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Expedient Synthesis of Heterobifunctional Triarylmethane Stoppers for Macromolecular Rotaxanes

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ABSTRACT: Increasingly complex rotaxane-based molecular devices are interfaced with polymers and surfaces but suitable bifunctional stoppering groups are lacking. Here we report a 2-step, high-yielding synthesis towards a new class of heterobifunctional triarylmethane stoppers. They possess hydroxyl and ester groups for further functionalization, as well as halogen substituents conferring a diagnostic spectroscopic signature. Their utility was demonstrated with the synthesis of a chain-centered macromolecular rotaxane. This new stopper architecture should prove useful to connect rotaxanes with polymers and surfaces, for applications in polymer mechanochemistry, single-molecule force spectroscopy, smart-materials, and molecular machines.

Heterobifunctional stoppers are particularly useful to interface rotaxane-based molecular machines and devices with polymers^{1a-e} and surfaces.^{2a-9} However, the most popular are only suitable for relatively small macrocycles and the increasing complexity of rotaxane-based molecular devices is often accompanied by the use of larger, tailored-made, macrocycles.^{3a-h} This need has been fulfilled with Gibson's very popular 'bulky stopper'⁴ and, increasingly, with commercially available alternatives such as **4** (Figure 1b),^{5a-f} which is slightly smaller but has the advantage of displaying an enhanced solubility in organic solvent, and a diagnostic fingerprint in NMR and MS spectra. Homobifunctional counterparts of the 'bulky stopper' are available⁶ but no, easily accessible, heterobifunctional equivalent exists. Here we report the rapid synthesis of heterobifunctional triarylmethane stoppers **3** derived from **4** with diagnostic spectroscopic signatures and/or sites for further functionalization (Figure 1a). These stoppers should prove useful to connect rotaxanes with polymers and surfaces, for applications in polymer mechanochemistry, single-molecule force spectroscopy, materials chemistry, and molecular machines. This concept is demonstrated with the synthesis of a chain-centered macromolecular [2]rotaxane.

Figure 1. (a) Synthetic strategy towards heterobifunctional stopper **3**. (b) Commercially available stopper **4**.

Our recent investigation of the mechanochemistry of the mechanical bond,^{5a-b, 7} lead us to assemble complex macromolecular [2]rotaxanes requiring a bulky heterobifunctional stopper.^{5a} Inspired by Gibson's synthesis,⁴ which proceeds by the acid-catalyzed addition of phenol on triarylmethanol derivatives, we devised a strategy based on the addition of phenol onto conjugated ester **2** (which is formed on gram-scale from cheap commercially available diaryl ketones **1** and a Wittig reagent, Figure 1). Our initial attempt, reproducing the conditions used by Gibson, lead entirely to the formation of decarboxylated

product **5a** (Entry 1, Table 1). Lowering the temperature enables the formation of a small amount of the desired product (**3a**) but at the expense of the total conversion (Entry 2-3). As chloride ions can assist decarboxylation via a Krapcho mechanism,⁸ we hypothesized that acids with non-nucleophilic counterion could prevent the formation of decarboxylated product **5a**. Indeed, the use of HBF₄ lead to the formation of **3a** as the major product (Entry 4). Hoping to further diminish the decarboxylation, we performed the reaction in presence of molecular sieve that could arise from the hydrolyzed ester but this proved unsuccessful (Entry 5). Using p-toluenesulfonic acid (TsOH) as a catalyst afforded **3a** with moderate yield and selectivity after 16h at 90°C (Entry 6). A slightly improved conversion was obtained with triflic acid (TfOH) in the same conditions (Entry 7). Reducing the reaction time to 1h significantly improved the formation of **3a** (Entry 8). Pleasingly, we found that **3a** could be formed quantitatively and with complete selectivity after 15min at 90°C (Entry 9) or by maintaining the reaction mixture just above the melting point of phenol (41°C) for 45min (Entry 10).

Table 1. Screening the reaction conditions^a

Entry	Catalyst	T (°C)	Time (h)	Yield of 3a (%) ^c	of 3a:5a ^d
1	HCl	170	16	-	1:100
2	HCl	90	16	7	1:6
3	HCl	65	16	7	1:3
4	HBf ₄	90	16	54	1:0.7
5 ^b	HBf ₄	90	16	17	1:1.2
6	TsOH	90	16	26	1:1.9
7	TfOH	90	16	31	1:2.2
8	TfOH	90	1	83	1:0.2

9	TfOH	90	0.25	99	>100:1
10	TfOH	45	0.75	99	>100:1

^a Reaction conditions: **2a** (0.2 mmol, 1.0 eq.), phenol (5.3 mmol, 26.5 eq), catalyst (0.08 mmol, 0.4 eq.) under N₂ atmosphere. ^b molecular sieve (1.0 eq.) was added. ^c Isolated yield. ^d Determined by ¹H NMR.

The scope of the reaction was explored by reacting phenol with a range of 3,3-diarylacrylates under the optimized conditions presented in Entry 10 of Table 1. All halogen-substituted substrates showed quantitative conversion (Entry 1-3, Table 2), with no detectable amount of decarboxylated product. However, the presence of electron-donating groups on the acceptor completely suppresses its reactivity (Entry 4). Advantageously, this reaction can be easily scaled-up to gram-scale, as demonstrated by the production of 1.5g of chloro derivative **3a** in 94% yield (See SI).

Table 2. Scope of the reaction^a

Reaction scheme showing the conversion of compound **2** (a 3,3-diarylacrylate derivative with substituent X) to compound **3** (a 3,3-diarylacrylate derivative with substituent X and a hydroxyl group) using TfOH at 45 °C for 45 min.

Entry	2	X	3	Yield of 3 ^b (%)
1	2a	Cl	3a	99
3	2b	Br	3b	96
4	2c	F	3c	99
5	2d	OMe	3d	-

^a Reaction conditions: **2** (0.2 mmol, 1.0 eq.), phenol (5.3 mmol, 26.5 eq), TsOH (0.08 mmol, 0.4 eq.) under N₂ atmosphere. ^b Isolated yield.

To further demonstrate the utility of this new stopper we devised the synthesis of a chain-centered rotaxane starting from ester **3c** (Figure 2a). We anticipated that the para-fluoro substituents would confer a distinctive pattern in the ¹H and ¹⁹F NMR spectra of the various synthetic intermediates (Figure 2b-c,e). Propargylation and subsequent hydrolysis of **3c** afford acid **7**, which adequately possesses an acid functionality, to connect to the axle of the rotaxane, and an alkyne, to append a polymer precursor by Cu-catalyzed azide-alkyne cycloaddition (CuAAC). Rotaxane **11** was obtained in 42% yield using Takata's method,⁹ by reacting activated stopper **8**, diethanolamine **9**, and dibenzo-24-crown-8 (DB24C8) macrocycle in presence of silver triflate. The ¹H NMR spectra (Figure 2e) of DB24C8 macrocycle, free-thread **10** (i.e. **11** without macrocycle) and rotaxane **11** confirms the interlocked structure. The upfield shift of axle protons *H_m* ($\Delta\delta H_m = -0.43$ ppm), ammonium protons *H_q* ($\Delta\delta H_q = -0.24$ ppm), and macrocycle protons *H₆* ($\Delta\delta H_6 = -0.16$ ppm), and downfield shift of axle protons *H_p* ($\Delta\delta H_p = 0.60$ ppm) in the rotaxane compared to the free-thread/macrocyle are indicative of the presence of the macrocycle around the ammonium station. The ¹⁹F NMR spectra (Figure 2b) clearly shows the peaks associated with the triflate anion (-78.1 ppm), and the fluorophenyl groups (-116.3 ppm). Rotaxane **11** was then appended with polymerisation initiators (**12**) by CuAAC to reach rotaxane **13**. This reaction was catalyzed by Cu(MeCN)₄PF₆ and ¹⁹F NMR analysis revealed the exchange of TfO⁻ counterion for PF₆⁻ in the process by the presence of a doublet at -72.6 ppm

(Figure 2c). Finally, chain-centered macromolecular rotaxane **14** was obtained by single electron transfer living radical polymerization (SET-LRP)¹⁰ of methyl acrylate initiated from both ends of the axle. GPC (*M_n* = 45 kDa, *D* = 1.16, Figure 2d) and ¹H NMR (see SI) indicate the successful incorporation of the rotaxane in the polymer.

Figure 2. (a) Synthetic route towards chain-centered polymer **11**. i) Propargyl bromide, K₂CO₃, MeCN, 70 °C, 12 h, 96%. ii) LiOH, H₂O/THF, 1M HCl, 12 h, rt, quantitative. iii) (COCl)₂, DCM, rt, 2h, quantitative. iv) DB24C8, diethanolamine **9**, AgOTf, 2 h, rt, 42%. v) **12**, Cu(MeCN)₄PF₆, DCM/MeCN, 12 h, rt, 74%. vi) Methyl acrylate, CuBr₂/Me₆TREN, Copper wire, DMSO, rt, 40 min. (b) ¹⁹F NMR comparison of **9**•H⁺ TfO⁻ (top), rotaxane **11** (middle) and free thread **10** (bottom). (c) ¹⁹F NMR comparison of rotaxane **11** (top) and rotaxane **13** (bottom). (d) GPC trace of rotaxane centered polymer **14**. (e) Partial ¹H NMR comparison of DB24C8 (top), rotaxane **11** (middle) and free thread **10** (bottom).

In conclusion, we have developed an expedient synthesis of a new class of heterobifunctional stoppers. These stoppers can be produced on gram-scale with high yields, and their halogen substituents provide them with a diagnostic spectroscopic signature and potential sites for further functionalization. The utility of these building blocks was demonstrated with the synthesis of a chain-centered macromolecular rotaxane. We anticipate that

this new stopper architecture should prove useful to connect rotaxanes with polymers and surfaces, for applications in polymer mechanochemistry, single-molecule force spectroscopy, materials chemistry, and molecular machines.

EXPERIMENTAL SECTION

Unless otherwise stated, all reagents and solvents were purchased from commercial suppliers and used without further purification. Cu(0) wire (diameter: 0.25 mm, purity 99.9%) was purchased from Sigma-Aldrich. Me₆TREN was purchased from Alfa Aesar. Compounds **2a**^{5a} and **12**¹¹ were prepared according to literature procedures. Gel permeation chromatography (GPC) analyses were performed in THF solution (~0.6 mg mL⁻¹) at 35 °C using a Malvern Viscotek GPCmax VE2001 solvent/sample module with 2 × PL gel 10 μm mixed-B and a PL gel 500 Å column, and equipped with a Viscotek VE3580 refractive index detector employing narrow polystyrene polystyrene standards (Agilent Technologies) as a calibration reference. Samples were filtered through a Whatman Pura-disc 4 mm syringe filter with 0.45 μm PTFE membrane before injection to equipment, and experiments were carried out with injection volume of 200 μL, flow rate of 1 mL min⁻¹. Results were analyzed using *n*-dodecane as internal marker using Malvern OmniSEC 5.10 software. Analytical TLC was performed on precoated silica gel plates (0.25 mm thick, 60 F254, Merck, Germany) and observed under UV light or stained with a phosphomolybdic acid solution. Preparative TLC was performed on precoated silica gel plates: 2 mm, UNIPLATE GF, Analtech Inc., DE, USA. Flash column chromatography was performed with silica gel 60 (230-400 mesh) from Sigma-Aldrich. ¹H and ¹³C NMR spectra were obtained using either a Bruker Avance III 500 MHz Prodigy instrument or a Bruker Avance III 400 MHz Prodigy instrument at the University of Manchester. Chemical shifts are reported in parts per million (ppm) from high to low frequency and referenced to the residual solvent resonance. Coupling constants (*J*) are reported in Hertz (Hz) and splitting patterns are designated as follows: b = broad, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet and m = multiplet. Mass spectra were obtained through the Mass Spectrometry services in the Department of Chemistry at the University of Manchester.

General procedure for the synthesis of 3,3-diarylacrylates **2**

A solution of **1** (2 mmol, 1.0 eq.) and methyl (triphenylphosphoranylidene) acetate (2.4 mmol, 1.2 eq.) in toluene (5 mL) was heated to reflux for 36 h in an oil bath. The solvent was removed and the crude product was purified by flash column chromatography (PE : EtOAc = 10:1) to give **2**.

Methyl 3,3-bis(4-bromophenyl)acrylate **2b**

White solid, mp 103.4-105.2 °C; yield 74% (586 mg); ¹H NMR (500 MHz, CDCl₃) δ = 7.52 (d, *J* = 7.0 Hz, 2H), 7.46 (d, *J* = 7.0 Hz, 2H), 7.13 (d, *J* = 7.0 Hz, 2H), 7.06 (d, *J* = 7.0 Hz, 2H), 6.35 (s, 1H), 3.64 (s, 3H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ = 166.1, 154.8, 139.4, 137.2, 131.9, 131.5, 131.0, 129.9, 124.4, 123.0, 117.7, 117.7, 51.6, 51.6; MS-ESI(+): *m/z* = 417.0(50, [M + Na]⁺); 419.0 (100, [M + Na]⁺); 421.0 (30, [M + Na]⁺); HRMS (ESI-FTMS) *m/z*: [M + H]⁺ Calcd for C₁₆H₁₃O₂Br₂ 394.9277; Found 394.9281.

Methyl 3,3-bis(4-fluorophenyl)acrylate **2c**

White solid, mp 46.1-48.0 °C; yield 99% (543 mg); ¹H NMR (500 MHz, CDCl₃) δ = 7.16 (dd, *J* = 8.5, 9.0 Hz, 4H, *H*_b), 7.02 (d, *J* = 8.5 Hz, 2H), 6.95 (dd, *J* = 8.5, 9.0 Hz, 4H), 6.72 (d, *J* = 8.5 Hz, 2H), 4.92 (s, 1H), 3.63 (s, 2H), 3.42 (s, 3H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ = 171.5, 161.3 (d, *J* = 246 Hz), 154.1, 142.5 (d, *J* = 3.3 Hz), 138.5, 130.7 (d, *J* = 7.8 Hz), 130.3, 114.9, 114.8 (d, *J* = 21.1 Hz), 54.3, 51.7 (d, *J* = 2.0 Hz), 46.6; ¹⁹F NMR (470 MHz, CDCl₃)

δ = -116.63; MS-ESI(-): *m/z* = 367.2 (100, [M - H]⁻); HRMS (ESI-FTMS) *m/z*: [M - H]⁻ Calcd for C₂₂H₁₇O₃F₂ 367.1151; Found 367.1159.

Methyl 3,3-bis(4-methoxyphenyl)acrylate **2d**

White solid, mp 35.5-37.0 °C; yield 21% (125 mg); ¹H NMR (500 MHz, CDCl₃) δ = 7.24 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.5 Hz, 2H), 6.91 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 6.23 (s, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 3.62 (s, 3H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ = 166.9, 160.9, 159.8, 157.1, 134.0, 131.2, 131.0, 130.2, 114.4, 114.5, 113.8, 113.4, 55.5, 55.5, 55.4, 55.3, 51.3, 51.3; MS-ESI(+): *m/z* = 321.2 (30, [M + Na]⁺); HRMS (ESI-FTMS) *m/z*: [M + Na]⁺ Calcd for C₁₈H₁₈O₄Na 321.1097; Found 321.1086.

General procedure for the synthesis of stopper **3**

TfOH (0.12 mmol, 40 mmol %) was added to a mixture of **2** (0.3 mmol, 1.0 eq.) and phenol (500 mg). The mixture was heated to 45 °C for 45 min in an oil bath. The crude product was washed with water and purified by flash column chromatography (PE : EtOAc = 5:1) to yield **3** as a solid.

Methyl 3,3-bis(4-chlorophenyl)-3-(4-hydroxyphenyl)propanoate **3a**

White solid, mp 145.3-147.2 °C; yield 99% (119 mg); ¹H NMR (400 MHz, CDCl₃) δ = 7.23 (d, *J* = 8.4 Hz, 4H), 7.13 (d, *J* = 8.8 Hz, 4H), 7.02 (d, *J* = 8.8 Hz, 2H), 6.73 (d, *J* = 8.8 Hz, 2H), 4.69 (b, 1H), 3.61 (s, 2H), 3.42 (s, 3H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ = 171.5, 154.4, 145.0, 137.7, 132.5, 130.5, 130.2, 128.2, 115.0, 54.5, 51.8, 46.2; MS-ESI(-): *m/z* = 399.1 (100, [M - H]⁻); 401.1 (80, [M - H]⁻); HRMS (ESI-FTMS) *m/z*: [M - H]⁻ Calcd for C₂₂H₁₇O₃Cl₂ 399.0560; Found 399.0566.

Methyl 3,3-bis(4-bromophenyl)-3-(4-hydroxyphenyl)propanoate **3b**

White solid, mp 162.9-164.7 °C; yield 96% (141 mg); ¹H NMR (500 MHz, CDCl₃) δ = 7.38 (d, *J* = 8.5 Hz, 4H), 7.07 (d, *J* = 8.4 Hz, 4H), 7.01 (d, *J* = 9.0 Hz, 2H), 6.72 (d, *J* = 8.5 Hz, 2H), 4.83 (b, 1H), 3.61 (s, 2H), 3.42 (s, 3H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ = 171.2, 154.2, 145.4, 137.9, 131.2, 130.9, 130.3, 120.7, 115.0, 54.6, 51.7, 46.0; MS-ESI(-): *m/z* = 487.1 (50, [M - H]⁻); HRMS (ESI-FTMS) *m/z*: [M - H]⁻ Calcd for C₂₂H₁₇O₃Br₂ 486.9550; Found 486.9545.

Methyl 3,3-bis(4-fluorophenyl)-3-(4-hydroxyphenyl)propanoate **3c**

White solid, mp 95.5-97.3 °C; yield 99% (109 mg); ¹H NMR (500 MHz, CDCl₃) δ = 7.16 (dd, *J* = 8.5, 9.0 Hz, 4H), 7.02 (d, *J* = 8.5 Hz, 2H), 6.95 (dd, *J* = 8.5, 9.0 Hz, 4H), 6.72 (d, *J* = 8.5 Hz, 2H), 4.92 (s, 1H), 3.63 (s, 2H), 3.42 (s, 3H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ = 171.5, 161.3 (d, *J* = 246 Hz), 154.2, 142.5 (d, *J* = 3.3 Hz), 138.5, 130.7 (d, *J* = 7.8 Hz), 130.3, 114.9, 114.8 (d, *J* = 21.1 Hz), 54.3, 51.7 (d, *J* = 2.0 Hz), 46.6; ¹⁹F NMR (470 MHz, CDCl₃) δ = -116.63; MS-ESI(-): *m/z* = 367.2 (100, [M - H]⁻); HRMS (ESI-FTMS) *m/z*: [M - H]⁻ Calcd for C₂₂H₁₇O₃F₂ 367.1151; Found 367.1159.

Synthesis of rotaxane **13**

Methyl 3,3-bis(4-fluorophenyl)-3-(4-(prop-2-yn-1-yloxy)phenyl)propanoate **6**

To a solution of **3c** (850 mg, 2.3 mmol, 1.0 eq.) and propargyl bromide (550 mg, 4.6 mmol, 2.0 eq.) in MeCN (5 mL) was added K₂CO₃ (476 mg, 3.45 mmol, 1.5 eq.). The mixture was heated to 70 °C in an oil bath overnight. The crude was washed with NH₄Cl (aq. 5 mL) and extracted with DCM (3 × 5 mL). The organic phase was combined and purified by flash column chromatography (PE : EtOAc = 10 : 1) to yield **6** as a white solid (900 mg, 96% yield), mp 39.5-41.4 °C. ¹H NMR (500 MHz, CDCl₃) δ = 7.16 (dd, *J* = 8.5, 9.0 Hz, 4H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.95 (dd, *J* = 8.5, 8.5 Hz, 4H),

6.83 (d, $J = 8.5$ Hz, 2H), 4.66 (d, $J = 2.0$ Hz, 2H), 3.64 (s, 2H), 3.41 (s, 3H), 2.52 (t, $J = 2.0$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) $\delta = 171.3, 161.4$ (d, $J = 246$ Hz), 156.2, 142.4 (d, $J = 3.4$ Hz), 139.5, 130.8 (d, $J = 7.9$ Hz), 130.1, 114.8 (d, $J = 21.1$ Hz), 114.3, 78.7 (d, $J = 2.1$ Hz), 75.7 (d, $J = 8.1$ Hz), 55.9, 54.3, 51.7 (d, $J = 2.1$ Hz), 46.6; ^{19}F NMR (470 MHz, CDCl_3) $\delta = -116.59$; MS-ESI(+): $m/z = 429.2$ (100, $[\text{M} + \text{Na}]^+$); 430.2 (20, $[\text{M} + \text{Na}]^+$); HRMS (ESI-FTMS) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{25}\text{H}_{20}\text{O}_3\text{F}_2\text{Na}$ 429.1273; Found 429.1262.

3,3-bis(4-fluorophenyl)-3-(4-(prop-2-yn-1-yloxy)phenyl)propionic acid **7**

To a solution of **6** (812 mg, 2.0 mmol, 1.0 eq.) in MeOH (2 mL) was added a solution of LiOH (384 mg, 8.0 mmol, 4.0 eq.) in H_2O (2 mL). The resulting solution was stirred at room temperature overnight. The solvent was removed and acidified using 1M HCl until pH = 2. The crude product was extracted by DCM (3 x 5 mL) and concentrated. The crude product was used directly without further purification, mp 95.2–97.0 °C. ^1H NMR (500 MHz, CDCl_3) $\delta = 7.12$ (dd, $J = 8.5, 9.0$ Hz, 4H), 7.07 (d, $J = 8.5$ Hz, 2H), 6.94 (dd, $J = 8.5, 8.5$ Hz, 4H), 6.87 (d, $J = 9.0$ Hz, 2H), 4.66 (d, $J = 2.5$ Hz, 2H), 3.63 (s, 2H), 2.52 (t, $J = 2.5$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) $\delta = 176.0, 161.3$ (d, $J = 246$ Hz), 156.2, 142.1 (d, $J = 3.4$ Hz), 139.3, 130.7 (d, $J = 7.8$ Hz), 130.1, 114.9 (d, $J = 21.2$ Hz), 114.4, 78.6 (d, $J = 2.0$ Hz), 75.8 (d, $J = 8.1$ Hz), 55.9, 54.0, 46.4; ^{19}F NMR (470 MHz, CDCl_3) $\delta = -116.59$.

3,3-bis(4-fluorophenyl)-3-(4-(prop-2-yn-1-yloxy)phenyl)propionyl chloride **8**

To a solution of **7** (588 mg, 1.5 mmol, 1.0 eq.) in DCM (3 mL) was added 2 drops of DMF. $(\text{COCl})_2$ (0.26 mL, 3 mmol, 2.0 eq.) was added dropwise. The resulting solution was stirred at room temperature for 2 h. The solvent was removed and dried under high vacuum. The crude product was used directly without further purification.

Free-thread **10**

To a dry flask was added diethanolamine **9** (50 mg, 79 μmol , 1.0 eq.) and AgOTf (45 mg, 158 μmol , 2.2 eq.). DCM (500 μL) was then added. The solution was cooled down in an ice bath before the addition of **8** (18 mg, 79 μmol , 1.2 eq.). The resulting solution was stirred at room temperature overnight. The crude product was purified by flash column chromatography (4% MeOH in DCM) yielding **10** as a white solid (15 mg, 19% yield). ^1H NMR (500 MHz, CDCl_3) $\delta = 7.76$ (bs, 2H), 7.14 (dd, $J = 8.5, 8.5$ Hz, 8H), 7.07 (d, $J = 9.0$ Hz, 4H), 6.92 (dd, $J = 8.5, 8.5$ Hz, 8H), 6.84 (d, $J = 9.0$ Hz, 4H), 4.63 (d, $J = 2.0$ Hz, 4H), 3.99 (t, $J = 5.0$ Hz, 4H), 3.70 (s, 4H), 2.92 (t, $J = 5.5$ Hz, 4H), 2.50 (t, $J = 2.5$ Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) $\delta = 171.1, 161.4$ (d, $J = 246$ Hz), 156.2, 147.61, 141.1 (d, $J = 3.3$ Hz), 138.9, 130.7 (d, $J = 7.6$ Hz), 130.2, 114.9 (d, $J = 21.3$ Hz), 114.4, 78.6 (d, $J = 2.1$ Hz), 75.9 (d, $J = 9.1$ Hz), 59.0, 55.9, 54.3, 47.3, 46.1; ^{19}F NMR (470 MHz, CDCl_3) $\delta = -78.28, -116.04$; MS-ESI(+): 854.5 (100, $[\text{M} - \text{OTf}]^+$); 855.5 (30, $[\text{M} - \text{OTf}]^+$); HRMS (ESI-FTMS) m/z : $[\text{M} - \text{OTf}]^+$ Calcd for $\text{C}_{52}\text{H}_{44}\text{NO}_6\text{F}_4$ 854.3099; Found 854.3086.

Rotaxane **11**

To a dry flask was added diethanolamine **9** (50 mg, 79 μmol , 1.0 eq.), dibenzo-24-crown-8 (51 mg, 118 μmol , 2.0 eq.) and AgOTf (45 mg, 158 μmol , 2.2 eq.). DCM (100 μL) was then added. The solution was stirred at room temperature for 2 h. The solution was cooled down in an ice bath before the addition of **8** (18 mg, 79 μmol , 1.2 eq.). The resulting solution was stirred at room temperature overnight. The crude product was purified by flash column chromatography (4% MeOH in DCM) yielding **11** as a white solid

(48 mg, 42% yield). ^1H NMR (500 MHz, CDCl_3) $\delta = 6.98$ (dd, $J = 8.5, 9.0$ Hz, 8H), 6.91 (d, $J = 8.5$ Hz, 4H), 6.89–6.84 (m, 16H), 6.81 (d, $J = 9.0$ Hz, 4H), 4.64 (d, $J = 2.4$ Hz, 4H), 4.11 (t, $J = 3.5$ Hz, 8H), 3.95 (t, $J = 4.5$ Hz, 4H), 3.81 (t, $J = 3.5$ Hz, 8H), 3.67 (s, 8H), 3.52 (t, $J = 4.0$ Hz, 4H), 3.22 (s, 4H), 2.54 (t, $J = 2.5$ Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) $\delta = 170.2, 161.3$ (d, $J = 246$ Hz), 156.1, 147.6, 142.0 (d, $J = 3.3$ Hz), 139.0, 130.6 (d, $J = 7.6$ Hz), 130.0, 122.1, 114.8 (d, $J = 21.0$ Hz), 114.3, 113.0, 78.7 (d, $J = 2.6$ Hz), 75.9 (d, $J = 10.3$ Hz), 71.0, 70.5, 68.3, 59.8, 55.9, 54.0, 47.4, 45.5; ^{19}F NMR (470 MHz, CDCl_3) $\delta = -78.10, -116.32$; MS-ESI(+): 1302.9 (100, $[\text{M} - \text{OTf}]^+$); 1304.9 (20, $[\text{M} - \text{OTf}]^+$); HRMS (ESI-FTMS) m/z : $[\text{M} - \text{OTf}]^+$ Calcd for $\text{C}_{76}\text{H}_{76}\text{NO}_{14}\text{F}_4$ 1302.5196; Found 1302.5155 (For isotopic distribution see SI).

Rotaxane **13**

To a dry flask was added **11** (10 mg, 6.9 μmol , 1.0 eq.) and **12** (5.0 mg, 20.7 μmol , 3.0 eq.). DCM (0.8 mL) and MeCN (0.2 mL) were added. The solution was degassed 4 times by freeze-thaw cycles. The mixture was then cannulated to a degassed vial containing $\text{Cu}(\text{MeCN})_4\text{PF}_6$ (5.1 mg, 13.8 μmol , 2.0 eq.). The resulting solution was stirred at room temperature overnight. The crude product was purified by flash column chromatography (4% MeOH in DCM) yielding **13** as a white solid (9.8 mg, 74% yield). ^1H NMR (500 MHz, CDCl_3) $\delta = 7.87$ (bs, 2H), 6.98 (dd, $J = 8.5, 8.5$ Hz, 8H), 6.89–6.82 (m, 24H), 5.16 (s, 4H), 4.70 (t, $J = 5.5$ Hz, 4H), 4.57 (t, $J = 5.5$ Hz, 4H), 4.10 (t, $J = 3.5$ Hz, 8H), 3.93 (t, $J = 4.5$ Hz, 4H), 3.79 (t, $J = 3.5$ Hz, 8H), 3.64 (s, 8H), 3.50 (t, $J = 4.0$ Hz, 4H), 3.19 (s, 4H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) $\delta = 171.2, 170.2, 161.3$ (d, $J = 246$ Hz), 156.9, 147.6, 144.2, 142.0 (d, $J = 3.4$ Hz), 138.4, 130.6 (d, $J = 7.8$ Hz), 130.0, 124.3, 122.2, 114.8 (d, $J = 21.0$ Hz), 114.3, 113.0, 70.9, 70.5, 68.2, 64.0, 61.9, 59.8, 55.6, 54.1, 50.0, 47.5, 45.6, 30.7; ^{19}F NMR (470 MHz, CDCl_3) $\delta = -72.63$ (d, $J = 712$ Hz), -116.32; MS-ESI(+): 1774.5 (100, $[\text{M}-\text{PF}_6]^+$); HRMS (ESI-FTMS) m/z : $[\text{M}-\text{PF}_6]^+$ Calcd for $\text{C}_{88}\text{H}_{96}\text{N}_7\text{O}_{18}\text{Br}_2\text{F}_4$ 1772.5109; Found 1772.5047 (For isotopic distribution see SI).

Synthesis of rotaxane **14**

Methyl acrylate was filtered through basic alumina to remove the inhibitor prior to use. A stock solution of Me_6TREN (16 μL , 0.060 mmol) and CuBr_2 (5.6 mg, 0.025 mmol) in dry DMSO (1 mL) was prepared. To a 5 mL vial was added rotaxane **13** (10 mg, 5.2 μmol , 1.0 eq.), 42 μL of catalytic solution (Me_6TREN : 3.0 μmol , 0.48 eq.; CuBr_2 : 1.2 μmol , 0.2 eq.), methyl acrylate (0.48 mL, 5.219 mmol, 1000.0 eq.) and dry DMSO (0.4 mL). This solution was degassed by bubbling with N_2 for 10 min. A Cu (0) wire (~2 cm, ~20 mg, 0.315 mmol, ~100.0 eq., cleaned in HCl_{conc} for 10 min) wrapped around a stirrer bar was added and the solution degassed for a further 2 min before being allowed to stir for 2 h. The solution was then precipitated out in stirring methanol, recovered and dried under a high vacuum for several days yielding a white polymer (230 mg, $M_n = 45$ kDa, $\bar{D} = 1.16$). Molecular weight and polydispersity indices were recorded using an analytical GPC that had been calibrated with polystyrene standards.

ASSOCIATED CONTENT

Supporting Information

^1H , ^{13}C , ^{19}F NMR spectra and rotaxanes isotopic patterns. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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The manuscript was written through contributions of all authors.

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