inert atmosphere. Rotaxane **23** (14 mg, 6.9×10^{-6} mol) was dissolved in a mixture of dichloromethane and acetonitrile (3 mL, 2:1) and was added $[Cu(CH_3CN)_4]PF_6$ (2.6 mg, 6.9×10^{-6} mol). The solution turned immediately deep red. The reaction mixture was then stirred for 1 h and the solvents were evaporated to give a red solid. The complexation process occurred quantitatively as evidenced by ^{1}H NMR. ^{1}H NMR (300 MHz, CD_2Cl_2): δ=8.68–8.30 (complex, 8H), 8.2–7.6 (complex, 12H), 7.40 (d, J=7.7 Hz, 4H), 7.29 (d, J=8.5 Hz, 12H), 7.18 (d, J=8.5 Hz, 12H), 6.94 (d, J=7.5 Hz, 4H), 6.16 (d, J=7.5 Hz, 4H), 5.35 (s), 3.58 (br m, 4H), 2.97 (br m, 4H), 2.24 (br m, 4H), 1.32 (s, 54H). HR ES-MS: m/z=2091.0241 $[M-PF_6]^+$, calcd for $C_{137}H_{137}CuN_{13}O_4$=2091.0207.

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