

Efficient synthesis of a labile copper(I)-rotaxane complex using click chemistry

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Abstract—Copper(I)-induced threading of 5,5'-diazidomethyl-2,2'-bipyridine through a coordinating ring followed by reaction of a propargyl ether attached to a stopper group leads to the desired rotaxane in 62% yield. The reaction is carried out under the 'click chemistry' conditions with 0.75 equiv of additional copper(I).

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The field of rotaxanes is particularly active, mostly in relation to molecular machines¹ and new materials.² The synthesis of these compounds is sometimes limited by the stoppering reaction, which has to be compatible with the other functions present in the precursor. Various organic³ or coordination⁴ chemistry reactions have been used but the yields are not always satisfactory particularly in the case of unstable rotaxane precursors.

Our group has extensively used copper(I) as a template,⁵ able to gather the various pieces of the future rotaxane and/or to induce threading of a coordinating string-like fragment through a ring. If the string and the ring contain sterically hindering chelates of the 2,9-dianisyl-1,10-phenanthroline (dap) family, a very stable copper(I)-complexed precursor is obtained which will most of the time survive, at least in part, the stoppering reaction conditions. In this respect, many such rotaxanes have been prepared which contain a $\text{Cu}(\text{dap})_2^+$ core. Very different is the situation when one of the two chelates coordinated to the copper(I) center is not encumbered. However, such rotaxanes would be particularly interesting as molecular machine prototypes since they are much faster-moving species than their highly shielded analogues.⁶ A reasonably efficient strategy has been (i) to attach a first stopper to the string, (ii) proceed to

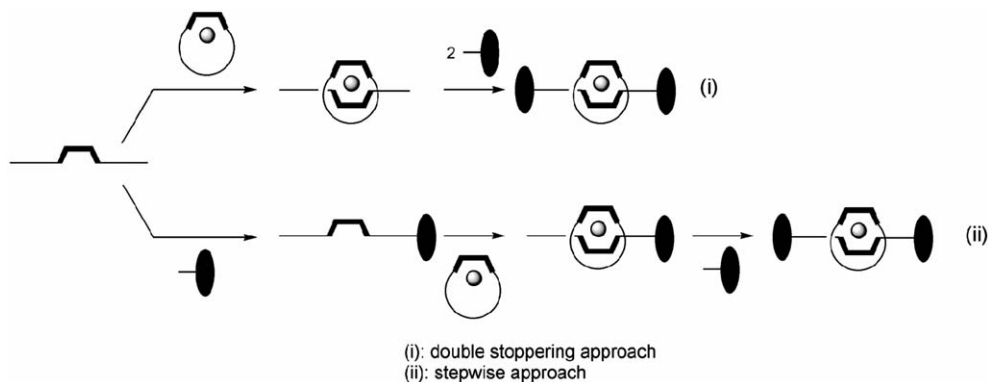
the threading reaction, and, finally, (iii) attach the second stopper. In such an approach, one can minimize the unthreading reaction leading to dissociation of the precursor. Both approaches are schematically represented in [Scheme 1](#).

The stepwise approach (ii) of [Scheme 1](#), using the Williamson reaction, has been applied recently when the fragment to be threaded incorporates a nonhindering chelate.⁶ The poor overall yield of this procedure, probably originating from the harsh Williamson reaction conditions used, prompted us to explore alternative stoppering reactions. So-called 'click chemistry', recently developed by Sharpless and coworkers,⁷ looked particularly attractive due to its mild conditions.

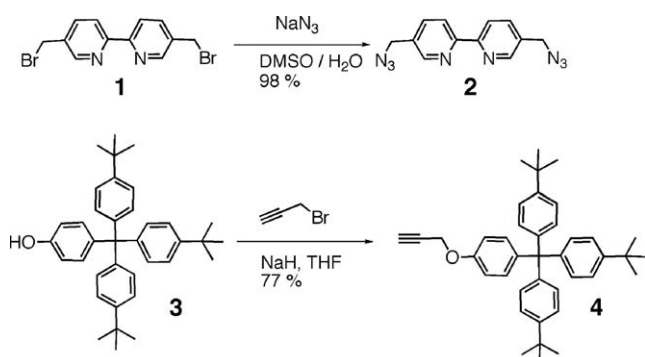
In fact, we could at the same time (1) circumvent the tedious two-step procedure (ii) of [Scheme 1](#) and replace it by the direct approach (i) and, (2) use a particularly unstable copper(I) complex as precursor, in which the threaded chelate is a 2,2'-bipyridine substituted at the 5 and 5' positions only. The synthesis of the precursors **2** and **4** bearing an azide or acetylenic function, respectively, is represented in [Scheme 2](#). Bipyridine **2** was prepared in excellent yield (98%) starting from the readily available compound **1**⁸ in presence of sodium azide (2.3 equiv) in a mixture of DMSO and water (2/1). Williamson ether synthesis led to the formation of stopper **4**. Compound **3**⁹ was reacted with an excess of propargyl bromide (NaH, THF, 45 °C, 24 h) to afford the propargyl-bearing stopper **4** in 77% yield.

Keywords: Rotaxane; Click chemistry.

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Scheme 1. Schematic representation of possible strategies to prepare the rotaxane.



Scheme 2. Synthesis of the precursors **2** and **4**.

The copper(I)-directed threading reaction between **2** and the 30-membered ring **5**¹⁰ is depicted in Figure 1, as well as the double stoppering reaction.

In a typical procedure, the macrocycle **5** (7.5×10^{-5} mol) was dissolved in a degassed solution of dichloromethane and acetonitrile (1 mL, (7/3)). Upon addition of the copper(I) salt (1 equiv), the solution turned immediately

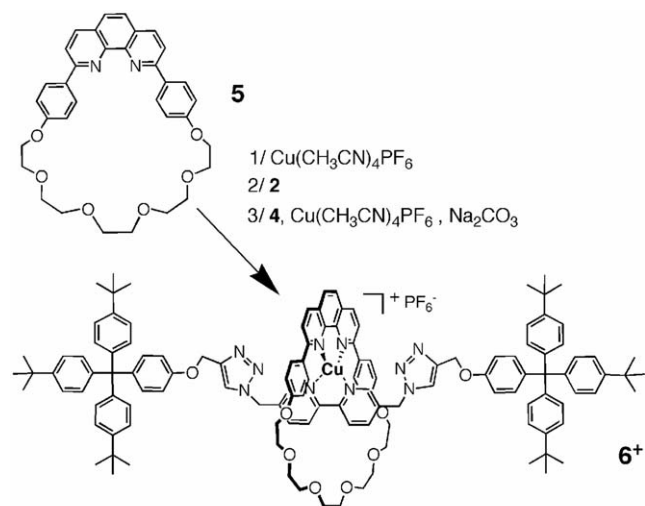


Figure 1. The threading and stoppering reactions leading to rotaxane **6**⁺.

to dark orange. The reaction mixture was stirred for 20 min and the bipyridine ligand **2** was then added. A dark red solution was instantaneously obtained. This color, which is characteristic of copper(I) complexes of aromatic diimine ligands, indicates that the threading process occurred efficiently. The next step concerned the stoppering reaction using a copper(I) catalyzed 1,3-dipolar cycloaddition reaction ('click' chemistry). To the solution containing the threaded complex generated in situ was added the acetylenic stopper **4** (2 equiv), 0.5 equiv of the copper(I) catalyst ($\text{Cu}(\text{CH}_3\text{CN})_4\text{PF}_6$), and a base (Na_2CO_3) (0.4 equiv). This reaction mixture was stirred for 5 h and then checked by TLC (Silica, $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (90/10), $R_f = 0.88$) which clearly showed the consumption of compound **4**. Nevertheless, the addition of an other portion of copper(I) salt (0.25 equiv), stopper **4**, and Na_2CO_3 and 16 h of stirring were necessary to observe the end of the reaction. Without work-up, the reaction mixture was directly purified over silica gel chromatography eluted with the degassed eluent ($\text{CH}_2\text{Cl}_2/\text{MeOH}$ (98.5/1.5) and a trace of hydrazine). The metallo-rotaxane **6**⁺ was obtained as a red solid (98 mg, 62%) and no other by-products as non-threaded species were isolated. It is noteworthy that the presence of the reducing agent in the eluent is crucial: without hydrazine, the isolated yield of the final rotaxane **6**⁺ dropped from 62% to 28%. ¹H NMR spectroscopy, as well as high-resolution ES-MS measurements ($m/z = 1979.9833$ for **6**⁺, calcd 1979.9833), confirmed the expected structure of the rotaxane **6**⁺. A cyclic voltammetric experiment in CH_3CN showed a reversible signal at 0.49 V versus a silver quasi-reference electrode, in agreement with previous electrochemical data on related compounds.

The mild reaction conditions of the 'click chemistry' methodology is clearly very well adapted to the synthesis of rotaxanes whose copper(I) complex precursors are relatively unstable, as in the present example. It is expected that such methodology applied here for the construction of a simple copper(I) [2]rotaxane will also be suitable for more elaborated rotaxanes. Noteworthy, a recent report describes the elegant preparation of another family of rotaxanes using click chemistry.¹¹ In this case, copper(I) plays the role of both the template and the catalyst.

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