J Incl Phenom Macrocycl Chem (2011) 71:507–515
DOI 10.1007/s10847-011-9986-6

ORIGINAL ARTICLE

Formation of copper(I)-templated [2]rotaxanes using "click" methodology: influence of the base, the thread and the catalyst

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Received: 4 May 2011 / Accepted: 6 May 2011 / Published online: 28 May 2011

Abstract Three new copper(I)-assembled [2]rotaxanes incorporating the same macrocycle and different axes containing a bipy, a phen or a terpy have been synthesized thanks to CuAAC reaction for attaching the stoppers. The influence of the nature of the base used for the stoppering reaction was investigated on the formation of the bipy-containing rotaxane. The yield of the [2]rotaxane synthesis was increased when using a phen as a coordinating unit in the thread with $[Cu(CH_3CN)_4](PF_6)$ as catalyst. The strong influence of the nature of the catalyst was clearly evidenced for the formation of the terpy rotaxane, increasing the yield of the stoppering reaction from 0 to 95% by just substituting the Cu(I) catalyst. Finally, the best conditions found for our systems are the use of Na_2CO_3 as a base and Cu(tren′)Br as a catalyst.

Keywords Rotaxane · Copper(I) · Click chemistry · Phenanthroline · Bipyridine · Terpyridine

Electronic supplementary material The online version of this article (doi:10.1007/s10847-011-9986-6) contains supplementary material, which is available to authorized users.

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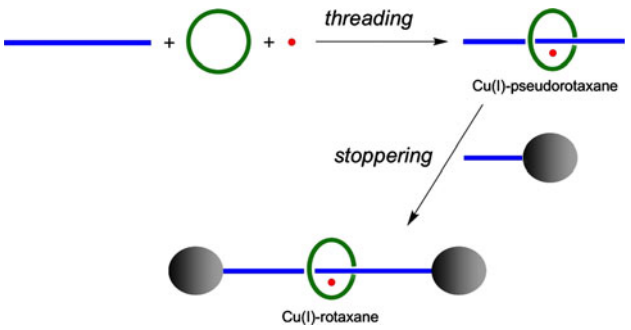
Introduction

[2]rotaxanes are nowadays considered as very accessible compounds, contrary to what was thought until the 80s [1–4]. One of the reasons for this change was the excellent yields obtained for preparing the rotaxane precursors by threading reactions [5–17]. Another important improvement was the yield increase of the stoppering reactions. However, although templated strategies are nowadays well documented, affording the desired rotaxanes or their precursors in high yields, substantial efforts are still needed to increase the yield of the stoppering reactions [18–23]. In the course of the last few years, "click reaction", which implies azides and alkynes to give 1,2,3-triazoles in a controlled fashion, [24, 25] has been extensively used and sometimes considered as the "holy grail" of stoppering reactions thanks to its generally good yields and high tolerance to many functions [26–28]. Indeed, many laboratories, including ours, currently use copper-catalyzed azide-alkyne cycloaddition (CuAAC) with much success for the elaboration of rotaxanes [29–32]. However, in most cases, the CuAAC has not really been studied methodologically in order to optimize the conditions and obtain the highest possible yields. In particular, there is a lack of information concerning the elaboration of rotaxane from Cu(I)-complexes, this family of compounds being particularly important in relation to molecular machine prototypes [33, 34].

We would now like to report the synthesis of several [2]rotaxanes whose axles contain different ligands, namely 2,2′-bipyridine (bipy), 1,10-phenanthroline (phen) and 2,2′,6′,2″terpyridine (terpy) by using the threading-stoppering strategy, as described in Scheme 1. Several reaction conditions for CuAAC stoppering reactions were investigated.



Scheme 1 Principle of formation of a [2]rotaxane by the threading and stoppering strategy; the *small spheres* represent Cu(I), and the *big spheres* represent stoppers

In order to test the influence of the base used during the stoppering reaction, we synthesized a [2]rotaxane containing a non-hindered bipy on the axle by changing the base. The use of a bipy rather than a phen is justified by the fact that bipy is a less powerful chelate than phen, and therefore the intermediate [2]pseudorotaxane should be more sensitive to the basic conditions of stoppering reaction.

As indicated on Fig. 1, [2]rotaxane $\mathbf{5}^+$ was prepared in a few steps from relatively easily accessible compounds. Ligands **1** and **2** were synthesized according to published procedures [35, 36]. As for preparing other copper(I)-complexed [2]rotaxanes, the synthesis sequence started with a threading reaction. Threading bipy **1** into the 30-membered ring **2** afforded the corresponding [2]pseudorotaxane $\mathbf{3}^+$. Subsequently, this compound was directly engaged in a stoppering reaction without any purification and characterization. The stoppering reaction was performed with $[Cu(CH_3CN)_4](PF_6)$ as catalyst in the presence of a base (0.5 equivalent). Various bases were tested: lutidine, sodium carbonate, and none. The stopper **4**, bearing an azide function, [37] was added in slight excess. The resulting copper(I)-complexed [2]rotaxane $\mathbf{5}^+$ was then purified by silica chromatography.

The nature of the base strongly influenced the reaction yield. Whereas 2,6-lutidine allowed to get the target [2]rotaxane in moderate yields (30%), the use of a base such as sodium carbonate led to compound $\mathbf{5}^+$ in a satisfying yield of 61%. Cu(I) complexes are sensitive to bases, which could explain the differences observed. Indeed, whereas lutidine is perfectly soluble in the mixture of solvents used for the stoppering reaction (CH_2Cl_2/CH_3CN: 3/1), sodium carbonate is hardly soluble. Consequently, whereas the number of equivalents of base added in the

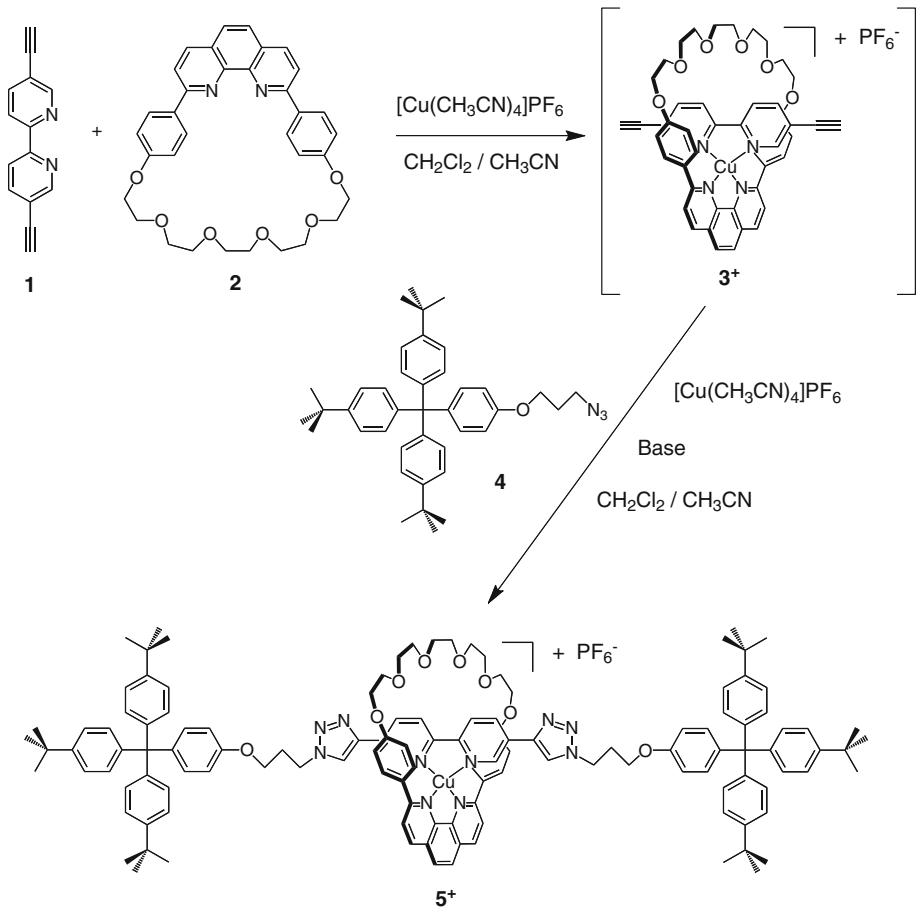


Fig. 1 Synthesis of copper(I)-complexed [2]rotaxane $\mathbf{5}^+$

mixture was the same, the real quantity of base present in the layer containing the Cu(I) complex was certainly lower in the case of sodium carbonate, making the medium less aggressive towards the copper complexes present in the solution. This solubility difference could explain why the yield increased when sodium carbonate was used. This yield is similar to that reported for a similar bipy-incorporating [2]rotaxane, synthesized from a diazide axle and a propargyl-bearing stopper [31].

An unexpected result was obtained when the stoppering reaction was performed without any base. Indeed, whereas we did not expect to form any rotaxane or only trace amounts, compound $\mathbf{5}^{+}$ was formed in 45% yield, which was even more than when lutidine was used. The product could not originate from the non-catalyzed Huisgen cycloaddition because this reaction occurs only at high temperature (except with activated acetylenes, [38] which was not the case here) and the mixture was reacted at room temperature. We suggest that partial decoordination of the thread, which could thus play the role of the catalytic base, could explain the formation of compound $\mathbf{5}^{+}$ in such a yield. This partial decoordination would be more limited than in the presence of a soluble base like 2,6-lutidine, as suggested by the comparison of the yields.

In order to compare the influence of the coordinating moiety belonging to the axle, we synthesized a [2]rotaxane incorporating a 2,9-diphenyl-1,10-phenanthroline unit in the axle instead of the bipy. The compounds used for the synthesis of the corresponding [2]rotaxane and the final rotaxane itself are represented in Fig. 2. We have already reported the synthesis of a phen bearing azide functions [39]. But its synthesis was tedious and involved low-

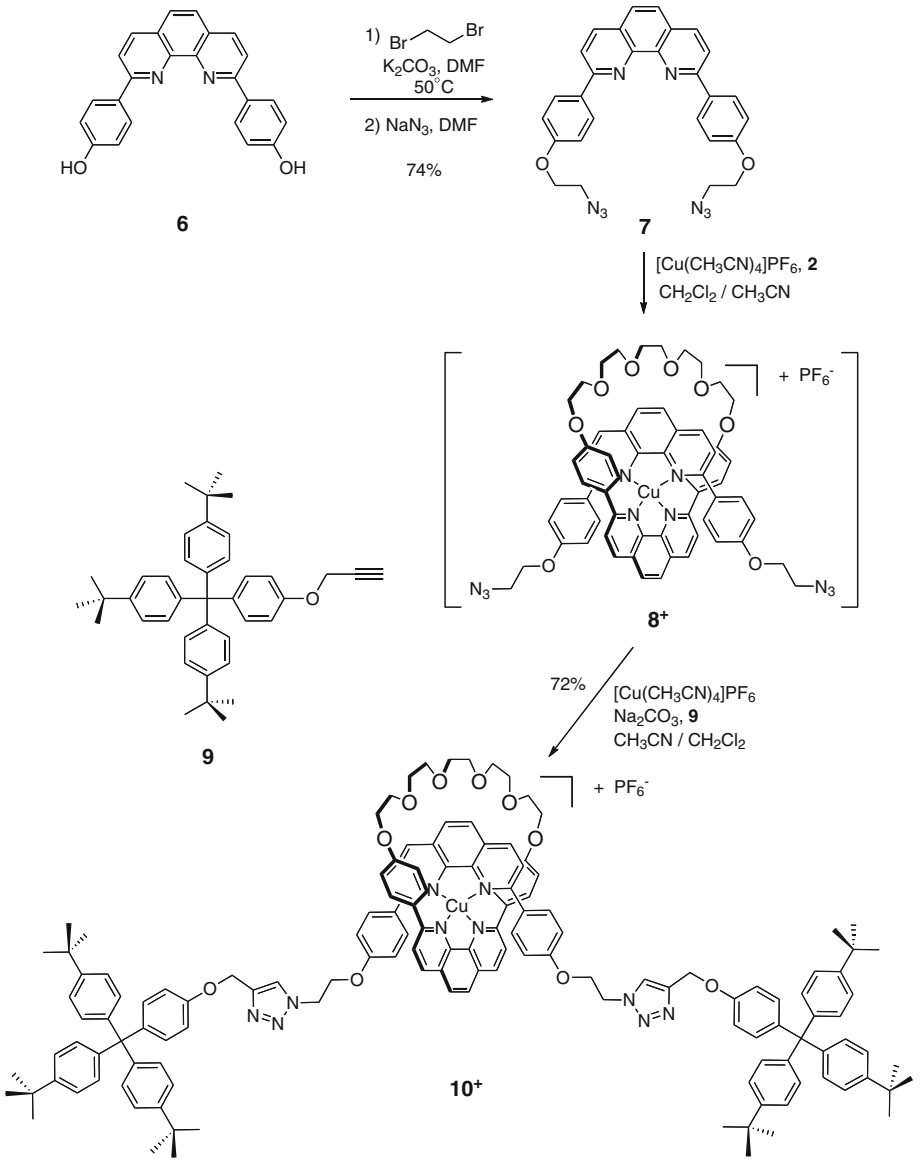


Fig. 2 Synthesis of [2]rotaxane $\mathbf{10}^{+}$

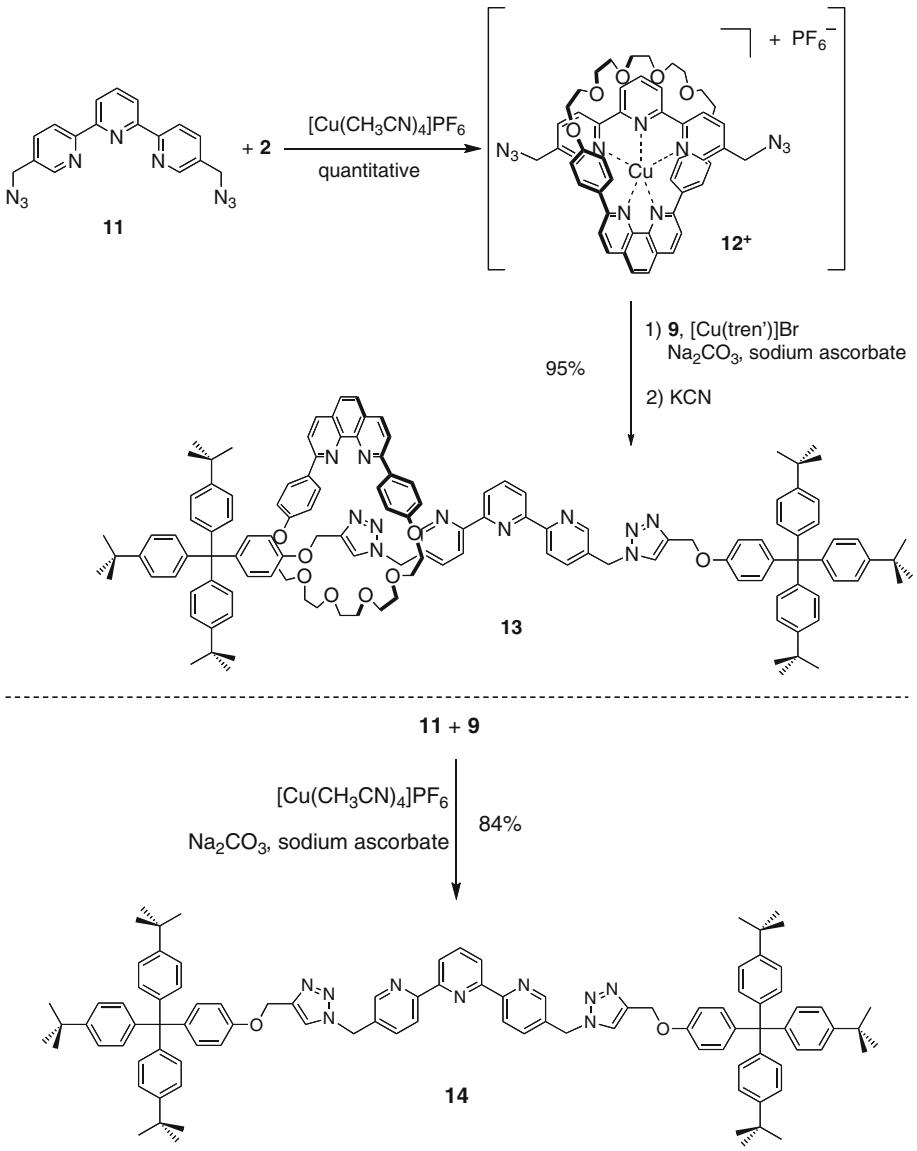


Fig. 3 Synthesis of a terpy-containing [2]rotaxane **13** by CuAAC, as well as the related dumbbell **14**

yielding steps. Therefore, a more accessible phen unit incorporating two azide functions was designed. Dialkylation of the 2,9-di(*p*-hydroxy-phenyl)-1,10-phenanthroline **6** in presence of dibromoethane, followed by substitution of the corresponding bromides by sodium azide in DMF led to diazide **7** with an overall yield of 74% (Fig. 2). [2]pseudorotaxane $\mathbf{8}^+$ was then obtained quantitatively by mixing an equimolar mixture of diazide **7**, macrocycle **2** and $[Cu(CH_3CN)_4](PF_6)$ in CH_2Cl_2/CH_3CN (3/1). This [2]pseudorotaxane $\mathbf{8}^+$ was subsequently stoppered in presence of propargyl stopper **9** [31], Na_2CO_3 and $[Cu(CH_3CN)_4](PF_6)$ to give the desired [2]rotaxane $\mathbf{10}^+$ with a good yield of 72%. On one hand, this better yield, in comparison with the one obtained with the bipy moiety, could be explained by a more stable pseudorotaxane $\mathbf{8}^+$ due to 2,9-substituents of phen and a longer axle. This observation stresses the importance of the chelating moiety in the axle: the more stable the intermediate copper(I) pseudorotaxane, the less unthreading during the synthesis of rotaxanes by CuAAC and the higher the yields. On the other hand, this yield is in good agreement with the yield of a previously published [2]rotaxane incorporating the same macrocycle and a similar axis, using the same conditions [39].

We also attempted to prepare a [2]rotaxane incorporating a terpy axle. Only few examples of reactions of click chemistry on terpyridinic compounds have been reported in the literature [40–45]. The threading reaction between the copper(I) complex of ring **2** and the terpy thread **11** [44, 45] led quantitatively to the expected [2]pseudorotaxane $\mathbf{12}^+$ (Fig. 3) as confirmed by a proton NMR study (Fig. 4). All the signals were assigned (see experimental part and supplementary materials), and the phenyl protons labeled o and m showed a strong upfield shift, resulting from their

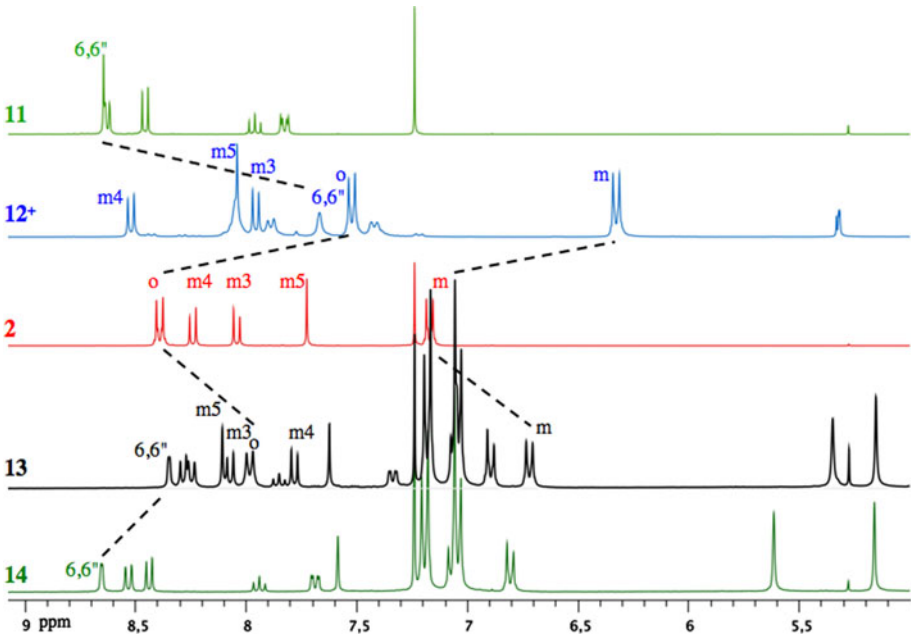


Fig. 4 Partial ^{1}H NMR spectra of a terpy-containing dumbbell **14**, the related [2]rotaxane **13**, the macrocycle **2**, the copper(I) pseudorotaxane $\mathbf{12}^+$ and the terpy precursor **11** in $CDCl_3$ (except for $\mathbf{12}^+$ in CD_2Cl_2)

presence in the anisotropy cone of the terpy axle. Similar upfield shifts were also observed for the 6 and 6″ protons of the terpy moiety.

The first attempt to synthesize the [2]rotaxane **13** (Fig. 3) by click chemistry was made using the following optimized "standard" conditions: a CH_2Cl_2/CH_3CN (2/1) mixture with Na_2CO_3 as a base and 0.5 equivalents of $[Cu(CH_3CN)_4](PF_6)$ for 5 days. No copper(I) [2]rotaxane could be isolated. By comparison with the results concerning the bipy-based [2]rotaxane $\mathbf{5}^+$ and the phen analog $\mathbf{10}^+$, we concluded that the presence of terpy was detrimental to the formation of the desired stoppered complex, probably because the copper(I) centers supposed to act as catalysts were not coordinated to any protective ligand. It thus appeared necessary to use an ancillary ligand, able to partially complex the catalytic copper(I) center and protect it towards potentially coordinating fragments of the compounds to be "clicked".

We recently reported the efficiency of such a protected catalyst, [Cu(tren′)]Br, first described and used by Vincent et al., [46, 47] in the synthesis of linear multi-rotaxanes, incorporating terpy [44, 45]. Consequently, we mixed the [2]pseudorotaxane $\mathbf{12}^+$ (Fig. 3) with the acetylenic stopper **9** (three equivalents), [Cu(tren′)]Br (0.25 equivalent), sodium carbonate as a base (0.5 equivalent), and sodium ascorbate (1.3 equivalent) as a reductant. After 3 days under argon, the NMR spectrum of the crude reaction mixture showed total conversion of azide functions to 1,2,3-triazoles. In order to confirm the threaded nature of the non-isolated corresponding copper(I) [2]rotaxane and to facilitate purification, the mixture was demetalated with an excess of KCN and submitted to purification by alumina chromatography. This treatment afforded the free [2]rotaxane **13** in 95% yield. This excellent yield emphasized the efficiency of [Cu(tren′)]Br as a catalyst, since it was the best yield of the double click stoppering reactions among the various [2]rotaxanes described in the present report.

The ES-MS and the ^{1}H NMR spectra were in accordance with the postulated structure of **13**. The ES-MS spectrum showed two peaks, one at *m/z* 1996.25 corresponding to $(\mathbf{13} + H^+)$ (calcd 1996.09), and the other at *m/z* 998.65 corresponding to $([\mathbf{13} + 2H]^{2+}/2)$ (calcd 998.55). The free dumbbell of rotaxane **14** has also been synthesized in 84% yield thanks to click chemistry by mixing compounds **9** and **11** in the presence of Cu(I). Thus, the ^{1}H NMR spectrum of this dumbbell-shaped molecule could be compared to that of the rotaxane as discussed below. It can be noticed that this reaction occurred very efficiently with $Cu(CH_3CN)_4PF_6$ whereas [Cu(tren′)]Br was detrimental to the formation of rotaxane **13**. It is likely that $Cu(CH_3CN)_4PF_6$ as a catalyst participates to the coordination of the terpy incorporated in the rotaxane and thus interferes too much with pseudorotaxane $\mathbf{12}^+$ to play its role of catalyst without destroying this precursor $\mathbf{12}^+$. On the contrary, [Cu(tren′)]Br is strongly protected and too hindered to interfere with this intermediate.

The ^{1}H NMR spectrum of rotaxane **13** (Fig. 4) was significantly different from the superposition of the spectra of both the macrocycle **2** and the symmetrical terpy dumbbell compound **14** (Fig. 3). This confirmed that compound **13** was a real rotaxane and that the stoppers prevented unthreading of the ring. The protons labeled o, m, 6 and 6″ were again upfield shifted, but less than in the presence of copper(I) like in the [2]pseudorotaxane $\mathbf{12}^+$.

Conclusion

To conclude, CuAAC was investigated in detail in order to optimize the yield of stoppering for the elaboration of copper(I)-complexed rotaxanes or their metal-free forms. We applied this reaction to the synthesis of three [2]rotaxanes containing each time the same macrocycle but a different axis. We could thus obtain rotaxanes encompassing a bipy, a phen or a terpy in the axis. Particularly noteworthy is the yield obtained for the terpy-containing [2]rotaxane which was dramatically improved by using the recently reported catalyst [46, 47] containing a copper(I) center protected with a tripodal chelate. As a consequence, this methodology paves the way to the elaboration of more complex structures, such as multi-rotaxanes with different kinds of chelating unit, in relation to new molecular machines incorporating several coordinating units in their axis or in the threaded rings.

Experimental part

General procedure for the synthesis of [2]rotaxane $\mathbf{5}^{+}$

Threading procedure Macrocycle **2** (143.2 mg, 250 μmol) was dissolved in 5 mL of distilled and degassed dichloromethane. 5 mL of a solution of $[Cu(CH_3CN)_4]PF_6$ (94.6 mg, 250 μmol) in distilled and degassed acetonitrile were subsequently added and the resulting solution was stirred for 15 min. Then, 5 mL of a solution of bipy **1** (51.7 mg, 250 μmol) were added to the previous solution and the mixture was stirred overnight. The solvents were evaporated, and the resulting precipitate was used as-is for the next step.

Stoppering procedure A third of the previous Cu(I)-complex (81 mg, 83 μmol), $Cu(CH_3CN)_4PF_6$ (16 mg, 43 μmol) and 0.5 equivalent of base were dissolved in 3 mL of degassed dichloromethane and 1 mL of acetonitrile. The mixture was stirred at room temperature under argon for 5 days. Then, the solvents were evaporated and the resulting residue was purified by silica chromatography (eluent: CH_2Cl_2/MeOH/CH_3CN: 98/1/1) to afford the desired [2]rotaxane $\mathbf{5}^{+}$.

^{1}H-NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 8.59$ (d, $^3J = 8.2$ Hz, 2H, H-m4), 8.44 (d, $^4J = 1.4$ Hz, 2H, H-3), 8.37 (dd, $^3J = 8.4$ Hz, $^4J = 2.0$ Hz, 2H, H-2), 8.30 (d, $^3J = 8.4$ Hz, 2H, H-1), 8.10 (s, 2H, H-m3), 8.09 (s, 2H, H-4), 8.03 (d, $^3J = 8.4$ Hz, 2H, H-m5), 7.45 (d, $^3J = 8.6$ Hz, 4H, H-o), 7.24 (d, $^3J = 8.6$ Hz, 12H, H-11), 7.18 (d, $^3J = 8.7$ Hz, 4H, H-9), 7.14 (d, $^3J = 8.6$ Hz, 12H, H-10), 6.80 (d, $^3J = 8.9$ Hz, 4H, H-8), 6.17 (d, $^3J = 8.8$ Hz, 4H, H-m), 4.66 (t, $^3J = 6.8$ Hz, 4H, H-5), 4.01 (t, $^3J = 5.7$ Hz, 4H, H-7), 4.80–4.60 (m, 20H, H-α, H-β, H-γ, H-δ, H-ε), 2.46 (q, $^3J = 6.1$ Hz, 4H, H-6), 1.29 (s, 54H, H-12) ppm. **MS (ES)** *m/z* (%) = 2009.101 (100) $[M–PF_6]^+$ (calcd: 2009.019 for $[C_{128}H_{140}CuN_{10}O_8]^+$).

Diazidophenanthroline 7 To a solution of 2,9-di(*p*-phenol)-1,10-phenanthroline **6** (500 mg, 1.372 mmol) in DMF (50 mL) was added successively 1,2-dibromoethane (6 mL, 68.7 mmol) and K_2CO_3 (3.8 g, 27.494 mmol) and the solution was stirred 48 h at 50 °C. DMF was removed under vacuum and the residue taking up in H_2O–CH_2Cl_2. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), the organic phases were combined, dried over $MgSO_4$, filtered and concentrated under vacuum. To the crude material in DMF was added NaN_3 (1.79 g, 27.44 mmol) and the solution was stirred overnight at 100 °C. DMF was removed under vacuum and the residue taking up in H_2O–CH_2Cl_2. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), the organic phases were combined, dried over $MgSO_4$, filtered and concentrated under vacuum. The residue was purified by flash column chromatography on silica gel eluting with CH_2Cl_2 to give the desired product as a white powder (512 mg, 1.017 mmol, 74% yield).

^{1}H RMN (300 MHz, CD_2Cl_2) $\delta = 8.44$ (d, $^3J = 8.8$ Hz, 4H, H-o), 8.31 (d, $^3J = 8.5$ Hz, 2H, H-4), 8.12 (d, $^3J = 8.5$ Hz, 2H, H-3), 7.79 (s, 2H, H-5), 7.16 (d, $^3J = 8.8$ Hz, 4H, H-m), 4.28 (t, $^3J = 5.1$ Hz, 4H, H-a), 3.67 (t, $^3J = 5.1$ Hz, 4H, H-b) ppm. **^{13}C RMN** (75 MHz, CD_2Cl_2) $\delta = 49.9$, 66.8, 114.5, 118.8, 125.3, 127.3, 128.5, 132.4, 136.4, 145.7, 155.4, 159.2 ppm. **MS (ES)** *m/z* (%) = 1027.36 (100) $[2M + Na]^+$ (calcd: 1027.36 for $[(C_{28}H_{22}N_8O_2)_2Na]^+$).

[2]Rotaxane $\mathbf{10}^{+}$ Macrocycle **2** (14.3 mg, 25.2 μmol) and $[Cu(CH_3CN)_4]PF_6$ (9.4 mg, 25.2 μmol) were dissolved in 2 mL of degassed CH_2Cl_2 and 1 mL of degassed CH_3CN. To this solution was subsequently added via *canula* a solution of diazide **7** (14.7 mg, 25.2 μmol) in 2 mL of degassed CH_2Cl_2. The resulting solution was stirred 1 h, and the solvents were then evaporated to give, without any further purification, the desired [2]pseudorotaxane $\mathbf{8}^{+}$ in quantitative yield according to the ^{1}H NMR spectrum. To a solution of the corresponding [2]pseudorotaxane $\mathbf{8}^{+}$, Na_2CO_3 (1.4 mg, 12.6 μmol), sodium ascorbate (10 mg, 50.4 μmol) and $Cu(CH_3CN)_4PF_6$ (4.7 mg, 12.6 μmol) in a mixture of dichloromethane (1 mL) and acetonitrile (1 mL) was added a solution of the stopper **9** (41 mg, 75.6 μmol) in dichloromethane (2 mL) and the resulting mixture was stirred overnight and concentrated under vacuum. The residue was purified by flash column chromatography on silica gel eluting with a mixture of CH_2Cl_2 and MeOH (99.5/0.5–97/3) to give the desired [2]rotaxane $\mathbf{10}^{+}$ as a dark red solid (40.9 mg, 18.4 μmol, 72% yield).

^{1}H RMN (300 MHz, $CDCl_3$) $\delta = 8.63$ (d, $^3J = 8.8$ Hz, 4H, H-4), 8.32 (d, $^3J = 8.4$ Hz, 2H, H-m4), 8.25 (s, 2H, H-5), 7.86 (d, $^3J = 8.4$ Hz, 2H, H-3), 7.84 (s, 2H, H-m5), 7.83 (s, 2H, H-g), 7.76 (d, $^3J = 8.3$ Hz, 4H, H-m3), 7.46 (d, $^3J = 8.6$ Hz, 4H, H-o′), 7.27 (d, $^3J = 8.6$ Hz, 4H, H-o), 7.24 (d, $^3J = 8.5$ Hz, 12H, H-b), 7.20 (d, $^3J = 8.9$ Hz, 4H, H-d), 7.15 (d, $^3J = 8.5$ Hz, 12H, H-c), 6.04 (d, $^3J = 8.6$ Hz, 4H, H-m′), 5.97 (d, $^3J = 8.6$ Hz, 4H, H-m), 5.30 (s, 4H, H-f), 4.65 (t, $^3J = 4.7$ Hz, 4H, H-h), 3.89 (t, $^3J = 4.7$ Hz, 4H, H-i), 3.83 (s, 4H, H-ε), 3.69-3.75 (m, 4H, H-δ), 3.58-3.62 (m, 4H, H-γ), 3.52-3.58 (m, 4H, H-β), 3.48 (t, $^3J = 4.7$ Hz, 4H, H-α), 1.28 (s, 54 H, H-a) ppm. **MS (ES)** *m/z* (%) = 2218.081 (100) $[M–PF_6]^+$ (calcd: 2218.071 for $[C_{142}H_{148}CuN_{10}O_{10}]^+$).

Diazido [2]pseudorotaxane 12^+ To a degassed solution of macrocycle **2** (15.3 mg, 27.0 μmol) in dry CH_2Cl_2 (0.7 mL) was added a solution of $[Cu(CH_3CN)_4]PF_6$ (10.2 mg, 27.0 μmol) in dry and degassed CH_3CN (0.3 mL) and it was stirred at room temperature during 15 min under inert atmosphere. A degassed solution of di(azidomethyl)terpyridine **11** (9.5 mg, 27.6 μmol) in dry CH_2Cl_2 (2.1 mL) was then added to this orange solution via canula; the mixture turned immediately intensely dark red and was reacted during 3 h. After evaporation of the solvents, the crude [2]pseudorotaxane **12^+** (35 mg, 27.0 μmol) was checked by ^{1}H NMR in CD_2Cl_2.

^{1}H-NMR (300 MHz, CD_2Cl_2, 25 °C): $\delta = 8.52$ (d, $^3J = 8.2$ Hz, 2H, H-m4), 8.05 (m, 3H, H-3′,4′,5′), 8.04 (s, 2H, H-m5), 7.96 (d, $^3J = 8.2$ Hz, 2H, H-m3), 7.89 (d, $^3J = 8.1$ Hz, 2H, H-3,3″), 7.67 (s, 2H, H-6,6″), 7.52 (d, $^3J = 8.6$ Hz, 4H, H-o), 7.42 (d, $^3J = 8.1$ Hz, 2H, H-4,4″), 4.15 (s, 4H), 3.93–3.90 (m, 4H, H-α), 3.82–3.72 (m, 16H, H-β, H-γ, H-δ, H-ε).

Demetalated [2]rotaxane 13 [2]pseudorotaxane **12^+** (35 mg, 27.0 μmol), acetylenic stopper **9** (44.2 mg, 81.4 μmol), Na_2CO_3 (1.6 mg, 15 μmol), [Cu(tren′)]Br catalyst (12.5 mg, 6.9 μmol), sodium ascorbate (6.9 mg, 35 μmol) were introduced in 1.4 mL of distilled and degassed CH_2Cl_2 and 0.7 mL of degassed anhydrous CH_3CN. The mixture was stirred for 3 days under argon. KCN (31 mg, 476 μmol) diluted in the minimum amount of distilled water was then added and the mixture was stirred for 4 h. Then, 20 mL of distilled water were added and this layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, the solvent was then evaporated and the resulting yellow residue was purified by alumina chromatography. A gradient of elution (CH_2Cl_2/MeOH) gave 52 mg (25.8 μmol) of pure [2]rotaxane **13** (95%).

^{1}H-NMR (500 MHz, CD_2Cl_2, 25 °C): $\delta = 8.43$ (d, $^4J = 1.6$ Hz, 2H, H-6,6″), 8.32 (d, $^3J = 7.8$ Hz, 2H, H-3′,5′), 8.27 (d, $^3J = 8.3$ Hz, 2H, H-3,3″), 8.13 (d, $^3J = 8.4$ Hz, 2H, H-m4), 8.11 (s, 2H, H-m5), 8.03 (d, $^3J = 8.4$ Hz, 2H, H-o), 7,88 (t, $^3J = 7.8$ Hz, 1H, H-4′), 7.85 (d, $^3J = 8.4$ Hz, 2H, H-m3), 7.67 (s, 2H, H-g), 7.43 (dd, $^3J = 8.3$ Hz, $^4J = 1.6$ Hz, 2H, H-4,4″), 7.23 (d, $^3J = 8.6$ Hz, 12H, H-b), 7.15 (d, $^3J = 8.6$ Hz, 12H, H-c), 7.13 (d, $^3J = 8.9$ Hz, 4H, H-d), 6.91 (d, $^3J = 8.9$ Hz, 4H, H-e), 6.74 (d, $^3J = 8.4$ Hz, 4H, H-m), 5.43 (s, 4H, H-h), 5.15 (s, 4H, H-f), 4.00 (t, $^3J = 5.9$ Hz, 4H, H-α), 3.60 (t, $^3J = 5.9$ Hz, 4H, H-β), 3.58 (s, 4H, H-ε), 3.53 (s, 8H, H-γ, H-δ), 1.28 (s, 54H, H-a) ppm. **MS (ES)** *m/z* (%) = 1996.25 (100) $[M + 1H]^+$ (calcd: 1996.09 for $[C_{131}H_{140}N_{11}O_8H_4]^+$), 998.65 (94) $[M + 2H]^{2+}$ (calcd: 998.55 for $[C_{131}H_{141}N_{11}O_8H_4]^{2+}/2$).

Terpy dumbbell 14 Di(azidomethyl)terpyridine **11** (0.040 g, 116 μmol) was dissolved in 750 μL of distilled and degassed CH_2Cl_2 under argon. $[Cu(CH_3CN)_4]PF_6$ (0.063 g, 170 μmol) dissolved in 350 μL of degassed CH_3CN was added under argon. The dark green solution was agitated for 2 h. Then, stopper **9** (158 mg, 291 μmol) was added under argon, as well as Na_2CO_3 (5.5 mg, 52.4 μmol) and sodium ascorbate (35 mg, 175 μmol). The mixture was stirred for 18 h under argon. KCN (111 mg, 1.7 mmol) diluted in the minimum amount of distilled water was then added and the mixture was stirred for 2 h 30 min. Then, 20 mL of distilled water were added and this layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, the solvent was then evaporated and the resulting yellow residue was purified by alumina chromatography (elution ether/ethylacetate) to give 140 mg (98 μmol) of pure **15** (84%).

^{1}H RMN (300 MHz, $CDCl_3$, 25 °C): δ (ppm) = 8.67 (d, $^4J = 2.1$ Hz, 2H, H-6,6″), 8.55 (d, $^3J = 8.2$ Hz, 2H, H-3,3″), 8.44 (d, $^3J = 7.7$ Hz, 2H, H-3′, H-5′), 7.94 (t, $^3J = 7.9$ Hz, 1H, H-4′), 7.69 (dd, $^3J = 8.2$, $^4J = 2.5$ Hz, 2H, H-4,4′), 7.59 (s, 2H, H-7), 7.20 (d, $^3J = 8.8$ Hz, 12H, H-12), 7.07 (d, $^3J = 9.0$ Hz, 4H, H-10), 7.05 (d, $^3J = 8.8$ Hz, 12H, H-11), 6.81 (d, 4H, H-9, $^3J = 9.0$ Hz), 5.61 (s, 4H, H-2), 5.16 (s, 4H, H-8), 1.26 (s, 54H, H-13) ppm.

Acknowledgments We thank the Agence Nationale de la Recherche (ANR no. 07-Blan-0174, MOLPress) for its financial support as well as the French Ministry of Research for a fellowship to YT.

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