[2]Rotaxane End-Capping Synthesis by Click Michael-Type Addition to the Vinyl Sulfonyl Group

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Abstract: Here we report the application of the click Michael-type addition reaction to vinyl sulfone or vinyl sulfonate groups in the synthesis of rotaxanes through the threading-and-capping method. This methodology has proven to be efficient and versatile as it allowed the preparation of rotaxanes using template approaches based on different non-covalent interactions (i.e. donor-acceptor π-π interactions or H bonding) in yields ranging generally 60%−80% and up to 91% thanks to the mild conditions required (room temperature or 0 ºC and a mild base such as Et_3N or DMAP). Furthermore, the use of vinyl sulfonate moieties, suitable motifs for coupling-and-decoupling (CAD) chemistry, implies another advantage as it allows the controlled chemical disassembly of the rotaxanes into their components through nucleophilic substitution of the sulfonates resulting from the capping step with a thiol under mild conditions (Cs_2CO_3 and room temperature).

Introduction

Rotaxanes are interlocked molecules composed of a linear component (thread or axle) threaded through a macrocycle with two bulky stopper groups at both sides of the axle to prevent the dethreading of the macrocycle.[1] Over the last two decades, rotaxanes,[2] along with other kinds of interlocked structures such as catenanes,[1,3] have become more and more relevant due to their unique structure and, mainly, because of their extensive application in the development of an increasing number of molecular devices able to perform different tasks.[4]

The quick progress achieved in the application of rotaxanes in molecular machines able to perform tasks of increasing complexity and relevance was only possible due to the development of efficient synthetic methodologies that allowed scientists to access such structures in a relatively simple and convenient manner. In this sense, the classic and most versatile strategies for the synthesis of rotaxanes, apart from the active metal template approach,[5] namely threading-and-capping (including snapping) and clipping, rely on the template effect that preorganizes the linear and macrocyclic (sub)components due to the establishment of non-covalent interactions,[6] mainly metal coordination,[7] hydrogen bonds,[8] π-π interactions[9] or hydrophobic forces,[10] to give supramolecular assemblies such as pseudorotaxanes. Nevertheless, a truly useful synthetic methodology for rotaxane or catenane synthesis also requires efficient and orthogonal closing reactions that proceed under mild conditions to covalently lock the intermediate supramolecular complexes, i. e. attach the stoppers to both ends of the linear component or close the macrocycle, without significantly altering the complexation equilibrium. Thus, among others, amide[11] and imine bond formation,[12] alkene metathesis[13] or click reactions[14] soon arose as suitable methodologies for the efficient synthesis of such interlocked architectures. Among the latter, the copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC)[15] became one of the most useful and extensively exploited synthetic tools in the field when the capping strategy is followed.[16]

Despite the great success of the CuAAC in the synthesis of rotaxanes, the availability of other synthetic tools is, as in other fields of organic synthesis, of key importance to expand the toolbox of methodologies to choose from to access any potential rotaxane design. In this fashion, some important pioneering effort has been done to employ other click reactions,[17] such as the radical thiol-ene/yne,[18] Diels-Alder reactions,[19] nitrile oxide cycloadditions[20] or Michael-type additions such as the thiol-maleimide[21] in the synthesis of rotaxanes.[22] At this point, we envisioned that the click Michael-type addition reaction of a nucleophile to the vinyl sulfonyl group,[17e,23] in particular to vinyl sulfone or vinyl sulfonate derivatives, could become an efficient and versatile tool in rotaxane synthesis. Click Michael-type addition reactions of thiols or amines to vinyl sulfone groups proceed under mild conditions, i.e. at room temperature or lower in the presence of mild bases, and in a variety of solvents, including aqueous media. Hence, these reactions have been exploited by ours and other research groups in a variety of immobilization and (bio)conjugation applications like protein labelling and immobilization,[24] enzyme inhibition,[25] functionalization of carbohydrates,[24d,e] development of carrier systems[26] or in polymer and materials chemistry.[27]

On the other hand, vinyl sulfonate derivatives[28] exhibit the same click features than vinyl sulfones as acceptors in Michael-type additions.[25b,29] However, the use of vinyl sulfonate derivatives gives the added value of allowing a later cleavage through nucleophilic substitution of the sulfonate moieties obtained after the Michael-type addition, as we recently demonstrated.[28] This behaviour, which enables vinyl sulfonates as promising reagents for the so-called coupling-and-decoupling (CAD) chemistry,[30] could be interesting in the development of cleavable[31] functional rotaxanes, especially relevant for applications such as controlled delivery or directional transport,[32] if the decoupling step that leads to the disassembly of the components takes place in mild conditions.

Therefore, here we report the development of a new efficient and versatile methodology for the synthesis of rotaxanes based on the click Michael-type addition reaction[33] of thiols[34] or amines to vinyl sulfone and vinyl sulfonate moieties as the key reaction for the capping step. We demonstrate its applicability to the synthesis of rotaxanes based on a variety of non-covalent

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interactions (Figure 1). Furthermore, we report the usefulness of the CAD chemistry features of the vinyl sulfonate group by presenting the controlled chemical disassembly into its components of a rotaxane displaying sulfonate moieties.

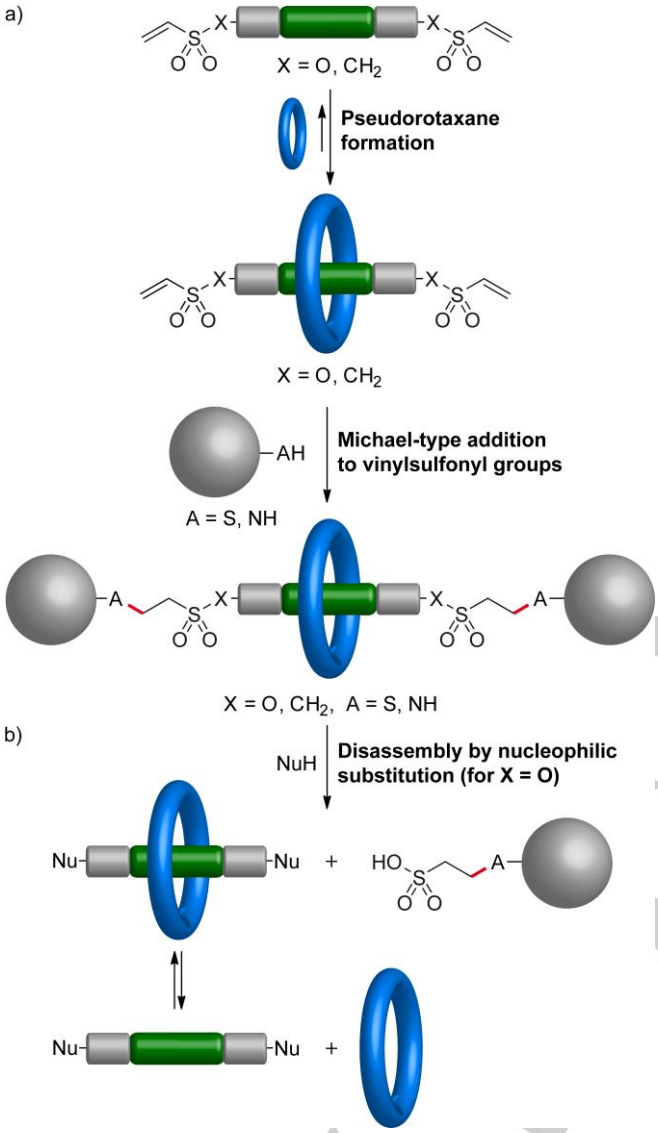


Figure 1. Proposed synthetic strategy for: a) the synthesis of rotaxanes through a capping approach based on Michael-type addition reactions to vinyl sulfone (X = CH_2) or vinyl sulfonate (X = O) groups as the key step for the blocking of the pseudorotaxanes, and b) the disassembly of the rotaxanes formed from vinyl sulfonates (X = O) by nucleophilic substitution.

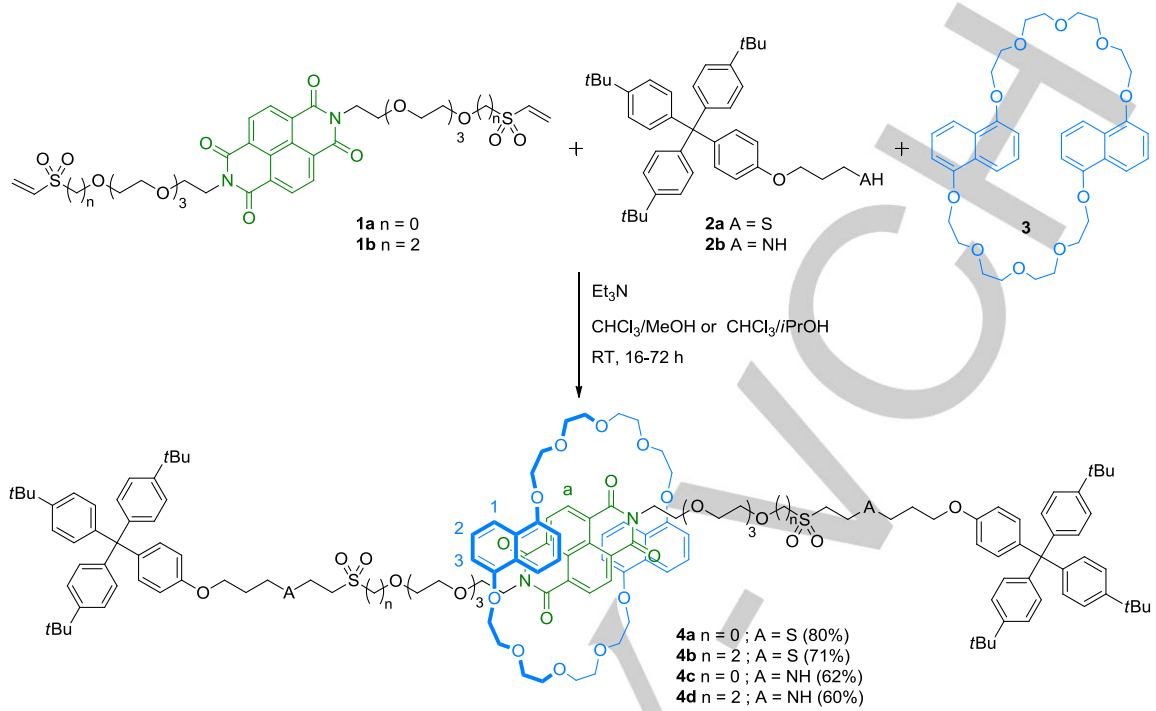
Results and Discussion

Synthesis of rotaxanes based on π-π interactions

Initially, we tested the proposed click Michael-type addition methodology in the synthesis of rotaxanes based on donor-acceptor π-π interactions (Scheme 1). We chose as recognition motif a π-acceptor naphthalene diimide unit which has been shown to interact with crown ether macrocycles with π-donor aromatic moieties. In particular it associates with dinaphto-38-crown-10 (DNP38C10, **3**) with a binding constant $K_a \approx 1 \times 10^2$ M^{-1} in $CHCl_3$/MeOH 98:2,[35] forming supramolecular entities exploited in the synthesis of rotaxane architectures.[21b,36] Hence, we synthesised thread precursors **1a,b** displaying the naphthalene diimide core functionalized with tetraethylenglycol chains with vinyl sulfonate (**1a**) or vinyl sulfone groups (**1b**) on both ends (see the Supporting Information for synthetic details), suitable to undergo click Michael-type addition reactions.

At first, we performed the reaction of the different naphthalene diimide derivatives **1a,b** with bulky stoppers exhibiting a thiol (**2a**) or an amine group (**2b**) that can act as nucleophiles in the Michael-type addition to vinyl sulfonyl derivatives in the presence of Et_3N at room temperature. We obtained the corresponding free threads in good yields, proving that this click reaction gives, as expected, good results under those mild conditions, suggesting its compatibility with rotaxane synthesis. Therefore, in the search of the target rotaxanes, we repeated the thia- or aza-Michael addition reactions of **1a,b** with **2a,b** after mixing the naphthalene diimide vinyl sulfonyl derivatives with macrocycle **3** to favour the assembly of the corresponding pseudorotaxanes (Scheme 1). The reaction afforded the corresponding rotaxanes **4a-d** in remarkable 60-80% isolated yields. Slightly higher yields were obtained when using thiol stopper **2a**, which can be attributed to its higher nucleophilic character compared to its amine counterpart **2b**. In addition, another factor influencing the yield outcome could be the relatively easier purification of the corresponding sulfur rotaxanes, especially **4a**, which could be purified by only one preparative TLC, respect to the isolation of **4c,d**, which required a sequence of column chromatography and successive runs of gel permeation chromatography.

Rotaxanes **4a-d** were characterized by means of 1D and 2D NMR spectroscopy, showing the expected shifting to lower frequencies for the signals of the aromatic H atoms of the macrocycle and the naphthalene diimide core due to the shielding caused by the establishment of π-π interactions between the naphthalene rings of the macrocycle and the naphthalene diimide unit ($\Delta\delta_{H1}$ = −0.95−0.96 ppm; $\Delta\delta_{H2}$ = −0.53 ppm; $\Delta\delta_{H3}$ = −0.40 ppm and $\Delta\delta_{Ha}$ = −0.48 ppm), thus supporting the formation of the target structures (for **4a**, see Figure S1 in the Supporting Information). Rotaxane **4b** was further studied by DOSY NMR experiments which showed that both thread and macrocycle diffuse as a whole as both sets of signals show the same diffusion coefficient, estimated as 7.04×10^{-6} cm^2 s^{-1}, also supporting the presence of an interlocked structure (see Figure S54 in the Supporting Information). Finally, the identity of the rotaxanes was confirmed by high resolution mass spectrometry (HRMS). The ESI-TOF mass spectra show peaks corresponding to the singly or doubly charged molecular ions with experimental exact masses and isotopic distributions in good agreement with the theoretical ones (see Figures S160-S170 in the Supporting Information).



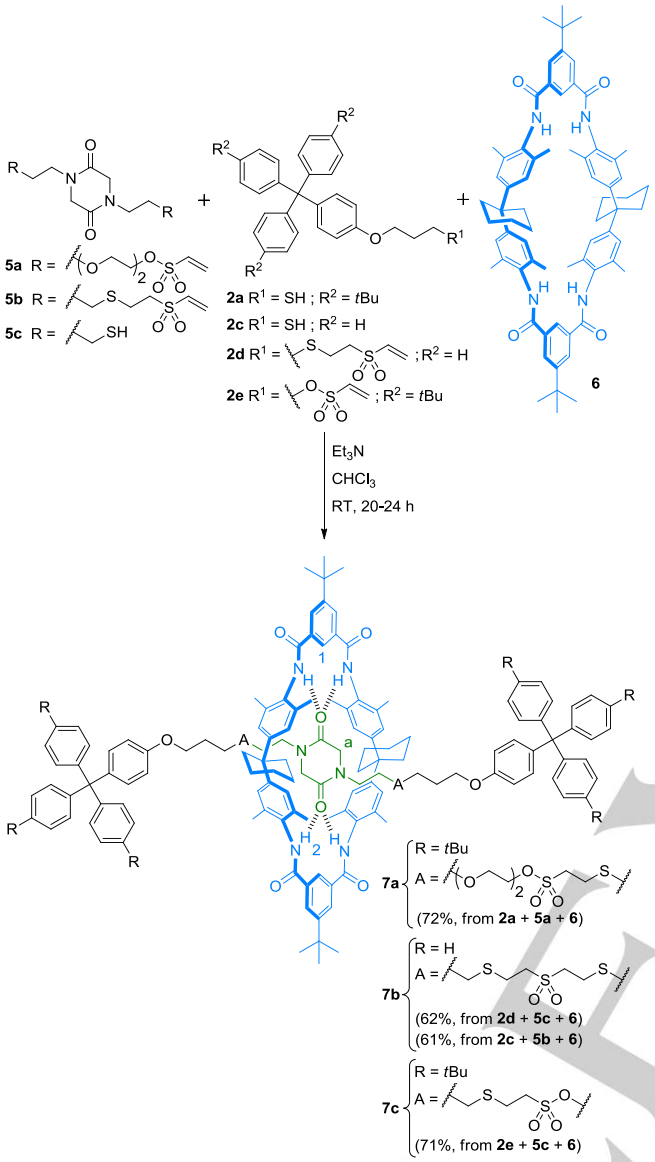
Scheme 1. Synthesis of rotaxanes based on π-π interactions **4a-d** through aza- and thia-Michael addition to the vinyl sulfonyl group.

Synthesis of rotaxanes based on hydrogen bonding

The good results obtained with this methodology based on Michael-type additions to the vinyl sulfonyl group in the synthesis of rotaxanes based on π-π interactions prompted us to extend its application to other systems based on different non-covalent interactions. Therefore, we decided to test this synthetic strategy in the assembly of rotaxanes based on hydrogen bonding (Scheme 2). Firstly, we focused on tetralactam rings as they are macrocyclic components that have been used in the synthesis of a variety of rotaxanes through the establishment of hydrogen bonds with a variety of acceptor templates. In particular, we chose the Hunter/Vögtle-type anilide macrocycle[37] as most of the usual Leigh-type benzylamide macrocycles exhibit a very low solubility which makes them incompatible with the capping approach and they are mostly used in clipping strategies.[11a,d,f,38] As recognition motif for the macrocyclic component we selected the diketopiperazine unit (Scheme 2), which was shown to act as template for tetralactam macrocycles (binding constant K_a = (1.08 ± 0.09) × 10^4 M^{-1} at 233K in $CDCl_3$) in rotaxane synthesis,[39] affording yields among the highest obtained for organic non-ionic recognition motifs with this macrocycle.[40]

Based on the results obtained for π-π rotaxanes, we decided to focus on the thia-Michael addition as higher yields were achieved. However, we used this system to investigate whether the position of the nucleophile or the Michael acceptor group on the thread or on the stopper would have any influence on the reaction outcome. Therefore, we prepared diketopiperazine derivatives **5a,b** functionalized with vinyl sulfonate or vinyl sulfone groups as Michael acceptors for thiol stopper **2a,c**, but also axle **5c** with thiol groups on both ends that could act as nucleophiles in the click thia-Michael addition to vinyl sulfonyl-functionalized stoppers **2d,e**. After the very good results attained in the preparation of the free threads (see the Supporting Information), we carried out the rotaxane formation following our methodology by reacting linear compounds **5a,b** or **5c** with stoppers **2a,c** or **2d,e**, respectively, in the presence of tetralactam macrocycle **6** (Scheme 2). Indeed, the thia-Michael addition to the vinyl sulfonyl group gave the corresponding [2]rotaxanes **7a-c** in good yields (61%−72%), quite similar to those observed for the naphthalene diimide rotaxanes.

Again, the structure of rotaxanes of **7a-c** was supported by 1D and 2D NMR experiments, which showed in all cases a downfield shift of the amide H atoms along with H1 due to the establishment of hydrogen bond interactions with the carbonyl groups of the diketopiperazine recognition motif on the thread ($\Delta\delta_{H1}$ = 0.44−0.46 ppm and $\Delta\delta_{H2}$ = 1.02−1.11 ppm). On the contrary, thread H atoms on or close to the diketopiperazine unit are shifted to lower frequencies due to the shielding induced by the aromatic rings on the macrocycle ($\Delta\delta_{Ha}$ = −1.29−1.38 ppm) (for **7a,b** see Figures S2-S3 in the Supporting Information). The structure of **7a,b** was also studied by DOSY NMR spectroscopy. The DOSY experiments show that all signals display the same diffusion coefficient, with estimated values of 9.29 × 10^{-6} cm^2 s^{-1} and 7.08 × 10^{-6} cm^2 s^{-1} for **7a** and **7b**, respectively, supporting



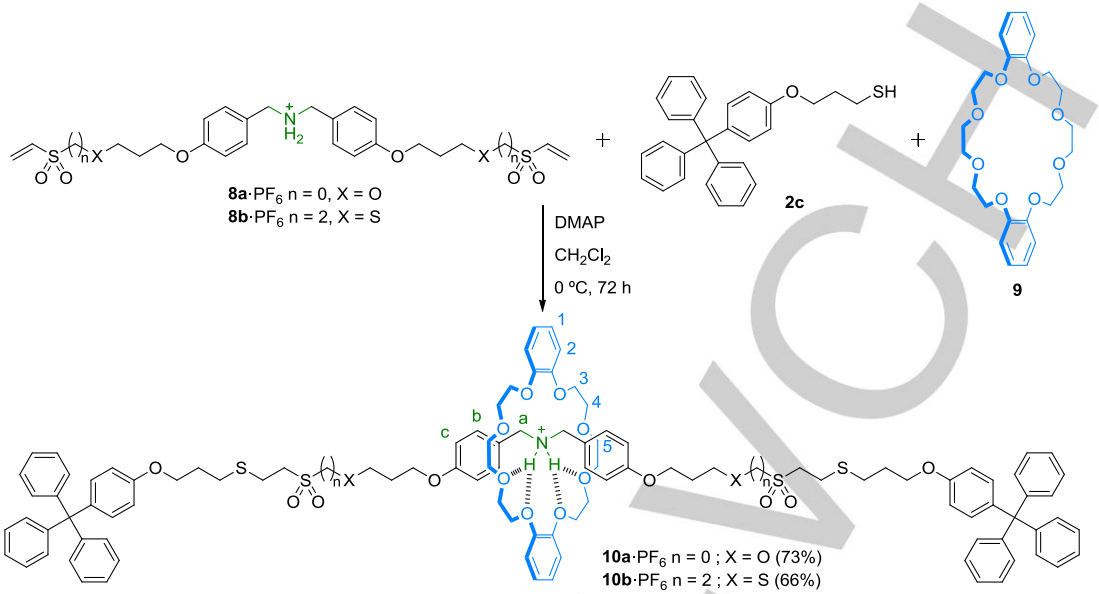
Scheme 2. Synthesis of hydrogen bonded rotaxanes **7a-c** via thia-Michael addition to vinyl sulfonyl groups placed on the thread precursor or the stopper.

the interlocked nature of the species (see Figures S78 and S86 in the Supporting Information). Finally, rotaxanes **7a-c** were also further characterized by means of HRMS (see Figures S171-S177 in the Supporting Information).

Prompted by these results, we decided to try the studied methodology for the synthesis of crown ether-based rotaxanes using ammonium salts as template. This represents a more challenging system for the proposed strategy, as the recognition motif for the macrocycle is a protonated secondary amine that could undergo deprotonation under the basic conditions required. We concentrated on the extensively used motif comprising dibenzo-24-crown-8 (DB24C8, **9**) as macrocycle and a dibenzylammonium derivative as the secondary ammonium salt (Scheme 3). This recognition pair, with a binding constant K_a = 2.7×10^4 M^{-1} at 298 K in $CHCl_3$,[41] has been exploited in the design of a vast number of rotaxane architectures.[32c,42, 43]

Initially, a series of model studies suggested that the use of substoichiometric amounts of Et_3N and PPh_3 could promote the thia-Michael addition reaction while keeping a high degree of association between macrocycle and the ammonium unit, meaning that the latter remained with a high extent of protonation. Thus, we prepared dibenzylammonium salts **8a,b**•PF_6 functionalized with vinyl sulfonate or vinyl sulfone groups and reacted them with stopper **2c** in the presence of DB24C8 (**9**) and a catalytic amount of Et_3N. However, the ^1H NMR analysis of the crude mixture did not show any evidence of the formation of the rotaxane but only the presence of free thread and macrocycle. Therefore, we tried milder conditions reported in the literature for a thiol maleimide reaction, consisting on the use of a catalytic amount of dimethylaminopyridine (DMAP) as base and performing the reaction at 0 ºC.[21a] The compatibility of the thia-Michael addition to the vinyl sulfonyl group with temperatures of 0−4 ºC[24c] is another of the advantages of this synthetic strategy as it enhances its scope, enabling its use with temperature-sensitive substrates (e.g. proteins), to avoid other side or decomposition reactions or in supramolecular systems to strengthen or not to disturb the host-guest interactions. The possibility of using DMAP as base was also confirmed by some model studies. Under these conditions, reaction of the pseudorotaxane assembled from **8a**•PF_6 and **9** with thiol stopper **2c** successfully afforded the target rotaxane **10a**•PF_6 in a good yield (73%) (Scheme 3), in line with those observed for previous systems. Similar results were obtained when using the vinyl sulfone analogue **8b**•PF_6, affording the corresponding rotaxane **10b**•PF_6 in a similar yield (66%) (Scheme 3).

1D and 2D NMR experiments support the rotaxane structure. Thus, there is a broadening and shift to higher frequencies of the benzylic CH_2 signals, typical of the establishment of hydrogen bonding between the crown ether and the ammonium unit ($\Delta\delta_{Ha}$ = 0.39 ppm).[18b,42d] On the contrary, the signals of the aromatic H atoms of the dibenzylammonium motif and the CH_2 groups of the macrocycle are slightly shifted upfield due to the shielding by the aromatics rings of the macrocycle or the dibenzylammonium unit, respectively ($\Delta\delta_{Hc}$ = −0.11 ppm and $\Delta\delta_{H5}$ = −0.42 ppm) (for **10a** see Figure S4 in the Supporting Information). DOSY NMR experiments also confirmed the interlocked nature of **10a**•PF_6 as the same diffusion coefficient (ca. 7.91×10^{-6} cm^2 s^{-1}) was observed for the sets of signals of the macrocycle and the thread (see Figure S115 in the Supporting Information). Finally, the identity of rotaxanes **10a,b** was also endorsed by the exact mass and isotopic distributions data obtained by HRMS (Figures S178-S181 in the Supporting Information).



Scheme 3. Synthesis of rotaxanes **10a,b**·PF_6 from dibenzylammonium derivatives functionalized with vinyl sulfonyl groups **8a,b**·PF_6 and thiol stopper **2c** in the presence of DB24C8 (**9**).

Synthesis of pillar[5]arene-based rotaxanes

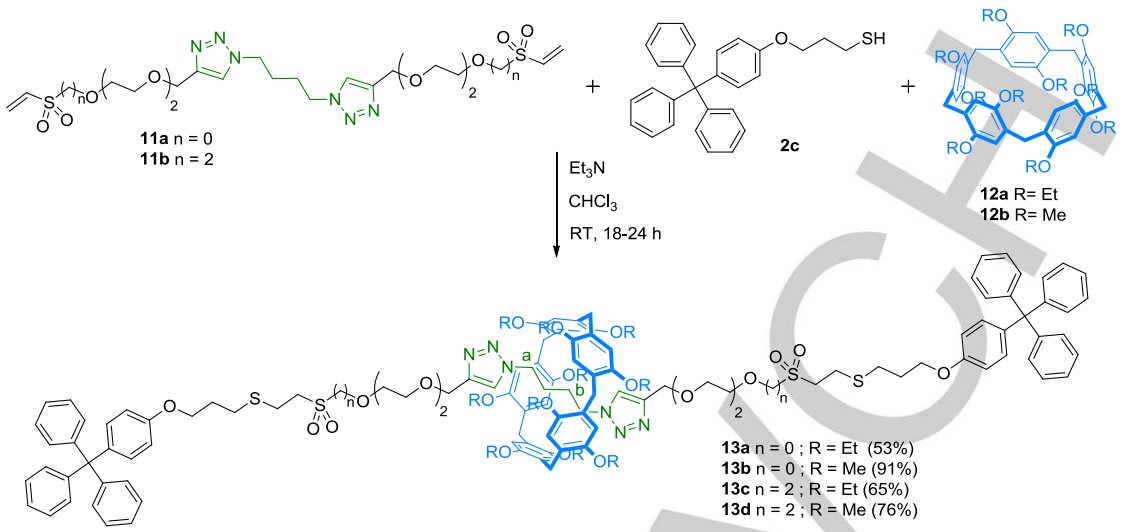
Finally, we applied the proposed synthetic methodology to the preparation of rotaxanes with pillar[5]arenes as the macrocyclic component. Pillar[n]arenes, firstly developed by Ogoshi and co-workers, are a relatively novel class of macrocycles formed by hydroquinone rings with two *para* positions bridged with CH_2 groups.[44] These macrocycles are attracting an increasing interest due to their interesting ability to act as supramolecular hosts in addition to its easy preparation and functionalization, which makes them interesting candidates for the development of supramolecular systems and molecular devices.[45] Hence, we found it relevant to test the capping strategy of click vinyl sulfonyl-based Michael-type reactions in the synthesis of rotaxanes incorporating this type of macrocycles. As templates we turned our attention to the 1,4-di(1,2,3-triazol-1-yl)butane unit, previously used in the synthesis of rotaxanes, due to its high binding constant (K_a = (1.6 ± 0.3) × 10^4 M^{-1} at 298 K in $CDCl_3$) with pillar[5]arene derivatives (Scheme 4).[46]

As in previous examples, we synthesised linear fragments **11a,b** with two terminal vinyl sulfone or vinyl sulfonate groups linked to the recognition core (see the Supporting Information). Thia-Michael addition of the bulky thiol **2c** to the vinyl sulfonyl moieties afforded the corresponding free threads in the usual efficient and high-yielding (82% and 94%) manner, which lead us to undertake the synthesis of the corresponding [2]rotaxanes. We reached the target structures by reacting a mixture of thread precursors **11a** or **11b** and *per*-ethyl or *per*-methyl pillar[5]arenes **12a,b**, which assemble into the corresponding pseudorotaxanes, with stopper **2c** under the same mild conditions employed with previous systems, affording rotaxanes **13a-d** in 53%−91% yield (Scheme 4). Especially remarkable is the 91% isolated yield, the highest found using this methodology, reached for the synthesis of **13b** using the *per*-methyl pillar[5]arene **12b**.

As previously, exhaustive characterization by means of 1D, 2D and DOSY NMR spectroscopy supported the proposed interlocked structures, showing the shielding of the H atoms of the central butylene unit by the macrocycle, which induces a strong shifting to lower frequencies ($\Delta\delta_{Ha}$ = −2.28−2.33 ppm and $\Delta\delta_{Hb}$ = −3.03−3.09 ppm) (for **13a,b**, see Figures S5-S6 in the Supporting Information), and the same diffusion coefficient, ranging 5.43 × 10^{-6} − 6.80 × 10^{-6} cm^2 s^{-1}, for all components in each of the interlocked structures (see Figures S141, S146, S152 and S157 in the Supporting Information). The identity of the structures was further confirmed by HRMS (see Figures S182-S191 in the Supporting Information).

Stability of the rotaxanes

After obtaining the different types of rotaxanes we studied the stability of representative examples to assess whether the presence of a sulfonate group or reactions like the retro-Michael addition could compromise the stability of the systems.[47] Therefore, the stability of rotaxanes **4a**, **7b,c** and **13b,d** in solution ($CDCl_3$) at room temperature was monitored over 7 d by ^{1}H NMR spectroscopy. No evidences of decomposition were observed as the spectra recorded after 3 and 7 days did not show any significant changes respect to those recorded straight after the preparation of the samples, thus, confirming the stability of the systems obtained from both vinyl sulfone or vinyl sulfonate groups (see Figures S13-S17 in the Supporting



Scheme 4. Synthesis of pillar[5]arene rotaxanes **13a-d** following a capping strategy involving thia-Michael reactions to vinyl sulfonyl-functionalized thread precursors **11a,b**.

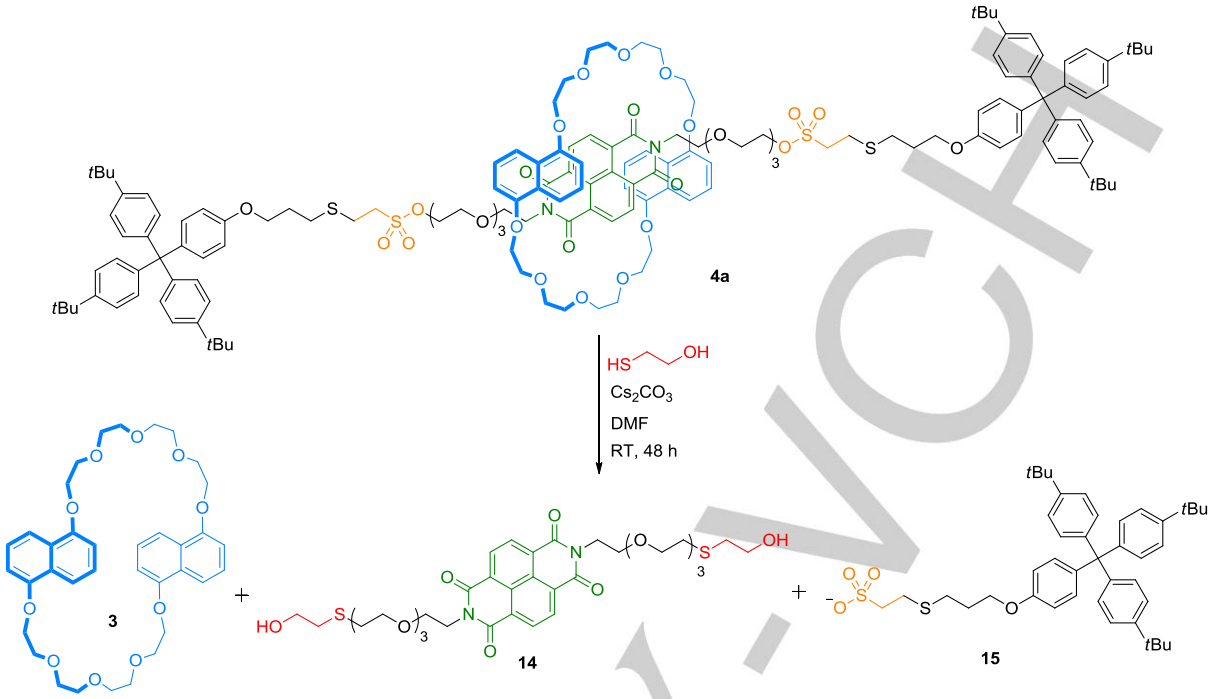
Information). Taking a step further, the stability of rotaxanes **4a** and **13d**, with a sulfonate or a sulfone group, respectively, was studied in the presence of an excess of Et_3N over 5 days. Again, the ^1H NMR spectra confirmed the stability of both rotaxanes under those conditions, as the spectra remained unchanged, except for the presence of Et_3N, compared to those in the absence of base, ruling out the retro Michael addition at room temperature in the presence of this mild base (see Figures S18-S19 in the Supporting Information).

Chemical disassembly of sulfonate rotaxane 4a

Inspired by our previous research on vinyl sulfonate CAD chemistry,[28] which showed its compatibility with biological systems, we decided to explore the possibility of disassembling into its components the rotaxanes obtained from vinyl sulfonate groups.

Hence, as proof-of-concept, we studied the disassembly of naphthalene diimide rotaxane **4a** by cleavage of the sulfonate groups through nucleophilic substitution (Scheme 5). We chose 2-mercaptoethanol as nucleophile as it can displace sulfonate moieties under mild conditions, i.e. a relatively mild base such as Cs_2CO_3 and room temperature in DMF.[48] In this manner, the reaction of rotaxane **4a** with 2-mercaptoethanol afforded a mixture of compounds which was analysed by HPLC. The main features of the chromatogram, both the retention time and the UV traces of the peaks observed, were analysed and compared to those of the starting rotaxane **4a**, its corresponding free thread, macrocycle **3** and compound **14**, the latter synthesised independently by nucleophilic substitution of the sulfonate moieties with 2-mercaptoethanol to be used as reference (see the Supporting Information). Free macrocycle **3** and axle **14** were identified as the major species in the mixture due to the presence of two peaks whose retention time and UV traces were in excellent agreement with those of the reference compounds **3** and **14**. We did not found any evidence of the presence of free thread or starting rotaxane **4a** (see Figures S8-S10 in the Supporting Information). Moreover, HRMS of the collected fractions unambiguously confirmed the identity of those species (see Figures S11-12 in the Supporting Information), supporting the proposed dethreading mechanism through cleavage or the stoppers by nucleophilic substitution of the sulfonates with a thiol. Treatment of **4a** with Cs_2CO_3 and room temperature without the thiol resulted in the recovery of the starting rotaxane as confirmed by ^1H NMR analysis of the crude mixture after workup, where only the signals of **4a** were observed, without any evidence of the presence of **14**, free **3** or their inclusion complex (see Figure S20 in the Supporting Information).

These experiments illustrate the chemical disassembly of a sulfonate rotaxane and the release of its components in a controlled manner triggered by the reaction with a suitable nucleophile. This feature exploits the CAD behaviour of the vinyl sulfonate group as it relies on the presence of a sulfonate which can undergo nucleophilic substitution but is stable under mild basic conditions in the absence of a nucleophilic species. Therefore, these results support our hypothesis of the vinyl sulfonate moiety as a general versatile group not only for the efficient synthesis of rotaxanes through click Michael-type additions, but also for their chemical disassembly and controlled release of their components.



Scheme 5. Chemical disassembly of rotaxane **4a** by nucleophilic attack of 2-mercaptoethanol to the sulfonate groups resulting from the click thia-Michael addition capping reaction.

Conclusions

As summary, we have demonstrated the application of the click thia- and aza-Michael addition to vinyl sulfone or vinyl sulfonate moieties in rotaxane synthesis through the capping strategy. The main strengths of this approach are its versatility and efficiency thanks to the mild conditions required. In this fashion, we applied the described synthetic methodology to the preparation of a series of rotaxanes based on different templates and recognition motifs, namely, naphthalene diimide units that establish donor-acceptor π-π interactions with dinaphto-38-crown-10, diketopiperazine units that interact with tetralactam macrocycles through H-bonding and 1,4-di(1,2,3-triazol-1-yl)butane derivatives as templates for pillar[5]arenes. In all cases the Michael-type addition reaction to the vinyl sulfonyl group proceeded under mild conditions, i.e. room temperature or 0 ºC and with a mild base such as Et_3N or DMAP without the need of a metal catalyst, affording the corresponding rotaxanes in around 60−90% yield in most cases. These results demonstrate the efficiency of this methodology and, in most cases, it matches or improves the yields for similar reported examples based on the same recognition motifs using alternative capping reactions. Therefore, the methodology described constitutes an efficient and convenient synthetic choice in the preparation of rotaxanes.

Moreover, the vinyl sulfonate group carries another advantage as it not only enables click Michael-type addition coupling reactions to form rotaxanes but also the controlled chemical disassembly of the rotaxanes obtained via nucleophilic substitution on the resulting sulfonates. As proof-of-concept to illustrate this behaviour, we presented the cleavage of a sulfonate rotaxane with a thiol under mild conditions, i. e. room temperature and cesium carbonate as base.

Therefore, the click Michael-type addition reaction to the vinyl sulfonyl group constitutes an interesting capping synthetic methodology and an alternative to consider when designing and synthesizing molecular devices based on rotaxane architectures.

Experimental Section

Synthesis of rotaxane 4a. A solution of **1a** (15 mg, 20 µmol) and **3** (25 mg, 40 µmol) in $CHCl_3$ (15 mL) was stirred for 10 minutes at room temperature. The solvent was removed under reduced pressure. The crude was redissolved in $CHCl_3$ (1 mL). Under Ar, to this solution were added a few drops of 2-propanol, **2a** (46 mg, 80 µmol) and 2 drops of Et_3N. The mixture was stirred for 18 h at room temperature. The solvent was evaporated under reduced pressure. The crude material was purified by a preparative TLC (SiO_2, CH_2Cl_2/MeOH 99:1) to afford **4a** (39 mg, 80%) as a red solid. See the Supporting Information for characterization details.

Synthesis of rotaxane 7c. Under inert atmosphere, to a solution of **5c** (5.0 mg, 18 µmol) and **6** (9.0 mg, 8.8 µmol) in $CHCl_3$ (8 mL) were added **2e** (45 mg, 71 µmol) and 2 drops of Et_3N. The solution was stirred for 20 h at room temperature. The solvent was removed under reduced pressure. The crude material was purified by gel permeation chromatography (Bio-Beads® S-X1, CH_2Cl_2) to afford **7c** (16 mg, 71%) as white solid. See the Supporting Information for characterization details.

Synthesis of rotaxane 10a·PF_6. **8a**·PF_6 (17 mg, 25 μmol) and **9** (57 mg, 0.13 mmol) were dissolved in CH_2Cl_2/CH_3CN (2:1, 15 mL). The solvent was removed under reduced pressure and the solid was redissolved in CH_2Cl_2 (0.8 mL). Under Ar, the solution was cooled to 0 ºC and was stirred for 1 h. **2c** (42 mg, 0.10 mmol) and a catalytic amount of DMAP were added. The mixture was stirred for 72 h at 0 ºC. The solvent was evaporated under vacuum. The crude material was purified by gel permeation chromatography (Bio-Beads® S-X1, CH_2Cl_2, and then Bio-Beads® S-X3, CH_2Cl_2). The crude was dissolved in CH_2Cl_2 (20 mL) and washed with HCl (1%, 3 × 20 mL). The organic phase was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to yield **10a**·PF_6 (36 mg, 73%) as a white solid. See the Supporting Information for characterization details.

Synthesis of rotaxane 13b. A solution of **11a** (26 mg, 43 μmol) and **12b** (160 mg, 0.21 mmol) in $CHCl_3$ (3 mL) was stirred for 5 h at room temperature under inert atmosphere. Stopper **2c** (70 mg, 0.17 mmol) and 2 drops of triethylamine were added. The resulting mixture was stirred for 24 h at room temperature. The solvent was evaporated under reduced pressure and the crude purified by two consecutive column chromatographies (firstly, SiO_2, CH_2Cl_2/hexane 30:70 to 100:0, to CH_2Cl_2/MeOH to 49:1; then SiO_2, CH_2Cl_2/MeOH 100:0 to 24:1) to afford **13b** (85 mg, 91%) as a colourless syrup. See the Supporting Information for characterization details.

Chemical disassembly of rotaxane 4a. Under an Ar atmosphere, to a solution of **4a** (16 mg, 6.2 μmol) in dry DMF (500 μL) was added 2-mercaptoethanol (2.0 μL, 31 μmol) and Cs_2CO_3 (10 mg, 31 μmol). The suspension was stirred for 48 hours under an Ar atmosphere. $LiCl_{(aq)}$ (5%, 25 mL) was added to the resulting mixture which was extracted with dichloromethane (3 × 25 mL). The combined organic phases were dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure. The resulting crude was analysed by HPLC (see the Supporting Information).

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Conflict of interest

There are no conflicts to declare.

Keywords: Rotaxanes • Michael addition • vinyl sulfonyl • coupling-and-decoupling chemistry • click chemistry

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[48] Deprotonated thiols were also used to promote stopper substitution in sulfur-containing rotaxanes through a Michael retro-Michael reaction sequence. See ref. [34c].

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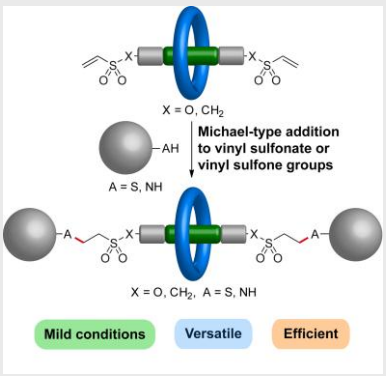
Layout 1:

FULL PAPER

Another tool in the box! The click Michael-type addition to vinyl sulfonyl groups emerges as a versatile and efficient tool for the threading-and-capping synthesis in mild conditions of rotaxanes based on different non-covalent interactions. The disassembly of the interlocked structures is also possible in designs based on vinyl sulfonate moieties.



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