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Synthesis of a pH-Sensitive Hetero[4]Rotaxane Molecular Machine that Combines [c2]Daisy and [2]Rotaxane Arrangements

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Abstract: The synthesis of a novel pH-sensitive hetero[4]rotaxane molecular machine through a self-sorting strategy is reported. The original tetra-interlocked molecular architecture combines a [c2]daisy chain scaffold linked to two [2]rotaxane units. Actuation of the system through pH variation is possible thanks to the specific interactions of the dibenzo-24-crown-8 (DB24C8) macrocycles for ammonium, anilinium, and triazolium molecular stations. Selective deprotonation of the anilinium moieties triggers shuttling of the unsubstituted DB24C8 along the [2]rotaxane units.

Introduction

The field of interlocked molecular machines appeared about twenty years ago, when the motion of one element with respect to another in a sole molecule was successfully achieved with control. Various more or less complicated interlocked molecular architectures have been reported to date. In the rotaxane series, doubly interlocked rotaxanes (i.e., [c2]daisy chain[1]) attracted chemists because of their peculiar interwoven architecture. In 2000, J.-P. Sauvage[2] was the first to report the synthesis of a metal-based doubly interlocked rotaxane that was able to act as a stimulus-responsive molecular machine.[3] This novel molecular machine was termed a "molecular muscle"[4] by the author, in reference to the contractile motion that occurs in human muscles. Indeed, such a molecular architecture can adopt different co-conformations from a stretched to a contracted state through the gliding of the macrocycles along the encircled threads (Figure 1).

Following this inspiring pioneer work, only a few teams had reported original molecular-muscle systems.[5] In 2008, we reported a straightforward chemical route to a pH-sensitive molecular muscle, which was based on ammonium and *N*-methyltriazolium stations for the dibenzo-24-crown-8 (DB24C8).[5a] Later, we synthesized several two- and three-station-based molecular muscles that adopted numerous co-conformational states, for which many induced conformational changes could be controlled.[5d] Daisy-chain precursors were also used by our group to prepare unique double-lasso rotamacrocycles that were likened to cyclic molecular muscles.[6] The challenging synthesis of new multi-interlocked[7] molecular architectures is of interest because it could lead to a wide variety of molecular motions in a single molecule. Herein, we report on the synthesis and study of an appealing pH-sensitive tetra-interlocked molecular machine **I** (Figure 2b). The molecular architecture consists of a [c2]daisy chain scaffold that is linked to two [2]rotaxane units. The molecular machinery, which is inherent to this hetero[4]rotaxane architecture, should allow for different possible co-conformational states (**I**, **J**, and **K**) that are a consequence of the gliding of the different interlocked components with respect to each other.

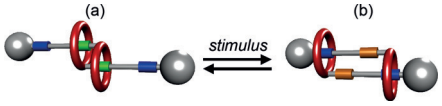

Figure 1. Representation of a [c2]daisy-chain-containing molecular muscle in a) the stretched state and b) the contracted state.

Until now, such a tetra-interlocked chemical architecture has been the subject of only one very recent publication by Tian, Qu et al. (Figure 2a).[8] They proposed a self-sorting strategy[9] that relies on the use of macrocycles with different sizes. The very well designed molecular precursors allow the various macrocycles to bind the ammonium template moieties that are present on the two different axles selectively. The self-sorting strategy is driven by the favorable daisy-chain arrangement and by the fact that the small macrocycles (in yellow) cannot thread the hermaphrodite molecule due to the presence of a too-hindering group on its axle. Moreover, in the final interlocked architecture, the small macrocycles act as stoppers for the DB24C8 (in red) and, therefore, prevent the [c2]daisy arrangement from disassembling. Herein, we propose a different self-sorting strategy for precursors **A**, **B**, and **C** by using different templates (ammonium and anilinium) for analogous DB24C8 macrocycles. On mixing **A**, **B**, and **C**, some supramolecular arrangements were formed preferentially from

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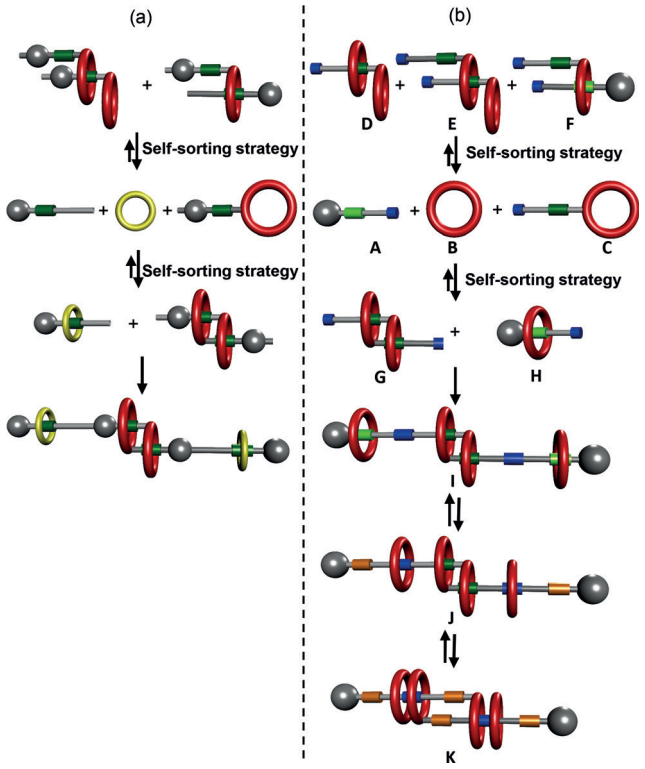


Figure 2. Two self-sorting strategies to give the targeted tetra-interlocked molecular architecture: a) self-sorting through selective recognition based on the use of different macrocycles for identical templates[8] and b) self-sorting strategy, reported herein, that relies on the selective recognition of different templates for analogous macrocycles and that could result in different possible co-conformational states. Benzylammonium template: dark green; anilinium template: light green; aniline: orange; triazolium: blue; DB24C8: red.

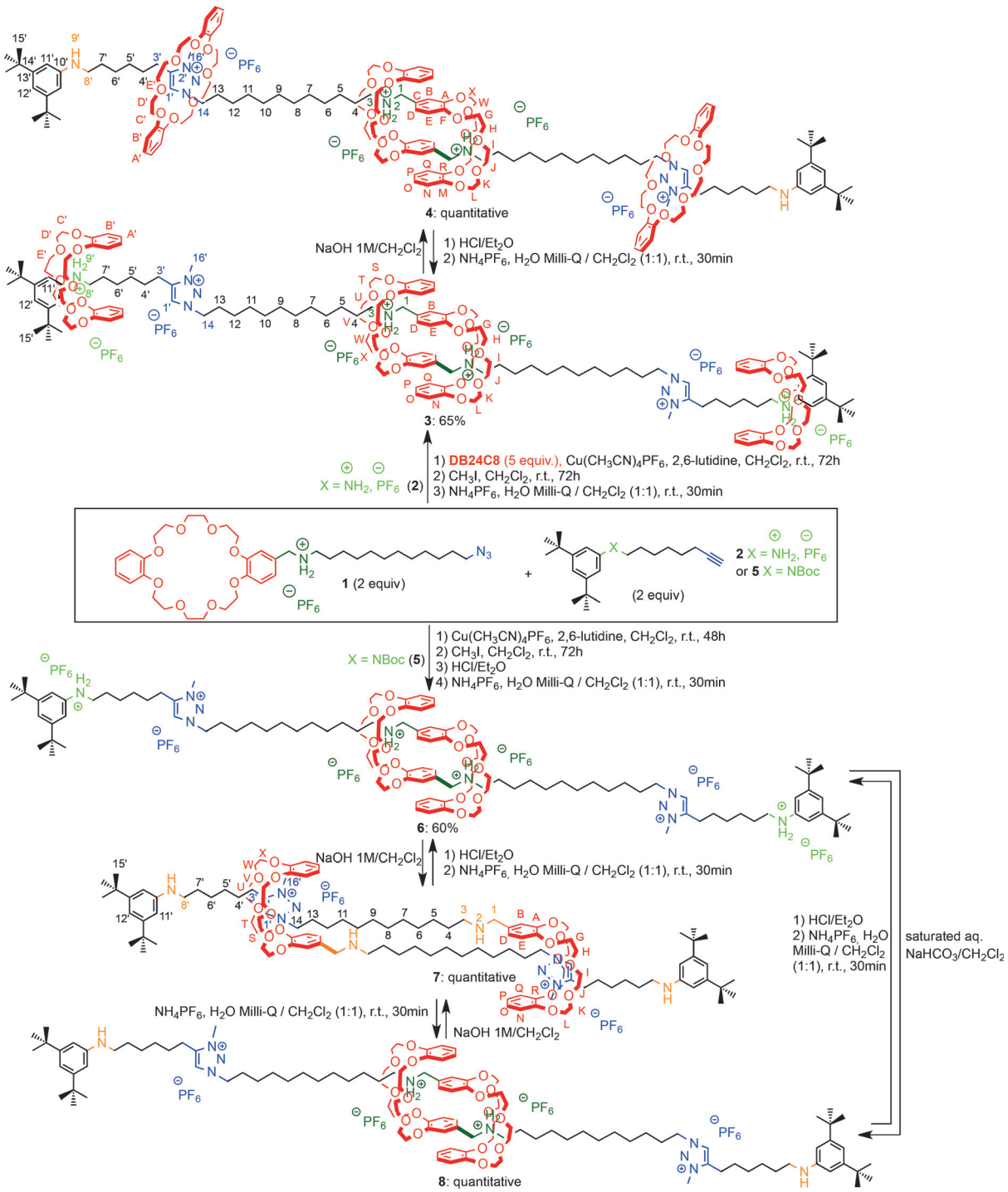
among the multiple different possible ones. Ammonium-containing hermaphrodite molecule **C** selectively assembled into an interwoven [c2]daisy chain **G**, rather than being encircled by either a free DB24C8 or another substituted macrocycle **C** to give [2]rotaxane species **D** or **E**. Similarly, hermaphrodite molecule **C** did not thread anilinium-containing axle **A** to give **F** in a preponderant fashion. On one hand, these results arise from the much greater affinity of the DB24C8 for the benzylammonium moiety than for the anilinium one. On the other hand, the possibility to achieve two binding sites between the templates and the macrocycles in a single molecule (i.e., the [c2]daisy chain) is favored in term of enthalpy with respect to the formation of single [2]rotaxanes in which interaction takes place at only one site. As a result, hermaphrodite molecule **C** could be entirely converted into [c2]daisy arrangement **G**, whereas excess DB24C8 **B** threaded chemical axle **A** quantitatively to give semi-rotaxane **H**. The subsequent chemical connection afforded tetra-interlocked architecture **I** and allowed for the incorporation of an extra unoccupied molecular station. The molecular machinery of this hetero[4]rotaxane was investigated by changing the pH.

Results and Discussion

Synthesis of pH-sensitive hetero[4]rotaxane molecular Machine 3/4 and molecular muscles 6, 7, and 8

The chemical design (i.e., macrocycle and molecular stations) of targeted hetero[4]rotaxane molecular machine **I** (compound **3**) is based on the system we published in 2008;[5a,11b] it contains ammonium, anilinium, and triazolium templates for DB24C8 macrocycles (Scheme 1). Because the ammonium moiety is a good template for DB24C8,[10] the presence of these two motifs in the same molecule (**1** is a hermaphrodite) results in the formation of a doubly interlocked rotaxane through a *meso* [c2]daisy supramolecular arrangement.[6b] The encircled molecular axles of the daisy chain scaffold have been chosen so that they also each include a *N*-methyltriazolium unit, which is known to be a site of interactions of poorer affinity than the ammonium site. They also have di-*tert*-butylanilinium molecular stations at the end of the axles, which prevent disassembly of the structure and allow us to drive the extra [2]rotaxane interlocking at each extremity of the [c2]daisy scaffold. The affinity of the anilinium group for DB24C8 is better than the triazolium station[11] but poorer than the ammonium group, which confers interesting shuttling behavior on the molecular target.

Targeted molecular machine **3** was synthesized in an overall yield of 65% from previously synthesized azido-containing hermaphrodite compound **1**, alkynanilinium **2**, and DB24C8 (Scheme 1). In the hydrogen-bond-promoting solvent CH_2Cl_2, the mixed components were self-sorted according to their affinities, and mainly self-assembled into two distinct supramolecular assemblies: a quite stable doubly interlocked [c2]daisy chain that quantitatively consumed **1** due to the two strong complementary interactions between the two hermaphrodite monomers, and a semi-rotaxane from compounds **2** and DB24C8 that both remain in solution.[12] The linkage between the two supramolecular arrangements was carried out in situ through a two-step sequence that started with a copper(I)-catalyzed Huisgen[13] alkyne–azide 1,3-dipolar cycloaddition,[14] followed by subsequent *N*-methylation of the triazole. The deprotonation of isolated hetero[4]rotaxane **3** was then studied to investigate its propensity to act as a molecular machine. Washing rotaxane **3** with an aqueous solution of sodium hydroxide (1 M) resulted in the sole deprotonation of the anilinium molecular stations, which triggered shuttling of the DB24C8 from the anilinium to the triazolium stations. No contraction of the [c2]daisy-chain-containing molecule, which would arise from a molecular-muscle actuation, was observed. ^{1}H NMR spectroscopy evidence relating to the actuation of the molecular machinery is discussed in detail below. The deprotonation of the anilinium is not a surprise if one considers its higher acidity with respect to the ammonium in the daisy arrangement. Moreover, deprotonation of the ammonium involved in the DB24C8-based [c2]daisy chain is obviously tougher than in a single ammonium-containing [2]rotaxane because twice the number of interactions exist between the ammonium groups and the DB24C8, all things being equal. However, what is very



Scheme 1. Preparations of pH-sensitive hetero[4]rotaxane molecular machines **3**/**4** and pH-sensitive molecular muscles **6**/**7**/**8**.

specific here is the impossibility of deprotonating the ammonium of the daisy-chain arrangement in the singular tetra-interlocked architecture regardless of the excess of NaOH used and the experimental conditions used.[15] This problem was not expected because deprotonation of analogous (albeit only bis-interlocked) synthesized molecular muscles **6** and **8**[16] could be easily achieved under the same experimental conditions, which trigger with efficacy contracted state **7** (Scheme 1). In bis-interlocked molecular muscle **8**, we assume that the free *N*-methyltriazolium molecular station may assist the deprotonation of the ammonium in the daisy arrangement. Certainly, in this case, the free triazolium site can be partially occupied by the daisy-DB24C8, although in a very minimal fashion in the protonated state. However, this possibility for the daisy-DB24C8 to move slightly from its more stable site is sufficient to help the deprotonation of the daisy ammonium due to thermodynamic factors. Indeed, it is known that an ammonium group encircled by a crown ether has a lower acidity than

a free ammonium group due to stabilization of the cationic species.[17] Therefore, in structure **8**, the possibility for the triazolium sites to be minimally occupied by the crown ethers of the daisy arrangement allows the ammonium groups to be much less hindered (i.e., in a very small population of protonated contracted co-conformers) and, therefore, more subject to deprotonation. In contrast, when the triazolium sites are occupied by the extra DB24C8 (as in **4** because of the easy and fast deprotonation of the anilinium moieties), the deprotonation of the ammonium-containing daisy chain is highly affected. With respect to **8**, the localization of the extra DB24C8 around the triazolium groups in **4** obviously decreases the population of a possible minimal ratio of a contracted protonated daisy scaffold due to the competitive interactions between the triazolium and, respectively, the extra DB24C8 or the daisy-DB24C8.

Interestingly, in the bis-interlocked molecular-muscle series, the selective diprotonation of contracted molecular muscle **7** was possible by washing with an aqueous solution of the weak acid NH_4PF_6. This very easy selective protonation of amine-containing [c2]daisy chain **7** triggers the extension of the molecular muscle and corroborates the high difference in pK_a observed between an anilinium-containing [2]rotaxane and an ammonium-including [c2]daisy chain. Moreover, the complete protonation of contracted molecular muscle **7** allowed isolation of molecular muscle **6**, which lies in an exclusive extended co-conformation and thus demonstrates the high preference of the daisy-DB24C8 for the benzylammonium compared with the anilinium stations. It is also worth noting that selective deprotonation of the anilinium moieties was possible for extended fully protonated molecular muscle **6** by washing with an aqueous saturated solution of sodium hydrogen carbonate, which again corroborates the high difference in pK_a observed between an anilinium-containing [2]rotaxane and an ammonium-including [c2]daisy chain.

^{1}H NMR spectroscopy evidence of the molecular machinery observed in molecular muscles 6, 7, and 8

The co-conformations adopted by molecular muscles **6**, **7**, and **8** are shown by comparison of their ^{1}H NMR spectra with those of their non-interlocked analogues (Figure 3).

The direct comparison between the ^{1}H NMR spectrum of doubly interlocked compound **6** with that of its non-interlocked analogue **6u** demonstrates the extended co-conformation of molecular muscle **6** (Figure 3a–b). In compound **6**, the methylene hydrogen atoms of the DB24C8, H^{G-L} and H^{S-X}, are all split because they are facing the two nonsymmetrical ends of the threaded axle. Moreover, the aromatic hydrogen atoms of the DB24C8, and in particular H^E, are all shifted upfield in the interlocked structure because they each experience the shielding effect of the other aromatic rings of the daisy arrangement. The upfield shift of H^E[5a,5d,19] is typical of the [c2]daisy arrangement in the stretched co-conformation of the molecular muscle because it indicates the sandwich-type conformation adopted by the aromatics of the two DB24C8 units. The extended co-conformation of **6** is corroborated by the downfield shift of H^1, H^3, and to a lesser extent H^4 ($\Delta\delta = 0.41$, 0.43 and 0.06 ppm, respectively) that belong to the ammonium sites. These chemical shift displacements are due to hydrogen-bond interactions with the oxygen atoms of DB24C8. Selective deprotonation of the anilinium moieties of **6** led to molecular muscle **8**, which remains in the same extended co-conformation. This was confirmed by a direct comparison of the ^{1}H NMR spectra of **6** and **8** (Figure 3b–c). Indeed, in **8** all the NMR signals remained unchanged, with the exception of the hydrogen atoms that are close to the anilinium sites. Only hydrogen atoms $H^{11'}$, $H^{12'}$, $H^{8'}$, and to a lesser extent $H^{7'}$ are shifted upfield in **8** ($\Delta\delta = -0.45$, -0.47, -0.16, and -0.09 ppm, respectively) because of the deprotonation of the anilinium. Fully deprotonated molecular muscle **7** could be obtained from either **6** or **8** by using an aqueous solution of sodium hydroxide. The contracted co-conformation of **7** was shown by the comparison of NMR spectra of **8** and **7** (Figure 3c–d). In this state (**7**), the DB24C8 units are localized around the triazolium stations. Obviously, H^1, H^3, and H^4 are shifted upfield in **7** ($\Delta\delta = -0.87$, -0.94, and -0.32 ppm, respectively) as a result of the deprotonation of the ammoniums of the daisy chain. More interestingly, the hydrogen atoms $H^{1'}$, H^{14}, $H^{3'}$, and $H^{16'}$ that belong to the triazolium station are now highly affected by the new localization of DB24C8. Indeed, on one hand, $H^{1'}$, $H^{3'}$, and H^{14} are all shifted downfield in **7** ($\Delta\delta = 0.77$, 0.59, and 0.45 ppm, respectively) because of their hydrogen-bonding interactions with the oxygen atoms of DB24C8. On the other hand, methyl hydrogen atoms $H^{16'}$ are shielded in **7** ($\Delta\delta = -0.41$ ppm) because they experience the shielding effect of the aromatic rings of DB24C8. Eventually, the contracted conformational state of molecular muscle **7** could be confirmed through the direct comparison of its ^{1}H NMR spectrum with that of uncomplexed analogue **7u** (Figure 3d–e). In that case, the same trend in chemical shift displacements was observed for the hydrogen atoms of the triazolium station ($H^{1'}$, $H^{3'}$, H^{14}, and $H^{16'}$; $\Delta\delta = 0.79$, 0.61, 0.48, and -0.40 ppm, respectively). This trend corroborates the new localization of DB24C8 around the triazolium stations in **7**, whereas the splitting of the methylene hydrogen atoms of DB24C8 in **7** accounts for the doubly interlocked molecular architecture.

^{1}H NMR spectroscopy evidence for the molecular machinery in hetero[4]rotaxanes 3/4

The molecular machinery observed upon a change in pH for hetero[4]rotaxanes **3**/**4** was shown by using ^{1}H NMR spectroscopy through a comparison of the spectra of the examined interlocked molecules with their non-interlocked analogues (Figure 4).

The direct comparison between specifically diprotonated molecular muscle **8** and its non-interlocked analogue **8u**[18] reveals both the doubly interlocked [c2]daisy arrangement and the extended co-conformation (Figure 4a, b). Indeed, the methylene hydrogen atoms of the daisy-chain macrocycles are all very split in **8** because they are facing the two nonsymmetrical ends of the [c2]daisy chain. Moreover, the hydrogen atoms of the aromatic ring of DB24C8 and, more particularly, H^E are

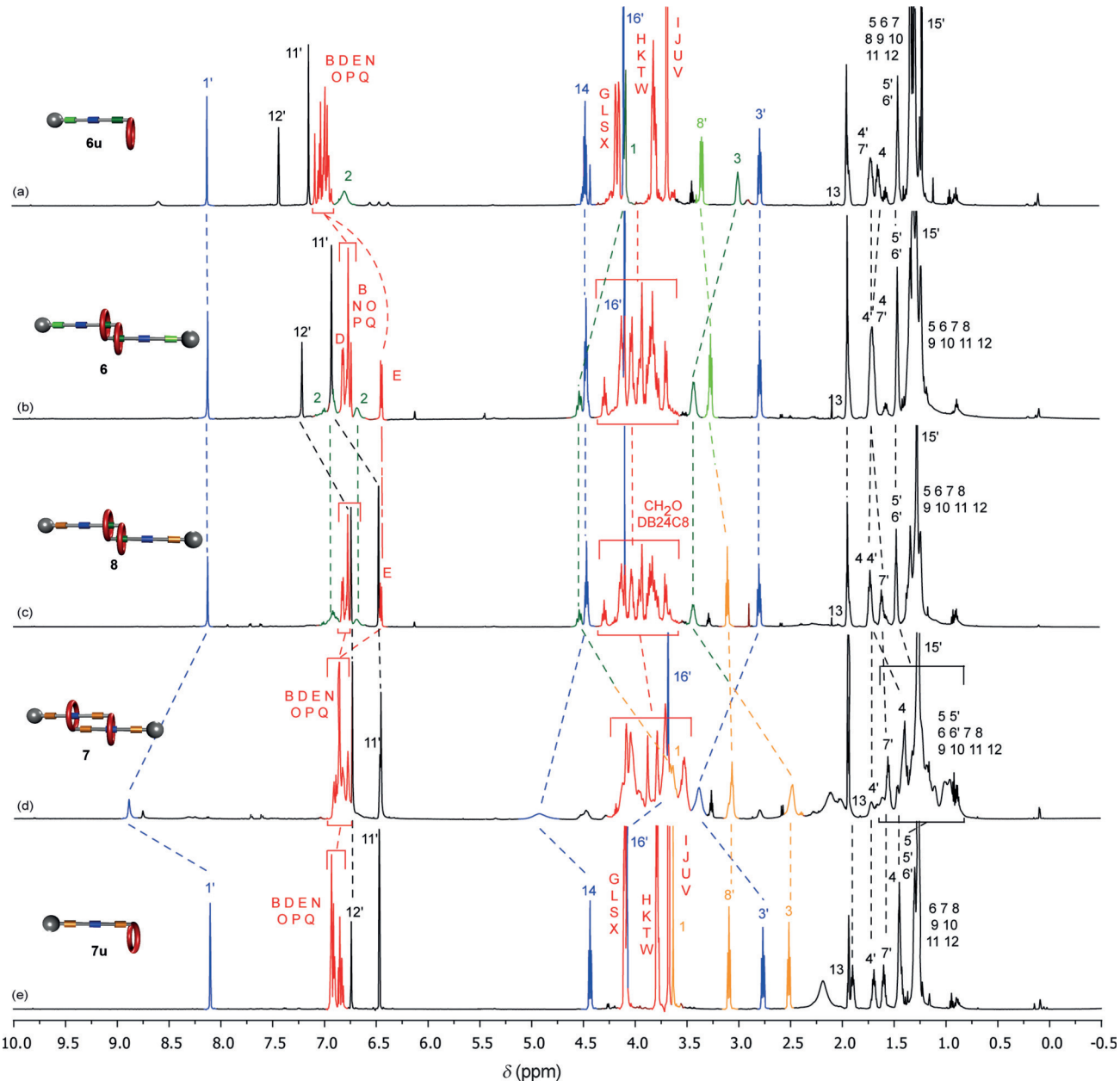


Figure 3. ^{1}H NMR spectra (CD_3CN, 298 K, 600 MHz) of a) fully protonated uncomplexed thread **6u**, b) tetra-protonated extended molecular muscle **6**, c) specifically diprotonated extended molecular muscle **8**, d) fully deprotonated molecular muscle **7**, e) fully deprotonated uncomplexed thread **7u**. The numbering and color of the signals correspond to those indicated in Scheme 1.

shielded in **8** ($\Delta\delta = -0.55$ ppm) because they undergo the shielding effect of the two aromatic rings of the other DB24C8 unit. The stretched doubly interlocked co-conformation is confirmed in **8** by the downfield shift of the hydrogen atoms that belong to the ammonium station H^1, H^3, and to a lesser extent H^4 ($\Delta\delta = 0.62$, 0.64, and 0.17 ppm, respectively) due to their hydrogen-bonding interactions with the oxygen atoms of the crown ether. No other chemical shift variation is noticed for the other hydrogen atoms between **8u** and **8**, which corroborates the structure drawn for **8** in Scheme 1. The direct comparison between molecular muscle **8** and hetero[4]rotaxane molecular machine **4** allows us to localize the extra DB24C8 around the triazolium station and the stretched state of molecular muscle **4** (Figure 4b, c). First, note the appearance in **4** of a new set of signals for the hydrogen atoms $H^{A'-E'}$ from the extra DB24C8. Moreover, the stretched state of the [c2]daisy chain is indicated by the absence of any variation in the signals of H^E, H^1, H^3, H^4, which accounts for the daisy chain as discussed above. However, the hydrogen atoms of the triazolium station are now affected by the presence of the extra DB24C8 units. Indeed, $H^{1'}$, $H^{3'}$, and H^{14} are all shifted downfield in **4** ($\Delta\delta = 0.64$, 0.63, and 0. 48 ppm, respectively) because of their hydrogen-bonding interactions with the oxygen atoms of the extra DB24C8. Concomitantly, the hydrogen atoms $H^{16'}$, $H^{4'-6'}$, and H^{10-12} experience the shielding effect of the extra DB24C8 ($\Delta\delta = -0.10 - -0.39$ ppm). The pH-sensitive molecular machi-

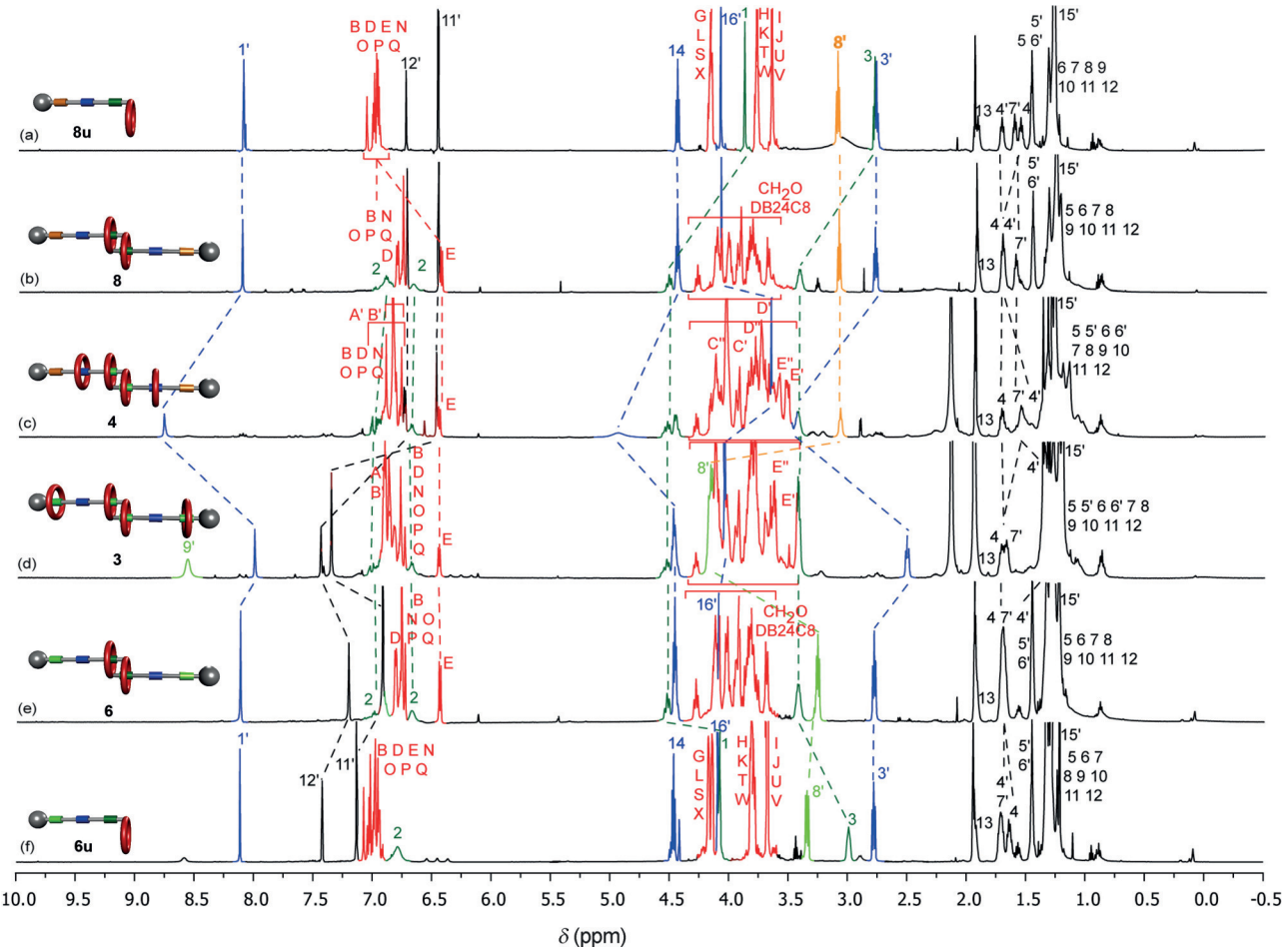


Figure 4. ^{1}H NMR spectra (CD_3CN, 298 K, 600 MHz) of a) specifically mono-protonated uncomplexed thread **8u**, b) specifically diprotonated molecular muscle **8**, c) specifically diprotonated hetero[4]rotaxane molecular machine **4**, d) tetra-protonated hetero[4]rotaxane molecular machine **3**, e) tetra-protonated molecular muscle **6**, f) diprotonated uncomplexed thread **6u**. The numbering and color of the signals correspond to those indicated in Scheme 1.

nery between specifically diprotonated hetero[4]rotaxane molecular machine **4** and tetra-protonated hetero[4]rotaxane molecular machine **3** was demonstrated by the direct comparison of their ^{1}H NMR spectra (Figure 4c, d). No variation in the chemical shifts of the hydrogen atoms of the daisy arrangement (in particular H^{E}, H^{1}, and H^{3-4}) was noted, which reveals a stretched co-conformation for both compounds. In protonated compound **3**, the localization of the extra DB24C8 around the anilinium is highlighted by the very high chemical shift of $H^{9'}$ (i.e., NH_2) and by the downfield shifts of $H^{8'}$, $H^{11'}$, $H^{12'}$, and to a lesser extent $H^{7'}$ of the anilinium site ($\Delta\delta = 1.10$, 0.98, 0.69, and 0.12 ppm, respectively), which are due to their implication in hydrogen bonding with the extra DB24C8. This matches perfectly with the upfield shifts observed in **3** for the hydrogen atoms of the triazolium station $H^{1'}$, $H^{3'}$, and to a lesser extent H^{14} and $H^{4'}$ ($\Delta\delta = -0.77$, -0.95, -0.47, and -0.17 ppm) as a result of the displacement of the extra DB24C8 away from the triazolium groups. Finally, $H^{E'-E''}$ of the extra DB24C8 are slightly shifted upfield in **3** due to their localization in the shielding region of the anilinium aromatic ring. The localization of the macrocycles in **3** was confirmed by the direct comparison with tetra-protonated molecular muscle **6** (Figure 4d, e). Briefly, in tetra-protonated compound **6**, the molecular muscle lies in an extended state, which reveals that the ammonium station has a better affinity for DB24C8 than the anilinium group. Indeed, the sandwich-type arrangement of DB24C8 is also observed (see the particular upfield chemical shift for H^{E}). The main difference in **3** resides in the downfield shift in the chemical shifts of the hydrogen atoms $H^{8'}$, $H^{11'}$, and $H^{12'}$ of the anilinium station due to their hydrogen bonding with the extra DB24C8 and the shielding of $H^{3'-4'-5'}$ due to their localization in the shielding cavity of the extra DB24C8. These comparisons between **3** and **6** illustrate the localization of DB24C8 around the anilinium site in **3** and the extended state of the muscle. This last extended co-conformation is finally corroborated by a direct comparison between the ^{1}H NMR spectra of **6** and its non-interlocked analogue **6u**[15] (Figure 4e, f), for which exactly the same trend in the displacement of chemical shifts can be observed between **6** and **6u** as between **8** and **8u**.

Conclusion

We report the self-assembled synthesis of a novel molecular architecture that contains a [c2]daisy scaffold linked to two [2]ro-

taxane units. The combination of different molecular stations (ammonium, anilinium, and triazolium) with DB24C8 units allowed for the molecular shuttling of the extra DB24C8 in the two rotaxane units. Nevertheless, the molecular muscle could not be actuated because of the impossibility of deprotonating the ammonium station regardless of the conditions. This result was unexpected because deprotonation of analogous molecular muscles, albeit only bis-interlocked and thus devoid of the extra DB24C8 on the axle linked to the daisy scaffold, could be protonated and deprotonated easily, to give at will an extended or a contracted co-conformational state. Chemical access to such tetra-interlocked molecular architectures now paves the way to the possibility of generating multiple different motions in a single molecule.

Experimental Section

Hetero[4]rotaxane 3

Step 1

Alkynanilinium **2** (55 mg, 2 equiv, 0.12 mmol) and dibenzo-24-crown-8 (135 mg, 5 equiv, 0.3 mmol) were added to a flask (volume: 5 mL) and dissolved in dry, degassed CH_2Cl_2 (1 mL). After stirring for 15 min at RT, hermaphrodite molecule **1** (100 mg, 2 equiv, 0.12 mmol) was added to the solution, followed by $Cu(CH_3CN)_4PF_6$ (22 mg, 1 equiv, 0.06 mmol) and a drop of 2,6-lutidine. The mixture was stirred at RT for 72 h. The residue was then diluted with CH_2Cl_2 (15 mL) and washed with aqueous disodium ethylenediaminetetraacetate dihydrate (0.1 M; 2×40 mL). The combined aqueous layers were extracted with CH_2Cl_2 (3×20 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude product was purified by using chromatography on a lipophilic Sephadex LH-20 column (solvent elution: CH_2Cl_2) to afford the pure hetero[4]rotaxane intermediate as a brown solid (yield: 143 mg, 69%). R_f: 0.55 (CH_2Cl_2/CH_3OH 9:1); ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): $\delta = 8.48$ (br s, 4H; $H^{9'}$), 7.45 (s, 2H; $H^{1'}$), 7.33 (s, 4H; $H^{11'}$), 7.31 (s, 2H; $H^{12'}$), 6.93–6.74 (m, 16H; $H^{A'}$ $H^{B'}$ H^{N} H^{O} H^{P} H^{Q}), 6.88 (d, $^3J(H^D,H^E) = 8.1$ Hz, 2H; H^D), 6.65 (d, $^3J(H^D,H^E) = 8.1$ Hz, 2H; H^E), 6.64 (s, 2H; H^B), 4.52–4.35 (m, 4H; H^1), 4.52–3.55 (m, 48H; H^G H^H H^I H^J H^K H^L H^S H^T H^U H^V H^W H^X), 4.33 (t, $^3J(H^{14},H^{13}) = 7.3$ Hz, 4H; H^{14}), 4.24–4.17 (m, 8H; $H^{C''}$), 4.13–4.08 (m, 8H; $H^{C'}$), 4.12 (m, 4H; $H^{8'}$), 3.87–3.79 (m, 16H; $H^{D'}$), 3.68–3.63 (m, 8H; $H^{E''}$), 3.55–3.35 (m, 12H; H^3 $H^{E'}$), 2.54 (t, $^3J(H^{3'},H^{4'}) = 7.6$ Hz, 4H; $H^{3'}$), 1.94–1.84 (m, 4H; H^{13}), 1.74–1.64 (quint., $^3J(H^3,H^4) = {}^3J(H^4,H^5) = 7.6$ Hz, 4H; H^4), 1.64–1.53 (m, 4H; $H^{7'}$), 1.42 (quint., $^3J(H^{4'},H^{3'}) = {}^3J(H^{4'},H^{5'}) = 7.6$ Hz, 4H; $H^{4'}$), 1.37–1.28 (m, 8H; H^5 H^{12}), 1.37–1.10 (m, 24H; H^6 H^7 H^8 H^9 H^{10} H^{11}), 1.28–1.10 (m, 8H; $H^{5'}$ $H^{6'}$), 1.19 ppm (s, 36H; $H^{15'}$); ^{13}C NMR (101 MHz, $CDCl_3$, 298 K): $\delta = 152.7$, 147.7, 147.6, 147.5, 146.4, 146.2, 135.3 (C^A C^C C^F C^M C^R $C^{2'}$ $C^{10'}$ $C^{13'}$ $C^{14'}$), 123.5 ($C^{12'}$), 121.6 ($C^{1'}$), 121.1, 121.0, 112.9, 112.8, 112.4, 111.8 ($C^{A'}$ C^B $C^{B'}$ C^D C^E C^N C^O C^P C^Q), 117.0 ($C^{11'}$), 72.2, 72.0, 70.9, 70.8, 70.3, 70.4, 68.4, 68.2, 67.5, 67.1, 66.9 (C^G C^H C^I C^J C^K C^L C^S C^T C^U C^V C^W C^X), 70.9 ($C^{E'}$ $C^{E''}$), 70.3 ($C^{D'}$), 68.2 ($C^{C'}$ $C^{C''}$), 52.2 (C^1), 50.9 ($C^{8'}$), 50.2 (C^{14}), 49.9 (C^3), 31.3 ($C^{15'}$), 30.5 (C^{13}), 29.5, 29.4, 29.3, 29.2, 29.1, 29.0, 26.6, 25.9 ($C^{4'}$ C^5 $C^{5'}$ C^6 $C^{6'}$ C^7 C^8 C^9 C^{10} C^{11} C^{12}), 27.7 ($C^{7'}$), 26.7 (C^4), 25.6 ppm ($C^{3'}$); HRMS (ESI): *m/z* calcd for $[C_{166}H_{254}N_{10}O_{32}]^{4+}$: 724.9639 $[M-4PF_6]^{4+}$; found: 724.9652.

Step 2

The previously isolated intermediate (143 mg, 1 equiv, 0.041 mmol) was dissolved in dry CH_2Cl_2 (0.5 mL). An excess of iodomethane (4 mL) was added to the solution and the mixture was stirred at RT for 72 h. The solution was then evaporated and the residue was diluted in Milli-Q water (2 mL). Ammonium hexafluorophosphate (39 mg, 6 equiv, 0.246 mmol) was introduced and CH_2Cl_2 (2 mL) was added to the solution. The resulting bilayer solution was vigorously stirred at RT for 30 min. After separation, the aqueous layer was extracted with CH_2Cl_2 (3×15 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to obtain fully protonated triazolium-containing hetero[4]rotaxane molecular machine **3** as a brown solid (yield: 146 mg, 94%). R_f: 0.60 (CH_2Cl_2/CH_3OH 9:1); ^{1}H NMR (600 MHz, CD_3CN, 298 K): $\delta = 8.55$ (br s, 4H; $H^{9'}$), 7.99 (s, 2H; $H^{1'}$), 7.43 (s, 2H; $H^{12'}$), 7.35 (s, 4H; $H^{11'}$), 7.04–6.94, 6.67 (m, 4H; H^2), 6.94–6.84 (m, 16H; $H^{A'}$ $H^{B'}$), 6.82 (d, $^3J(H^D,H^E) = 8.2$ Hz, 2H; H^D), 6.79–6.71 (m, 10H; H^B H^N H^O H^P H^Q), 6.44 (d, $^3J(H^E,H^D) = 8.2$ Hz, 2H; H^E), 4.59–4.41 (m, 4H; H^1), 4.47 (t, $^3J(H^{14},H^{13}) = 7.3$ Hz, 4H; H_{14}), 4.21–3.38 (m, 48H; H^G H^H H^I H^J H^K H^L H^S H^T H^U H^V H^W H^X), 4.21–4.06 (m, 16H; $H^{C'}$), 4.17 (m, 4H; $H^{8'}$), 4.04 (s, 6H; $H^{16'}$), 3.89–3.72 (m, 16H; $H^{D'}$), 3.65–3.58 (m, 8H; $H^{E''}$), 3.46–3.38 (m, 12H; H^3 $H^{E'}$), 2.51 (t, $^3J(H^{3'},H^{4'}) = 7.8$ Hz, 4H; $H^{3'}$), 1.94 (m, 4H; H^{13}), 1.71 (quint., $^3J(H^4,H^3) = {}^3J(H^4,H^5) = 7.8$ Hz, 4H; H^4), 1.67 (m, $^3J(H^{7'},H^{6'}) = {}^3J(H^{7'},H^{8'}) = 7.5$ Hz, 4H; $H^{7'}$), 1.41–1.35 (m, 4H; $H^{4'}$), 1.41–1.17 (m, 40H; H^5 $H^{5'}$ H^6 $H^{6'}$ H^7 H^8 H^9 H^{10} H^{11} H^{12}), 1.20 ppm (s, 36H; $H^{15'}$); ^{13}C NMR (151 MHz, CD_3CN, 298 K): $\delta = 153.9$, 148.6, 147.1, 145.6, 136.2, 128.5, 126.4, 123.7 (C^A C^C C^F C^M C^R $C^{2'}$ $C^{10'}$ $C^{13'}$ $C^{14'}$), 125.1 ($C^{12'}$), 122.4, 122.3, 121.7, 114.3, 113.6, 113.5, 113.1, 112.8 ($C^{A'}$ C^B $C^{B'}$ C^D C^E C^N C^O C^P C^Q), 121.7 ($C^{1'}$), 117.9 ($C^{11'}$), 73.1, 71.6, 71.5, 71.3, 71.2, 69.8, 69.3, 69.1, 68.6, 68.3, 68.2, 68.1 (C^G C^H C^I C^J C^K C^L C^S C^T C^U C^V C^W C^X), 71.7 ($C^{E'}$ $C^{E''}$), 71.2 ($C^{D'}$), 69.3 ($C^{C'}$), 54.7 (C^{14}), 52.9 (C^1), 51.7 ($C^{8'}$), 49.9 (C^3), 38.3 ($C^{16'}$), 31.5 ($C^{15'}$), 30.4, 30.3, 30.2, 30.0, 29.3, 28.3, 27.4, 26.7, 26.5 ($C^{4'}$ C^5 $C^{5'}$ C^6 $C^{6'}$ C^7 C^8 C^9 C^{10} C^{11} C^{12}), 29.7 (C^{13}), 27.4 (C^4 $C^{7'}$), 23.7 ppm ($C^{3'}$); HRMS (ESI): *m/z* calcd for $[C_{168}H_{260}N_{10}O_{32}]^{6+}$: 488.3171 $[M-6PF_6]^{6+}$; found: 488.3181.

Hetero[4]rotaxane 4

A solution of tetra-protonated triazolium-containing hetero[4]rotaxane molecular machine **3** (42 mg, 1 equiv, 0.011 mmol) in CH_2Cl_2 (15 mL) was washed with aqueous sodium hydroxide (1 M; 2× 15 mL). The aqueous layer was extracted with CH_2Cl_2 (3×15 mL), then the combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to obtain selectively dideprotonated triazolium-containing hetero[4]rotaxane molecular muscle **4** quantitatively as a brown solid (yield: 38 mg). R_f: 0.53 (CH_2Cl_2/CH_3OH 9:1); ^{1}H NMR (600 MHz, CD_3CN, 298 K): $\delta = 8.76$ (s, 2H; $H^{1'}$), 6.68–6.92, 6.67 (m, 4H; H^2), 6.92–6.75 (m, 10H; H^B H^N H^O H^P H^Q), 6.87–6.79 (m, 16H; $H^{A'}$ $H^{B'}$), 6.81 (d, $^3J(H^D,H^E) = 8.2$ Hz, 2H; H^D), 6.74 (br t, 2H; $H^{12'}$), 6.47 (br d, 4H; $H^{11'}$), 6.44 (d, $^3J(H^E,H^D) = 8.2$ Hz, 2H; H^E), 4.94 (br s, 4H; H^{14}), 4.59–4.41 (m, 4H; H^1), 4.18–3.61 (m, 48H; H^G H^H H^I H^J H^K H^L H^S H^T H^U H^V H^W H^X), 4.15–4.06 (m, 8H; $H^{C''}$), 4.06–3.98 (m, 8H; $H^{C'}$), 3.82–3.76 (m, 8H; $H^{D''}$), 3.76–3.69 (m, 8H; $H^{D'}$), 3.65 (s, 6H; $H^{16'}$), 3.62–3.55 (m, 8H; $H^{E''}$), 3.55–3.47 (m, 8H; $H^{E'}$), 3.47–3.37 (m, 8H; H^3 $H^{3'}$), 3.07 (t, $^3J(H^{8'},H^{7'}) = 6.4$ Hz, 4H; $H^{8'}$), 1.96–1.89 (m, 4H; H^{13}), 1.72 (quint., $^3J(H^4,H^3) = {}^3J(H^4,H^5) = 7.9$ Hz, 4H; H^4), 1.61–1.49 (m, 8H; $H^{4'}$ $H^{7'}$), 1.49–0.96 (m, 40H; H^5 $H^{5'}$ H^6 $H^{6'}$ H^7 H^8 H^9 H^{10} H^{11} H^{12}), 1.27 ppm (s, 36H; $H^{15'}$); ^{13}C NMR (151 MHz, CD_3CN, 298 K): $\delta = 152.5$, 149.7, 148.8, 148.6, 147.3, 147.1, 126.4 (C^A C^C C^F C^M C^R $C^{2'}$ $C^{10'}$ $C^{13'}$ $C^{14'}$), 129.8 ($C^{1'}$), 123.7, 123.2, 122.5, 121.8, 121.7, 114.3, 113.6, 113.1, 112.8, 112.1 ($C^{12'}$ $C^{A'}$ C^B $C^{B'}$ C^D C^E C^N C^O C^P C^Q), 108.2 ($C^{11'}$), 73.1, 71.9, 71.7, 71.6, 71.5, 71.4, 71.2, 71.1, 70.9, 70.3, 70.2, 70.0, 69.2, 68.6, 68.3, 68.2, 68.1 ($C^{C'}$ $C^{C''}$ $C^{D'}$ $C^{D''}$ $C^{E'}$ $C^{E''}$ C^G C^H C^I C^J C^K C^L C^S C^T C^U C^V C^W C^X), 54.5 (C^{14}), 52.9 (C^1), 49.9 ($C^{3'}$), 49.9 (C^3), 44.5 ($C^{8'}$), 31.8 ($C^{15'}$), 37.1 ($C^{16'}$), 31.9, 31.6, 31.5, 31.4, 30.4, 30.3, 30.1, 30.0, 29.9, 29.7, 29.5, 27.5, 27.4, 27.2 ppm (C4 $C^{4'}$ C^5 $C^{5'}$ C^6 $C^{6'}$ C^7 $C^{7'}$

C^8 C^9 C^{10} C^{11} C^{12} C^{13}); HRMS (ESI): *m/z* calcd for $[C_{168}H_{260}N_{10}O_{32}]^{5+}$: 614.9733 $[M-3PF_6+2H]^{5+}$, found: 614.9746.

Extended molecular muscle 6

Step 1

Carbamoylated compound **5** (49 mg, 2 equiv, 0.12 mmol) was dissolved in dry and degassed CH_2Cl_2 (2.5 mL), then hermaphrodite molecule **1** (100 mg, 2 equiv, 0.12 mmol) was added to the solution, followed by $Cu(CH_3CN)_4PF_6$ (22 mg, 1 equiv, 0.06 mmol) and a drop of 2,6-lutidine. The reaction mixture was stirred at RT for 48 h, then CH_2Cl_2 (15 mL) was added to the mixture. The solution was washed with aqueous disodium ethylenediaminetetraacetate dihydrate (0.1 M; 3×30 mL). The combined aqueous layers were extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude product was purified by using chromatography on a silica gel column (solvent elution: CH_2Cl_2/CH_3OH 100:0 to 98:2) to afford the pure di-*N*-carbamoylated triazole-containing molecular muscle as a white solid (yield: 96 mg, 65%). R_f: 0.60 (CH_2Cl_2/CH_3OH 95:5); ^{1}H NMR (400 MHz, CD_3CN, 298 K): δ = 7.45 (s, 2H; $H^{1'}$), 7.30 (br t, $^4J(H^{12'},H^{11'})$ = 1.3 Hz, 2H; $H^{12'}$), 7.03 (d, 4H; $^4J(H^{11'},H^{12'})$ = 1.3 Hz, $H^{11'}$), 6.97–6.85, 6.68 (m, 4H; H^2), 6.85–6.71 (m, 10H; H^B H^N H^O H^P H^Q), 6.82 (d, $^3J(H^D,H^E)$ = 8.2 Hz, 2H; H^D), 6.44 (d, $^3J(H^E,H^D)$ = 8.2 Hz, 2H; H^E), 4.59–4.41 (m, 4H; H^1), 4.27 (t, $^3J(H^{14},H^{13})$ = 7.1 Hz, 4H; H^{14}), 4.19–3.65 (m, 48H; H^G H^H H^I H^J H^K H^L H^S H^T H^U H^V H^W H^X), 3.60 (t, $^3J(H^{8'},H^{7'})$ = 7.2 Hz, 4H; $H^{8'}$), 3.49–3.35 (m, 4H; H^3), 2.60 (t, $^3J(H^{3'},H^{4'})$ = 7.5 Hz, 4H; $H^{3'}$), 1.82 (quint., $^3J(H^{13},H^{14})$ = $^3J(H^{13},H^{12})$ = 7.1 Hz, 4H; H^{13}), 1.72 (quint., $^3J(H^4,H^3)$ = $^3J(H^4,H^5)$ = 7.2 Hz, 4H; H^4), 1.65–1.53 (m, 4H; $H^{4'}$), 1.53–1.43 (m, 4H; $H^{7'}$), 1.40 (s, 18H; $H^{9'}$), 1.42–1.17 (m, 40H; H^5 $H^{5'}$ H^6 $H^{6'}$ H^7 H^8 H^9 H^{10} H^{11} H^{12}), 1.30 ppm (s, 36H; $H^{15'}$); ^{13}C NMR (101 MHz, CD_3CN, 298 K): δ = 155.5, 152.2, 148.8, 148.5, 147.2, 147.0, 143.3 (C^A C^C C^F C^M C^R $C^{2'}$ $C^{10'}$ $C^{13'}$ $C^{14'}$), 123.6, 121.7, 114.2, 113.0, 112.8 (C^B C^D C^E C^N C^O C^P C^Q), 122.5 ($C^{11'}$), 122.0 ($C^{1'}$), 120.7 ($C^{12'}$), 73.1, 71.6, 71.5, 71.3, 71.1, 68.6, 68.3, 68.1, 68.0 (C^G C^H C^I C^J C^K C^L C^S C^T C^U C^V C^W C^X), 52.9 (C^1), 50.7 ($C^{8'}$), 50.6 (C^{14}), 49.9 (C^3), 31.7 ($C^{15'}$), 31.0 (C^{13}), 30.2, 30.1, 30.0, 29.7, 29.6, 29.5, 29.1, 27.3, 27.1 ($C^{4'}$ C^5 $C^{5'}$ C^6 $C^{6'}$ C^7 $C^{7'}$ C^8 C^9 C^{10} C^{11} C^{12}), 27.7 ($C^{9'}$), 27.3 (C^4), 26.2 ppm ($C^{3'}$); HRMS (ESI): *m/z* calcd for $[C_{128}H_{205}N_{10}O_{20}]^{3+}$: 734.5121 $[M-2PF_6+1H]^{3+}$, found: 734.5139.

Step 2

The previously isolated di-*N*-carbamoylated triazole-containing molecular muscle (96 mg, 1 equiv, 0.039 mmol) was dissolved in dry CH_2Cl_2 (0.5 mL) and an excess of iodomethane (3 mL) was added to the solution. The reaction mixture was stirred at RT for 72 h, then the solution was evaporated and the residue was diluted in Milli-Q water (2.5 mL). Ammonium hexafluorophosphate (38 mg, 6 equiv, 0.234 mmol) was introduced and CH_2Cl_2 (2.5 mL) was added to the solution. The resulting bilayer solution was vigorously stirred at RT for 1 h. After separation, the aqueous layer was extracted with CH_2Cl_2 (3×15 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to obtain the triazolium-containing molecular muscle as a white solid (yield: 100 mg, 92%). R_f: 0.30 (CH_2Cl_2/CH_3OH 95:5); ^{1}H NMR (600 MHz, CD_3CN, 298 K): δ = 8.11 (s, 2H; $H^{1'}$), 7.32 (t, $^4J(H^{12'},H^{11'})$ = 1.7 Hz, 2H; $H^{12'}$), 7.04 (d, $^4J(H^{11'},H^{12'})$ = 1.7 Hz, 4H; $H^{11'}$), 6.91, 6.67 (m, 4H; H^2), 6.84–6.79 (m, 2H; H^D), 6.84–6.71 (m, 10H; H^B H^N H^O H^P H^Q), 6.44 (d, $^3J(H^E,H^D)$ = 8.2 Hz, 2H; H^E), 4.56–4.42 (m, 4H; H^1), 4.46 (t, $^3J(H^{14},H^{13})$ = 7.2 Hz, 4H; H^{14}), 4.19–3.65 (m, 48H; H^G H^H H^I H^J H^K H^L H^S H^T H^U H^V H^W H^X), 4.07 (s, 6H; $H^{16'}$), 3.61 (t, $^3J(H^{8'},H^{7'})$ = 7.3 Hz, 4H; $H^{8'}$), 3.47–3.37 (m, 4H; H^3), 2.76 (t, $^3J(H^{3'},H^{4'})$ = 7.6 Hz, 4H; $H^{3'}$), 1.97–1.87 (m, 4H; H^{13}), 1.72 (quint., $^3J(H^4,H^3)$ = $^3J(H^4,H^5)$ = 7.3 Hz, 4H; H^4), 1.67 (quint., $^3J(H^{4'},H^{3'})$ = $^3J(H^{4'},H^{5'})$ = 7.6 Hz, 4H; $H^{4'}$), 1.51 (quint., $^3J(H^{7'},H^{6'})$ = $^3J(H^{7'},H^{8'})$ = 7.3 Hz, 4H; $H^{7'}$), 1.42–1.17 (m, 40H; H^5 $H^{5'}$ H^6 $H^{6'}$ H^7 H^8 H^9 H^{10} H^{11} H^{12}), 1.39 (s, 18H; $H^{9'}$), 1.31 ppm (s, 36H; $H^{15'}$); ^{13}C NMR (151 MHz, CD_3CN, 298 K): δ = 155.6, 152.3, 148.8, 147.3, 147.1, 145.7, 143.2 (C^A C^C C^F C^M C^R $C^{2'}$ $C^{10'}$ $C^{13'}$ $C^{14'}$), 128.6 ($C^{1'}$), 123.7, 122.5, 121.7, 114.3, 113.1, 112.8 (C^B C^D C^E C^N C^O C^P C^Q), 122.5 ($C^{11'}$), 120.8 ($C^{12'}$), 73.1, 73.0, 71.6, 71.5, 71.3, 71.1, 68.6, 68.3, 68.2, 68.1 (C^G C^H C^I C^J C^K C^L C^S C^T C^U C^V C^W C^X), 54.6 (C^{14}), 52.9 (C^1), 50.6 ($C^{8'}$), 49.9 (C^3), 38.2 ($C^{16'}$), 31.7 ($C^{15'}$), 30.3, 29.9, 29.7, 29.6, 29.1, 28.9, 27.5, 27.4, 26.9, 26.7 (C^4 $C^{4'}$ C^5 $C^{5'}$ C^6 $C^{6'}$ C^7 $C^{7'}$ C^8 C^9 C^{10} C^{11} C^{12}), 30.2 (C^{13}), 28.7 ($C^{9'}$), 23.7 ppm ($C^{3'}$); HRMS (ESI): *m/z* calcd for $[C_{130}H_{210}N_{10}O_{20}]^{4+}$: 588.1439 $[M-4PF_6]^{4+}$; found: 588.1444.

Step 3

The previously isolated triazolium-containing molecular muscle (63 mg, 1 equiv, 0.021 mmol) was dissolved in dry CH_2Cl_2 (0.5 mL). An excess of hydrogen chloride (2 M) in diethyl ether (15 mL) was added to the solution and the mixture was stirred at 0 °C for 2 h. The solution was evaporated, and the residue was then diluted with Milli-Q water (2 mL). Ammonium hexafluorophosphate (25 mg, 6 equiv, 0.15 mmol) was introduced and CH_2Cl_2 (2 mL) was added to the solution. The resulting bilayer solution was vigorously stirred at RT for 30 min. After separation, the aqueous layer was extracted with CH_2Cl_2 (3×15 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to obtain protonated molecular muscle **6** quantitatively as a beige solid. R_f: 0.66 (CH_2Cl_2/CH_3OH 9:1); ^{1}H NMR (600 MHz, CD_3CN, 298 K): δ = 8.12 (s, 2H; $H^{1'}$), 7.21 (s, 2H; $H^{12'}$), 6.97–6.87, 6.67 (m, 4H; H^2), 6.92 (s, 4H; $H^{11'}$), 6.81 (dd, $^4J(H^D,H^B)$ = 1.7 Hz, $^3J(H^D,H^E)$ = 8.2 Hz, 2H; H^D), 6.79–6.72 (m, 10H; H^B H^N H^O H^P H^Q), 6.44 (d, $^3J(H^E,H^D)$ = 8.2 Hz, 2H; H^E), 4.57–4.41 (m, 4H; H^1), 4.46 (t, $^3J(H^{14},H^{13})$ = 7.2 Hz, 4H; H^{14}), 4.19–3.60 (m, 48H; H^G H^H H^I H^J H^K H^L H^S H^T H^U H^V H^W H^X), 4.09 (s, 6H; $H^{16'}$), 3.47–3.37 (m, 4H; H^3), 3.26 (t, $^3J(H^{8'},H^{7'})$ = 7.4 Hz, 4H; $H^{8'}$), 2.78 (t, $^3J(H^{3'},H^{4'})$ = 7.6 Hz, 4H; $H^{3'}$), 1.97–1.88 (m, 4H; H^{13}), 1.76–1.63 (m, 12H; H^4 $H^{4'}$ $H^{7'}$), 1.49–1.41 (br quint., 8H; $H^{5'}$ $H^{6'}$), 1.40–1.14 (m, 32H; H^5 H^6 H^7 H^8 H^9 H^{10} H^{11} H^{12}), 1.30 ppm (s, 36H; $H^{15'}$); ^{13}C NMR (101 MHz, CD_3CN, 298 K): δ = 153.7, 148.7, 147.2, 147.0, 145.7 (C^A C^C C^F C^M C^R $C^{2'}$ $C^{10'}$ $C^{13'}$ $C^{14'}$), 128.6 ($C^{1'}$), 119.0 ($C^{12'}$), 114.2, 113.1, 112.8, 112.7 (C^B C^D C^E C^N C^O C^P C^Q), 113.4 ($C^{11'}$), 73.0, 71.6, 71.5, 71.3, 71.1, 68.5, 68.3, 68.1, 68.0 (C^G C^H C^I C^J C^K C^L C^S C^T C^U C^V C^W C^X), 54.6 (C^{14}), 52.9 (C^1), 49.9 (C^3), 49.5 ($C^{8'}$), 38.2 ($C^{16'}$), 31.5 ($C^{15'}$), 30.3, 30.2, 30.1, 29.9, 29.6, 29.0, 28.0, 26.8, 26.7 (C^5 $C^{5'}$ C^6 $C^{6'}$ C^7 C^8 C^9 C^{10} C^{11} C^{12}), 29.6 (C^{13}), 27.4 (C^4 $C^{4'}$ $C^{7'}$), 23.6 ppm ($C^{3'}$); HRMS (ESI): *m/z* calcd for $[C_{120}H_{195}N_{10}O_{16}]^{5+}$: 406.6957 $[M-6PF_6-H]^{5+}$; found: 406.6957.

Contracted molecular muscle 7

Extended molecular muscle **6** (61 mg, 1 equiv, 0.021 mmol) was dissolved in CH_2Cl_2 (15 mL) and washed with aqueous sodium hydroxide (1 M; 2×10 mL), then the aqueous layer was extracted with CH_2Cl_2 (3×15 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to obtain the deprotonated contracted molecular muscle **7** quantitatively as a brown solid (yield: 49 mg). R_f: 0.60 (CH_2Cl_2/CH_3OH 9:1); ^{1}H NMR (600 MHz, CD_3CN, 298 K): δ = 8.89 (s, 2H; $H^{1'}$), 6.95–6.75 (m, 14H; H^B H^D H^E H^N H^O H^P H^Q), 6.73 (t, $^4J(H^{12'},H^{11'})$ = 1.6 Hz, 2H; $H^{12'}$), 6.46 (d, $^4J(H^{11'},H^{12'})$ = 1.6 Hz, 4H; $H^{11'}$), 6.45 (br s, 2H; $H^{9'}$), 4.91 (br s, 4H; H^{14}), 4.11–3.46 (m, 48H; H^G H^H H^I H^J H^K H^L H^S H^T H^U H^V H^W H^X), 3.68 (s, 6H; $H^{16'}$), 3.63 (m, 4H; H^1), 3.46–3.30 (m, 4H; $H^{3'}$), 3.06 (t, $^3J(H^{8'},H^{7'})$ = 6.5 Hz, 4H; $H^{8'}$), 2.54–2.43 (m, 4H; H^3), 2.05–1.95 (m, 4H; H^{13}), 1.77–1.59 (m, 4H; $H^{4'}$), 1.59–1.51 (m, 4H; $H^{7'}$), 1.46–1.35 (m,

4H; H^4), 1.46–0.80 (m, 40H; H^5 $H^{5'}$ H^6 $H^{6'}$ H^7 H^8 H^9 H^{10} H^{11} H^{12}), 1.26 ppm (s, 36H; $H^{15'}$); ^{13}C NMR (101 MHz, CD_3CN, 298 K): $\delta =$ 152.4, 149.9, 149.7, 148.7, 148.6, 147.4 (C^A C^C C^F C^M C^R $C^{2'}$ $C^{10'}$ $C^{13'}$ $C^{14'}$), 122.2 ($C^{1'}$), 121.8, 114.9, 112.9, 108.1 (C^B C^D C^E C^N C^O C^P C^Q), 112.0 ($C^{12'}$), 108.1 ($C^{11'}$), 71.9, 71.7, 70.9, 70.6, 70.0, 69.9, 69.0 (C^G C^H C^I C^J C^K C^L C^S C^T C^U C^V C^W C^X), 54.4 (C^1), 54.0 (C^{14}), 50.0 ($C^{3'}$), 49.9 (C^3), 44.4 ($C^{8'}$), 39.6, 37.3, 30.9, 30.4, 30.2, 29.9, 29.7, 29.5, 29.2, 28.2, 27.5, 27.3, 26.9, 23.6 (C^4 $C^{4'}$ C^5 $C^{5'}$ C^6 $C^{6'}$ C^7 $C^{7'}$ C^8 C^9 C^{10} C^{11} C^{12} C^{13}), 35.4 ($C^{16'}$), 31.7 ppm ($C^{15'}$); HRMS (ESI): *m/z* calcd for $[C_{120}H_{195}N_{10}O_{16}]^{5+}$: 406.4951 $[M-2PF_6+3H]^{5+}$; found: 406.4951.

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[12] The ^{1}H NMR spectroscopy evidence for the self-sorting strategy is reported in the Supporting Information. In particular, the [c2]daisy chain (i.e., the supramolecular interwoven dimer of hermaphrodite compound **1**; 1 equiv) proved to be very stable in the presence of anilinium thread **2** (2 equiv) and/or the extra DB24C8 (3 and even 5 equiv), whereas anilinium-containing thread **2** was entirely encircled by the excess DB24C8.

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[15] The use of sodium hydroxide in methanol or methanol/water, or of various alkoxides in methanol, did not allow deprotonation of the daisy chain. Use of the stronger base P1-*t*Bu-tris(tetramethylene)phosphazen resulted in degradation of the compound.

[16] Molecular muscles **6**, **7**, and **8** were initially synthesized with the aim of demonstrating both the interlocked structure and the localizations of the macrocycles in hetero[4]rotaxanes **3** and **4**. Interestingly, they proved to behave very differently towards deprotonation compared with hetero[4]rotaxanes **3** and **4**. Their preparation was very similar to that of **3**, although capping of the daisy chain was realized by using Boc-protected aniline **5**.

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