DOI: 10.1002/ejoc.201500657

A Cholesterol Containing pH-Sensitive Bistable [2]Rotaxane

Martin Berg,[a] Senada Nozinovic,[b] Marianne Engeser,[a] and Arne Lützen*[a]

Keywords: Supramolecular chemistry / Molecular recognition / Rotaxanes / Crown compounds / Interlocked molecules / Molecular shuttles

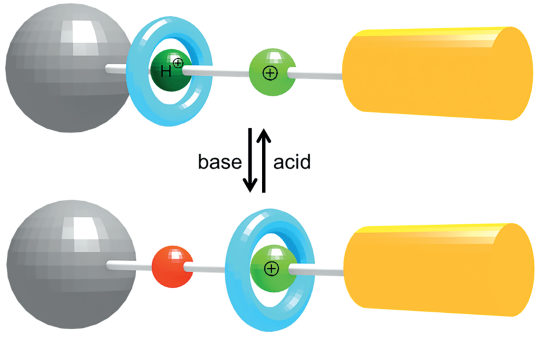
A non-symmetrical pH-sensitive bistable [2]rotaxane that bears a cholesterol unit and a tetraphenylmethane group as stopper groups was designed and synthesized in 18 steps. The successful formation of the rotaxane was proven by NMR spectroscopy and MS/MS. Besides a permanent cationic alkylated triazolium unit, the axle contains a secondary amine that can act as a second pH-sensitive binding site for a crown ether. Depending on the protonation state of this amine function, the crown ether reversibly changes its position by moving between the two binding sites along the axle, as revealed by NMR spectroscopy.

Introduction

Control of mechanical motions on the molecular level is a crucial point in the design of (supra-)molecular switches and machines.[1,2] Among the different approaches, bistable mechanically interlocked molecules, like catenanes and rotaxanes, have attracted considerable attention to access functional systems[3] because the mechanical bonds between the molecular components offer a unique possibility to restrict the freedom of motion to some well-defined pathways, such as the translational motion of a rotaxane's ring along its axis in a shuttling manner.[4] In bistable rotaxanes this ring displacement results from an external stimulus that alters the non-covalent interaction patterns between the ring and different parts of the axis. Among the repertoire of external stimuli for actuating this movement, the application of light,[5] redox-agents,[6] and changes of the pH[7] are probably used the most.

To affect stimulus induced motion, like a muscle-like contraction or relaxation[8] or an opening or closing of a channel, pore, or valve,[9] such systems need to be anchored to a support.[10] Cholesterol can act as an anchor in lipid membranes but so far there has only been a single report that describes the synthesis of a bistable redox-sensitive rotaxane that bears cholesterol as a stopper unit.[11]

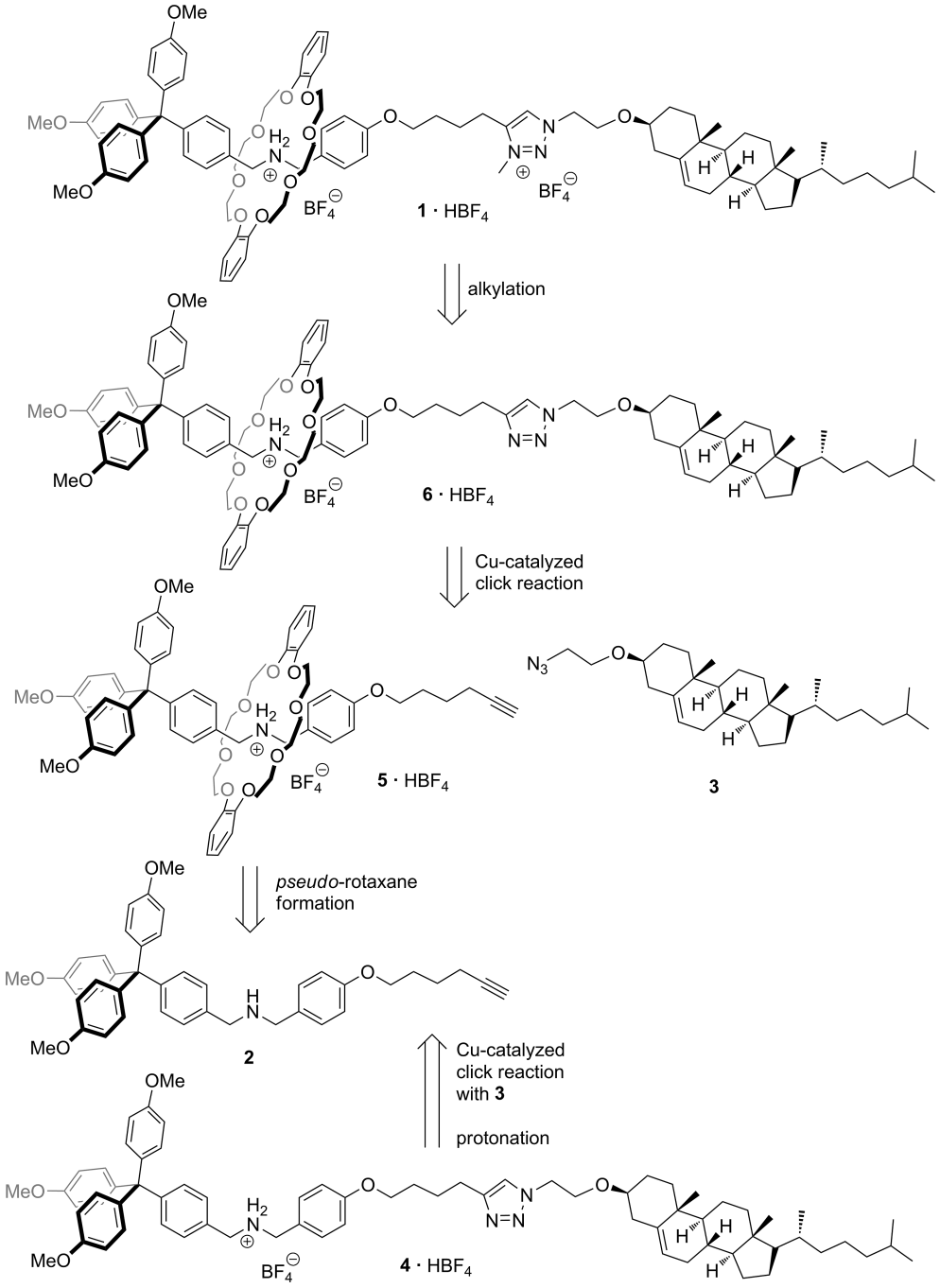
Hence, we decided to develop another non-symmetrical bistable pH-sensitive rotaxane with a cholesterol stopper on the one end and another stopper group at the other end, the ring of which can undergo a shuttle-movement along the axis depending on the protonation state of a suitable functional group as depicted schematically in Scheme 1. Several successful approaches can be found in the literature that employ a permanent cationic function that can act as a medium-strong binding site for an ionophore, such as a crown ether and a secondary amine functionality that can act as a strong binding site for an ionophore in the protonated state but not in its neutral form.[12] Three permanent cationic units have been used most in this context: dialkylated 4,4′-bipyridinium ions as pioneered by J. F. Stoddart in the late 1990s[13] and more recently alkylated pyridinium ions as employed by S.-H. Chiu,[14] F. Coutrot,[15] T. Ogoshi,[16] and U. Lüning,[17] or alkylated triazolium ions as used by F. Coutrot,[18] Y. Liu,[19] C.-F. Chen,[20] P. D. Beer,[21] and D. A. Leigh.[22] Among these, the latter one is very appealing because the triazole unit can also act as a key structural element to actually synthesis the rotaxane by means of a copper-catalysed azide-alkyne cycloaddition (CuAAC).[23]



Scheme 1. Schematic representation of a bistable pH-sensitive [2]-rotaxane shuttle.

Therefore, we decided to follow this strategy to design bistable [2]rotaxane **1** that contains a cholesterol and the

[a] Kekulé-Institut für Organische Chemie und Biochemie, Rheinische Friedrich-Wilhelms-Universität Bonn, Gerhard-Domagk-Str. 1, 53121 Bonn, Germany
E-mail: arne.luetzen@uni-bonn.de
www.chemie.uni-bonn.de/oc/forschung/arbeitsgruppen/ak_lue
[b] Institut für Anorganische Chemie, Rheinische Friedrich-Wilhelms-Universität Bonn, Gerhard-Domagk-Str. 1, 53121 Bonn, Germany
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201500657.



Scheme 2. Retrosynthetic analysis of bistable pH-sensitive [2]rotaxane **1**·HBF_4.

well-established tetraphenylmethane stopper which has a secondary amine function and a triazolium ion in its axis (Scheme 2). Its synthesis, structural characterization, and shuttling behaviour as analysed by NMR spectroscopic and ESI mass spectrometric means is reported here.

Results and Discussion

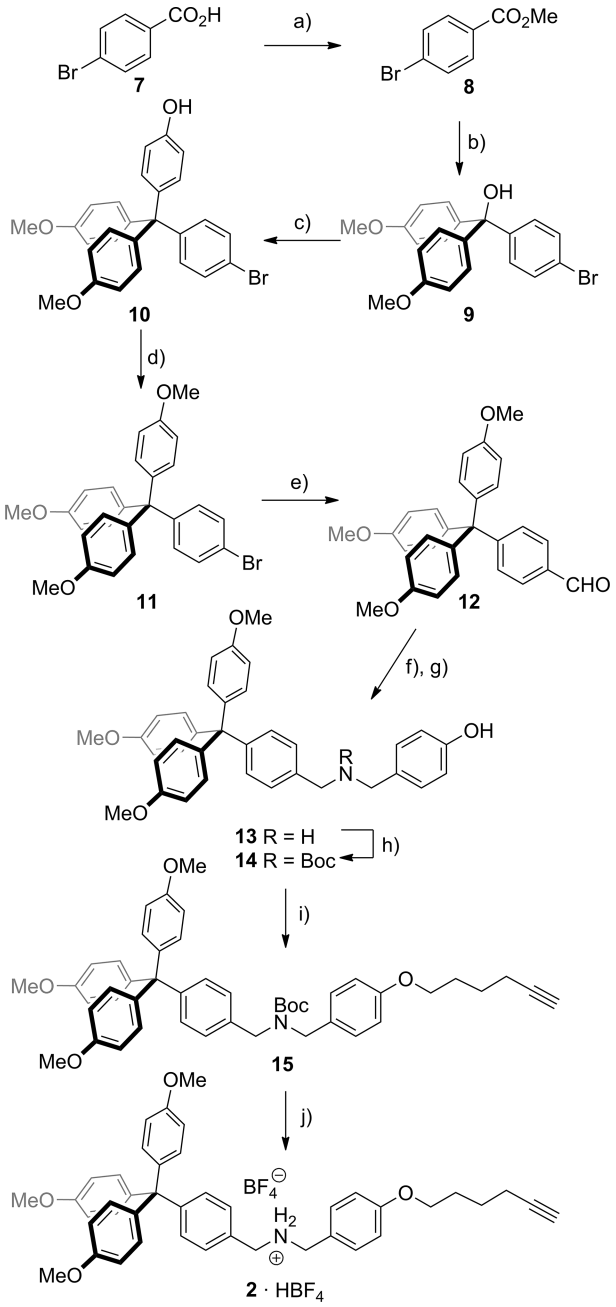
Synthesis

The retrosynthetic analysis of **1** (Scheme 2) asks for the preparation of two half-axes: tetraphenylmethane stoppered **2** and cholesterol derivative **3** that contains a terminal alkyne and a terminal azide function, respectively. These two building blocks can be combined by means of a copper-catalysed Click-reaction to give rise to isolated axes **4**, which is needed for comparison later on to prove the threaded structure of the rotaxane.

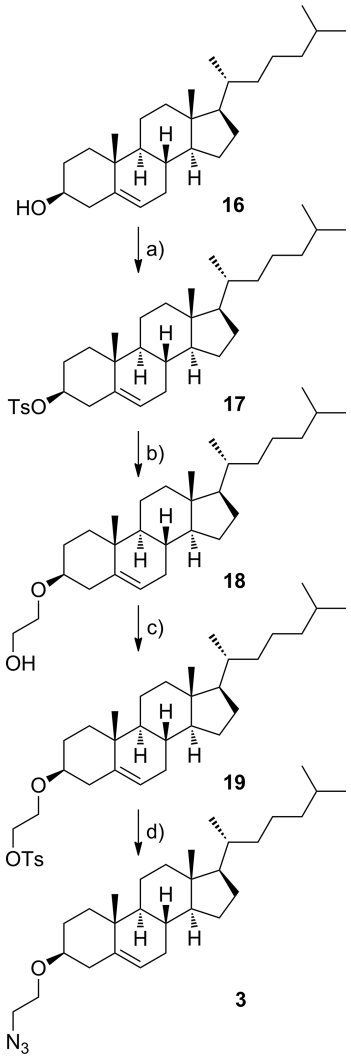
Because the cholesterol group is not as bulky as the tetraphenylmethane stopper, the size of the ring had to be chosen with great care to ensure reasonable binding to the triazolium ion or the secondary ammonium ion and to avoid dethreading of the axis. Dibenzo-24-crown-8 (db-24-c-8) perfectly fulfils these requirements because its cavity is

small enough not to slip over the cholesterol but still offers ample opportunities to interact with the axis through hydrogen bonds, cation-π, and CH-π interactions.[24] Hence, we thought to use half axis **2** to form *pseudo*-rotaxane **5**·HBF_4 upon subsequent treatment with acid and the crown ether moiety. Combination of this *pseudo*-rotaxane with cholesterol derivative **3** was then planned to give rotaxane **6**·HBF_4, which could finally be transformed into desired bistable rotaxane **1**·HBF_4 upon alkylation of the triazole moiety.

Schemes 3 and 4 show the syntheses of half-axes **2** and **3**. Alkyne half-axis **2** was prepared in ten steps by starting from 4-bromobenzoic acid (**7**) (Scheme 3). By following literature procedures, **7** was first transformed into corresponding methyl ester **8** before it was subjected to a twofold Grignard addition reaction to give tertiary alcohol **9**. Compound **9** was then condensed with phenol under acidic conditions to give tetraphenylmethane derivative **10**[25], which was subsequently methylated to give tris(4-methoxyphenyl)(4-bromophenyl)methane (**11**).[26]



Scheme 3. Synthesis of alkyne half-axes **2**: (a) MeOH, H_2SO_4, Δ, 24 h, 64%, (b) 4-MeOPhMgBr, THF, room temp., 18 h, 62%, (c) PhOH, HBr, Δ, 18 h, 48%, (d) NaH, MeI, room temp., 78%, (e) *t*BuLi, THF, 1 h, –78 °C, then DMF, HCl, 1.5 h, room temp., quant.; (f) 4-(aminomethyl)phenol, EtOH, 24 h, Δ, quant.; (g) $NaBH_4$, MeOH/THF, 1:1, 18 h, room temp., 64%; (h) di-*tert*-butyl dicarbonate, CH_2Cl_2, 18 h, room temp., 83%; (i) 6-chloro-1-hexyne, Cs_2CO_3, KI, DMF, 18 h, 70 °C, 77%; (j) HCl (2 N), CH_2Cl_2, 18 h, room temp., then aq. NH_4BF_4, 18 h, room temp., 74%.



Scheme 4. Synthesis of azide half axis **3**: (a) *p*TsCl, pyridine, room temp., 1 h, 78%, (b) $HOCH_2CH_2OH$, 1,4-dioxane, Δ, 18 h, 86%, (c) *p*TsCl, pyridine, 0 °C, 18 h, 76%, (d) NaN_3, DMPU, 18 h, 50 °C, 90%.

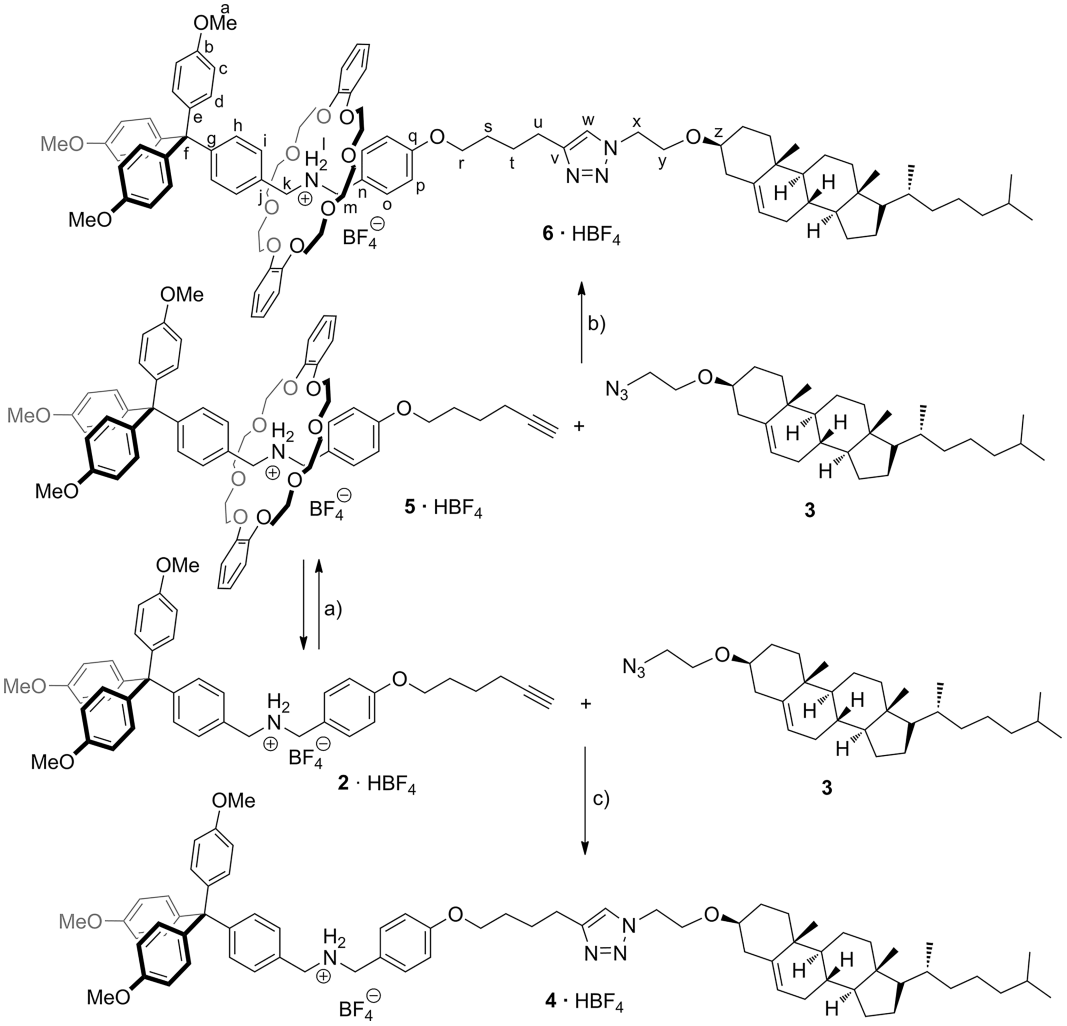
To achieve formylation of **11** a bromine lithium exchange had to be performed first. Interestingly, we found that this could only be done with *tert*-butyllithium, whereas neither *n*- nor *sec*-butyllithium was successful in this reaction. Addition of *N*,*N*-dimethylformamide to the lithium organyl

followed by quenching with aqueous HCl then gave rise to desired aldehyde **12** in quantitative yield. Reductive amination upon reaction of **12** with 4-(aminomethyl)phenol in anhydrous ethanol, but without the typical use of anhydrous magnesium sulfate, and subsequent reduction of the intermediate imine by $NaBH_4$ in tetrahydrofuran (THF)/MeOH gave amine **13** in 64% yield over both steps.

To be able to perform the desired alkylation with 6-chlorohex-1-yne regioselectively, as in a Williamson ether synthesis, the more nucleophilic secondary amine had to be protected first. Therefore, base stable *tert*-butyloxycarbonyl (Boc) protecting group was introduced by reacting **13** with di-*tert*-butyl dicarbonate to give **14** in 83% yield. Boc protected phenol **14** was then deprotonated with caesium carbonate and the reaction with the chloroalkyne in the presence of catalytic amounts of potassium iodide gave desired alkynylated ether **15** in 77% yield. Next, the Boc protecting group was removed by treatment with HCl (2 N) in diethyl ether to form the ammonium ion. To make this an even better template for the formation of the *pseudo*-rotaxane with dibenzo-24-crown-8, the counterion was finally exchanged against the much weaker coordinating tetrafluoroborate by using a saturated aqueous solution of ammonium tetrafluoroborate to give protonated alkyne-terminated half-axis **2**·HBF_4 in 74% yield.

Azide half-axis **3** was prepared in four steps starting from commercially available cholesterol (**16**; Scheme 4). By following literature protocols,[27] **16** was first tosylated to give sulfonate **17** in 78% yield. Nucleophilic substitution with ethylene glycol then afforded chain-elongated alcohol **18** with retention of stereochemistry in 86% yield. Another tosylation gave **19** in 76% yield, which was finally transformed into desired azide **3** upon treatment with sodium azide in 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU). In this way cholesterol derivative **3** could be isolated in 90% yield after recrystallization from ethanol.

With both building blocks in hands the next task was to prepare isolated axis **4** and the formation of rotaxane **6**·HBF_4 through CuAAC (Scheme 5). Therefore, alkyne-terminated half-axis **2**·HBF_4 was mixed with dibenzo-24-



Scheme 5. Synthesis of rotaxane **6**·HBF_4 and isolated axis **4**·HBF_4: (a) dibenzo-24-crown-8, CH_2Cl_2, 2 h, room temp., (b) $Cu(CH_3CN)_4BF_4$, tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (TBTA), CH_2Cl_2, 2 d, 5%, (c) $Cu(CH_3CN)_4BF_4$, CH_2Cl_2, 2 d, 55%.

crown-8 and stirred for two hours in degassed dichloromethane to achieve formation of *pseudo*-rotaxane **5**·HBF_4. This was treated with **3** for 2 d in dichloromethane with $Cu(CH_3CN)_4BF_4$ as catalyst and tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (TBTA) as a copper(I) stabilizing ligand[28] to afford desired rotaxane **6**·HBF_4 in a yield of 4% after recrystallization from ethanol and additional column chromatography. Interestingly, the same conditions were not successful to prepare the isolated axis from **2**·HBF_4 and **3** because we were unable to remove TBTA from the desired product. Only when we repeated the synthesis without the stabilizing ligand we were able to isolate axis **4**·HBF_4 in a reasonable yield of 55% after column chromatography.

NMR Spectroscopic and Mass Spectrometric Characterization

The threaded topology of rotaxane **6**·HBF_4 could be unambiguously characterized in the gas phase, and in solution. Thus, two independent pieces of evidence for the rotaxane structure are available.

(i) Evidence for the successful formation of the rotaxane structure in solution is available from NMR experiments. Figure 1 analyses the ^{1}H NMR spectra of the free crown ether (trace a), rotaxane **6**·HBF_4 (trace b), free axis **4**·HBF_4 (trace c), and a 1:1 mixture of crown ether and **4**·HBF_4 (trace d) in CD_2Cl_2 at 293 K. Although the mixture of the ring and the axle component more or less results in a summation of the individual spectra, some of the signals in the spectrum of the rotaxane show significant changes relative to the positions of these signals for the free components as a result of the threaded topology of the mechanically interlocked structure. This could also be seen in (i) splitting and (ii) a significant shift both aromatic protons ($H_{Ar,\,W}$) and aliphatic protons ($CH_{2,\,W}$) of the dibenzo-24-crown-8 wheel. Furthermore the signals of the two different pairs of benzylic protons k and m are shifted downfield $\Delta\delta$ = 0.64 and 0.62 ppm, respectively. This is most likely a result of C-H···O hydrogen bonds between these protons and the oxygen atoms on the crown ether.

These changes clearly indicate that the preferred position of the crown ether wheel is in close proximity to the ammonium ion at room temperature. This interpretation is

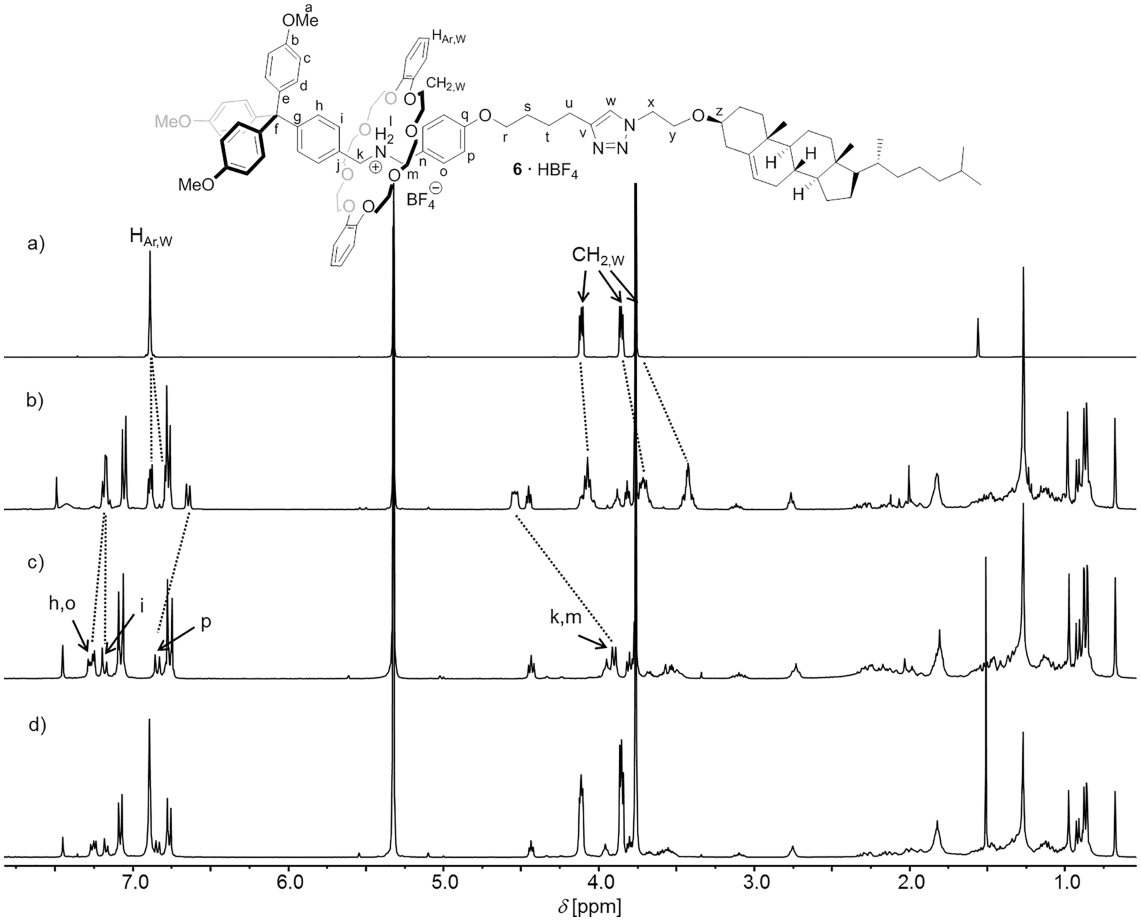


Figure 1. ^{1}H NMR spectra (400.1 MHz, CD_2Cl_2, 293 K) of (a) dibenzo-24-crown-8, (b) rotaxane **6**·HBF_4, (c) free axis **4**·HBF_4, and (d) 1:1 mixture of dibenzo-24-crown-8 and **4**·HBF_4. Dashed lines indicate changes in shifts between selected nuclei of the individual components relative to the rotaxane (letters a–z mark protons of the axis, whereas $CH_{2,W}$ and $H_{Ar,W}$ mark protons of the wheel).

further corroborated by the results of 2D NOESY experiments (see the Supporting Information) that reveal NOE contacts between the benzylic protons k and m of the axis and the ethylene glycol protons ($CH_{2,\,W}$) of the crown ether unit.

(ii) Evidence for the interlocked structure also comes from the positive-mode ESI mass spectra of rotaxane **6**·HBF_4 and a 1:1 mixture of axle **4**·HBF_4 and dibenzo-24-crown-8 (Figure 2). The spectrum of the rotaxane (Figure 2, a) does show a very intense signal at *m*/*z* = 1530 that corresponds to the positive [**6**+H]$^+$ ion, but no signal for the isolated protonated axis [**4**+H]$^+$. In marked contrast, strong signals for protonated axle [**4**+H]$^+$ at *m*/*z* = 1082 and for [db-24-c-8 + Na]$^+$ at *m*/*z* = 471 are observed under the same conditions when we analysed the 1:1 mixture of the crown ether and protonated axis **4**·HBF_4 (Figure 2, f), and only a minor signal at *m*/*z* = 1530 is observed that results from the corresponding non-threaded (most probably) hydrogen-bonded complex [db-24-c-8·**4**+H]$^+$.

Even better proof for this assignment comes from a series of positive ion MS/MS experiments shown in Figure 2 (b–e and g–j).[29] In both cases we mass-selected the full isotope pattern of the ions at *m*/*z* 1530 and subjected the ions to collision-induced dissociation (CID). The molecular ion for rotaxane [**6**+H]$^+$ proved to be remarkably stable and only decomposed by fragmentation of the axis after applying collision energies of about 50 eV. Upon fragmentation of the axle the crown ether is released which is why we could only detect fragments that resulted from the axis, e.g. at *m*/*z* 536, but no signal for the intact protonated axle at *m*/*z* =

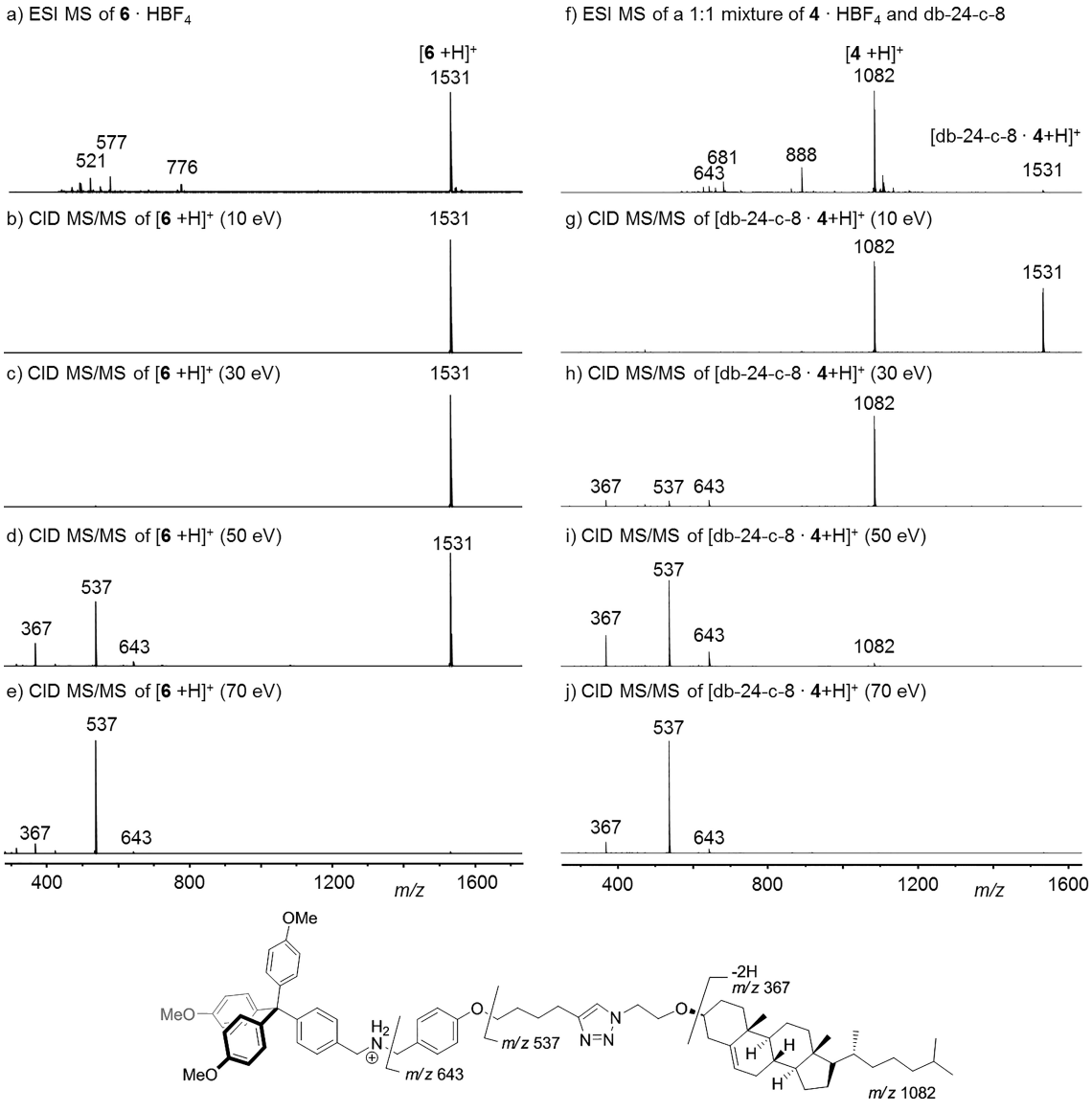


Figure 2. ESI mass spectra of **6**·HBF_4 (a) and a 1:1 mixture of **4**·HBF_4 and dibenzo-24-crown-8 (f, please note that the signal of the crown ether sodium complex [db-24-c-8+Na]$^+$ at *m*/*z* = 471 is so intense that the mass region below *m*/*z* = 500 had to be suppressed to get observable intensities of the ion at *m*/*z* = 1531) and CID MS/MS spectra of [**6**+H]$^+$ (b–e) and [db-24-crown-8·**4**+H]$^+$ (g–j). The inset shows the fragmentation pathways observed for the axis that gives rise to the signals at *m*/*z* 643, 537, and 367.

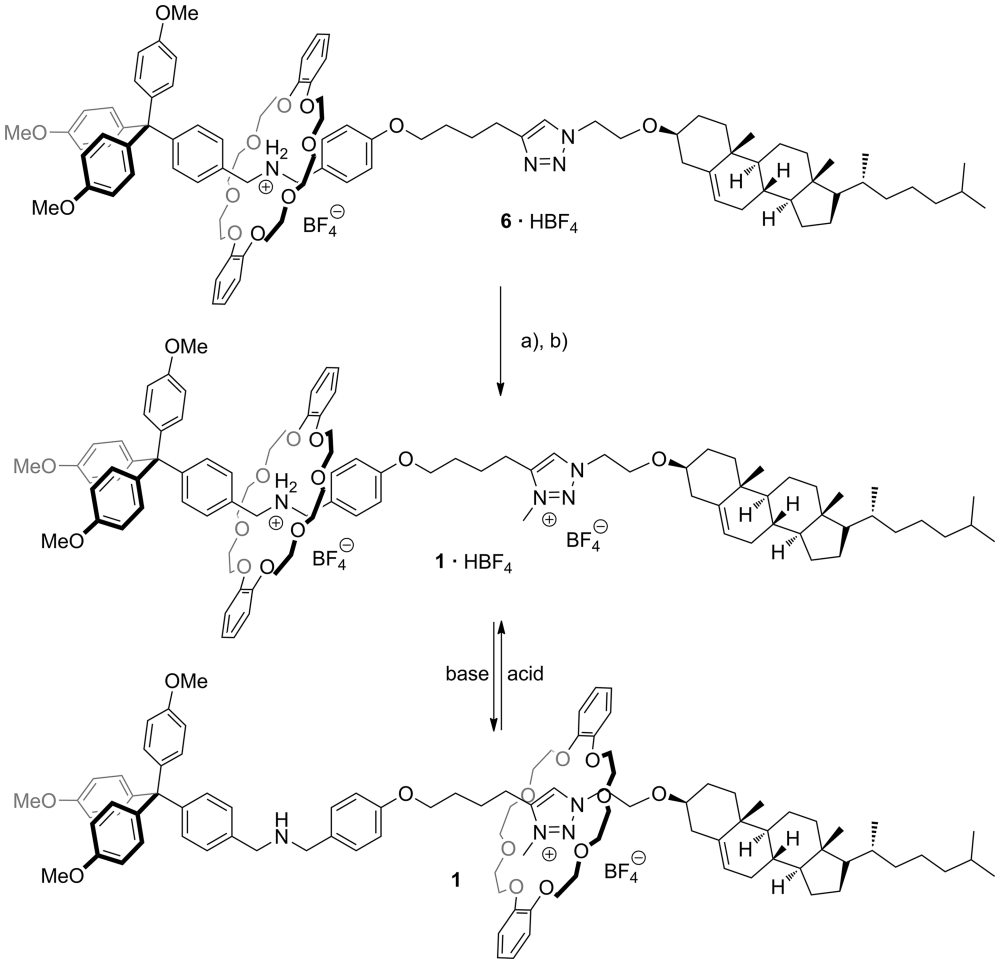
1082. This can also be traced back to a significantly more energy demanding cleavage of the covalent bonds of the crown ether. Thus, fragmentation of covalent bonds within the axle leads to simultaneous cleavage of the mechanical bond.

The ion of the non-threaded axis-crown-ether complex [db-24-c-8·**4**+H]$^+$, when treated in the same way as the rotaxane, behaves very differently. As expected for a noncovalently bonded species, the crown ether is lost very easily in the CID experiments and positively charged axle [**4**+H]$^+$ is formed as the major product at m/z = 1082 upon application of a collision energy of only ≈ 10 eV. The consecutive fragmentations of the axle that start to occur at 50 eV are similar to the fragments observed for the rotaxane. These experiments confirm the threaded nature of the rotaxane and permit us to distinguish the mechanically bound species from a non-covalently-bonded complex of axis and crown ether. They also reflect the much weaker bond strength of the non-covalently assembled complex versus the strength of the mechanical bond of the rotaxane, which requires cleavage of a covalent bond for fragmentation.

Synthesis of the Bistable pH-Sensitive Rotaxane and Its Shuttling Behaviour

After having confirmed the mechanically interlocked structure of rotaxane **6**·HBF_4 by NMR spectroscopy and mass spectrometry, the next task was to introduce a second permanent cationic binding site within the axis to make the rotaxane a bistable pH-sensitive molecular shuttling system. Therefore, we decided to methylate the triazole moiety to a triazolium ion by treatment with excess methyl iodide. A prolonged reaction time of 3 d ensured quantitative methylation and finally we performed an anion exchange by treatment with sodium tetrafluoroborate to obtain **1**·HBF_4 as a white solid (Scheme 6).

The permanent cationic function within the axis the rotaxane should undergo a shuttling motion upon deprotonation of the secondary ammonium ion with a base. The resulting neutral amine has a significantly reduced binding affinity towards the crown ether, and hence, the ring shifts towards the triazole moiety that is a better binding site for the ionophore. Reprotonation of the amine function by ad-



Scheme 6. Synthesis of the rotaxane **1**·HBF_4: (a) MeI, 3 d, (b) $NaBF_4$, quant. (top) and its pH-sensitive shuttling of the crown ether (please note that the counterions might be exchanged upon the addition of base and acid).

dition of acid changes the affinity again, which causes the crown ether to move back to the ammonium ion.

This pH dependent shuttling of the crown ether along the axis could be easily monitored by NMR spectroscopic experiments (Figure 3 and the Supporting Information). After addition of aq. NaOH to rotaxane **1**·HBF_4 the signal that arises from the ammonium protons (l) at around δ = 7.45 ppm disappears and a broad signal that arises from the secondary amine proton appears upfield at δ = 4.88 ppm that indicates successful deprotonation.

The shifts of the protons of the crown ether moiety ($H_{Ar,W}$, $CH_{2,W}$) also change significantly to indicate that the crown ether is located in a different environment. The same is true for the shifts of the signals assigned to the nuclei around the triazolium ion. The proton of the triazolium ring (p) is shifted downfield by $\Delta\delta$ = 0.37 ppm, probably as a result of formation of C–H···O hydrogen bonding with the oxygen atoms of the crown ether. The signal of the protons of the methyl group that is bound to the triazolium nitrogen (NCH_3) is shifted upfield owing to the shielding effect of the wheel, and finally, the signals of the protons of the alkyl chains neighbouring the triazolium moiety (k, l, m, n, q, and r) are all significantly shifted. This indicates that the crown ether has shuttled to the triazole unit.

This shuttling action is completely reversible, and addition of HCl in diethyl ether leads to a reprotonation of triazolene function, which causes the ring to move back to the ammonium ion and results in the same NMR spectrum as before (Figure 4). Further addition of base again results in deprotonation of the ammonium ion and shuttling of the crown ether to the triazolium ion. This process can be repeated several times (for four reversible shuttling motions see the Supporting Information).

Although not the focus of our project, we also checked whether rotaxane **1**·HBF_4 has some liquid crystalline properties and whether these are dependent on its protonation state by using polarised optical microscopy. Unsurprisingly with respect to their structures with the bulky arene and cholesterol moieties, neither of the rotaxanes (**1** or **1**·HBF_4) show any such phase transition but both rather become isotropic liquids upon heating and solidify into amorphous solids without forming any observable structurally ordered mesophase.

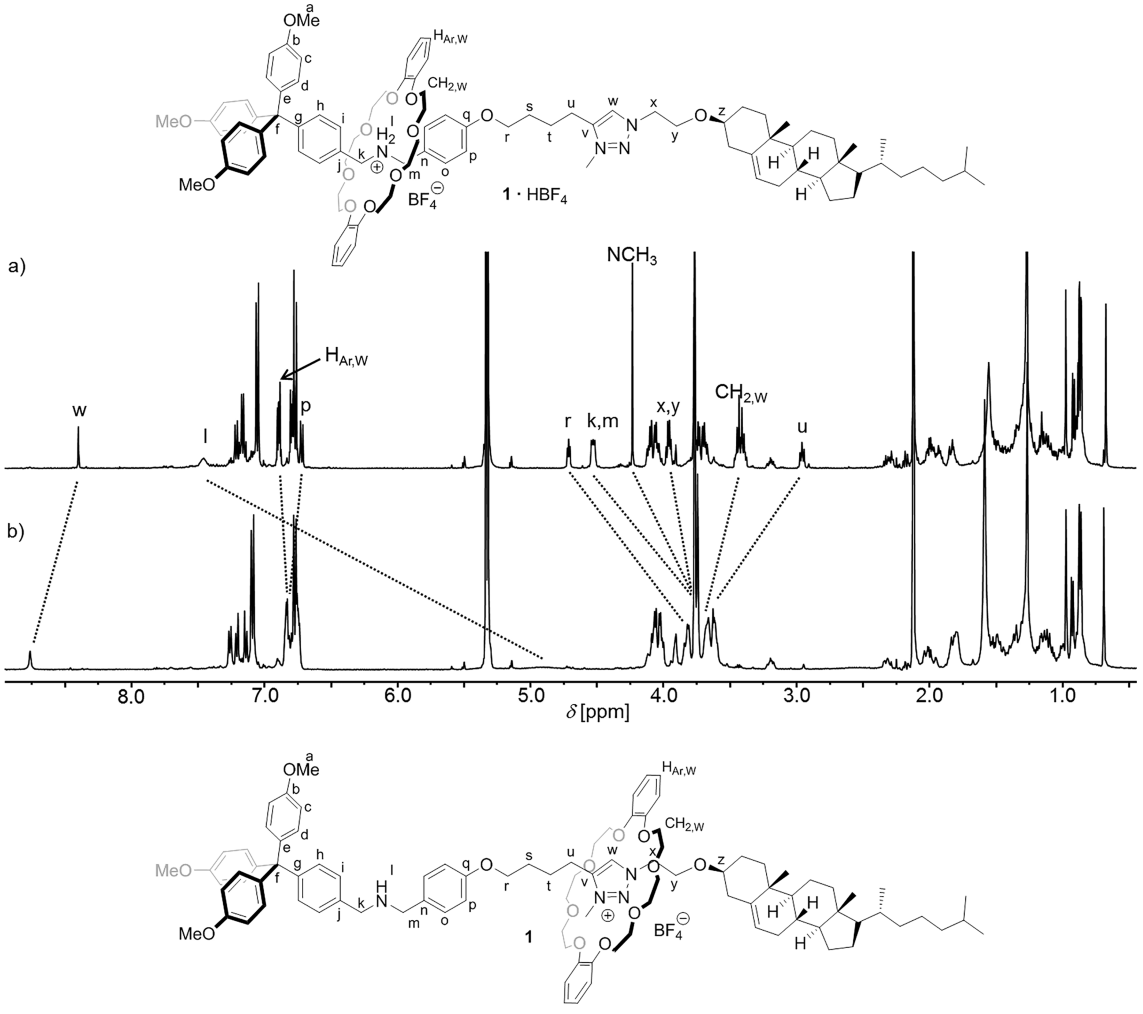


Figure 3. ^{1}H NMR spectra (500.1 MHz, in CD_2Cl_2, 293 K) of (a) rotaxane **1**·HBF_4, (b) rotaxane **1** obtained by deprotonation of rotaxane **1**·HBF_4 through addition of NaOH (1 M; letters a–z mark protons of the axis, whereas $CH_{2,W}$ and $H_{Ar,W}$ mark protons of the wheel).

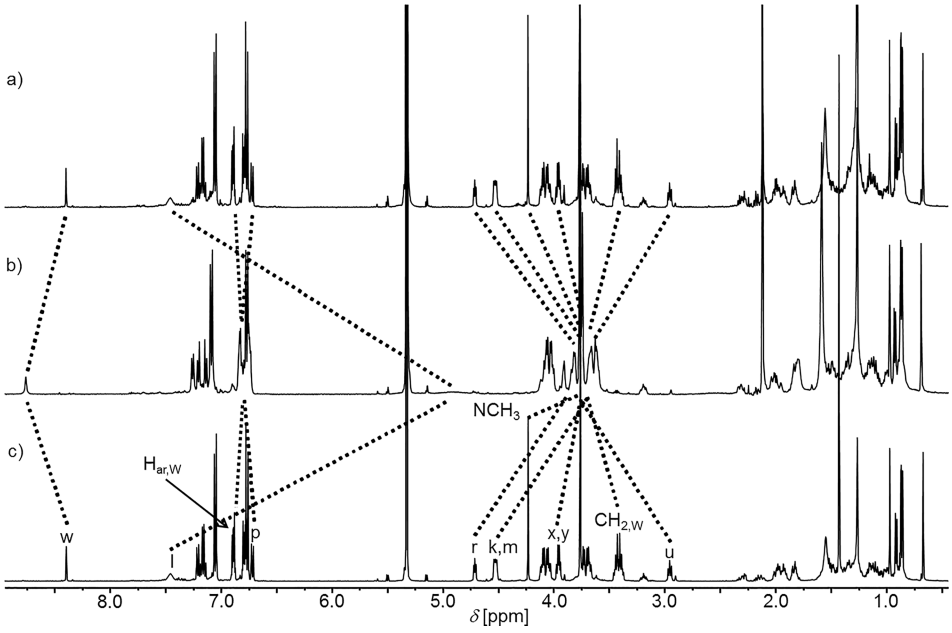


Figure 4. Reversible pH-sensitive shuttle motion of the crown ether moiety along the rotaxane axis. ^{1}H NMR spectra (500.1 MHz, 293 K, CD_2Cl_2) of (a) **1**·HBF_4, (b) **1** obtained after deprotonation of **1**·HBF_4, and (c) **1**·HBF_4 obtained upon reprotonation of **1**.

Conclusions

We were able to synthesis rotaxane **6**·HBF_4 that contained a crown ether threaded onto a non-symmetrical axis with a tetraphenylmethane and a cholesterol stopper unit in a CuAAC reaction of an azide and an alkyne terminated half axis through an ammonium-ion template effect. Its mechanically interlocked structure was unambiguously assigned by NMR spectroscopy and mass spectrometry. Upon alkylation of the triazole ring we obtained pH-sensitive bistable rotaxane **1**·HBF_4 in which the crown ether part changes its preferred position on the axis as a result of the protonation state of a secondary amine function. In the protonated form the crown ether is located around the secondary ammonium ion as the best binding site for the ionophore. Upon deprotonation of the ammonium ion the triazolium ion becomes the better binding site, which causes the ring to shuttle along the axis towards this position as evidenced by NMR spectroscopy. After this proof of principle, further studies will aim to develop amphiphilic bistable rotaxanes with a lipophilic and a hydrophilic stopper unit, to investigate their self-assembly and shuttling behaviour, or their implementation as functional devices in lipophilic barriers.

Experimental Section

General: Reactions under inert gas atmosphere were performed under argon by using standard Schlenk techniques and oven-dried glassware prior to use. Thin-layer chromatography was performed on aluminium TLC plates (silica gel 60F_{254} from Merck). Detection was carried out under UV light (254 and 366 nm). Products were purified by column chromatography on silica gel 60 (70–230 mesh) from Merck. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker DRX 500 spectrometer (300 K) operating at 500.1 and 125.8 MHz, a Bruker AM 400 (298 K) spectrometer operating at 400.1 MHz and 100.6 MHz, or with a Bruker Avance 300 (298 K) spectrometer operating at 300.1 MHz and 75.5 MHz. ^{1}H and ^{13}C NMR chemical shifts are reported on the δ scale (ppm) relative to signals of residual non-deuterated solvent (^{1}H) or the deuterated solvent (^{13}C) as the internal standard. ^{19}F NMR chemical shifts are reported on the δ scale (ppm) relative to $CFCl_3$ as an external standard. Signals were assigned on the basis of ^{1}H, ^{13}C, HMQC, HMBC, and NOESY NMR experiments. For the numbering of the individual nuclei in the compounds see Figures 1 and 3 and the Supporting Information. Mass spectra were recorded with a Finnigan 95XL (EI) or a Bruker micrOTOF-Q (ESI). Argon was used as collision gas for CID. The given collision energies are uncorrected values E_{lab} because the isolated ions have the same mass in this case, and E_{lab} is sufficient for a relative comparison. Elemental analyses were carried out with a Heraeus Vario EL. Please note that our equipment does not allow for analysis of fluorine containing samples, therefore HRMS data is given in these cases. Polarized optical microscopy measurements were performed on a Leica DMLB microscope with a hot stage and a home-built control unit. Images were acquired with a Canimpex digital camera connected to a personal computer. Most solvents were dried, distilled, and stored under argon in accordance with standard procedures. All chemicals were used as received from commercial sources. 4-Bromobenzoic acid methyl ester (**8**),[25] bis(4-methoxyphenyl)-(4-bromophenyl)methane (**9**),[25] bis(4-methoxyphenyl)-(4-bromophenyl)methane (**10**),[25] tris(4-methoxyphenyl)(4-bromophenyl)-methane (**11**),[26] cholest-5-en-3β-tosylate (**17**),[27] cholest-5-en-3β-oxyethanol (**18**),[27] and 2-(cholest-5-en-3β-oxy)ethyl tosylate (**19**) [27] were prepared in accordance to literature protocols.

4-[Tris(4-methoxyphenyl)methyl]benzaldehyde (12): *t*BuLi (21.51 mL, 1.9 M in pentane, 40.87 mmol, 5.0 equiv.) were added to dry THF (200 mL) at –78 °C and stirred for 10 min. To this solution tris(*p*-methoxyphenyl)(*p*-bromphenyl)methane (**11**; 4.00 g, 8.17 mmol, 1.0 equiv.) was added and stirred for another 1 h at

–78 °C. Afterwards, dry dimethylformamide (DMF; 6.30 mL, 81.37 mmol, 10.0 equiv.) was added and the solution was warmed to room temperature over 1.5 h. The reaction was quenched by addition of aq. HCl (4*N*, 11.24 mL, 44.95 mmol, 5.5 equiv.) and stirred for 0.5 h. The layers were separated and the organic layer was washed with aq. HCl (0.5 M, 150 mL), saturated aq. $NaHCO_3$ solution (150 mL), and brine (150 mL), dried with $MgSO_4$, and concentrated in vacuo. The resultant white solid was used without further purification (3.35 g, 8.17 mmol, quant.). ^{1}H NMR (400.1 MHz, $CDCl_3$, 293 K): δ = 3.79 (*s*, 9 H, H_a), 6.79 (*d*, $^3J_{c,d}$ = 9.0 Hz, 6 H, H_c), 7.08 (d, $^3J_{d,c}$ = 9.0 Hz, 6 H, H_d), 7.40 (d, $^3J_{h,i}$ = 8.4 Hz, 2 H, H_h), 7.76 (d, $^3J_{i,h}$ = 8.4 Hz, 2 H, H_i), 9.98 (s, 1 H, CHO) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, 293 K): δ = 55.3 (C_a), 63.4 (C_f), 113.1 (*C*$_c$), 128.9 (C_h), 131.6 (C_i), 132.0 (C_d), 134.2 (C_j), 138.7 (C_e), 154.9 (C_g), 157.8 (C_b), 192.1 (C_k) ppm. MS (ESI): *m*/*z* (%) = 461.2 (100) $[C_{29}H_{26}O_4 + Na]^+$. HRMS (ESI): *m*/*z* (%) calcd. for $[C_{29}H_{26}O_4Na]^+$ 461.1723; found 461.1704. $C_{29}H_{26}O_4{\cdot}0.5H_2O$ (438.51): calcd. C 77.84, H 6.17; found C 77.83, H 6.08.

4-({4-[Tris(4methoxyphenyl)methyl]benzylideneamino}methyl)-phenol: To a solution of **12** (3.35 g, 7.63 mmol, 1.0 equiv.) in anhydrous EtOH (153 mL), 4-(aminomethyl)phenol (0.94 g, 7.63 mmol, 1.0 equiv.) was added. The mixture was heated to reflux for 24 h. After that the solvent was evaporated and the resultant yellowish solid was used without further purification (4.15 g, 7.63 mmol, quant.). ^{1}H NMR (400.1 MHz, CD_2Cl_2, 293 K): δ = 3.77 (*s*, 9 H, H_a), 4.68 (*s*, 2 H, H_m), 6.70 (*d*, $^3J_{p,o}$ = 8.0 Hz, 2 H, H_p), 6.78 (*d*, $^3J_{c,d}$ = 8.4 Hz, 6 H, H_c), 7.09–7.11 (*m*, 8 H, H_d, H_o), 7.28 (*d*, $^3J_{h,i}$ = 8.1 Hz, 2 H, H_h), 7.65 (*d*, $^3J_{i,h}$ = 8.1 Hz, 2 H, H_i), 8.36 (*s*, 1 H, H_k) ppm. ^{13}C NMR (100.6 MHz, CD_2Cl_2, 293 K): δ = 55.3 (C_a), 63.4 (C_f), 64.9 (C_m), 113.2 (*C*$_c$), 115.8 (C_p), 127.8 (C_h), 129.7 (Ci), 130.8 (C_n), 131.5 (C_o), 132.2 (C_d), 133.9 (C_j), 139.5 (C_e), 151.2 (C_g), 156.0 (C_q), 158.0 (C_b), 162.0 (C_k) ppm. MS (ESI): *m*/*z* (%) = 544.2 (100) $[C_{36}H_{33}NO_4 + H]^+$, 566.2 (16) $[C_{36}H_{33}NO_4 + Na]^+$. HRMS (ESI): *m*/*z* (%) calcd. for $[C_{36}H_{34}NO_4]^+$ 544.2482; found 544.2480. $C_{36}H_{33}NO_4{\cdot}0.5CH_2Cl_2{\cdot}$EtOH (543.65): calcd. C 73.14, H 6.38, N 2.22; found C 72.61, H 6.21, N 1.91.

4-({4-[Tris(4-methoxyphenyl)methyl]benzylamino}methyl)phenol (13): The Schiff Base derived from **12** (212 mg, 0.39 mmol, 1.0 equiv.) was dissolved in THF (5.8 mL) and MeOH (5.8 mL), and then $NaBH_4$ (59 mg, 1.56 mmol, 4.0 equiv.) was added slowly. After stirring overnight at room temperature, the reaction was quenched by addition of saturated aqueous ammonium chloride. The solvents were removed under reduced pressure. The residue was extracted with CH_2Cl_2 and dried with Na_2SO_4. Removal of the solvent under reduced pressure and purification by column chromatography with silica gel and a gradient of cyclohexane/ethyl acetate (1:1 to 1:9) as eluent gave the target compound as a yellowish amorphous solid, yield 136 mg (0.25 mmol, 64%). ^{1}H NMR (400.1 MHz, CD_2Cl_2, 293 K): δ = 3.72 (*s*, 2 H, H_k)*, 3.76 (*s*, 9 H, H_a), 3.78 (*s*, 2 H, H_m)*, 6.65 (*d*, $^3J_{p,o}$ = 8.4 Hz, 2 H, H_p), 6.77 (*d*, $^3J_{c,d}$ = 8.9 Hz, 6 H, H_c), 7.11 (*d*, $^3J_{d,c}$ = 8.9 Hz, 6 H, H_d), 7.13 (*d*, $^3J_{h,i}$ = 8.5 Hz, 2 H, H_h), 7.14 (*d*, $^3J_{i,h}$ = 8.5 Hz, 2 H, H_i), 7.21 (*d*, $^3J_{o,p}$ = 8.4 Hz, 2 H, H_o) ppm (* assignment of signals might be interchanged). ^{13}C NMR (100.6 MHz, CD_2Cl_2, 293 K): δ = 53.0 (C_k)*, 53.1 (C_m)*, 55.5 (C_a), 63.1 (C_f), 113.0 (*C*$_c$), 115.8 (C_p), 127.7 (C_h), 130.0 (Ci), 131.2 (C_o), 131.4 (C_n), 132.2 (C_d), 137.5 (C_j), 139.9 (C_e), 146.9 (C_g), 156.0 (C_q), 157.9 (C_b) ppm (* assignment of signals might be interchanged). MS (ESI): *m*/*z* (%) = 546.3 (100) $[C_{36}H_{35}NO_4 + H]^+$, 568.2 (5) $[C_{36}H_{35}NO_4 + Na]^+$. HRMS (ESI): *m*/*z* (%) calcd. for $[C_{36}H_{36}NO_4]^+$ 546.2639; found 546.2640. $C_{36}H_{35}NO_4{\cdot}0.5CH_2Cl_2{\cdot}H_2O$ (545.65): calcd. C 72.32 H 6.32 N 2.31; found C 72.18, H 6.45, N 2.18.

***tert*-Butyl-4-hydroxybenzyl{4-[tris(4-methoxyphenyl)methyl]-benzyl} Carbamate (14):** Boc_2O (0.62 g, 2.86 mmol, 1.0 equiv.) was added to a stirred solution of **13** (1.56 g, 2.86 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (50 mL). The solution was stirred overnight at room temperature and then washed with water (20 mL) and brine (10 mL). The organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was subjected to column chromatography on silica gel with cyclohexane/ethyl acetate (1:1) as eluent to afford the desired product as a white solid (1.53 g, 2.36 mmol, 83%). ^{1}H NMR (400.1 MHz, CD_2Cl_2, 293 K): δ = 1.47 (*s*, 9 H, *tert*-butyl-H), 3.77 (*s*, 9 H, H_a), 4.27–4.40 (br., 4 H, H_k, H_m), 5.75 (*s*, 1 H, O-H), 6.75–6.80 (*m*, 8 H, H_c, H_p), 7.06–7.11 (*m*, 10 H, H_d, H_h, H_i), 7.14 (*d*, $^3J_{o,p}$ = 8.4 Hz, 2 H, H_o) ppm. ^{13}C NMR (100.6 MHz, CD_2Cl_2, 293 K): δ = 28.5 [C(*C*H$_3$)$_3$], 55.5 (C_a), 63.1 (C_f), 80.3 [*C*(CH$_3$)$_3$], 113.1 (*C*$_c$), 115.6 (C_p), 127.1 (C_h), 131.2 (C_o), 132.2 (C_d), 139.9 (C_e), 146.9 (C_g), 155.6 (C_q), 156.3 (*C*OO), 157.9 (C_b) ppm. MS (ESI): *m*/*z* (%) = 668.3 (100) $[C_{41}H_{43}NO_6 + Na]^+$. HRMS (ESI): *m*/*z* (%): calcd. for $[C_{41}H_{43}NO_6Na]^+$ 668.2983; found 668.2983. $C_{41}H_{43}NO_6{\cdot}0.5CH_2Cl_2$ (645.78): calcd. C 72.42, H 6.44, N 2.04; found C 72.91, H 6.70, N 1.96.

***tert*-Butyl 4-(Hex-5-ynyloxy)benzyl{4-[tris(4-methoxyphenyl)-methyl]benzyl}carbamate (15):** A mixture of **14** (500 mg, 0.77 mmol, 1.0 equiv.), Cs_2CO_3 (505 mg, 1.55 mmol, 2 equiv.), KI (65 mg, 0.39 mmol, 0.5 equiv.), and 6-chloro-1-hexyne (136 mg, 1.16 mmol, 1.5 equiv.) in anhydrous DMF (8 mL) was heated to 70 °C overnight. After cooling to room temperature, the mixture was diluted with EtOAc (10 mL) and washed with water (3 × 15 mL) and brine (3 × 15 mL). The organic layer was dried with $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography with silica gel and cyclohexane/ethyl acetate (1:1) as eluent to give **15** as a yellow viscous oil (430 mg, 77%). ^{1}H NMR (500.1 MHz, $CDCl_3$, 293 K): δ = 1.47 (s, 9 H, *tert*-butyl-H), 1.72 (*q*, $^3J_{t,s}$ = 7.0 Hz, 2 H, H_t), 1.88–1.90 (*m*, 2 H, H_s), 1.96 (*t*, $^4J_{w,u}$ = 2.7 Hz, 1 H, H_w), 2.27 (td, $^3J_{u,t}$ = 7.0 Hz, $^4J_{u,w}$ = 2.7 Hz, 2 H, H_u), 3.78 (*s*, 9 H, H_a), 3.97 (*d*,$^3J_{r,s}$ = 6.4 Hz, 2 H, H_r), 4.27 (br., 2 H, H_m)*, 4.35 (br., 2 H, H_k)*, 6.78 (*d*, $^3J_{c,d}$ = 8.9 Hz, 6 H, H_c), 6.82 (*d*, $^3J_{p,o}$ = 8.6 Hz, 2 H, H_p), 7.05–7.09 (*m*, 8 H, H_d, H_h), 7.10–7.12 (*m*, 4 H, H_i, H_o) ppm (* assignment of signals might be interchanged). ^{13}C NMR (125.8 MHz, $CDCl_3$, 293 K): δ = 18.3 (C_u), 25.2 (C_t), 28.4 (C_s), 28.6 [C(*C*H$_3$)$_3$], 48.7 (C_k)*, 49.0 (C_m)*, 55.3 (C_a), 62.7 (C_f), 67.4 (C_r), 68.7 (C_w), 80.1 [*C*(CH$_3$)$_3$], 84.2 (C_v), 112.7 (*C*$_c$), 114.5 (C_p), 126.8 (C_h), 128.9 (C_j), 129.5 (Ci) 130.1 (C_n) 131.1 (C_o), 132.1 (C_d), 139.5 (C_e), 146.5 (C_g), 156.0 (*C*OO), 157.5 (C_b), 158.3 (C_q) ppm (* assignment of signals might be interchanged). MS (EI): *m*/*z* (%) = 725.4 (4) $[C_{47}H_{51}NO_6]^{+\cdot}$, 669.3 (9) $[C_{43}H_{43}NO_6]^+$, 625.3 (4) $[C_{42}H_{43}NO_4]^+$, 439.2 (13) $[C_{29}H_{29}NO_3]^+$, 333.1 (100) $[C_{22}H_{23}NO_2]^+$. HRMS (EI): *m*/*z* (%) calcd. for $[C_{47}H_{51}NO_6]^{+\cdot}$ 725.3721; found 725.3721. $C_{47}H_{51}NO_6{\cdot}2H_2O$ (725.91): calcd. C 74.09, H 7.28, N 1.84; found C 73.80, H 7.63, N 1.94.

***N*-[4-(Hex-5-ynyloxy)benzyl]-1-{4-[tris(4-methoxyphenyl)methyl]-phenyl}methanammonium Tetrafluoroborate (2·HBF$_4$):** HCl (2 M in Et_2O, 5.17 mL, 10.33 mmol, 15.0 equiv.) was added to a stirred solution of **15** (500 mg, 0.69 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (20 mL) and stirred overnight at room temperature. The solvent was evaporated and Et_2O (30 mL) was added to the resultant viscous oil. To this solution HCl (2 M in Et_2O, 3 mL, 6 mmol) was added and stirred until the mixture became clear. The solvents were removed under reduced pressure. The residue was dissolved in a 1:1 mixture of CH_2Cl_2 (40 mL) and saturated aqueous NH_4BF_4 (40 mL) and stirred overnight. The layers were separated and the organic layer was washed with water (100 mL), dried with $MgSO_4$, and concentrated in vacuo. The resultant pink solid was used with-

out further purification (364 mg, 0.51 mmol, 74%). ^{1}H NMR (400.1 MHz, CD_2Cl_2, 293 K): δ = 1.69 (*q*, $^3J_{t,u}$, $^3J_{t,s}$ = 7.2 Hz, 2 H, H_t), 1.88 (*q*, $^3J_{s,t}$, $^3J_{s,r}$ = 6.8 Hz, 2 H, H_s), 2.00 (*t*, $^4J_{w,u}$ = 2.6 Hz, 1 H, H_w), 2.25 (*td*, $^3J_{u,t}$ = 7.2, $^4J_{u,w}$ = 2.6 Hz, 2 H, H_u), 3.75 (*s*, 9 H, H_a), 3.91–4.02 (*m*, 6 H, H_k, H_m, H_r), 4.02–4.14 (br., 2 H, H_l), 6.75 (*d*, $^3J_{c,d}$ = 8.9 Hz, 6 H, H_c), 6.87 (*d*, $^3J_{p,o}$ = 8.6 Hz, 2 H, H_p), 7.05 (*d*, $^3J_{d,c}$ = 8.9 Hz, 6 H, H_d), 7.24–7.27 (*m*, 6 H, H_h, H_i, H_o) ppm. ^{13}C NMR (100.6 MHz, CD_2Cl_2, 293 K): δ = 18.4 (C_u), 25.4 (C_t), 28.6 (C_s), 50.9 (C_m)*, 51.1 (C_k)*, 55.5 (C_a), 63.1 (C_f), 67.8 (C_r), 68.8 (C_w), 84.4 (C_v), 113.1 (*C*$_c$), 115.3 (C_p), 124.5 (C_n), 128.8 (C_o), 130.2 (C_j), 131.3 (C_h), 131.9 (Ci), 132.2 (C_d), 139.4 (C_e), 149.3 (C_g), 159.0 (C_b), 160.1 (C_q) ppm (* assignment of signals might be interchanged). ^{19}F NMR (282.4 MHz, CD_2Cl_2, 293 K): δ = –149.48 (br., $^{10}BF_4$), –149.54 (br., $^{11}BF_4$) ppm. MS (ESI): *m*/*z* (%) = 626.4 (100) $[C_{41}H_{44}NO_6]^+$. HRMS (ESI): *m*/*z* (%) calcd. for $[C_{41}H_{44}NO_6]^+$ 626.3265; found 626.3276.

3β-(2-Azido)ethoxycholest-5-ene (3): 2-(Cholest-5-en-3β-oxy)ethyl tosylate (**19**) (500 mg, 0.85 mmol, 1 equiv.) was dissolved in DMPU (24 mL) under an argon atmosphere. Sodium azide (111 mg, 1.71 mmol, 2 equiv.) was added and the mixture was stirred at 50 °C for 24 h. After this time Et_2O (100 mL) was added and the organic phase was washed with aq. HCl (10%; 2× 30 mL) and brine (50 mL), and dried with $MgSO_4$. The solvents were removed under reduced pressure. Crystallization from ethanol gave **3** as white crystalline needles (430 mg, 90%). ^{1}H NMR (400.1 MHz, $CDCl_3$, 293 K): δ = 0.67 (*s*, 3 H, $H_{cholesterol}$) 0.85–2.29 (*m*, 38 H, $H_{cholesterol}$), 3.17–3.25 (m, 1 H, Hz), 3.36 (t, $^3J_{x,y}$ = 5.2 Hz, 2 H, H_x), 3.66 (t, $^3J_{y,x}$ = 5.2 Hz, 2 H, H_y), 5.33–5.38 (m, 1 H, H_{olefin}) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 293 K): δ = 12.0, 18.8, 19.5, 21.2, 22.7, 22.9, 23.9, 24.4, 28.1, 28.3, 32.0, 32.1, 35.9, 36.3, 36.9, 37.3, 39.1, 39.6, 39.9, 42.4, 50.3, 51.7, 56.3, 56.9, 66.9, 79.8, 121.9, 140.8 ppm (individual assignment of the signals was not possible). MS (EI): *m*/*z* (%) = 455.2 (7) $[C_{29}H_{49}N_3O]^{+\cdot}$, 440.2 (12) $[C_{28}H_{46}N_3O]^+$, 425.2 (51) $[C_{27}H_{43}N_3O]^+$, 410.1 (28) $[C_{26}H_{40}N_3O]^+$, 368.2 (100) $[C_{27}H_{44}]^+$, 353.2 (25) $[C_{26}H_{41}]^+$, HRMS (EI): *m*/*z* (%) calcd. for $[C_{29}H_{49}N_3O]^{+\cdot}$ 425.3668; found 425.3665.

***N*-[4-(4-{1-[2-(Cholest-5-en-3b-oxy)ethyl]-*H*-1,2,3-triazol-4-yl}butoxy)-benzyl]-1-{4-[tris(4-methoxyphenyl)methyl]phenyl}-methylammonium Tetrafluoroborate (4·HBF$_4$):** A solution of **2**·HBF_4 (40 mg, 0.06 mmol, 1.0 equiv.), **3** (38 mg, 0.08 mmol, 1.5 equiv.), and $Cu(CH_3CN)_4BF_4$ (3.53 mg, 0.01 mmol, 0.2 equiv.) in degassed CH_2Cl_2 (2 mL) was stirred in the dark for 48 h at room temperature. The reaction was diluted with CH_2Cl_2 (10 mL) and washed with EDTA·$2Na_{(aq.)}$ solution (0.1 M, 2× 14 mL) and H_2O (2× 14 mL). The organic layer was dried with $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography with silica gel and EtOAc/MeOH/CH_2Cl_2 (1:1:1) as eluent to give **4**·HBF_4 as a yellowish solid (38 mg, 55%). ^{1}H NMR (400.1 MHz, CD_2Cl_2, 293 K): δ = 0.67 (*s*, 3 H, $H_{cholesterol}$) 0.85–2.30 (*m*, 42 H, $H_{cholesterol}$, H_s, H_t), 2.73 (t, $^3J_{u,t}$ = 6.6 Hz, 2 H, H_u), 3.04–3.15 (*m*, 1 H, Hz), 3.76 (*s*, 9 H, H_a), 3.80 (*t*, $^3J_{y,x}$ = 5.1 Hz, 2 H, H_y), 3.89 (*s*, 2 H, H_m)*, 3.91 (s, 2 H, H_k)*, 3.95 (*t*, $^3J_{x,y}$ = 5.5 Hz, 2 H, H_x), 4.43 (*t*, $^3J_{r,s}$ = 6.0 Hz, 2 H, H_r), 6.76 (*d*, $^3J_{c,d}$ = 8.9 Hz, 6 H, H_c), 6.84 (*d*, $^3J_{p,o}$ = 8.5 Hz, 2 H, H_p), 7.08 (*d*, $^3J_{d,c}$ = 8.9 Hz, 6 H, H_d), 7.18 (*d*, $^3J_{i,h}$ = 8.5 Hz, 2 H, H_i), 7.25–7.29 (*m*, 4 H, H_h, H_o), 7.45 (*s*, 1 H, H_w) ppm. ^{13}C NMR (125.8 MHz, CD_2Cl_2, 293 K): δ = 12.0, 18.9, 19.5, 21.4, 22.7, 22.9, 23.1, 24.2, 24.6, 25.7, 26.4, 28.4, 28.6, 28.6, 29.2, 30.1, 32.2, 32.3, 36.2, 36.6, 37.1, 37.4, 39.3, 39.9, 40.2, 50.6, 50.9, 53.0, 53.1, 55.3, 56.6, 57.1, 63.0, 66.8, 68.0, 80.0, 113.0, 114.6, 122.1, 122.2, 127.5, 128.5, 129.3, 129.6, 131.1, 132.2, 139.9, 140.9, 146.6, 147.8, 157.9, 158.5 ppm (an individual assignment of the signals was not possible). ^{19}F NMR (282.4 MHz, CD_2Cl_2, 293 K) δ = –151.22 (br., $^{10}BF_4$), –151.27 (br., $^{11}BF_4$) ppm. MS (ESI): *m*/*z* (%) = 1081.7 (100) $[C_{71}H_{93}N_4O_5]^+$, 1103.6 (23) $[C_{71}H_{92}N_4O_5 + Na]^+$. HRMS (ESI): *m*/*z* (%) calcd. for $[C_{71}H_{92}N_4O_5Na]^+$ 1103.6960; found 1103.6980.

Rotaxane·6·HBF$_4$: A solution of **2**·HBF_4 (100 mg, 0.14 mmol, 1.0 equiv.) and db-24-C-8 (126 mg, 0.28 mmol, 2.9 equiv.) in degassed CH_2Cl_2 (2 mL) was stirred at room temperature for 2 h under argon. To this solution **3** (96 mg, 0.21 mmol, 1.5 equiv.), $Cu(CH_3CN)_4BF_4$ (9 mg, 0.03 mmol, 0.2 equiv.), and TBTA (15 mg, 0.03 mmol, 0.2 equiv.) were added and the reaction was stirred in the dark for 48 h at room temperature. The reaction was diluted with CH_2Cl_2 (21 mL) and washed with EDTA·$2Na_{(aq.)}$ solution (0.1 M, 2× 28 mL) and H_2O (2× 28 mL). The organic layer was dried with $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was recrystallized from ethanol and further purified by flash column chromatography on silica gel with a gradient of ethyl acetate to ethyl acetate/MeOH/CH_2Cl_2 (1:1:1) as eluent to give **6**·HBF_4 as a yellowish solid (8 mg, 0.005 mmol, 4%). ^{1}H NMR (400.1 MHz, CD_2Cl_2, 293 K): δ = 0.67 (*s*, 3 H, $H_{cholesterol}$) 0.85–2.29 (*m*, 42 H, $H_{cholesterol}$, H_s, H_t), 2.76 (*t*, $^3J_{u,t}$ = 7.0 Hz, 2 H, H_u), 3.08–3.15 (*m*, 1 H, Hz), 3.38–3.47 (*m*, 8 H, $H_{CH2,\ w}$), 3.66–3.76 (*m*, 8 H, $H_{CH2,\ w}$), 3.77 (*s*, 9 H, H_a), 3.82 (*t*, $^3J_{y,x}$ = 5.5 Hz, 2 H, H_y), 3.88 (*t*, $^3J_{x,y}$ = 5.5 Hz, 2 H, H_x), 4.03–4.13 (*m*, 8 H, $H_{CH2,\ w}$), 4.45 (*t*, $^3J_{r,s}$ = 6.0 Hz, 2 H, H_r) 4.53–4.55 (*m*, 4 H, H_k, H_m), 6.64 (*d*, $^3J_{p,o}$ = 8.7 Hz, 2 H, H_p), 6.76–6.79 (*m*, 10 H, H_c, $H_{Ar,\ w}$), 6.87–6.90 (*m*, 4 H, $H_{Ar,\ w}$), 7.06 (*d*, $^3J_{d,c}$ = 8.9 Hz, 6 H, H_d), 7.15–7.19 (*m*, 6 H, H_h, H_i, H_o), 7.40–7.46 (br., 2 H, H_l), 7.49 (*s*, 1 H, H_w) ppm. ^{13}C NMR (100.6 MHz, CD_2Cl_2, 293 K): δ = 12.0, 14.2, 18.9, 19.5, 21.4, 22.7, 22.9, 24.2, 24.6, 25.6, 26.4, 28.4, 28.5, 28.6, 29.0, 29.7, 30.1, 32.3, 36.2, 36.5, 37.1, 37.4, 39.5, 39.8, 40.2, 42.6, 50.6, 50.9, 52.6, 55.6, 56.5, 57.1, 63.2, 66.8, 68.0, 68.6, 70.1, 70.6, 71.0, 71.1, 80.0, 113.1, 113.2, 114.6, 122.0, 122.1, 122.2, 123.8, 128.8, 129.7, 131.2, 131.5, 132.1, 139.4, 140.9, 147.7, 147.9, 149.4, 158.0, 160.1 ppm (an individual assignment of the signals was not possible). MS (ESI): *m*/*z* (%) = 1530.9 ($[C_{95}H_{125}N_4O_{13} - BF_4^-]^+$, 100). HRMS (ESI): *m*/*z* (%) calcd. for $[C_{95}H_{125}N_4O_{13}]^+$ 1530.9271; found 1530.9240.

Rotaxane·1·HBF$_4$. Method A from (6·HBF$_4$): A solution of rotaxane (**6**·HBF_4) (7 mg, 4.32×10^{-3} mmol, 1.0 equiv.) in iodomethane (0.5 mL) was stirred at room temperature for 3 d under argon. The solvent was removed under reduced pressure and the residue was dissolved in a 1:1:2 mixture of CH_2Cl_2/acetone/water (2 mL). An excess of $NaBF_4$ was added and the mixture was stirred for 18 h at room temperature. CH_2Cl_2 (7 mL) and water (5 mL) were added, the phases separated and the aqueous layer extracted with CH_2Cl_2 (2× 15 mL). The combined organic layers were washed with water (5 mL), dried with $MgSO_4$, and concentrated under reduced pressure to afford **1**·HBF_4 (7 mg, quant.) as a yellowish solid.

Method B from 1: Rotaxane **1** (7 mg, 4.32×10^{-3} mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (0.7 mL). HCl (2.5 μL, 2 M in Et_2O, 5×10^{-3} mmol, 1.15 equiv.) was added and the mixture was stirred at room temperature for 1 h. The solvent was removed under reduced pressure and the residue was dissolved in a 1:4:2 mixture of CH_2Cl_2/acetone/water (2.3 mL). An excess of $NaBF_4$ was added and the mixture was stirred for 18 h at room temperature. CH_2Cl_2 (7 mL) and water (5 mL) were added, the phases separated and the aqueous layer extracted with CH_2Cl_2 (2× 15 mL). The combined organic layers were washed with water (5 mL), dried with $MgSO_4$, and concentrated under reduced pressure to afford **1**·HBF_4 (7 mg, quant.) as a yellowish solid. ^{1}H NMR (500.1 MHz, CD_2Cl_2, 293 K): δ = 0.67 (*s*, 3 H, $H_{cholesterol}$) 0.86–2.33 (*m*, 42 H, $H_{cholesterol}$, H_s, H_t), 2.96 (*t*, $^3J_{u,t}$ = 7.6 Hz, 2 H, H_u), 3.16–3.22 (*m*, 1 H, Hz), 3.37–3.46 (*m*, 8 H, $H_{CH2,\ w}$), 3.66–3.75 (*m*, 8 H, $H_{CH2,\ w}$), 3.76 (*s*,

9 H, H_a), 3.94–3.98 (*m*, 4 H, H_y, H_x) 4.03–4.12 (*m*, 8 H, $H_{CH2, w}$), 4.23 (*s*, 3 H, NCH_3) 4.52–4.55 (*m*, 4 H, H_k, H_m), 4.71 (*t*, $^3J_{r,s}$ = 5.0 Hz, 2 H, H_r) 6.72 (*d*, $^3J_{p,o}$ = 8.6 Hz, 2 H, H_p), 6.77 (*d*, $^3J_{c,d}$ = 8.9 Hz, 6 H, H_c), 6.78–6.81 (*m*, 4 H, $H_{Ar, w}$), 6.87–6.90 (*m*, 4 H, $H_{Ar, w}$), 7.05 (*d*, $^3J_{d,c}$ = 8.9 Hz, 6 H, H_d), 7.15 (*d*, $^3J_{i,h}$ = 8.6 Hz, 2 H, H_i)*, 7.18 (*d*, $^3J_{h,i}$ = 8.6 Hz 2 H, H_h)*, 7.21 (*d*, $^3J_{o,p}$ = 8.6 Hz, 2 H, H_o) 7.41–7.47 (br., 2 H, H_l), 8.39 (*s*, 1 H, H_w) ppm (* assignment of signals might be interchanged). ^{13}C NMR (125.8 MHz, CD_2Cl_2, 293 K): δ = 12.0, 14.2, 18.9, 19.5, 21.4, 22.7, 22.9, 23.1, 23.3, 23.8, 24.2, 24.6, 27.3, 28.4, 28.5, 30.0, 30.1, 32.2, 32.3, 36.2, 36.5, 37.1, 37.3, 37.9, 39.1, 39.9, 40.1, 42.6, 50.5, 52.3, 52.6, 54.8, 55.6, 56.8, 57.1, 63.2, 64.9, 67.4, 68.7, 70.6, 71.0, 80.1, 113.1, 113.2, 114.8, 122.0, 122.3, 123.9, 128.8, 129.0, 129.8, 131.3, 131.4, 132.1, 139.4, 140.7, 144.8, 148.0, 149.3, 158.0, 159.7 ppm (an individual assignment of the signals was not possible). ^{19}F NMR (282.4 MHz, CD_2Cl_2, 293 K): δ = –152.98 (br., $^{10}BF_4$), –153.04 (*m*, $^{11}BF_4$) ppm. MS (ESI): *m*/*z* (%) = 772.5 (100) $[C_{96}H_{128}N_4O_{13} – 2BF_4^-]^{2+}$, 1633.0 (7) $[C_{96}H_{128}N_4O_{13} – BF_4^-]^+$. HRMS (ESI): *m*/*z* (%) calcd. for $[C_{96}H_{128}N_4O_{13}]^{2+}$ 772.9750; found 772.9747: calcd. for $[C_{96}H_{128}N_4O_{13}BF_4]^+$ 1631.9506; found 1631.9522.

Rotaxane·1: Aq. NaOH (1 mL, 1 M) was added to a solution of **1**·HBF_4 (7 mg, 4.32×10^{-3} mmol, 1.0 equiv.) in CH_2Cl_2 (0.7 mL) and the mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with CH_2Cl_2 (10 mL), the layers separated, and the aqueous layer extracted with CH_2Cl_2 (10 mL). The combined organic layers were dried with $MgSO_4$, and concentrated under reduced pressure to afford rotaxane **1** as a yellow solid (7 mg, quant.). ^{1}H NMR (500.1 MHz, CD_2Cl_2, 293 K): δ = 0.69 (*s*, 3 H, $H_{cholesterol}$) 0.86–2.34 (*m*, 42 H, $H_{cholesterol}$, H_s, H_t), 3.16–3.23 (*m*, 1 H, Hz), 3.59–4.12 (*m*, 46 H, H_a, H_k, H_m, H_p, H_u, H_x, H_y, $H_{CH2, w}$, NCH_3), 4.80–5.05 (br., 1 H, H_l), 6.73–6.90 (*m*, 16 H, H_c, H_p, $H_{Ar, w}$), 7.09 (*d*, $^3J_{d,c}$ = 8.7 Hz, 6 H, H_d), 7.14 (*d*, $^3J_{i,h}$ = 8.2 Hz, 2 H, H_i)*, 7.20 (*d*, $^3J_{h,i}$ = 8.2 Hz, 2 H, H_h)*, 7.26 (*d*, $^3J_{o,p}$ = 8.1 Hz, 2 H, H_o), 8.76 (*s*, 1 H, H_w) ppm (* assignment of the signals might be interchanged). ^{13}C NMR (125.8 MHz, CD_2Cl_2, 293 K): δ = 12.0,14.2, 15.5, 18.9, 19.5, 21.4, 22.7, 22.9, 23.1, 24.2, 24.6, 28.4, 28.6, 32.2, 32.3, 36.2, 36.6, 37.1, 37.5, 39.9, 40.2, 42.7, 50.6, 55.5, 56.6, 57.2, 66.0, 68.7, 70.4, 71.4, 79.9, 112.4, 113.0, 113.1, 114.4, 121.4, 127.4, 129.7, 130.7, 131.1, 132.2, 133.1, 138.5, 139.9, 146.7, 148.1, 157.9 ppm (an individual assignment of the signals was not possible). MS (ESI): *m*/*z* (%) = 772.5 (100) $[C_{96}H_{127}N_4O_{13} + H]^{2+}$, 1544.1 (6) $[C_{96}H_{127}N_4O_{13}]^+$. HRMS (ESI): *m*/*z* calcd. for $[C_{96}H_{127}N_4O_{13}]^+$ 1544.9427; found 1544.9423.

Acknowledgments

Financial support by the Deutsche Forschungsgemeinschaft (DFG) is gratefully acknowledged.

[1] B. L. Feringa, W. R. Browne (Eds.), *Molecular Switches*, 2nd ed., Wiley-VCH, Weinheim, Germany, **2011**.

[2] a) V. Balzani, A. Credi, F. Raymo, J. F. Stoddart, *Angew. Chem. Int. Ed.* **2000**, *39*, 2248–2291; *Angew. Chem.* **2000**, *112*, 3485–3530; b) T. Kelley, *Molecular Machines*, *Top. Curr. Chem.* **2005**, *262*; c) K. Kinbara, T. Aida, *Chem. Rev.* **2005**, *105*, 1377–1400; d) R. E. Kay, D. A. Leigh, F. Zerbetto, *Angew. Chem. Int. Ed.* **2007**, *46*, 72–191; *Angew. Chem.* **2007**, *119*, 72–196; e) V. Balzani, A. Credi, M. Venturi, *Molecular Devices and Machines - Concepts and Perspectives for the Nanoworld*, 2nd ed., Wiley-VCH, Weinheim, Germany, **2008**.

[3] S. F. M. van Dongen, S. Cantekin, J. A. A. W. Elemans, A. E. Rowan, R. J. M. Nolte, *Chem. Soc. Rev.* **2014**, *43*, 99–122.

[4] a) A. Rescifina, C. Zagni, D. Iannazzo, P. Merino, *Curr. Org. Chem.* **2009**, *13*, 448–481; b) A. Rescifina, U. Chiacchio, A. Corsaro, G. Romeo, *Curr. Org. Chem.* **2012**, *16*, 127–160; c) W. Yang, Y. Li, H. Liu, L. Chi, Y. Li, *Small* **2012**, *8*, 504–516.

[5] a) S. Saha, J. F. Stoddart, *Chem. Soc. Rev.* **2007**, *36*, 77–92; b) D.-H. Qu, H. Tian, *Curr. Phys. Chem.* **2011**, *1*, 261–274; c) A. Credi, S. l Silvi, M. Venturi, *Photochemically Driven Molecular Devices and Machines*, in: *Supramolecular Chemistry – From Molecules to Nanomaterials* (Eds.: P. A: Gale, J. W. Steed), Wiley-VCH, Chichester, UK, **2012**, vol. 8, 3719–3750; d) P. Ceroni, A. Credi, M. Venturi, *Chem. Soc. Rev.* **2014**, *43*, 4068–4083.

[6] a) B. Champin, P. Mobian, J.-P. Sauvage, *Chem. Soc. Rev.* **2007**, *36*, 358–366; b) C. A. Nijhuis, B. J. Ravoo, J. Huskens, D. N. Reinhoudt, *Coord. Chem. Rev.* **2007**, *251*, 1761–1780; c) A. C. Fahrenbach, C. J. Bruns, D. Cao, J. F. Stoddart, *Acc. Chem. Res.* **2012**, *45*, 1581–1592; d) A. Coskun, J. M. Spruell, G. Barin, W. R. Dichtel, A. H. Flood, Y. Y. Botros, J. F. Stoddart, *Chem. Soc. Rev.* **2012**, *41*, 4827–4859; e) A. C. Fahrenbach, C. J. Bruns, H. Li, A. Trabolsi, A. Coskun, J. F. Stoddart, *Acc. Chem. Res.* **2014**, *47*, 482–493.

[7] K. C.-F. Leung, C.-P. Chak, C.-M. Lo, W.-Y. Wong, S. Xuan, C. H. K. Cheng, *Chem. Asian J.* **2009**, *4*, 364–381.

[8] C. J. Bruns, J. F. Stoddart, *Acc. Chem. Res.* **2014**, *47*, 2186–2199.

[9] a) K. K. Cotí, M. E. Belowich, M. Liong, M. W. Ambrogio, Y. A. Lau, H. A. Khatib, J. I. Zink, N. M. Kashab, J. F. Stoddart, *Nanoscale* **2009**, *1*, 16–39; b) M. W. Ambrogio, C. R. Thomas, Y.-L. Zhao, J. I. Zink, J. F. Stoddart, *Acc. Chem. Res.* **2011**, *44*, 903–913; c) P. Yang, S. Gai, J. Lin, *Chem. Soc. Rev.* **2012**, *41*, 3679–3698.

[10] Y.-W. Yang, Y.-L. Sun, N. Song, *Acc. Chem. Res.* **2014**, *47*, 1950–1960.

[11] Y.-L. Zhao, I. Aprahamian, A. Trabolsi, N. Erina, J. F. Stoddart, *J. Am. Chem. Soc.* **2008**, *130*, 6348–6350.

[12] Z.-J. Zhang, Y. Liu, *Synlett* **2012**, *23*, 1733–1750.

[13] a) M.-V. Martínez-Díaz, N. Spencer, J. F. Stoddart, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1904–1907; *Angew. Chem.* **1997**, *109*, 1991–1994; b) P. R. Ashton, R. Ballardini, V. Balzani, I. Baxter, A. Credi, M. C. T. Fyfe, M. T. Gandolfi, M. Gómez-López, M.-V. Martínez-Díaz, A. Piersanti, N. Spencer, J. F. Stoddart, M. Venturi, A. J. P. White, D. J. Williams, *J. Am. Chem. Soc.* **1998**, *120*, 11932–11942.

[14] a) C.-F. Lin, C.-C. Lai, Y.-H. Liu, S.-M. Peng, S.-H. Chiu, *Chem. Eur. J.* **2007**, *13*, 4350–4355; b) C.-J. Chuang, W.-S. Li, C.-C. Lai, Y.-H. Liu, S.-H. Peng, I. Chao, S.-H. Chiu, *Org. Lett.* **2009**, *11*, 385–388.

[15] F. Coutrot, E. Busseron, *Chem. Eur. J.* **2009**, *15*, 186–190.

[16] T. Ogoshi, D. Yamafuji, T. Aoki, K. Kitajima, T. Yamagishi, Y. Hayashi, S. Kawauchi, *Chem. Eur. J.* **2012**, *18*, 7493–7500.

[17] B. Hesseler, M. Zindler, R. Herges, U. Lüning, *Eur. J. Org. Chem.* **2014**, 3885–3901.

[18] a) F. Coutrot, C. Romuald, E. Busseron, *Org. Lett.* **2008**, *10*, 3741–3744; b) E. Busseron, C. Romuald, F. Coutrot, *Chem. Eur. J.* **2010**, *16*, 10062–10073.

[19] a) Q. Jiang, H.-Y. Zhang, M. Han, Z.-J. Ding, Y. Liu, *Org. Lett.* **2010**, *12*, 1728–1731; b) Z.-J. Zhang, M. Han, H.-Y. Zhang, Y. Liu, *Org. Lett.* **2013**, *15*, 1698–1701.

[20] Y. Jiang, J.-B. Guo, C.-F. Chen, *Org. Lett.* **2010**, *12*, 4248–4251.

[21] G. T. Spence, M. B. Pitak, P. D. Beer, *Chem. Eur. J.* **2012**, *18*, 7100–7108.

[22] V. Blanco, A. Carlone, K. D. Hänni, D. A. Leigh, B. Lewandowski, *Angew. Chem. Int. Ed.* **2012**, *51*, 5166–5169; *Angew. Chem.* **2012**, *124*, 5256–5259.

[23] I. Aprahamian, O. Š. Miljanić, W. R. Dichtel, K. Isoda, T. Yasuda, T. Kato, J. F. Stoddart, *Bull. Chem. Soc. Jpn.* **2007**, *80*, 1856–1869.

[24] a) W. Jiang, H. D. F. Winkler, C. A. Shalley, *J. Am. Chem. Soc.* **2008**, *42*, 13852–13853; b) D. A. Leigh, V. Marcos, M. R. Wilson, *Compr. Asymmetric Catal. Suppl.* **2014**, *4*, 4490–4497.

[25] A. Tanatani, T. S. Hughes, J. S. Moore, *Angew. Chem. Int. Ed.* **2002**, *41*, 325–328; *Angew. Chem.* **2002**, *114*, 335–338.

[26] T. Hatano, T. Kato, *Tetrahedron* **2008**, *64*, 8368–8360.
[27] S. Bhattacharya, Y. Krishnan-Ghosh, *Langmuir* **2001**, *17*, 2067–2075.
[28] T. R. Chan, R. Hilgraf, K. Barry Sharpless, V. V. Fokin, *Org. Lett.* **2004**, *17*, 2853–2855.
[29] a) C. A. Schalley, J. Hoernschemeyer, X.-y. Li, G. Silva, P. Weis, *Int. J. Mass Spectrom.* **2003**, *228*, 373–388; b) C. A. Schalley, P. Ghosh, M. Engeser, *Int. J. Mass Spectrom.* **2004**, *232*, 249–258; c) P. Ghosh, G. Federwisch, M. Kogej, C. A. Schalley, D. Haase, W. Saak, A. Lützen, R. M. Gschwind, *Org. Biomol. Chem.* **2005**, *3*, 2691–2700.

Received: May 21, 2015
Published Online: August 6, 2015

