

A Strategy Utilizing a Recyclable Macrocycle Transporter for the Efficient Synthesis of a Triazolium-Based [2]Rotaxane

Sovy Chao, Camille Romuald, Karine Fournel-Marotte, Caroline Clavel, and Frédéric Coutrot*

Abstract: A general synthesis of triazolium-containing [2]rotaxanes, which could not be accessed by other methods, is reported. It is based on a sequential strategy starting from a well-designed macrocycle transporter which contains a template for dibenzo-24-crown-8 and a *N*-hydroxysuccinimide (NHS) moiety. The sequence is: 1) synthesis by slippage of a [2]rotaxane building-block; 2) its elongation at its NHS end; 3) the delivery of the macrocycle to the elongated part of the axle by an induced translational motion; 4) the contraction process to yield the targeted [2]rotaxane and recycle the initial transporter.

Interlocked molecules like [2]rotaxanes^[1] constitute a family of molecules of growing interest since it has been found that the presence and the localization of a macrocycle around a molecular axle tremendously change the physical and chemical properties of the encircled molecular thread.^[2] The first interlocked compound (a catenane) was synthesized by Wasserman in 1960 using a statistical approach.^[3] Since then, many endeavors have been realized to prepare more efficiently interlocked compounds. In 1964, Schill and Lüttringhaus were the first to use dynamic covalent bonding to prepare catenanes.^[4] One may also notice the effort reported by Harrison and Harrison in 1967 to improve the poor yields generally encountered using statistical methods.^[5] They proposed the synthesis of a [2]rotaxane using a resin to immobilize a macrocycle, the latter statistically captured a molecular thread in solution before it was capped at both ends. Only 6% of the desired [2]rotaxane was obtained after 70 runs of the end-capping reaction and cleavage of the interlocked compound from the resin. More recently acquired knowledge about supramolecular interactions has permitted the development of various and much more efficient template-directed syntheses based on coordinative or noncovalent bonding interactions as the driving force to interlock the elements for assembly.^[6] As part of our research concerning the synthesis of mechanically interlocked molecular machines, we reported an operating system based on a dibenzo-24-crown-8 (DB24C8) macrocycle which is asso-

ciated with either anilinium or ammonium and either *N*-methyl- or *N*-benzyltriazolium molecular stations.^[7] In this system, we demonstrated the efficient role of the ammonium template for rotaxane formation, and we found that the triazolium group was an effective moiety for the DB24C8, albeit of poorer affinity than that of DB24C8 with an ammonium group. Indeed, in such a system, triazolium only interacts with the crown ether under basic conditions, that is, when the ammonium is deprotonated. To quantify the binding affinity of the triazolium moiety for DB24C8, and to evaluate the possibility of using a triazolium group as a new template for rotaxane preparation, we investigated, using ¹H NMR spectroscopy, the possible intermolecular interactions in hydrogen-bond-promoting solvents between DB24C8 and a triazolium-containing molecule.^[8] It appeared that no complexation occurred at all between the two components, thus demonstrating the impossibility of preparing DB24C8-based [2]rotaxanes with such a moiety.^[9] We logically pursued our investigation by wondering if it was possible to synthesize, in another way, rotaxanes devoid of any effective template moiety while containing a site for only very weak intramolecular interactions, for example, a triazolium group. Generally speaking, and contrary to strong interactions, very weak interactions between the macrocycle and the thread (such as those between DB24C8 and triazolium) in a [2]rotaxane should give rise to interlocked compounds which are much more sensitive to external stimuli. With this aim, we report herein a strategy based on the efficient synthesis of the [2]rotaxane building block **B** from the template-containing molecular thread **A** (Figure 1).

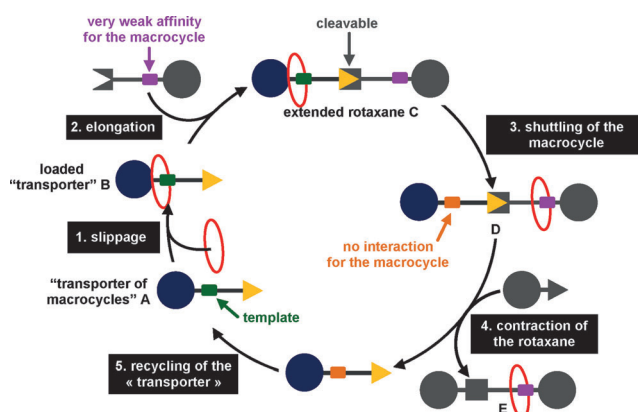


Figure 1. Cartoon representation of our synthetic strategy, using a five-step sequence: 1) Slip-on to yield a [2]rotaxane building-block, 2) elongation of the [2]rotaxane, 3) translation of the macrocycle, 4) contraction of the [2]rotaxane, 5) recycling of the macrocycle transporter.

[*] S. Chao, Dr. C. Romuald, Dr. K. Fournel-Marotte, Dr. C. Clavel, Dr. F. Coutrot
Supramolecular Machines and ARchitectures Team
Institut des Biomolécules Max Mousseron (IBMM) UMR 5247 CNRS
UM1-UM2, Université Montpellier 2, Place Eugène Bataillon, case
courrier 1706, Bât 17, 3ème étage, 34095 Montpellier Cedex 5
(France)
E-mail: frederic.coutrot@univ-montp2.fr
Homepage: <http://www.glycorotaxane.fr>
Supporting information for this article is available on the WWW
under <http://dx.doi.org/10.1002/anie.201403765>.

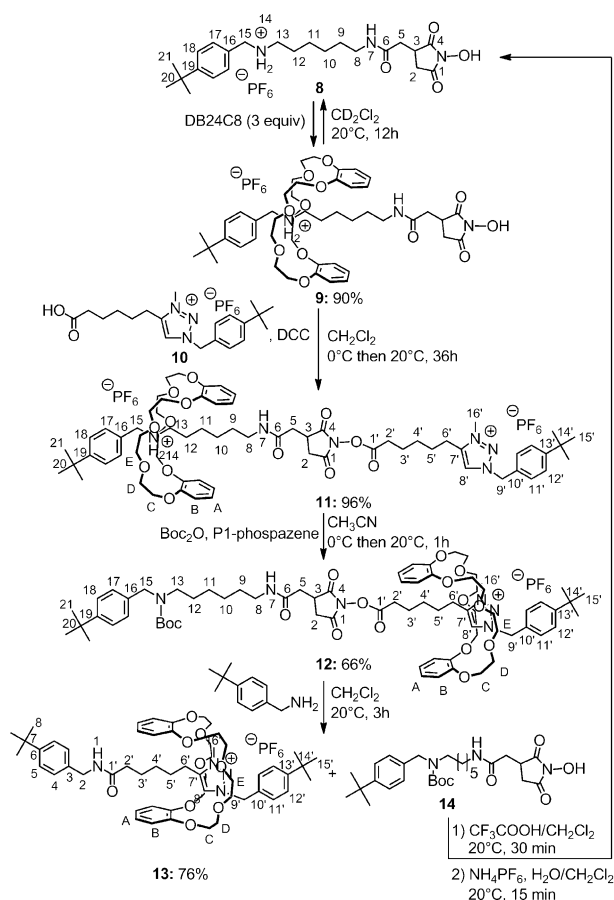
The building block **B** contains the macrocycle and a molecular axle, otherwise called a macrocycle transporter, since it templates and threads the macrocycle before delivering it to another docked axle, which does not contain a template of sufficient affinity to permit the direct synthesis of the rotaxane by classical methods. This stepwise sequence was achieved by elongation of the building block **B**, shuttling of the macrocycle along the thread in **C**, and contraction of **D** to yield the triazolium-based [2]rotaxane **E**. It is interesting to note that this strategy allows recycling of **A**. To the best of our knowledge, only one similar conceptual approach to the synthesis of rotaxanes, devoid of any template, has been published to date.^[10] In this case, a mechanically interlocking auxiliary was necessary for the success of the synthesis.

The targeted macrocycle transporter **A** (**8** in Schemes 1 and 2) contains an ammonium moiety, which is well known to bind with DB24C8,^[11] a *tert*-butylbenzyl moiety as a stopper at one end of the axle, and a *N*-hydroxysuccinimide (NHS) moiety at the other end. The NHS moiety proved to be small enough to allow interlocking between DB24C8 and the thread in hydrogen-bond-promoting solvents. Nevertheless, the NHS groups was also large enough to slow down the threading to allow the isolation of the [2]rotaxane **B** as a stable molecular architecture at ambient temperature, in the solid state. This feature makes the method similar to a slippage strategy,^[12] rather than a simple threading one. The NHS moiety was also utilized to extend the thread through the hydroxy group by forming an active ester^[13] bond, which is very sensitive to nucleophilic amines, with a carboxylic-acid-containing triazolium compound. The shuttling of the macrocycle around the extended triazolium part of the encircled axle was then envisaged to occur before cleaving the active ester bond, using a hindered amine, to afford the contracted triazolium based [2]rotaxane **E** (**13**).

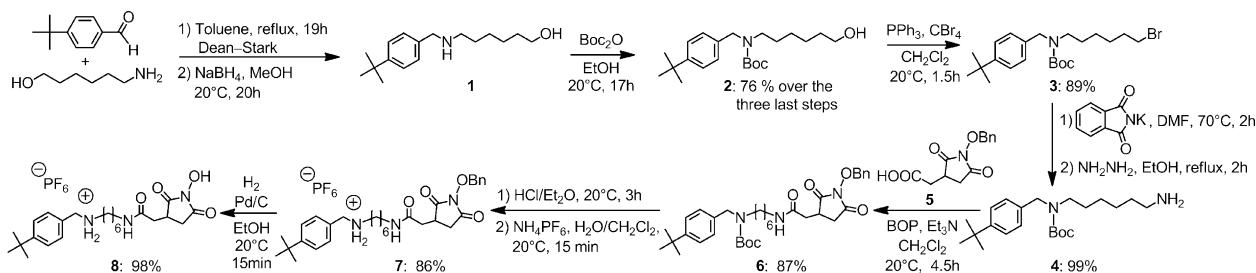
The first part of the reported work concerns the synthesis of the macrocycle transporter **8** (Scheme 1). It was obtained, in a 49% overall yield, from the commercially available *p*-*tert*-butylbenzaldehyde and 6-aminohexanol according to a multi-step sequence, and without any noticeable difficulty. A reductive amination first afforded the *tert*-butylbenzylamino-hexanol **1**, which was selectively *N* carbamoylated. The alcohol moiety was then brominated to yield **3**, before undergoing a Gabriel synthesis. The primary amino compound **4** was isolated and engaged in a coupling-type reaction with the previously prepared NHS derivative **5**^[14] using the Castro reagent BOP^[15] and triethylamine. The carbamoylated

amine of the compound **6** was deprotected using a solution of hydrogen chloride in ether and the resulting salt was subjected to anion exchange using ammonium hexafluorophosphate. The compound **7** was eventually debenzylated by hydrogenolysis to afford **8**, which contains the ammonium template for interlocking and the terminal NHS moiety for reaction with an activated acid for the extension of the molecule.

We then focused on the interlocking between **8** and DB24C8 (Scheme 2). Contrary to the very fast threading that we already reported between DB24C8 and ammonium- or anilinium-containing threads, devoid of any succinimide extremity,^[7,16] we were astonished to observe, here, that the formation of the [2]rotaxane **9**, using 3 equivalents of



Scheme 2. Synthesis of the triazolium-based [2]rotaxane **13**.



Scheme 1. Preparation of the macrocycle transporter **8**. Boc = *tert*-butoxycarbonyl, BOP = benzotriazolyl-oxy-tris(dimethylamino) phosphonium hexafluorophosphate, DMF = *N,N*-dimethylformamide.

DB24C8, proceeded very slowly. The threading could be assessed over time by ^1H NMR spectroscopy since the chemical exchange between **9** and **8** appears slow on the NMR time scale, thus giving rise to a distinguishable set of signals for each compound. In acetonitrile at room temperature, a maximum of 83 % of **9** was achieved after about 48 hours (Figure 2a). The rate of the slippage process

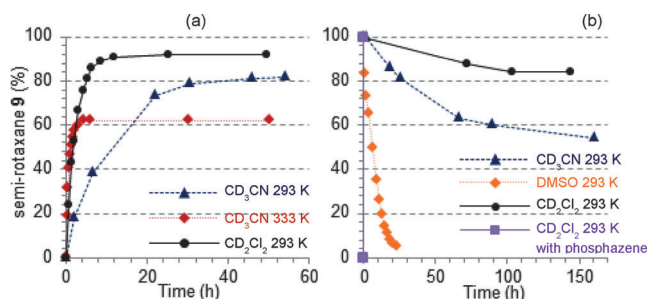


Figure 2. Kinetic studies of: a) the formation of the rotaxane **9** from **8** [3.6×10^{-2} M] and DB24C8 (3 equiv) in CD_2Cl_2 at 293 K and in CD_3CN at 293 and 333 K; b) the slip-off process for **9** [2×10^{-2} M] in CD_2Cl_2 , CD_3CN , and $[\text{D}_6]\text{DMSO}$ at 293 K.

increased by heating the mixture at 60°C (only 3 h are necessary to reach the plateau), albeit with a maximum of only 62 % of **9**. The same trend was observed in the less polar dichloromethane at room temperature, although a much better ratio of 92 % for **9** was achieved after about 12 hours. Whereas the driving force of the rotaxane formation relies on the noncovalent interactions between DB24C8 and the ammonium template, the different kinetics and ratio of the slippage can be attributed to the NHS end of **8**, whose size is somewhat comparable to the size of the cavity of DB24C8. Unsurprisingly, giving energy to the system by heating helps DB24C8 to slip-on the NHS end faster. However, the smaller ratio of **9** obtained at higher temperature indicates that the slipping-off process is competitive with the slipping-on one. This competition is due to the weaker hydrogen bonds between the ammonium template and DB24C8 at higher temperature. In dichloromethane, the better yield for **9** is related to the stronger hydrogen-bonding interactions in this less dissociating solvent.

The crude material obtained under the best experimental conditions was purified by sephadex LH20 chromatography using dichloromethane as the eluent, and allowed the isolation of 90 % of **9**. At room temperature, **9** is perfectly stable over time as a dried powder and its disassembly is very slow in solution in a hydrogen-bond-promoting solvent like dichloromethane. Indeed, after 144 hours, 84 % of **9** still remains interlocked (Figure 2b). These results attest to the efficient role of the NHS stopper under these reaction conditions and explain the feasible purification of **9** by exclusion chromatography using this solvent as the eluent. However, at room temperature in the more polar solvent acetonitrile, the disassembly of **9** appears to be faster, although still slow, and the slip-off rate is increased in dimethylsulfoxide. Indeed, the slip-off reached 46 % after

160 hours in acetonitrile, whereas the half-life of **9** is about 6.5 hours in dimethylsulfoxide, a half-life which is still impressive in terms of stability considering the solvent polarity. In comparison, the immediate and total disassembly of **9** was observed in dichloromethane after deprotonating the ammonium template by using 2 equivalents of P1-*t*Bu-tris(dimethyl)phosphazene.

The isolated [2]rotaxane **9** was elongated by esterification at the NHS end using dicyclohexylcarbodiimide (DCC) as the coupling reagent and the previously prepared triazolium acid **10** (see the Supporting Information; Scheme 2). The [2]rotaxane **11** was purified by sephadex chromatography and isolated in a 96 % yield. The shuttling of DB24C8 from the ammonium moiety toward the triazolium moiety was then achieved by deprotonation/carbamoylation of the ammonium group. This one-pot two-step sequence was preferred to the sole deprotonation, so as to avoid any side reaction of the generated amine on the active NHS ester. Hünig's base,^[17] diisopropylethylamine, proved to react too slowly with the ammonium, even when used in large excess, thus resulting in very slow carbamoylation.^[18]

P1-*t*Bu-tris(dimethyl)phosphazene (1 equiv), Schwesinger's base,^[19] was employed instead to quantitatively deprotonate the encircled ammonium, thus revealing the amine moiety, which was immediately trapped in situ by Boc_2O (3 equiv). The carbamoylated [2]rotaxane **12** was obtained in a 66 % yield after silica gel and sephadex chromatographic purifications.^[20] Unsurprisingly, the shuttling of DB24C8 was observed around the triazolium site in the absence of the ammonium group. More interesting is the rate of the translation of DB24C8 along the encircled molecular axle from one end to the other, a movement which appears, here, to be instantaneous. Indeed, after 1 hour of reaction in acetonitrile, only one ^1H NMR signal, corresponding to the triazolium hydrogen $\text{H}8'$ interacting with DB24C8 (at $\delta = 8.88$ ppm, Figure 3c), was observed and absolutely no triazolium hydrogen remained free in **12**, thus showing the absence of any DB24C8 on the left side of the axle and demonstrating that DB24C8 has no difficulty in gliding along in the absence of the ammonium template.

The comparison between the ^1H NMR spectra of the protonated **11**, its non-interlocked analogue **11_n**, the carbamoylated **12**, and its non-interlocked analogue **12_n** provided evidence of the molecular machinery (Figure 3 and Figure 5).

The direct comparison of the NMR spectra of **11_n** and **11** indicates the presence and the localization of DB24C8 around the ammonium moiety in **11** (Figure 3a,b). Firstly, the signals corresponding to the methylene hydrogen atoms $\text{H}_{\text{C-E}}$ of DB24C8 are split in **11**, with respect to the free DB24C8, and is due to their non-equivalence. Indeed, in the interlocked structure, they are facing the two nonsymmetrical ends of the encircled molecular axle. Contrary to **11_n**, the chemical shift of the hydrogen atom $\text{H}14$ in **11** appears downfield ($\delta = 7.11$ ppm), and those of $\text{H}13$ and $\text{H}15$, belonging to the ammonium moiety, are shifted downfield in the rotaxane (respectively $\Delta\delta = 0.24$ and 0.42 ppm) as a result of their hydrogen-bonding interactions with the oxygen atoms of DB24C8. Interestingly, no variations at all in the chemical shifts for the hydrogen atoms $\text{H}6'$, $\text{H}8'$, $\text{H}9'$, and $\text{H}16'$ of the triazolium moiety are noticed. The same is observed for all

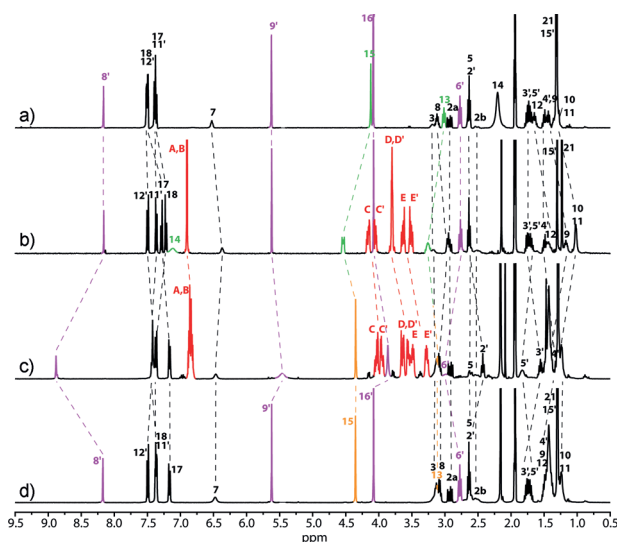


Figure 3. ^1H NMR spectra (400 MHz, CD_3CN , 298 K) of a) the uncomplexed protonated thread **11_u**, b) the protonated elongated [2]rotaxane **11**, c) the N carbamoylated [2]rotaxane **12**, and d) the N-carbamoylated and uncomplexed thread **12_u**. The numbering and coloring correspond to the hydrogen assignments indicated in Figure 5.

hydrogen atoms of the right part of the molecule, thus indicating the exclusive localization of DB24C8 around the ammonium group. At the same time, H7-12 are all shifted upfield in **11** (respectively $\Delta\delta = -0.15, -0.17, -0.25, -0.29, -0.28$, and -0.23 ppm) because they experience the shielding effect of the aromatic rings of DB24C8.

In **12**, the new localization of DB24C8 around the triazolium group is deduced from the direct comparison between the ^1H NMR spectra of **11** and **12** (Figure 3b,c). The hydrogen atoms H13 and H15 are shifted upfield in **12** (respectively, $\Delta\delta = -0.14$ and -0.19 ppm) as a result of both the N carbamoylation and the displacement of DB24C8. Simultaneously, the hydrogen atoms H8' and H6' of the triazolium group are shifted downfield in **12** (respectively $\Delta\delta = 0.72$ and 0.22 ppm) because of their hydrogen-bonding interactions with DB24C8. It is noteworthy that H9' and H16' are shifted upfield ($\Delta\delta = -0.17$ and -0.22 ppm), since the triazolium charge is concealed as a result of ion/dipole interactions with the oxygen atoms of DB24C8. The hydrogen atoms H7-12 are all deshielded in **12**, because they are not experiencing the shielding effect of DB24C8 anymore, whereas H2'-4' of the right-part of the axle are now shielded by the aromatic ring of DB24C8 (respectively $\Delta\delta = -0.21, -0.20$, and -0.17 ppm). The localization of DB24C8 around the triazolium moiety in **12** can be confirmed by comparing the NMR spectra of **12** and its unthreaded analogue **12_u** (Figure 3c,d). The same trend of chemical shift differences is observed concerning the hydrogen atoms which are either implicated in hydrogen bonding or shielded by the aromatic rings of DB24C8.

Once DB24C8 was displaced around the triazolium site by translational motion, the active-ester-containing **12** was shortened by adding the *tert*-butylbenzylamine in dichloromethane (Scheme 2). The [2]rotaxane **13** was obtained pure in a 76% yield after sephadex chromatography, and the

collected **8** was recycled with the help of trifluoroacetic acid and anion exchange. Evidence of the new interlocked structure is given by the comparison of the ^1H NMR spectra of **13** and its unthreaded analogue **13_u** (Figure 4 and Figure 5).

Obviously, the signals for the hydrogen atoms H_{A-E} belonging to DB24C8 appear in **13**. More interestingly, and

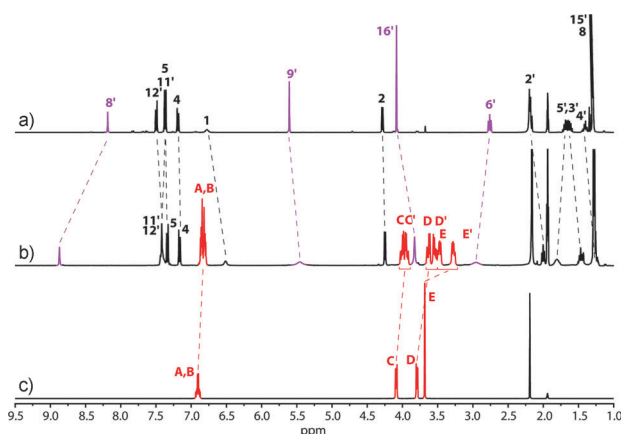


Figure 4. ^1H NMR spectra (400 MHz, CD_3CN , 298 K) of a) the uncomplexed thread **13_u**, b) the [2]rotaxane **13**, and c) DB24C8. The numbering and coloring correspond to the hydrogen assignments indicated in Figure 5.

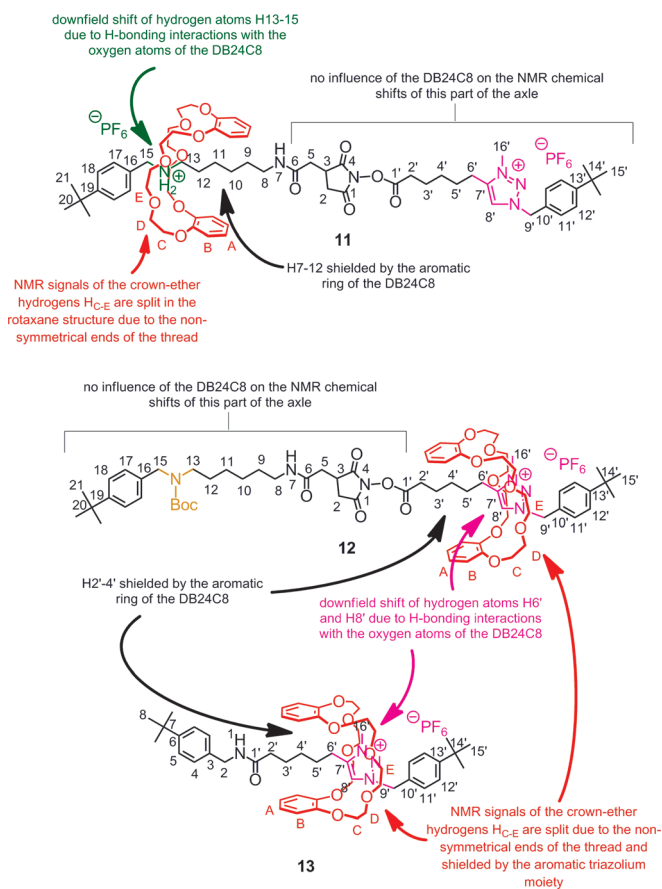


Figure 5. Summary of the influence of DB24C8 on the ^1H NMR chemical shifts of the encircled threads in the rotaxanes **11–13**.

as in rotaxanes **11** and **12**, the hydrogen atoms H_{C-E} all become split in **13**, with respect to the free DB24C8, since they are facing the two nonsymmetrical ends of the thread (Figure 4b,c). Moreover, the hydrogen atoms H_E , and to a lesser extent H_{C-D} , are shielded in **13** because they are more or less located in the shielding cavity of the aromatic triazolium moiety. By comparing **13** with **13_u**, the signals for the triazolium $H8'$ and $H6'$ atoms are shifted downfield in **13** (respectively $\Delta\delta = 0.69$ and 0.2 ppm) because of their hydrogen-bonding interactions with the oxygen atoms of DB24C8, whereas those of $H16'$ and $H9'$ are shielded because of the concealed triazolium charge (respectively $\Delta\delta = -0.25$ and -0.15 ppm; Figure 4a,b). Finally, $H1$ and $H2'-4'$ are all shielded by the aromatic rings of DB24C8 in **13** (respectively $\Delta\delta = -0.27$, -0.18 , -0.16 , and -0.14 ppm).

In conclusion, we have reported an efficient strategic chemical route to triazolium [2]rotaxanes. It is based on the synthesis of a new isolable [2]rotaxane building block containing a terminal NHS moiety as a point of attachment. The attachment of a triazolium-containing compound to this [2]rotaxane led to an extended [2]rotaxane having a labile active ester link at the middle of the encircled axle. The delivery of the macrocycle, through a translational motion from one end to the other (i.e. from ammonium to triazolium), was triggered by deprotonation/carbamoylation. The [2]rotaxane was contracted by the attack of an amine on the active ester moiety, thereby recycling the initial transporter for DB24C8 after acidic treatment. Notably, no other method for synthesizing such a DB24C8/triazolium-based rotaxane, devoid of a template moiety, has been reported to date. Indeed, **13**, which contains a triazolium group as a very weak site of interaction for DB24C8, could not be prepared by the usual classical template strategy. With our reported strategy, **13** was prepared from **10** in a three-step sequence with an overall yield of 48%. The generalization of our method, using the recyclable rotaxane building-block **9**, to a wide variety of rotaxanes holds potential for future endeavors.

Received: March 27, 2014

Published online: June 6, 2014

Keywords: macrocycles · rotaxanes · structure elucidation · supramolecular chemistry · template synthesis

- [1] E. R. Kay, D. A. Leigh, F. Zerbetto, *Angew. Chem.* **2007**, *119*, 72–196; *Angew. Chem. Int. Ed.* **2007**, *46*, 72–191.
- [2] For some examples, see: a) A. Fernandes, A. Viterisi, F. Coutrot, S. Potok, D. A. Leigh, V. Aucagne, S. Papot, *Angew. Chem.* **2009**, *121*, 6565–6569; *Angew. Chem. Int. Ed.* **2009**, *48*, 6443–6447; b) E. Arunkumar, C. C. Forbes, B. D. Smith, *Eur. J. Org. Chem.* **2005**, 4051–4059; c) V. Blanco, D. A. Leigh, V. Marcos, J. A. Morales-Serna, A. L. Nussbaumer, *J. Am. Chem. Soc.* **2014**, *136*, 4905–4908; d) J. Berná, D. A. Leigh, M. Lubomska, S. M. Mendoza, E. M. Pérez, P. Rudolf, G. Teobaldi, F. Zerbetto, *Nat. Mater.* **2005**, *4*, 704–710; e) J. M. Belitsky, A. Nelson, J. D. Hernandez, L. G. Baum, J. F. Stoddart, *Chem. Biol.* **2007**, *14*, 1140–1151; f) J. Berná, C. Franco-Pujante, M. Alajarin, *Org. Biomol. Chem.* **2014**, *12*, 474–478.
- [3] E. Wasserman, *J. Am. Chem. Soc.* **1960**, *82*, 4433–4434.
- [4] G. Schill, A. Lüttringhaus, *Angew. Chem.* **1964**, *76*, 567–568; *Angew. Chem. Int. Ed. Engl.* **1964**, *3*, 546–547.
- [5] I. T. Harrison, S. J. Harrison, *J. Am. Chem. Soc.* **1967**, *89*, 5723–5725.
- [6] a) D. B. Amabilino, J. F. Stoddart, *Chem. Rev.* **1995**, *95*, 2725–2828; b) *Molecular Catenanes, Rotaxanes and Knots* (Eds.: J. P. Sauvage, C. Dietrich-Buchecker), Wiley-VCH, Weinheim, **1999**; c) *From Non-Covalent Assemblies to Molecular Machines* (Eds.: J.-P. Sauvage, P. Gaspard), Wiley-VCH, Weinheim, **2011**; d) J. E. Beves, B. A. Blight, C. J. Campbell, D. A. Leigh, R. T. McBurney, *Angew. Chem.* **2011**, *123*, 9428–9499; *Angew. Chem. Int. Ed.* **2011**, *50*, 9260–9327; e) K. E. Griffiths, J. F. Stoddart, *Pure Appl. Chem.* **2008**, *80*, 485–506.
- [7] a) F. Coutrot, E. Busseron, J.-L. Montero, *Org. Lett.* **2008**, *10*, 753–756; b) F. Coutrot, C. Romuald, E. Busseron, *Org. Lett.* **2008**, *10*, 3741–3744; c) E. Busseron, F. Coutrot, *J. Org. Chem.* **2013**, *78*, 4099–4106.
- [8] E. Busseron, PhD Thesis, Montpellier University, **2009**.
- [9] Notably, triazolium moiety has been used for rotaxane formation through chloride anion template formation: a) N. G. White, P. J. Costa, S. Carvalho, V. Félix, P. D. Beer, *Chem. Eur. J.* **2013**, *19*, 17751–17765; b) N. G. White, H. G. Lovett, P. D. Beer, *RSC Adv.* **2014**, *4*, 12133–12147.
- [10] J. S. Hannam, S. M. Lacy, D. A. Leigh, C. G. Saiz, A. M. Z. Slawin, S. G. Stitchell, *Angew. Chem.* **2004**, *116*, 3322–3326; *Angew. Chem. Int. Ed.* **2004**, *43*, 3260–3264.
- [11] A. G. Kolchinski, D. H. Busch, N. W. Alcock, *J. Chem. Soc. Chem. Commun.* **1995**, 1289–1291.
- [12] a) P. R. Ashton, I. Baxter, M. C. T. Fyfe, F. M. Raymo, N. Spencer, J. F. Stoddart, A. J. P. White, D. J. Williams, *J. Am. Chem. Soc.* **1998**, *120*, 2297–2307; b) Y. Tokunaga, N. Wakamatsu, A. Ohbayashi, K. Akasaka, S. Saeki, T. Hisada, T. Goda, Y. Shimomura, *Tetrahedron Lett.* **2006**, *47*, 2679–2682; c) F. M. Raymo, K. N. Houk, J. F. Stoddart, *J. Am. Chem. Soc.* **1998**, *120*, 9318–9322; d) F. M. Raymo, J. F. Stoddart, *Pure Appl. Chem.* **1997**, *69*, 1987–1997; e) M. Händel, M. Plevoets, S. Gestermann, F. Vögtle, *Angew. Chem.* **1997**, *109*, 1248–1250; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1199–1201; f) S.-Y. Hsueh, C.-C. Lai, Y.-H. Liu, Y. Wang, S.-M. Peng, C.-C. Hsu, *Org. Lett.* **2007**, *9*, 4523–4526; g) J.-J. Lee, A. G. White, J. M. Baumes, B. D. Smith, *Chem. Commun.* **2010**, 46, 1068–1069; h) A. J. McConnell, P. D. Beer, *Chem. Eur. J.* **2011**, *17*, 2724–2733; i) P. R. Ashton, M. Belohradsky, D. Philp, J. F. Stoddart, *J. Chem. Soc. Chem. Commun.* **1993**, 1269–1274; j) M. Asakawa, P. R. Ashton, R. Ballardini, V. Balzani, M. Belohradsky, M. T. Gandolfi, O. Kocian, L. Prodi, F. M. Raymo, J. F. Stoddart, M. Venturi, *J. Am. Chem. Soc.* **1997**, *119*, 302–310; k) M. A. Bolla, J. Tiburcio, S. J. Loeb, *Tetrahedron* **2008**, *64*, 8423–8427; l) P. Linnartz, S. Bitter, C. A. Schalley, *Eur. J. Org. Chem.* **2003**, 4819–4829; m) H. W. Gibson, N. Yamaguchi, Z. Niu, J. W. Jones, C. Slebodnick, A. L. Rheingold, L. N. Zakharov, *J. Polym. Sci. Part A* **2010**, *48*, 975–985.
- [13] G. W. Anderson, J. E. Zimmerman, F. M. Callahan, *J. Am. Chem. Soc.* **1963**, *85*, 3039.
- [14] I. Schlemminger, D. R. Mole, L. A. McNeill, A. Dhanda, K. S. Hewitson, Y.-M. Tian, P. J. Ratcliffe, C. W. Pugh, C. J. Schofield, *Bioorg. Med. Chem. Lett.* **2003**, *13*, 1451–1454.
- [15] B. Castro, J. R. Dormoy, G. Evin, C. Selve, *Tetrahedron Lett.* **1975**, *14*, 1219–1222.
- [16] a) C. Romuald, G. Cazals, C. Enjalbal, F. Coutrot, *Org. Lett.* **2013**, *15*, 184–187; b) C. Romuald, A. Arda, C. Clavel, J. Jimenez-Barbero, F. Coutrot, *Chem. Sci.* **2012**, *3*, 1851–1857; c) C. Romuald, E. Busseron, F. Coutrot, *J. Org. Chem.* **2010**, *75*, 6516–6531; d) E. Busseron, C. Romuald, F. Coutrot, *Chem. Eur. J.* **2010**, *16*, 10062–10073; e) F. Coutrot, E. Busseron, *Chem. Eur. J.* **2009**, *15*, 5186–5190.
- [17] S. Hünig, M. Kiessel, *Chem. Ber.* **1958**, *91*, 380–392.

- [18] The introduction of a functional group on the ammonium template of [2]rotaxanes were reported to be a challenge. See Ref. [16c] and a) Y. Tachibana, H. Kawasaki, N. Kihara, T. Takata, *J. Org. Chem.* **2006**, *71*, 5093–5104; b) S. Suzuki, K. Nakazono, T. Takata, *Org. Lett.* **2010**, *12*, 712–715; c) Y. Koyama, T. Matsumura, T. Yui, O. Ishitani, T. Takata, *Org. Lett.* **2013**, *15*, 4686–4689.
- [19] R. Schwesinger, J. Willaredt, H. Schlemper, M. Keller, D. Schmitt, H. Fritz, *Chem. Ber.* **1994**, *127*, 2435–2454.
- [20] Notably, the rotaxane **12** was contaminated by 10% of a side product which holds a second *tert*-butoxycarbonyl group on the amide moiety (see the Supporting Information).
-