ChemistryOPEN

Supporting Information

Reversible Mechanical Switching of Magnetic Interactions in a Molecular Shuttle

Valentina Bleve, Christian Schäfer, Paola Franchi, Serena Silvi, Elisabetta Mezzina,* Alberto Credi,* and Marco Lucarini*[a]

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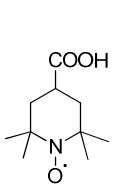
General procedures

EPR spectra has been recorded on Bruker-ELEXYS spectrometer by using the following instrument settings: microwave power 0.79 mW, modulation amplitude 0.04 mT, modulation frequency 100 kHz, scan time 180 s, 2K data points.

^{1}H NMR spectra of the rotaxane **1**H•3PF_6, the dumbbell **3**H•3PF_6, the spin labeled ring **2**, and 1D Roesy spectrum of **[2]rotaxane DB24C8_CH_2OH•3PF_6** were recorded at 298 K on a Varian Inova spectrometer operating at 600 MHz in CD_3CN solutions using the solvent peak as internal standard (1.94 ppm). Chemical shifts are reported in parts per million (δ scale).

ESI-MS spectra were recorded with Micromass ZMD spectrometer by using the following instrumental settings: positive ions; desolvation gas (N2) 230 L/h; cone gas (skimmer): 50 L/h; desolvation temp. 120° C; capillary voltage: 3.2 kV; cone voltage: 40 and 100 V; hexapole extractor: 3 V.

All substances, included radical stoppers **5** and **7**, and solvents were used without further purification and were commercially available. Dry solvents were bought dry and used directly.



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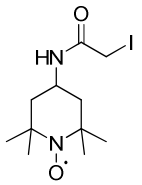

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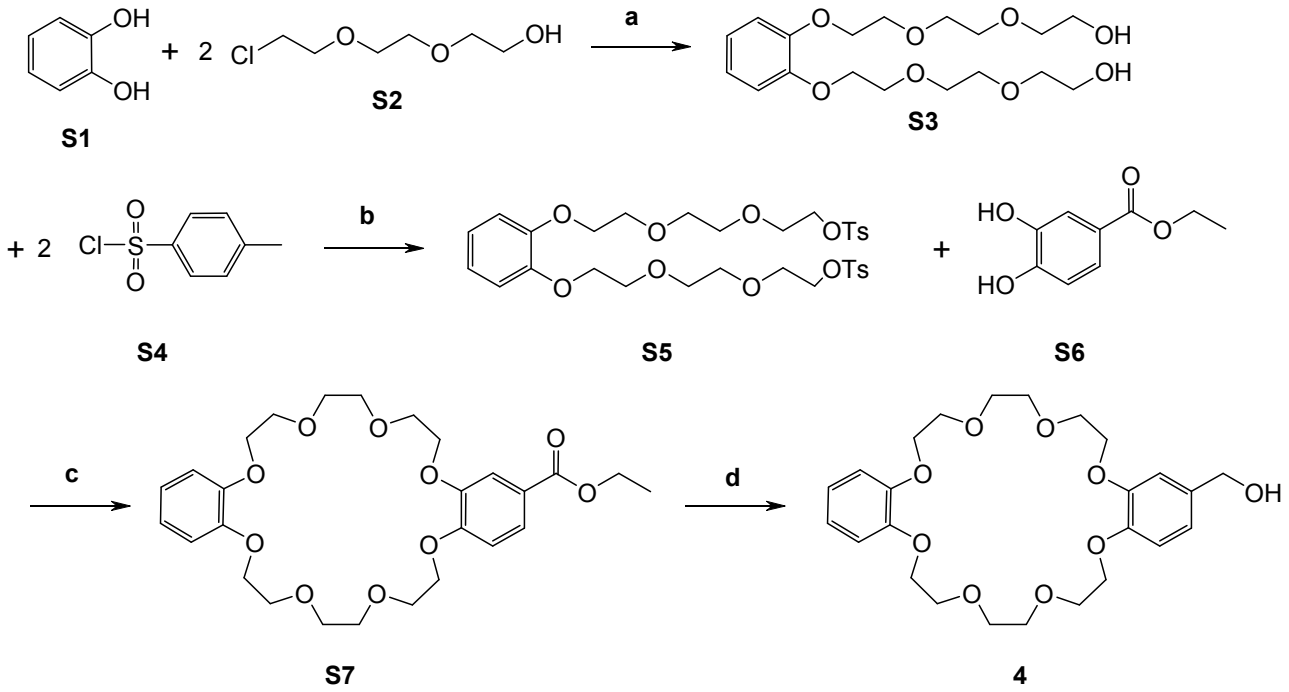
Compound **6**H•2PF_6 was prepared according to literature.[S1]

Preparation of compound 4

Compound **4** was prepared by a modified synthetic protocol based on the procedure reported by Pak *et al.*[S2] and Gale *et al.*[S3]
Catechol **S1** and two equivalents of 2-[2-(2-chloro-ethoxy)-ethoxy]-ethanol **S2** were used to obtain compound **S3** in 96% yield after column chromatography on silica gel. The hydroxy groups were then transformed into the corresponding tosylates by reaction with 4-toluenesulfonyl chloride **S4**, which gave compound **S5** in 74% yield after column chromatography. To obtain the mono-functionalized dibenzo crown ether **S7**, compound **S5** reacted in a 1:1 rate with ethyl 3,4-hydroxybenzoate **S6** under highly diluted conditions and over a period of 24 h. Crown ether **S7** was collected in 89% yield and reduced with lithium aluminium hydride to give compound **4** in 91% yield after the proper work-up.



Scheme S1: a) K_2CO_3, DMF, 120°C, 96%; b) 4-DMAP, Et_3N, DCM, rt, 74%; c) Cs_2CO_3, ACN, reflux, 89%; d) 1. $LiAlH_4$, THF, reflux; 2. H_2O/HCl, 91%.

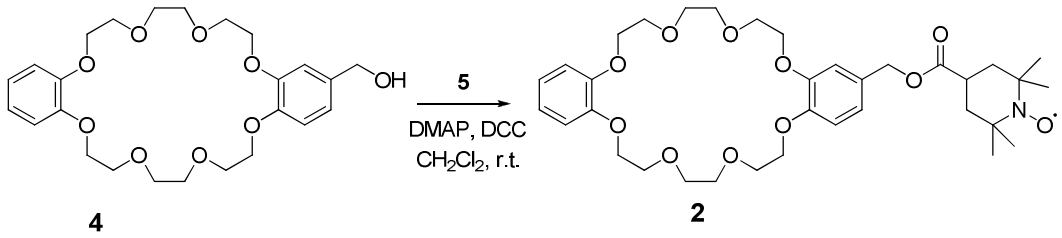
Compound **S3**: Catechol (2.80 g, 25.4 mmol) was dissolved in 50 mL dry DMF under nitrogen atmosphere and potassium carbonate (3 equivalents, 10.54 g, 76.2 mmol) was added followed by 2-[2-(2-chloro-ethoxy)-ethoxy]-ethanol (2.2 equivalents, 9.43 g, 56 mmol). The reaction was heated to 120°C (bath temperature). After 20 h, the suspension was allowed to cool down and the solvent was removed in vacuo. The residue was dissolved in water and chloroform, the phases were separated and the water layer was extracted with chloroform three more times. The combined org. layers were dried over $MgSO_4$ and the solvent was removed in vacuo. The residue was submitted to column chromatography on silica gel, using ethyl acetate/methanol (4:1, v/v) as eluent. Yield: 9.097 g, 24 mmol, 96%.
^{1}H NMR ($CDCl_3$, 400 MHz): δ [ppm] = 3.08 (br, OH, 2 H), 3.57-3.61 (m, CH_2, 4 H), 3.64-3.69 (m, CH_2, 4 H), 3.69-3.75 (m, CH_2, 8 H), 3.84-3.88 (m, CH_2, 4 H), 4.14-4.18 (m, CH_2, 4 H), 6.89 (s, ArH, 4 H). ^{13}C-NMR ($CDCl_3$): δ [ppm] = 61.65, 68.61, 69.70, 70.28, 70.78, 72.61 (CH_2), 114.41 ($C_{Ar}H$), 121.64 ($C_{Ar}H$), 148.68 ($C_{Ar}O$).

Compound **S5**: The reagent **S3** (9.51 g, 24.4 mmol) was dissolved in 150 mL DCM under nitrogen atmosphere and triethylamine (13.5 mL) and 4-(Dimethylamino)-pyridine (38 mg) were added. The solution was cooled down in an ice bath and 4-toluenesulfonyl chloride (2.2 equivalents, 10.65 g, 55.9 mmol) dissolved in 75 mL DCM was added dropwise at this temperature over 1 h. The ice bath was removed and stirring continued at rt over night. Some dichloromethane was removed in vacuo and 100 mL HCl (5 M) were added. The phases were separated and the org. layer was washed with 2 M HCl, brine, dried over $MgSO_4$ and the solvent was removed in vacuo. The product was isolated by column chromatography on silica gel, starting with pure DCM as solvent and continuing with DCM/EtOAc, 9:1 (v/v). Yield: 12.36 g, 18.1 mmol, 74%.
^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] = 2.40 (s, CH_3, 6 H), 3.56-3.60 (m, CH_2, 4 H), 3.62-3.68 (m, CH_2, 8 H), 3.77-3.81 (m, CH_2, 4 H), 4.09-4.15 (m, CH_2, 8 H), 6.88 (s, ArH, 4 H), 7.30 (d, ^3J=7.9 Hz, ArH, 4 H), 7.76 (d, ^3J=8.4 Hz, ArH, 4 H).

Compound **S7**: Cs_2CO_3 (25.28 g) was suspended in 630 mL acetonitrile under nitrogen atmosphere and heated to reflux (120 °C bath temperature). A solution of **S5** (10.594 g, 15.5 mmol) and ethyl 3,4-hydroxybenzoate (2.827 g, 15.5 mmol) in 90 mL acetonitrile was added over 24 h via syringe pump to the boiling suspension. Afterwards, reflux continued for 24 h before the suspension was allowed to cool down. The solvent was removed in vacuo und the residue was dissolved in ethyl acetate and water. The phases were separated and the water layer was extracted with ethyl acetate four more times. The combined org. layers were washed with water, dried over $MgSO_4$ and the solvent was removed in vacuo. The product was crystallized from DCM and *n*-hexane. If necessary, the product can be further purified by column chromatography on silica gel with DCM/MeOH, 49:1 (v/v) as eluent. Yield: 7.163 g; 13.76 mmol; 89%.
^{1}H NMR ($CDCl_3$, 400 MHz): δ [ppm] = 1.35 (t, ^3J=7.1 Hz, CH_3, 3 H), 3.80-3.83 (m, CH_2, 8 H), 3.88-3.94 (m, CH_2, 8 H), 4.11-4.15 (m, CH_2, 4 H), 4.15-4.19 (m, CH_2 4 H), 4.32 (q, ^3J=7.1 Hz, CH_2, 2 H), 6.81-6.89 (m, ArH, 5 H), 7.50 (d, ^4J=2.0 Hz, ArH, 1 H), 7.63 (dd, ^3J=8.4 Hz, ^4J=2.0 Hz, ArH, 1 H). ^{13}C-NMR ($CDCl_3$): δ [ppm] = 14.30 (CH_3), 60.67 (CH_2), 69.20, 69.26, 69.32, 69.41, 69.54, 69.68, 69.84, 71.18, 71.26, 71.36 (CH_2), 111.89 ($C_{Ar}H$), 113.94 ($C_{Ar}H$), 114.25 ($C_{Ar}H$), 121.30 ($C_{Ar}H$), 121.32 ($C_{Ar}H$), 123.12 ($C_{Ar,q}$), 123.72 ($C_{Ar}H$), 148.12 ($C_{Ar}O$), 148.81 ($C_{Ar}O$), 148.82 ($C_{Ar}O$), 152.70 ($C_{Ar}O$), 166.22 (C=O).

Compound **4**: The reagent **S7** (2.07 g, 3.98 mmol) was dissolved in 50 mL dry THF and added dropwise over 1 h to an ice cooled suspension of $LiAlH_4$ (5 equivalents, 755 mg) in 100 mL dry THF under nitrogen atmosphere. After addition, the reaction stirred at rt for 1 h und was then heated to reflux for 2 h. Afterwards, the suspension was allowed to cool down and quenched carefully with water and diluted HCl. THF was removed in vacuo and the product was extracted with dichloromethane several times. The combined org. layers were washed with water and brine, dried over $MgSO_4$ and the solvent was removed in vacuo. If necessary, the product can be further purified by column chromatography on silica gel with DCM/MeOH, 19:1 (v/v). Yield: 1.738 g; 3.63 mmol; 91%.
^{1}H NMR ($CDCl_3$, 400 MHz): δ [ppm] = 1.93 (br, OH, 1 H), 3.80 (s, CH_2, 8 H), 3.84-3.90 (m CH_2, 8 H), 4.08-4.14 (m, CH_2, 8 H), 4.54 (s, CH_2, 2 H), 6.77-6.91 (m, ArH, 7 H). ^{13}C-NMR ($CDCl_3$): δ [ppm] = 65.02 (CH_2OH), 69.32, 69.48, 69.84, 71.19 (CH_2), 112.94 ($C_{Ar}H$), 113.86 ($C_{Ar}H$), 114.06 ($C_{Ar}H$), 119.82 ($C_{Ar}H$), 121.36 ($C_{Ar}H$), 134.25 ($C_{Ar,q}$), 148.31 ($C_{Ar}O$), 148.88 ($C_{Ar}O$), 148.95 ($C_{Ar}O$).

Preparation of TEMPO-functionalized DB24C8 derivative 2



An ice-cooled solution of **4** (0.15 g, 0.313 mmol), 4-carboxy-TEMPO **5** (0.075 g, 0.376 mmol), 1,3-dicyclohexylcarbodiimide (DCC) (0.077 g, 0.376 mmol), and 4-dimethylaminopyridine (DMAP) (0.011 g, 0.094 mmol) in CH_2Cl_2 (20 mL) was stirred for 15 min and then for 24 h at room temperature under nitrogen atmosphere. The resulting suspension was filtered, and the filtrate was evaporated and subjected to column chromatography (SiO_2: h 13 cm, i.d. 2 cm, dichloromethane/ethyl acetate, 1:1) to furnish compound **2** as an orange-brown solid in 70% yield.

^{1}H NMR (600 MHz, CD_3CN): δ 3.68 (s, 8H), 3.80 (s, 8H), 4.05-4.15 (m, 8H), 5.06 (s, 2H), 6.80-7.00 (m, 7H). ESI-MS: *m/z* 683.1 $(M+Na)^+$.

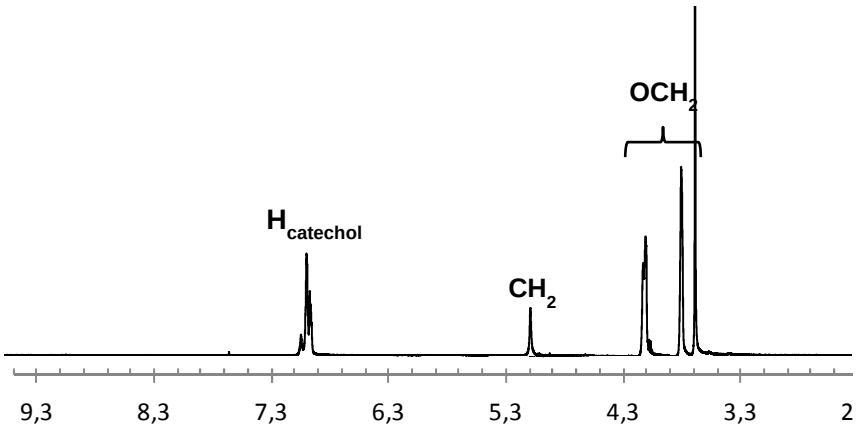


Figure. S1. ^{1}H NMR spectrum (600 MHz, CD_3CN, 298 K) of spin labelled ring **2**.

The ^{1}H NMR spectrum of *N*-hydroxy amine of **2** (**2**-OH) was also recorded after *in situ* reduction of the sample containing the nitroxide **2** by using phenylhydrazine.

2-OH: ^{1}H NMR (600 MHz, CD_3CN): δ 1.08 (s, 6H), 1.11 (s, 6H), 1.52 (t, J = 12.3 Hz, 2H), 1.77 (d, J = 12.3 Hz, 2H), 2.70 (dt, J = 12.3 and 3.0 Hz, 1H), 3.68 (s, 8H), 3.78-3.81 (m, 8H), 4.08-4.13 (m, 8H), 4.98 (s, 2H), 6.88-6.95 (m, 7H)

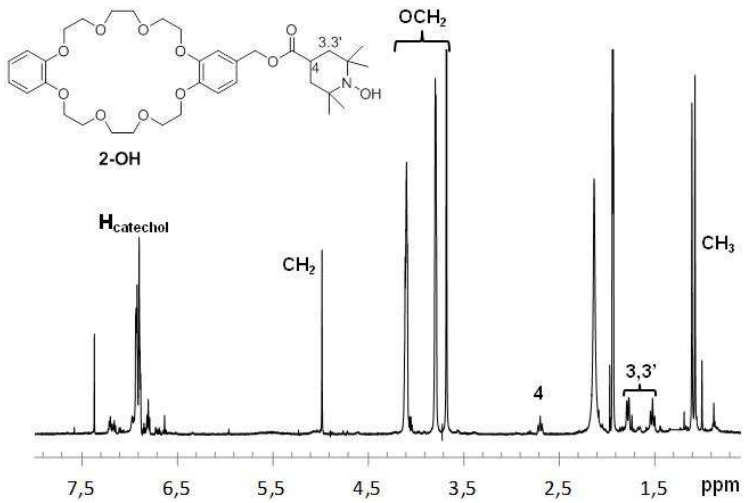
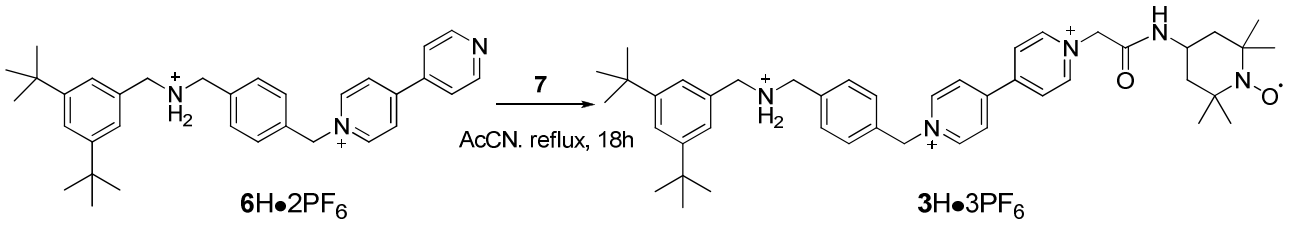


Figure S2. ^{1}H NMR spectrum (600 MHz, CD_3CN, 298 K) of **2**-OH obtained after in situ reduction of the sample containing the nitroxide **2** by using phenylhydrazine.

Preparation of dumbell 3H•3PF$_6$



A CH_3CN solution (2 mL) of **6**H•2PF_6 (0.030 g, 0.0389 mmol) and 4-(2-iodoacetamido)-TEMPO (**7**, 0.0527 g, 0.156 mmol) was heated under reflux for 18 h under nitrogen atmosphere. After cooling the solution was concentrated in vacuo and the reaction mixture was purified by silica gel column (h 8 cm, i.d. 2 cm, CH_2Cl_2-CH_3OH 9:1, then CH_3OH-NH_4Cl 2M-H_2O 7:0.5:2.5). The fractions containing the product were concentrated in vacuo, dissolved in a minimum volume of water, and treated with NH_4PF_6 aqueous solution. The resulting solid was collected by filtration, washed with water to remove the excess of NH_4PF_6, and dried to afford the dumbell **3**H•3PF_6 as a pink flesh powder (0.022 g, 50% yield).

3H•3PF_6: ^{1}H NMR (600 MHz, CD_3CN, CF_3COOH): δ 1.30-1.35 (m, 18H), 4.26 (*br* s, 2H), 4.32 (*br* s, 2H), 5.28 (*br* s, 2H), 5.83 (*br* s, 2H), 7,34 (br s, 2H) -7.46-7.68 (m, 5H), 8.35-8.44 (m, 4H), 8.78-8.86 (m, 2H), 8.93-8.99 (m, 2H). ESI-MS: *m/z* 690.5 $(M\text{-}3PF_6)^+$.

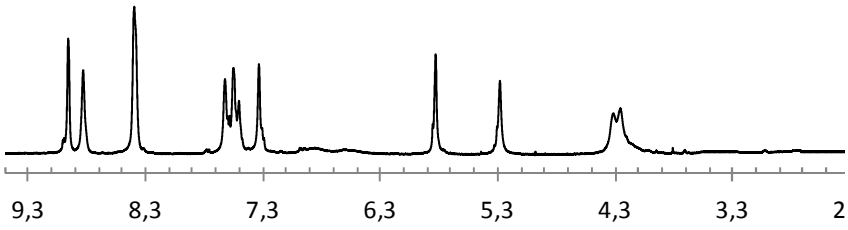
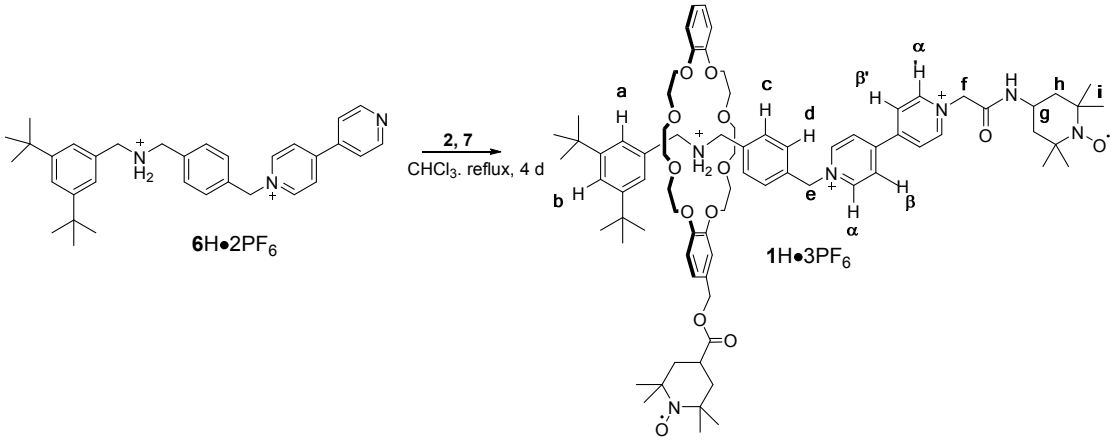


Figure. S3. Partial ^{1}H NMR spectrum (600 MHz, CD_3CN, CF_3COOH, 298 K) of dumbell **3**H•3PF_6

The ^{1}H NMR spectrum of *N*-hydroxy amine of **3**H•3PF$_6$ (**3**H•3PF$_6$-OH) was also recorded after *in situ* reduction of the sample containing the nitroxide dumbbell **3**H•3PF$_6$ by using phenylhydrazine.
3H•3PF$_6$-OH: ^{1}H NMR (600 MHz, CD_3CN): δ 1.14 (s, 6H), 1.15 (s, 6H), 1.32 (s, 18H), 1.42-1.50 (m, 2H), 1.82 (*br* d, *J* = 9.6 Hz, 2H), 3.64 (s, 2H), 3.69 (s, 2H), 5.27 (s, 2H), 5.81 (s, 2H), 7.38-7.52 (m, 7H), 8.35 (d, *J* = 6.6 Hz, 2H), 8.37 (d, *J* = 6.6 Hz, 2H), 8.79 (d, *J* = 6.6 Hz, 2H), 8.95 (d, *J* = 6.6 Hz, 2H).

Preparation of rotaxane 1H•3PF$_6$



A $CHCl_3$ (1 mL) solution of 4-(2-iodoacetamido)-TEMPO (**7**, 0.0725 g, 0.214 mmol) was added to a stirred suspension of compound **6**H•2PF$_6$ (0.030 g, 0.039 mmol) and **2** (0.046 g, 0.0972 mmol) in $CHCl_3$ (3 mL) and the mixture was heated under reflux for 4 d under nitrogen atmosphere, until it became a clear solution. After cooling the solution was concentrated in vacuo and the reaction mixture was purified by silica gel column (h 10 cm, i.d. 20 mm, CH_2Cl_2-CH_3OH 9:1, then CH_3OH-NH_4Cl 2M-H_2O 7:0.5:2.5). The fractions containing the product were concentrated in vacuo, dissolved in a minimum volume of water, and treated with NH_4PF_6 aqueous solution. The resulting solid was collected by filtration, washed with water to remove the excess of NH_4PF_6, and dried to afford the rotaxane **1**H•3PF$_6$ as a pink flesh powder (0.021 g, 30% yield).
1H•3PF$_6$: ^{1}H NMR (600 MHz, CD_3CN): δ 1.20 (s, 18H), 3.48-3.88 (m, 16H), 3.93-4.16 (m, 8H), 4.68-4.80 (m, 4H), 5.05 (br s, 2H), 5.30 (br s, 2H), 5.49 (s, 2H), 6.69-6.76 (m, 3H), 6.78-6.82 (m, 3H), 6.83-6.90 (m, 1H), 6.94-7.02 (m, 2H), 7.26-7.37 (m, 2H), 7.34 (s, 2H), 7.46 (s, 1H), 7.60-7.72 (m, 2H), 8.41 (br s, 4H), 8.77 (br s, 2H), 8.81-8.90 (m, 2H). ESI-MS: *m/z* 1810.8 $(M+Na)^+$, 1642.9 $(M-PF_6)^+$.

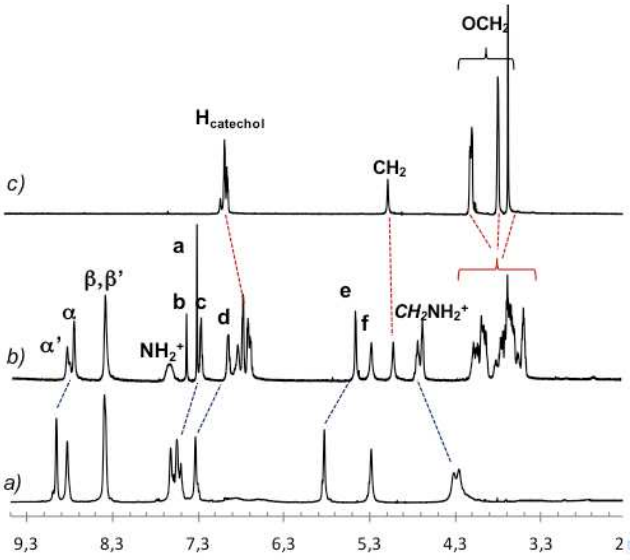


Figure S4. Partial ^{1}H NMR spectra (600 MHz, CD_3CN, 298 K) of *a*) dumbbell 3H•3PF$_6$; *b*) rotaxane 1H•3PF$_6$; *c*) spin-labeled ring **2**. Blue dashed lines evidence the shielding of some guest protons caused by the presence of the paramagnetic crown ether and red dashed lines show the broadening and splittings of the macrocyclic signals. The labels correspond to the hydrogen assignments indicated in previous scheme. The direct comparison between the ^{1}H-NMR spectra of the rotaxane **1H•3PF$_6$** and its non-interlocked analogue **3H•3PF$_6$** indicate the presence and the localization of paramagnetic DB24C8 around the ammonium moiety in former one. The signal of ammonium protons were detected only in the case of the complexed form owing to their hydrogen-bonding interactions with the oxygen atoms of the host, also, as a result of this, both CH_2 protons adjacent to the binding site are shifted downfield in the rotaxane ($\Delta\delta$=0.45 and 0.44 ppm, respectively). Other important shifts detected by the spectrum of the rotaxane concern i) α protons of the viologen moiety, ii) CH_2(e) and iii) *p*-xilene unit (c and d protons) signals which fall upfield ($\Delta\delta$ = -0.11, -0.34 and -0.27 and -0.36 ppm, respectively) respect to those of the dumbbell, indicating that this portion of the axle experiences the shielding effect of the aromatic rings of DB24C8 **2**. No variations at all in the chemical shifts for the hydrogen atoms $H_{\alpha'}$, $H_{\beta,\beta'}$, and CH_2 (f) belonging to the right part of the molecule are noticed, thus suggesting again the exclusive localization of the crown ether around the ammonium group. With regard to the host, the three sharp peaks corresponding to the OCH_2 proton of **2** are split upon the rotaxane formation, with respect to the free DB24C8 derivative as a consequence of their non-equivalence. Indeed, in the interlocked structure, they are facing the two nonsymmetrical ends of the encircled molecular axle. Similar behavior is displayed by catechol protons which are also shielded of ca 0.13 ppm upon complexation.

The ^{1}H NMR spectrum of *N*-hydroxy amine of **1**H•3PF$_6$ (**1**H•3PF$_6$-OH) was also recorded after *in situ* reduction of the sample containing **1**H•3PF$_6$: by using phenylhydrazine.

1H•3PF$_6$-OH: ^{1}H NMR (600 MHz, CD_3CN): δ 1.08 (s, 6H), 1,10 (s, 6H), 1.11 (s, 6H), 1.13 (s, 6H), 1.20 (s, 18H), 1.42 (t, *J* = 12.3 Hz, 2H), 1.52 (t, *J* = 13.2 Hz, 2H), 1.75-1.81 (m, 4H), 2.68-2.74 (m, 1H), 3.50-3.86 (m, 16H), 3.93-4.03 (m, 5H), 4.05-4.13 (m, 4H), 4.69-4.80 (m, 4H), 4.97 (s, 2H), 5.29 (s, 2H), 5.48 (s, 2H), 5.62 (br s, 1H), 6.63-6.86 (m, 7H), 6.95 (d, *J* = 7.8 Hz, 2H), 7.28 (d, *J* = 7.8 Hz, 2H), 7.37 (s, 2H), 7.46 (s, 1H), 7.67 (br s, 2H), 8.39 (d, *J* = 6.0 Hz, 2H), 8.41 (d, *J* = 6.6 Hz, 2H), 8.77 (d, *J* = 6.0 Hz, 2H), 8.82 (d, *J* = 6.6 Hz, 2H).

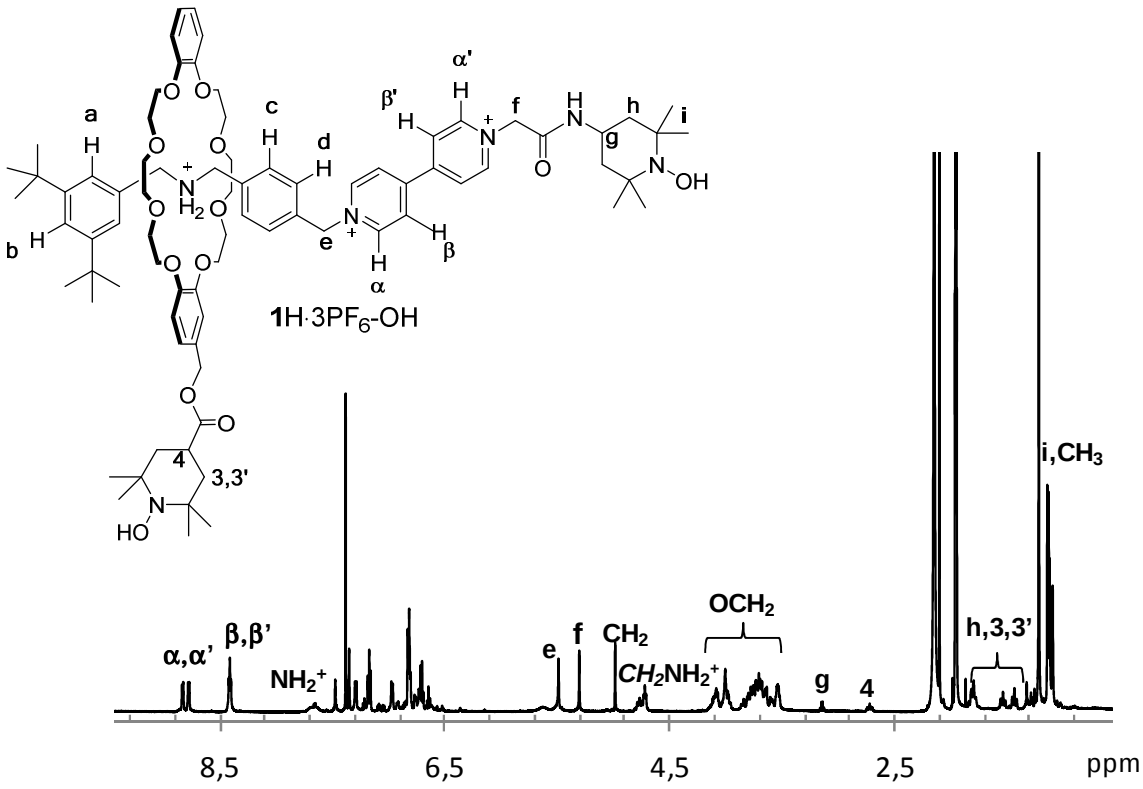


Figure S5. ^{1}H NMR spectrum (600 MHz, CD_3CN, 298 K) of **1**H•3PF_6-OH obtained after in situ reduction of the sample containing the rotaxane **1**H•3PF_6 by using phenylhydrazine.

Preparation of the diamagnetic [2]rotaxane containing 4 (DB24C8_CH_2OH)

A $CHCl_3$ (1 mL) solution of iodoacetamido-TEMPO (**7**, 0.0725 g, 0.214 mmol) was added to a stirred suspension of compound **3**H•2PF_6: (0.030 g, 0.0389 mmol) and **4** (0.046 g, 0.0972 mmol) in $CHCl_3$ (3 mL) and the mixture was heated under reflux for 4 d under nitrogen atmosphere, until it became a clear solution. After cooling the solution was concentrated in vacuo and the reaction mixture was purified by silica gel column (h 8 cm, i.d. 2 cm, CH_2Cl_2-CH_3OH 9:1, then CH_3OH-NH_4Cl 2M-H_2O 7:0.5:2.5). The fractions containing the product were concentrated in vacuo, dissolved in a minimum volume of water, and treated with NH_4PF_6 aqueous solution. The resulting solid was collected by filtration, washed with water to remove the excess of NH_4PF_6, and dried to afford the **[2]rotaxane DB24C8_CH_2OH •3PF_6** as a pink flesh powder (0.018 g, 30% yield).
^{1}H NMR (600 MHz, CD_3CN): δ 1.22 (s, 18H), 3.28-3.34 (m, 1H), 3.48-3.60 (m, 4H), 3.64-3.83 (m, 12H), 3.94-3.98 (m, 2H), 3.99-4.10 (m, 7H), 4.45 (*br* s, 2H), 4.70-4.78 (m, 4H), 5.29 (br s, 2H), 5.47 (s, 2H), 6.66 (d, *J* = 7.8 Hz, 1H), 6.73-6.84 (m, 6H), 6.89 (d, *J* = 7.8 Hz, 2H), 7.26 (d, *J* = 7.8 Hz, 2H), 7.37 (s, 2H), 7.49 (s, 1H), 7.67 (br s, 2H), 8.36-8.46 (m, 4H), 8.73-8.77 (m, 2H), 8.85 (br s, 2H). ESI-MS: *m/z* 1460.8 $(M\text{-}PF_6)^+$, 657.3 $(M\text{-}2PF_6)^{2+}$.

The ^{1}H NMR spectrum of the corresponding *N*-hydroxy amine was also recorded after *in situ* reduction of the sample containing the **[2]rotaxane DB24C8_CH_2OH•3PF_6** by using phenylhydrazine.

^{1}H NMR (600 MHz, CD_3CN): δ 1.13 (s, 6H), 1.14 (s, 6H), 1.22 (s, 18H), 1.45 (t, *J* = 12.0 Hz, 2H), 1.81 (d, *J* = 12.0 Hz, 2H), 3.22 (t, J = 4.8 Hz, 1H), 3.48-3.60 (m, 4H), 3.65-3.81 (m, 12H), 3.93-3.98 (m, 2H), 4.00-4.10 (m, 6H), 4.45 (s, 2H), 4.71-4.76 (m, 4H), 5.29 (s, 2H), 5.47 (s, 2H), 6.63-6.83 (m, 7H), 6.89 (d, *J* = 7.8 Hz, 2H), 7.26 (d, *J* = 7.8 Hz, 2H), 7.37 (s, 2H), 7.49 (s, 1H), 7.67 (br s, 2H), 8.38-8.44 (m, 4H), 8.74 (d, *J* = 6.6 Hz, 2H), 8.82 (d, *J* = 7.2 Hz, 2H).

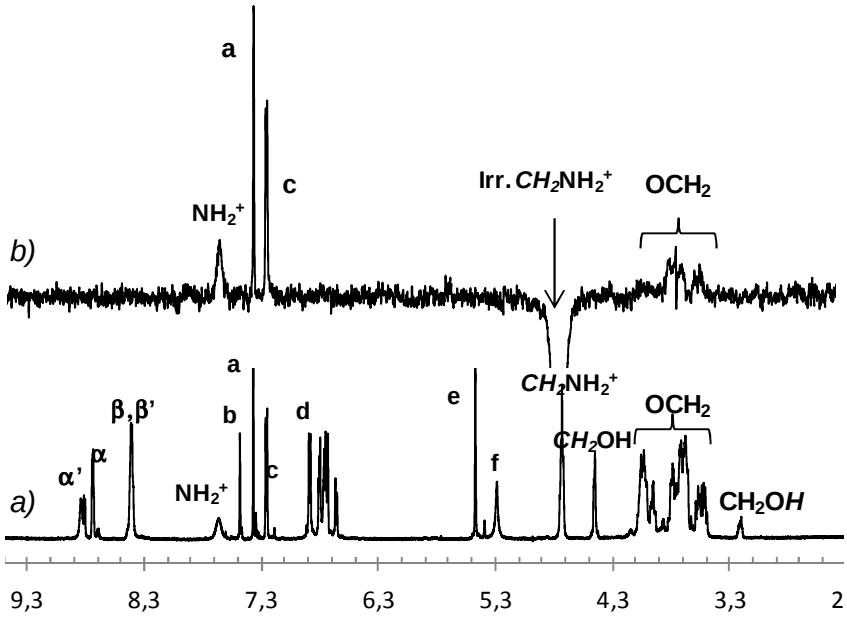


Figure S6. a) ^{1}H NMR spectrum (600 MHz, CD_3CN, 298 K) of **[2]rotaxane DB24C8_CH_2OH·3PF_6**. b) 1D Roesy spectrum obtained by selective irradiation of the protons $CH_2NH_2^+$. The labels correspond to the hydrogen assignments indicated in the previous scheme.

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