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A pH-Sensitive Lasso-Based Rotaxane Molecular Switch

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Abstract: The synthesis of a pH-sensitive two-station [1]rotaxane molecular switch by self-entanglement of a non-interlocked hermaphrodite molecule, containing an anilinium and triazole moieties, is reported. The anilinium was chosen as the best template for the macrocycle benzometaphenylene[25]-crown-8 (BMP25C8) and allowed the self-entanglement of the molecule. The equilibrium between the hermaphrodite molecule and the pseudo[1]rotaxane was studied by ^{1}H NMR spectroscopy: the best conditions of self-entanglement were found in the less polar solvent CD_2Cl_2 and at high dilution. The triazole moiety was then benzylated to afford a benzyltriazolium moiety, which then played a dual role. On one hand, it acts as a bulky gate to trap the BMP25C8, thus to avoid any self-disentanglement of the molecular architecture. On another hand, it acts as a second molecular station for the macrocycle. At acidic pH, the BMP25C8 resides around the best anilinium molecular station, displaying the lasso [1]rotaxane in a loosened conformation. The deprotonation of the anilinium molecular station triggers the shuttling of the BMP25C8 around the triazolium moiety, therefore tightening the lasso.

Keywords: crown complexes · lasso · molecular switch · self-entanglement · rotaxanes

Introduction

Stimuli-responsive multicomponent molecular machines have been the subject of many efforts during the past decades, especially in designing new interlocked molecular architectures, new sites of interactions and in improving the efficiency of template-synthesis. Interlocked architectures, such as rotaxanes,[1] catenanes,[2] foldaxanes,[3] molecular muscles,[4] molecular turnstiles,[5] molecular jump-rope,[6] molecular springs,[7] and so on, have been synthesized and utilized as molecular machines by controlling the movement of one of the different interlocked components upon a specific stimulus. Among these structures, pseudo[1]rotaxanes, which consist of a macrocycle covalently linked to a molecular axle that can be threaded or not in a reversible manner, have been rather intensively studied.[8] On the contrary, the synthesis of [1]rotaxanes, in which no equilibrium takes place with their non-interlocked analogues, have been the subject of only a few reports.[9] To the best of our knowledge, no lasso molecular-machine, based on a [1]rotaxane molecular architecture and exhibiting a large amplitude movement, has been reported to date. However, new lasso-type structures with changeable conformations triggered by external stimuli appear to be appealing targets, especially because the properties of a molecule are well known to rely tremendously on its topology.[10] Bioactive molecules found in nature, like lasso-peptides, demonstrate the utility of such an interlocked lasso architecture. Indeed, the natural lasso-peptides, which consist of 16–21 amino acid residues, share a lasso structure that is responsible for the biological activity as a receptor antagonist or an enzymatic inhibitor.[11]

As part of our study devoted to the synthesis of interlocked molecular machines, we were interested in the synthesis of lasso-based molecular architectures. With this aim, we recently reported the synthesis of a unique pH-sensitive double-lasso rota-macrocycle from an ends-activated [c2]daisy chain building-block.[6] Here we present the synthesis of a new mono-lasso-based molecular switch by using a self-entanglement strategy[12] of a "hermaphrodite" molecule; this molecule is composed of a benzometaphenylene[25]crown-8 (BMP25C8) macrocyclic head and a molecular tail containing an anilinium template moiety for the BMP25C8 and terminated by a bulky di-*tert*-butylphenyl extremity. In the smaller dibenzo[24]crown-8 macrocycle (DB24C8), the triethylene glycol substituents are in *ortho* positions to each other on the aromatic rings, so that DB24C8 interacts perfectly with the ammonium moieties. On the contrary, the BMP25C8 displays a bigger cavity holding the tail and the glycol substituents of one aromatic ring in the *meta* position to each other. Even though the affinity of the anilinium template[13] for the BMP25C8 appeared to be weaker than for the DB24C8, interlocking was

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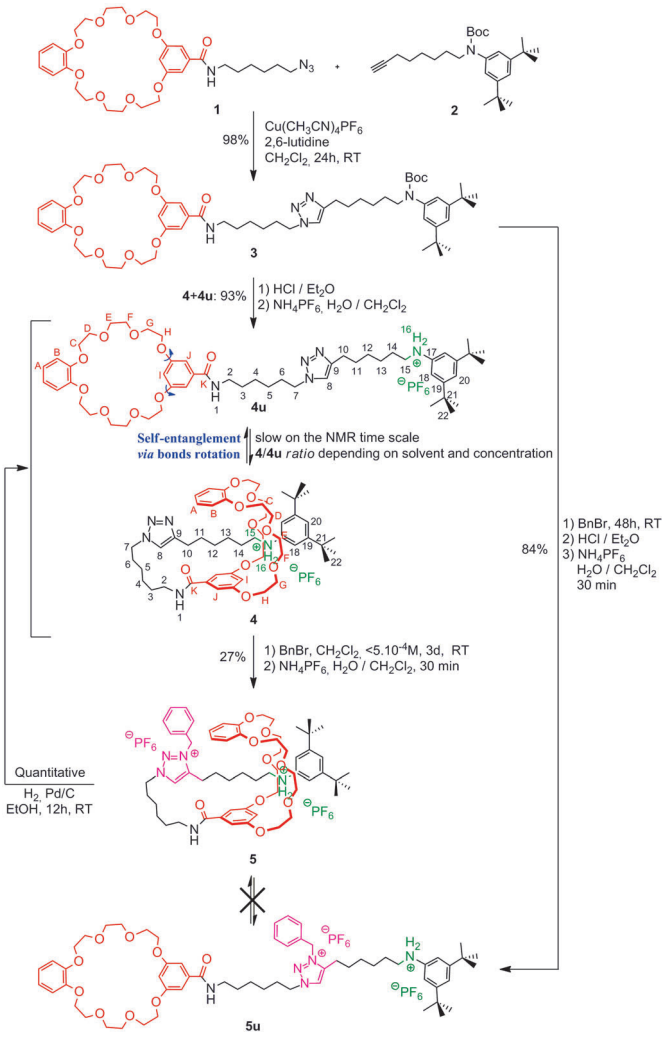
possible in some specific conditions by self-entanglement of the non-interlocked hermaphrodite molecule including the anilinium template and a triazole moiety. The subsequent benzylation of the triazole allowed, at the same time, for the creation of a second site of interactions for the BMP25C8 and for the trapping of the lasso structure by hindering the axle between the anilinium template and the BMP25C8. Variations in pH were then envisaged to obtain a tightened or a loosened lasso.

Results and Discussion

The uncomplexed thread **3** was almost quantitatively prepared from the previously synthesized macrocycle azide **1** and the *N*-Boc protected aniline alkyne **2** by using the copper(I)-catalyzed Huisgen alkyne–azide 1,3-dipolar cycloaddition in the presence of $Cu(MeCN)_4PF_6$ (1 equiv) and 2,6-lutidine (0.1 equiv)[14] (Scheme 1). The subsequent deprotection of the *N*-Boc moiety in an acidic medium revealed the anilinium moiety, which could then freely interact with the BMP25C8 macrocycle. This was achieved by using a solution of hydrochloric acid in diethyl ether, followed by a counter-anion exchange, and led, after silica gel chromatographic column, to a mixture of uncomplexed thread **4u** and pseudo[1]rotaxane **4** in 93% yield. The presence of the bulky di-*tert*-butyl anilinium extremity prevented the tail of the molecule to thread the macrocycle. However, the *meta* substitution of the aromatic ring of the macrocycle allowed for its rotation around the two carbon–oxygen σ bonds (blue arrows in Scheme 1), causing the self-entanglement of the compound. Interestingly, this self-entanglement equilibrium between **4** and **4u**, could be displaced either upon variation in solvent polarity or concentration.



Scheme 1. Synthesis of the lasso-based molecular switch **5** and its non-interlocked analogue **5u**.

The ratio **4**/**4u** was easily determined by ^{1}H NMR spectroscopy; because the equilibrium between pseudo[1]rotaxane **4** and uncomplexed thread **4u** appeared to be slow on the NMR timescale, one family of ^{1}H NMR signals for each compound was detected (Table 1 and Figures 1 and 2). The formation of the pseudo[1]rotaxane **4** proved to be dependent on the solvent polarity (Figure 1). Unsurprisingly, in the more polar $[D_6]$DMSO solvent (Figure 1a), no self-entanglement was observed, due to the high solvation of the anilinium template by DMSO, preventing from any kind of interactions between the BMP25C8 and the anilinium template. Traces of pseudo[1]rotaxane **4** were detected in CD_3OD (Figure 1b), whereas the amount of interlocked compound **4** is no longer negligible in CD_3CN (Figure 1c) and significant in the less polar solvent CD_2Cl_2 (Figure 1d).

Table 1. Ratio between [1]rotaxane **4** and uncomplexed thread **4u** depending on both concentration and solvent.

C (**4**/**4u**) [M][a]	$[D_6]$DMSO	CD_3OD	CD_3CN	CD_2Cl_2
5×10^{-2}	–	–	–	23:77
5×10^{-3}	0:100	4:96	14:86	36:64
5×10^{-4}	–	–	–	45:55

[a] Based on the integration of the ^{1}H NMR signal corresponding to H_{10}.

Variation in the concentration in CD_2Cl_2 was then realized to determine the best parameters for the self-entanglement of **4**. The ^{1}H NMR experiments at three concentrations are reported in Figure 2. It appeared that the formation of the pseudo[1]rotaxane **4** proved also to be concentration-dependent. The best experimental conditions of lasso formation were found at the lowest concentration and in the less polar solvent (i.e., CD_2Cl_2 at 5×10^{-4} M; Table 1). The pseudo[1]rotaxane was generated in a 45% ratio, which is less than the complexation that could be observed with the smaller DB24C8 macrocycle, in optimized conditions, by using the usual di-component threading method.[15] The *meta* substitutions of one aromatic ring of the BMP25C8, which cause a bigger cavity of the macrocycle and orientate the two phenoxy-oxygen atoms outside its cavity, should account for the lowering of the hydrogen-bonding interactions between the BMP25C8 and the anilinium. However, and contrary to the smaller macrocycle, here it could take ad-

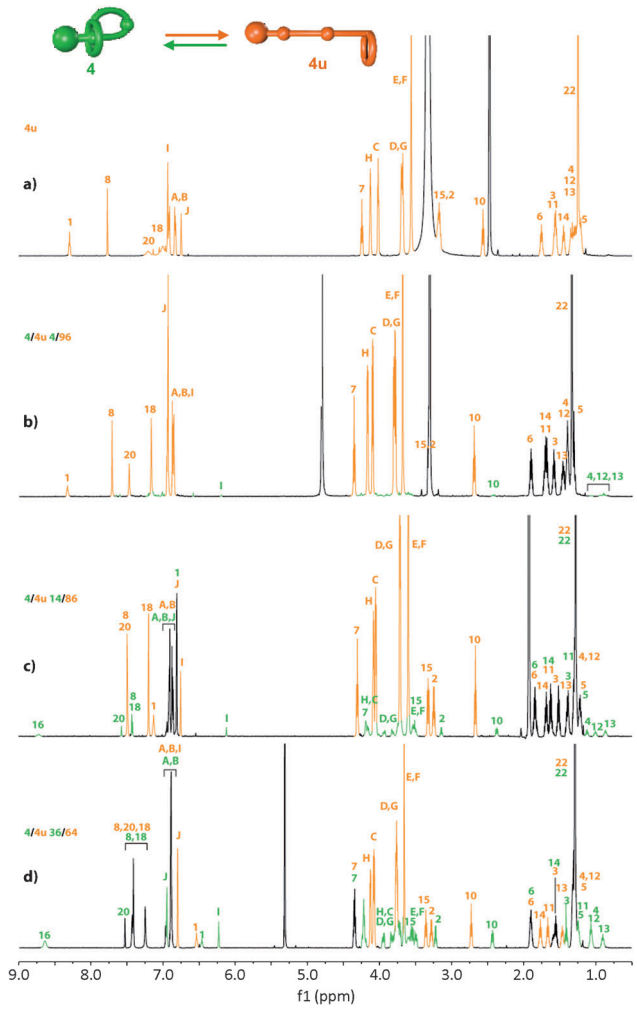


Figure 1. ^{1}H NMR spectra (600 MHz, 298 K) of a mixture of compounds **4**/**4u** at 5×10^{-3} M in: a) [D$_6$]DMSO, b) CD_3OD, c) CD_3CN, and d) CD_2Cl_2. The lettering and numbering correspond to the proton assignments indicated in Scheme 1. The green color corresponds to the lasso compound **4**, whereas the orange color corresponds to compound **4u**.

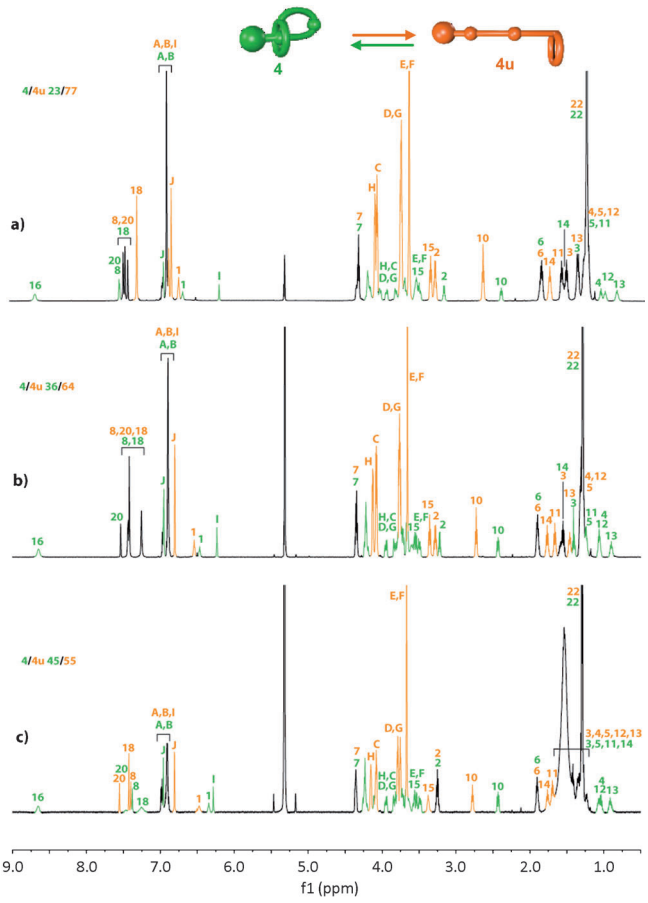
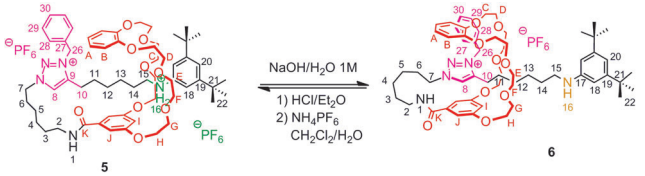


Figure 2. ^{1}H NMR spectra (600 MHz, 298 K) of compounds **4**/**4u** in CD_2Cl_2 at: a) 5×10^{-2} M, b) 5×10^{-3} M, and c) 5×10^{-4} M. The lettering and numbering correspond to the proton assignments indicated in Scheme 1. The green color corresponds to the lasso compound **4**, whereas the orange color corresponds to compound **4u**.

vantage of the bigger size of the cavity to self-entangle the structure.

Incorporation of a bulky gate[16] in the thread was subsequently realized to trap the macrocycle around the thread and to prevent the structure from any self-disentanglement. This was achieved by benzylation of the triazole moiety, with the additional aim to create a second molecular station for the BMP25C8. To favor the formation of the lasso structure, the triazole moiety was benzylated at a very low concentration ($<5\times10^{-4}$ M) by slowly adding a solution of **4**/**4u** in CH_2Cl_2 over a period of 24 h to a very large excess of benzyl bromide dissolved in dichloromethane. After stirring for a further 48 h, benzyl triazoliums **5** and **5u** were recovered separately after chromatographic columns in yields of 27 and 38%, respectively. No self-disentanglement of the lasso structure **5** towards thread **5u** was noticed by NMR spectroscopy, regardless of the solvent used, demonstrating the role of stopper of the benzyl side-chain for the BMP25C8. This was also demonstrated by synthesizing **5u** in 84% yield from the *N*-Boc thread **3**. By using this multistep synthetic strategy, no self-entanglement could be possible as long as compound **3** contains no template moiety for BMP25C8. Unmasking the anilinium template after the benzylation of the triazole did not cause any self-entanglement, signifying the absence of any equilibrium between **5u** and **5**. Nevertheless, conversion of [1]rotaxane **5** to a mixture of pseudo[1]rotaxane **4** and thread **4u** could be easily achieved by hydrogenolysis.

Variations in pH were then envisaged to tighten and loosen the lasso structure **5** (Scheme 2). At acidic pH, the BMP25C8 resides around the best anilinium molecular sta-



Scheme 2. Actuation of the lasso-based molecular switch **5**/**6** by variation of pH.

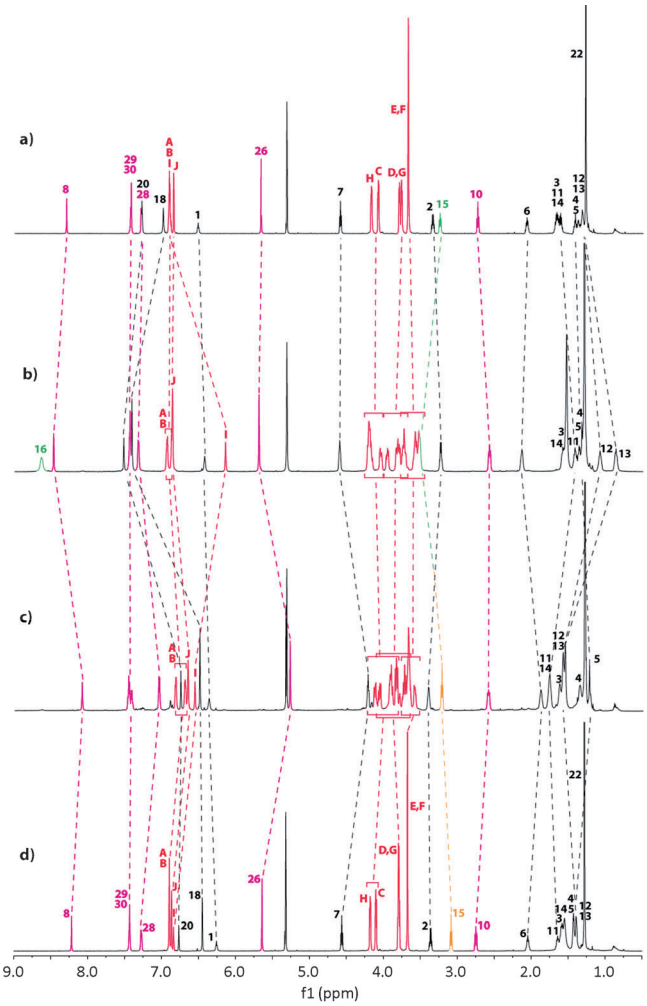


Figure 3. ^{1}H NMR spectra (600 MHz, CD_2Cl_2, 298 K) of: a) the protonated non-interlocked thread **5u**; b) the protonated lasso-based compound **5**; c) the deprotonated lasso-based compound **6**; d) the deprotonated non-interlocked thread **6u**. The coloring, lettering, and numbering correspond to the proton assignments indicated in Scheme 2.

tion. This was confirmed by the direct comparison between the ^{1}H NMR spectra of the non-interlocked thread **5u** and the [1]rotaxane **5** (Figure 3, a and b).

In the ^{1}H NMR spectrum of [1]rotaxane **5**, the NMR signals of the methylenic hydrogens H_{C-H} and the aromatic hydrogens H_{A-B} of the BMP25C8 are split, revealing the interlocked architecture. Indeed, in this structure, they are facing the two non-symmetrical extremities of the encircled molecular axle. The hydrogen H_I belonging to the BMP25C8 is importantly shifted upfield ($\Delta\delta = -0.75$ ppm) in the rotaxane **5**, as it experiences the shielding effect of the anilinium aromatic ring. This is consistent with the localization of the macrocycle around the anilinium station. It is also corroborated by the appearance of the ^{1}H NMR signal for the hydrogens H_{16} at very high chemical shift ($\delta = 8.64$ ppm) in **5**, and by the downfield shift of hydrogens H_{15} ($\Delta\delta = 0.27$ ppm) caused by their interaction through hydrogen bonds with the oxygen atoms of the crown ether. Furthermore, H_{13} and in a lesser extent H_{10-12} are all shifted upfield (respectively $\Delta\delta = -0.45$ and -0.16; -0.20; -0.24 ppm), because they experience the shielding effect of the aromatic rings of the BMP25C8. Eventually, an unexpected slight downfield shift of H_8 was observed in **5** ($\Delta\delta = 0.17$ ppm), which could be attributed to an interaction by hydrogen bonding between H_8 and the oxygen atom of the amide moiety. This interaction is certainly allowed by the spatial proximity of the two atoms, due to the bent structure.

After the deprotonation of [1]rotaxane **5**, the BMP25C8 moves from its initial localization and tightens the lasso structure. It is noteworthy that absolutely no uncomplexed thread **6u** was observed after deprotonation, which corroborates the already discussed fact that no self-disentanglement can be possible when a benzyl gate is covalently linked to the triazolium moiety. The new deprotonated tightened lasso structure can be explained by the direct comparison of the ^{1}H NMR spectra of [1]rotaxanes **5** and **6**. (Figure 3, b and c) Obviously, the signals corresponding to hydrogens H_{15}, H_{18}, and H_{20} are all shifted upfield since they all undergo the deprotonation of the anilinium station and the displacement of the macrocycle. Although we expected to observe a downfield shift of the triazolium hydrogen H_8, as already mentioned by us with DB24C8 in [2]rotaxane architectures,[13b] an upfield shift of H_8 ($\Delta\delta = -0.38$ ppm) was instead detected. Actually, we suggest that the bigger BMP25C8 macrocycle does not allow any efficient hydrogen bond with the triazolium moiety, due to the *meta* substitution of the aromatic ring, which displays the two phenoxy groups of the crown ether too far away from the inside BMP25C8 cavity. Moreover, the two catechol alkoxy groups (i.e., in the *ortho* position) of the other aromatic ring of the BMP25C8 cannot interact through a hydrogen bond with H_8 because the benzyl group held by the triazolium can only be situated outside the lasso cavity due to its bulkiness, which is not compatible with a close spatial arrangement between H_8 and these oxygen atoms. Hydrogen H_8 rather experiences a shielding effect of the aromatic rings of the BMP25C8, with no more hydrogen bonding with the oxygen atom of the amide. At the same time, whereas hydrogens H_J, H_A, H_B belonging to the BMP25C8 experience a shielding effect of the benzyltriazolium moiety (respectively $\Delta\delta = -0.37$, -0.12 and -0.17 ppm), hydrogen H_I is deshielded ($\Delta\delta = 0.60$ ppm) since it no longer experiences the strong shielding effect of the aniline extremity. In **6**, the shuttling of the BMP25C8 toward the triazolium moiety is corroborated by the fact that the benzylic hydrogens H_{26} are shielded by the aromatic rings of the BMP25C8 ($\Delta\delta = -0.42$ ppm). The same trend is observed for hydrogens H_5, H_6, and H_7 ($\Delta\delta = -0.14$, -0.26, and -0.38 ppm, respectively). Meanwhile, displacement of the BMP25C8 toward the triazolium site causes a deshielding of hydrogens H_{11}–H_{14} (respectively $\Delta\delta = 0.34$, 0.50, 0.71, and 0.18 ppm).

The direct comparison between the ^{1}H NMR spectra of the tightened lasso-based [1]rotaxane **6** and of its uncomplexed analogue **6u** corroborates the localization of the BMP25C8. (Figure 3, c and d) In the [1]rotaxane **6**, the

chemical shifts of hydrogens H_{5-8} are more or less shifted upfield ($\Delta\delta = -0.20$, -0.16, -0.34 and -0.12 ppm, respectively) due to their localization in the shielding cavity of the aromatic rings of the BMP25C8. At the same time, the chemical shift of hydrogens H_J, and in a lesser extent H_I, are shifted upfield ($\Delta\delta = -0.37$ and -0.09 ppm, respectively) due to their localization in the shielding cavity of the benzyltriazolium unit. Eventually, the benzyl hydrogens H_{26} are rather importantly shielded ($\Delta\delta = -0.36$ ppm) by the aromatic rings of the BMP25C8 in lasso compound **6**.

All these observations in relation to the tightening or the loosening of the lasso upon pH variation were confirmed by ROE spectroscopy on a Bruker Avance III spectrometer (600 MHz) (Figures 4 and 5).

The ROESY ^{1}H NMR experiment of the protonated lasso **5** is reported in Figure 4. The correlation peaks, which are highlighted by blue-cyan frames, reveal the localization of the BMP25C8 around the anilinium station. In particular, the correlation peaks observed between respectively the hydrogens H_{13}, H_{14}, H_{15}, H_{18}, and the methylenic hydrogens H_{C-H} of the BMP25C8 indicate the localization of the BMP25C8 around the anilinium site. The same spatial proximity is observed for hydrogens H_2 and H_8 pointing out the looped backbone, which displays these two hydrogens face to face. At the same time, no correlation peaks are observed between the methylenic hydrogens H_{H-C} of the BMP25C8 with the triazolium part of the molecular lasso.

By comparison with **5**, the 2D-ROESY ^{1}H NMR spectrum appears very different for the deprotonated lasso **6** and demonstrates the shuttling of the BMP25C8 around the triazolium moiety triggering the tightening of the lasso. Indeed, the new correlation peaks observed now respectively concern the hydrogens H_{10}, H_{11}, H_{12} (belonging to the alkyl chain), H_{26} and H_8 (belonging to the triazolium site) with the methylenic hydrogens H_{C-H} of the BMP25C8. Similarly, the hydrogens H_B and H_J, belonging to the aromatic rings of the BMP25C8, are spatially close to the hydrogen H_7 in **6**. All these observations are supported by the position of hydrogen H_I of the BMP25C8, which was correlated with H_{18} in **5**, and with H_{10}, H_{11}, and H_{12} in **6**.

Conclusion

We have described a straightforward synthesis of a lasso-based [1]rotaxane from a hermaphrodite non-interlocked precursor. Formation of an intermediate interlocked pseudo[1]rotaxane occurred by self-entanglement through the rotation of a *meta*-substituted aromatic ring of the BMP25C8 around two σ-bonds. The best conditions to obtain these pseudo[1]rotaxanes were found to be in the non-polar solvent dichloromethane and at the highest dilution. Although the anilinium group is not a very good template moiety for the large size of the BMP25C8, the pseudo[1]rotaxane could be detected by ^{1}H NMR spectroscopy in a 45% ratio. Furthermore, benzylation of the triazole enabled us to trap the macrocycle and isolate the [1]rotaxane molecular architecture. Therefore, the benzyltriazolium played the dual role of molecular station and gate for the BMP25C8: on one hand it interacts with the BMP25C8, whereas on the other hand, it avoids any disassembly of the interlocked structure. At acidic pH, the lasso

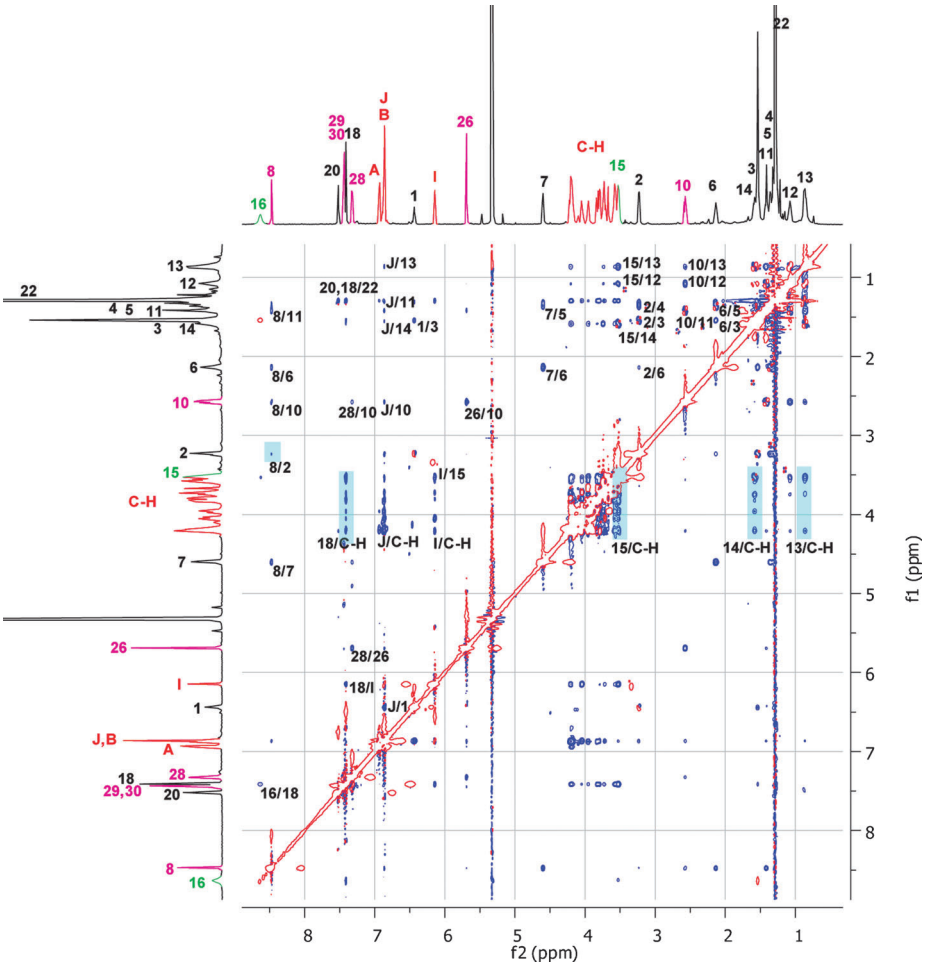


Figure 4. ^{1}H NMR ROESY experiment (600 MHz, 298 K, CD_2Cl_2) of the protonated [1]rotaxane **5**. The coloring, lettering, and numbering correspond to the proton assignments indicated in Scheme 2.

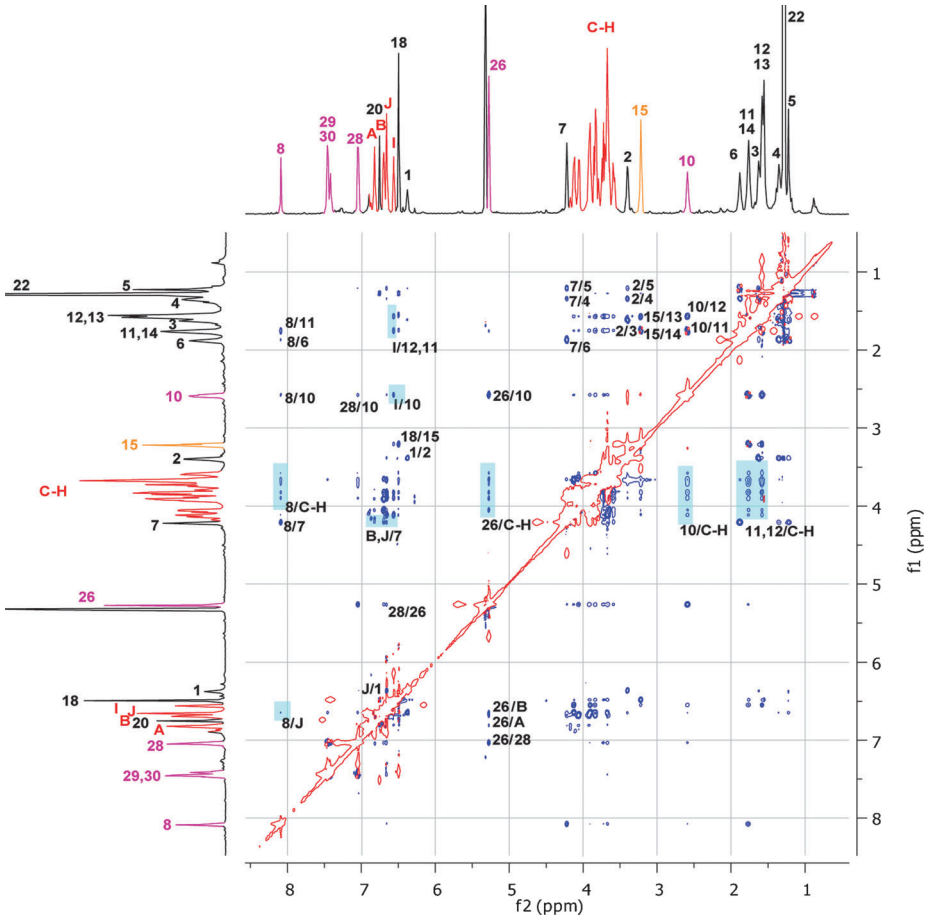


Figure 5. ^{1}H NMR ROESY experiment (600 MHz, 298 K, CD_2Cl_2) of the deprotonated [1]rotaxane **6**. The coloring, lettering, and numbering correspond to the proton assignments indicated in Scheme 2.

displayed a loosened shape in which the BMP25C8 is localized around the anilinium molecular station. After deprotonation of the anilinium, the macrocycle shuttles around the triazolium station, thus tightening the lasso structure.[17] To the best of our knowledge, the molecular switch **5**/**6** constitutes the first example of a pH-sensitive mono-lasso structure. An extension to the peptidic series by incorporating amino acid residues in the backbone of such a lasso molecular switch is in progress: less or more bending of the peptide should give rise to the modulation of the bio-properties of an active peptidic sequence depending on the pH stimulus.

Experimental Section

General: All reactions were performed under an atmosphere of argon unless otherwise indicated. All reagents were purchased from Aldrich and were used as received without further purification. The preparations and characterizations of the macrocycle **1** and the threads **5u** and **6u** are described in the Supporting Information. The *N*-carbamoylated aniline alkyne **2** has been synthesized according to the experimental procedure previously described by Coutrot et al.[18] Dichloromethane was distilled over P_2O_5 and was degassed by bubbling Ar gas for 20 min. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel 60 F254 plates. Compounds were visualized by dipping the plates in an ethanolic solution of 10% sulphuric acid, ninhydrine, or $KMNO_4$, followed by heating. ^{1}H NMR and ^{13}C NMR spectra were obtained on a Bruker DRX-400 and Bruker Avance III spectrometers (at 400.13 MHz or 600.13 MHz, and 100.62 MHz or 150.95 MHz, respectively). The chemical shifts of the ^{1}H NMR and ^{13}C NMR spectra are given by using $CHCl_3$, CH_3CN or CH_2Cl_2 as references (for ^{1}H spectrum: 7.27, 1.94, and 5.32 ppm, respectively, and for ^{13}C spectrum: 77.00 ppm, 118.26 ppm and 54 ppm, respectively). Coupling constants (J) are reported in Hertz (Hz). Standard abbreviations indicating multiplicity were used as follows: s (singlet), br (broad), d (doublet), t (triplet), q (quartet), and m (multiplet). High-resolution mass spectra (HRMS) and mass spectra were recorded on a Q-TOF Micro (water) apparatus.

Compound 3: $Cu(CH_3CN)_4PF_6$ (746 mg, 2 mmol, 1 equiv) and 2,6-lutidine (23 μL, 0.2 mmol, 0.1 equiv) were added successively to a solution of the azido macrocycle **1** (1.233 g, 2 mmol, 1 equiv) and the alkyne **2** (911 mg, 2.2 mmol, 1.1 equiv) in dry CH_2Cl_2 (10 mL). The mixture was stirred for 24 h at RT. The solvent was evaporated under vacuum and the crude product was directly purified by chromatography on a silica gel column (solvent gradient elution CH_2Cl_2/acetone 80:20 to 70:30) to give compound **3** (2.03 g, 98%) as a white foam. R_f 0.40 (CH_2Cl_2/acetone 80:20); ^{1}H NMR (300 MHz, CD_3CN, 298 K): $\delta = 7.49$ (s, 1H, H_8), 7.29 (t, 1H, $^{4}J_{H20-H18} = 1.6$ Hz, H_{20}), 7.04–6.99 (m, 3H, H_{18} H_1), 6.95–6.85 (m, 6H, H_A H_B H_J), 6.77 (t, 1H, $^{4}J_{HI-HJ} = 2.1$ Hz, H_I), 4.27 (t, 2H, $^{3}J_{H7-H6} = 7.1$ Hz, H_7), 4.21–4.13 (m, 4H, H_H), 4.10–4.02 (m, 4H, H_C), 3.80–3.68 (m, 8H, H_D H_G), 3.62 (s, 8H, H_E H_F), 3.64–3.55 (m, 2H, H_{15}), 3.32–3.23 (m, 2H, H_2), 2.66–2.53 (br t, 2H, H_{10}), 1.89–1.76 (m, 2H, H_6), 1.63–1.42 (m, 6H, H_3 H_{11} H_{14}), 1.39 (s, 9H, H_{25}), 1.29 (s, 9H, H_{22}), 1.36–1.23 ppm (m, 8H, H_4 H_5 H_{12} H_{13}); ^{13}C NMR (150 MHz, CD_3CN, 298 K): $\delta = 167.5$ (C_K), 161.1, 149.6, and 138.3 ($C_{IV\ arom\ BMP25C8}$), 155.6 (C_{23}), 152.2 (C_{19}), 143.3 (C_{17}), 122.5, 122.4, and 115.2 (C_8 C_{18} C_A C_B), 120.7 (C_{20}), 107.4 (C_J), 106.3 (C_1), 80.2 (C_{24}), 71.4 and 71.3 (C_E C_F), 70.5 and 70.3 (C_D C_G), 69.3 and 69.2 (C_C C_H), 51.4 (C_7), 50.7 (C_{15}), 40.3 (C_2), 35.6 (C_{21}), 31.7 (C_{22}), 30.6 (C_6), 28.7 (C_{25}), 30.0, 29.5, 29.1, 27.1, 26.9, and 26.8 (C_3 C_4 C_5 C_{10} C_{11} C_{12} C_{13} C_{14}); HRMS (ESI): $[M+H]^+$ calcd for $C_{58}H_{88}N_5O_{11}$: 1030.6480, found: 1030.6470.

Pseudo[1]rotaxane 4 and thread 4u from 3: A solution of HCl 1 M in Et_2O (20 mL, 20 mmol, 11 equiv) was added to a solution of compound **3** (1.814 g, 1.76 mmol, 1 equiv) in CH_2Cl_2 (5 mL). The mixture was stirred for 30 min before being evaporated to give a yellow foam. The solid was diluted in CH_2Cl_2 (40 mL). NH_4PF_6 (717 mg, 4.4 mmol, 2.5 equiv) and H_2O milliQ (20 mL) were added to this solution and the biphasic solution was stirred vigorously for 20 min. The aqueous layer was extracted with CH_2Cl_2 (×3) and the combined organic layers were dried over $MgSO_4$ and concentrated to give compounds **4**/**4u** (1.748 g, 93%) as a white foam. R_f 0.60 (CH_2Cl_2/acetone 70:30). HRMS (ESI): m/z calcd for $C_{53}H_{80}N_5O_9$: 930.5956 $[M+H]^+$; found: 930.5938.

Thread 4u from 5: Pd/C (10%, 20 mg) and 2 drops of NEt_3 were added to a solution of rotaxane **5** (20 mg, 0.015 mmol, 1 equiv) in EtOH (5 mL) were added. The reaction mixture was stirred at RT under H_2 for 24 h.

The reaction mixture was then filtered through celite and concentrated to give compound **4u** (16 mg, quantitative) as a white foam.

Uncomplexed form 4u: ^{1}H NMR (600 MHz, 5.10^{-2} M in CD_2Cl_2, 298 K): $\delta = 7.47$ (s, 1H, H_8), 7.45 (s, 1H, H_{20}), 7.30 (s, 2H, H_{18}), 6.92–6.87 (m, 4H, H_A H_B), 6.87 (br t, 1H, H_I), 6.83 (d, 2H, $^4J_{HJ-HI} = 1.9$ Hz, H_J), 6.74 (br t, 1H, H_I), 4.33 (t, 2H, $^3J_{H7-H6} = 6.6$ Hz, H_7), 4.13–4.10 (m, 4H, H_H), 4.10–4.07 (m, 4H, H_C), 3.79–3.73 (m, 8H, H_D H_G), 3.66 (s, 8H, H_E H_F), 3.37 (t, 2H, $^3J_{H15-H14} = 7.4$ Hz, H_{15}), 3.31 (q, 2H, $^3J_{H2-H3} = {}^3J_{H2-H1} = 6.7$ Hz, H_2), 2.67 (t, 2H, $^3J_{H10-H11} = 7$ Hz, H_{10}), 1.94–1.84 (m, 2H, H_6), 1.81–1.74 (m, 2H, H_{14}), 1.65–1.59 (m, 2H, H_{11}), 1.58–1.52 (m, 2H, H_3), 1.44–1.37 (m, 2H, H_{13}), 1.35–1.24 (m, 6H, H_4 H_5 H_{12}), 1.29 ppm (s, 18H, H_{22}); ^{13}C NMR (150 MHz, 5.10^{-2} M in CD_2Cl_2, 298 K): $\delta = 168.6$(C_K), 160.9, 149.1 and 137.0 ($C_{IV\ arom\ BMP25C8}$), 154.2 (C_{19}), 147.5 (C_{17}), 129.5 or 128.7 (C_9), 123.0 (C_{20}), 122.5 (C_8), 122.3 and 115.2 (C_A C_B), 116.4 (C_{18}), 107.2 (C_J), 106.5 (C_I), 71.1 and 71.0 (C_E C_F), 70.5 and 69.9 (C_D C_G), 69.1 and 68.9 (C_C C_H), 53.2 (C_{15}), 50.9 (C_7), 40.6 (C_2), 35.6 (C_{21}), 31.5 (C_{22}), 30.3 (C_6), 29.5 (C_3), 29.3 (C_{11}), 28.2 (C_{12}), 26.6 (C_{14}), 26.7 and 26.3 (C_4 C_5), 26.1 (C_{13}), 25.1 ppm (C_{10}).

Pseudo[1]rotaxane 4: ^{1}H NMR (600 MHz, 5.10^{-2} M in CD_2Cl_2, 298 K): $\delta = 8.65$ (br s, 2H, H_{16}), 7.53 (s, 1H, H_{20}), 7.52 (s, 1H, H_8), 7.42 (s, 2H, H_{18}), 6.97–6.93 and 6.90–6.86 (2 m, 4H, H_A H_B), 6.94 (d, 2H, $^4J_{HJ-HI} = 2$ Hz, H_J), 6.68 (br t, 1H, H_I), 6.20 (br t, 1H, H_I), 4.37–4.34 (m, 2H, H_7), 4.42–4.14 and 4.06–4.02 (2 m, 8H, H_H H_C), 3.98–3.93, 3.85–3.81, and 3.79–3.63 (3 m, 8H, H_D H_G), 3.79–3.63 and 3.60–3.49 (2 m, 8H, H_E H_F), 3.60–3.54 (m, 2H, H_{15}), 3.19 (q, 2H, $^3J_{H2-H3} = {}^3J_{H2-H1} = 6.4$ Hz, H_2), 2.43 (t, 2H, $^3J_{H10-H11} = 8$ Hz, H_{10}), 1.94–1.87 (m, 2H, H_6), 1.63–1.56 (m, 2H, H_{14}), 1.43–1.37 (m, 2H, H_3), 1.35–1.24 (m, 4H, H_5 H_{11}), 1.29 (s, 18H, H_{22}), 1.13–1.07 (m, 2H, H_4), 1.07–1.01 (m, 2H, H_{12}), 0.91–0.84 ppm (m, 2H, H_{13}); ^{13}C NMR (150 MHz, 5.10^{-2} M in CD_2Cl_2, 298 K): $\delta = 167.3$(C_K), 160.1, 148.2, 137.8, and 137.2 ($C_{IV\ arom\ BMP25C8}$), 154.2 (C_{19}), 135.6 (C_{17}), 129.5 or 128.7 (C_9), 124.9 (C_{20}), 122.8 and 113.2 (C_A C_B), 122.3 (C_8), 117.3 (C_{18}), 107.6 (C_I), 106.4 (C_J), 72.1 and 71.3 (C_E C_F), 70.8 (C_D C_G), 69.0 and 68.7 (C_C C_H), 52.3 (C_{15}), 50.9 (C_7), 39.9 (C_2), 35.7 (C_{21}), 31.6 (C_{22}), 29.9 and 29.1 (C_3 C_{11}), 29.4 (C_{12}), 28.8 (C_6), 27.7 (C_{14}), 26.2 (C_{13}), 25.8 (C_5), 25.6 (C_{10}), 25.4 ppm (C_4).

[1]Rotaxane 5: A solution of compound **4** (300 mg, 0.28 mmol, 1 equiv) dissolved in CH_2Cl_2 (10 mL) was added dropwise over 24 h to a solution of benzyl bromide (139 mL) and CH_2Cl_2 (418 mL). The mixture was stirred for further 72 h at RT. CH_2Cl_2 was then evaporated and the excess of benzyl bromide was removed by filtration on a silica gel column (solvent gradient elution CH_2Cl_2 to CH_2Cl_2/MeOH 95:5). The remaining solid (290 mg) was then diluted in CH_2Cl_2 (20 mL). To this solution was added NH_4PF_6 (189 mg, 1.16 mmol, 5 equiv) and H_2O milliQ (10 mL): the biphasic solution was stirred vigorously for 30 min. The aqueous layer was extracted with CH_2Cl_2 (3×20 mL) and the combined organic layers were dried over $MgSO_4$ and concentrated under vacuum. The crude was purified successively by chromatography on a silica gel column (CH_2Cl_2/MeOH 99:1) and LH20 sephadex column (CH_2Cl_2/MeOH 50:50) to give [1]rotaxane **5** (96 mg, 27%) and deprotonated thread **6u** (123 mg, 38%) as white foams. R_f 0.52 (CH_2Cl_2/Acetone 70/30); ^{1}H NMR (600 MHz, 5.10^{-3} M in CD_2Cl_2, 298 K): $\delta = 8.64$ (br s, 2H, H_{16}), 8.47 (s, 1H, H_8), 7.52 (s, 1H, H_{20}), 7.47–7.43 (m, 3H, H_{29} H_{30}), 7.42 (s, 2H, H_{18}), 7.35–7.30 (m, 2H, H_{28}), 6.97–6.92 and 6.90–6.85 (2 m, 4H, H_A H_B), 6.87 (s, 2H, H_J), 6.43 (br t, 1H, H_I), 6.15 (s, 1H, H_I), 5.70 (s, 2H, H_{26}), 4.60 (t, 2H, $^3J_{H7-H6} = 5.6$ Hz, H_7), 4.25–4.14 and 4.08–4.02 (2 m, 8H, H_H H_C), 3.99–3.93 and 3.86–3.77 and 3.77–3.69 (3 m, 8H, H_D H_G), 3.77–3.69 and 3.63–3.55 and 3.55–3.49 (3 m, 8H, H_E H_F), 3.55–3.49 (m, 2H, H_{15}), 3.27–3.20 (m, 2H, H_2), 2.58 (t, 2H, $^3J_{H10-H11} = 8$ Hz, H_{10}), 2.18–2.20 (m, 2H, H_6), 1.62–1.54 (m, 2H, H_{14}), 1.57–1.50 (m, 2H, H_3), 1.46–1.39 (m, 2H, H_{11}), 1.40–1.33 (m, 2H, H_5), 1.34–1.29 (m, 2H, H_4), 1.29 (s, 18H, H_{22}), 1.12–1.04 (m, 2H, H_{12}), 0.91–0.82 ppm (m, 2H, H_{13}); ^{13}C NMR (150 MHz, 5.10^{-2} M in CD_2Cl_2, 298 K): $\delta = 167.9$ (C_K), 160.8, 160.1, 149.5, 147.5, and 138.6 ($C_{IV-arom\ BMP25C8}$), 154.2 (C_{19}), 145.8 (C_9), 135.6 (C_{17}), 131.8 (C_{27}), 130.1 and 130.0 (C_{29} C_{30}), 128.9 (C_{28}), 128.8 (C_8), 124.9 (C_{20}), 122.7, 122.1, 115.4, and 113.2 (C_A C_B), 117.3 (C_{18}), 107.5 (C_I), 106.2 (C_J), 72.2, 71.4, and 71.3 (C_E C_F), 70.8, 70.7, 70.4, and 70.2 (C_D C_G), 69.3, 68.9, and 68.6 (C_C, C_H), 55.4 (C_{26}), 54.8 (C_7), 52.4 (C_{15}), 39.3 (C_2), 35.7 (C_{21}), 31.6 (C_{22}), 29.1 (C_{12}), 28.8 (C_3), 28.0 (C_6), 27.6 (C_{14}), 27.0 (C_{11}), 26.3 (C_{13}), 25.0 (C_4), 24.6 (C_5), 24.0 ppm (C_{10}); HRMS (ESI): calcd for $C_{60}H_{87}F_6N_5O_9P$: 1166.6095 $[M-PF_6]^+$, found: 1166.6146.

[1]rotaxane 6: A solution of the [1]rotaxane **5** (52 mg, 0.040 mmol, 1 equiv) in CH_2Cl_2 (10 mL) was washed with an aqueous solution of NaOH 1 M (2×5 mL). After extraction of the aqueous layer with CH_2Cl_2 (10 mL), the combined organic layers were dried over $MgSO_4$ and evaporated to obtain the deprotonated [1]rotaxane **6** (43 mg, 94%) as a white foam. R_f 0.50 (CH_2Cl_2/Acetone 70:30); ^{1}H NMR (600 MHz, 5.10^{-3} M in CD_2Cl_2, 298 K): $\delta = 8.09$ (s, 1H, H_8), 7.49–7.39 (m, 3H, H_{29} H_{30}), 7.07–7.02 (m, 2H, H_{28}), 6.85–6.79 and 6.72–6.67 (2 m, 4H, H_A H_B), 6.75 (s, 1H, H_{20}), 6.66 (s, 2H, H_J), 6.56 (s, 1H, H_I), 6.50 (s, 2H, H_{18}), 6.37 (br t, 1H, H_I), 5.28 (s, 2H, H_{26}), 4.22 (t, 2H, $^3J_{H7-H6} = 6$ Hz, H_7), 4.25–4.10 and 3.95–3.87 and 3.87–3.81 (3 m, 8H, H_H H_C), 4.09–4.04 and 3.94–3.88 and 3.70–3.63 (3 m, 8H, H_D H_G), 3.76–3.69 and 3.69–3.63 and 3.61–3.56 (3 m, 8H, H_E H_F), 3.43–3.37 (m, 2H, H_2), 3.22 (t, 2H, $^3J_{H15-H14} = 6.9$ Hz, H_{15}), 2.59 (t, 2H, $^3J_{H10-H11} = 7.9$ Hz, H_{10}), 1.91–1.85 (m, 2H, H_6), 1.80–1.72 (m, 4H, H_{11} H_{14}), 1.66–1.59 (m, 2H, H_3), 1.60–1.55 (m, 4H, H_{12} H_{13}), 1.39–1.32 (m, 2H, H_4), 1.29 (s, 18H, H_{22}), 1.25–1.19 ppm (m, 2H, H_5); ^{13}C NMR (150 MHz, 5.10^{-2} M in CD_2Cl_2, 298 K): $\delta = 166.6$ (C_K), 160.8, 160.4, 148.8, and 137.4 ($C_{IV-arom\ BMP25C8}$), 152.2 (C_{19}), 149.6 and 149.0 ($C_{IV-arom\ BMP25C8}$ and C_{17}), 146.6 (C_9), 132.4 (C_{27}), 129.8 and 129.7 (C_{29} C_{30}), 129.0 (C_8), 128.7 (C_{28}), 122.2, 122.1, and 114.1 (C_A C_B), 112.0 (C_{20}), 107.9 (C_{18}), 107.6 (C_I), 104.8 (C_J), 71.7, 71.5, 71.4, 71.3, and 71.2 (C_E C_F), 70.5, 70.4, and 70.0 (C_D C_G), 69.5, 68.9, and 68.6 (C_C, C_H), 54.8 (C_7), 54.0 (C_{26}), 44.6 (C_{15}), 40.5 (C_2), 35.3 (C_{21}), 31.8 (C_{22}), 30.3 (C_{14}), 30.1, 28.0, and 27.9 (C_6 C_{12} C_{13}), 28.1 (C_3), 27.1 (C_4), 26.7 (C_5), 26.3 (C_{11}), 23.5 (C_{10}); HRMS (ESI): *m/z* calcd for $C_{60}H_{87}F_6N_5O_9P$: 1166.6156 $[M+H]^+$; found: 1166.6146.

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