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Note

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Directional Transportation of a Helic[6]arene Along a Nonsymmetric Molecular Axle

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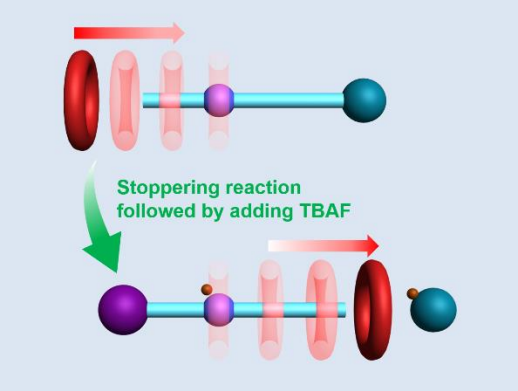


ABSTRACT: Directional transportation of a helic[6]arene along a nonsymmetric molecular axle was achieved, which was easily performed in dichloromethane by stopper reaction and subsequent addition of fluoride ions. In this system, the fluoride ions could act as a versatile stimulus to unidirectionally release the macrocycle that not only destroyed the host-guest interaction, but also removed the silyl stopper.

In nature, the biomolecular machines and motors are capable of converting energy into unidirectional transportation for their metabolic processes, such as cargo delivery,[1] cellular locomotion,[2] and proteins synthesis.[3] Inspired by these biological processes, the artificial molecular machines (AMMs)[4] have been designed and

constructed for directional motion.[5] And these system have been harnessed to perform special functions, such as sequence-specific peptide synthesis,[6] surface functionalization[7] and active transport.[8] Mechanically interlocked molecules (MIMs),[9] especially rotaxanes and catenanes, provide a perfect prototype to achieve directed motion at the molecular level.[10] The directed transport in MIMs is that a ring exhibit a directionally biased translational or circumrotational movement. For this purpose, chemists have introduced ratchet mechanisms to MIMs, including energy ratchets and information ratchets,[11] which require precise molecular design to change the kinetic energy barrier and energy well under the external stimulus.[12] Leigh and co-workers demonstrated rotary and linear molecular motor by utilizing chemical fuel.[13] Stoddart and co-workers reported the macrocycle directionally threaded and dethreaded along an axle fueled by redox stimuli.[14] Credi et al. also described the unidirectional transit of a non-symmetric axle through a ring driven by photo stimuli.[15] However, developing additional means of controlling directional molecular motion remains formidable challenge.[16]

Previously, we[17] have reported directional molecular transportation based on a stopper-leaving rotaxane system, which provided a new strategy for construction of directional transportation. In this system, the macrocycle was directionally released in the presence of DBU after heating. Based on this strategy, we hope to develop a more effective way to release the macrocycle from a rotaxane at a single versatile stimulus. Recently, we report a new macrocyclic arene named helic[6]arenes (**HA**),[18] which had found applications in recognition of organic guests, switchable complexation and

interlocked molecules.[19] In particular, the complexation between **HA** and protonated tertiary ammonium salts could be reversibly controlled by anions such as chloride ion and fluoride ion.[20] The latter was commonly used to remove silyl ether protecting groups.[21] These facts encouraged us to design and construct directional macrocycle transportation system controlled by fluoride ions.

Herein, we report a directional transportation of a helic[6]arene along a nonsymmetric molecular axle (Figure 1). A semi-dumbbell axle containing protonated tertiary ammonium as a central recognition site and *tert*-butyldiphenylsilyl group as one of the stopper was designed and synthesized. **HA** was initially allowed to thread onto the axle from the open side, affording a pseudorotaxane. Subsequently the terminal OH group was covalently captured[22] by the stoppering reaction, giving a nonsymmetric [2]rotaxane. Then, the unidirectional dethreading process of **HA** was triggered by addition of fluoride ions that not only destroyed the host-guest interaction, but also removed the silyl stopper. The whole unidirectional threading and dethreading process occurs easily in dichloromethane.

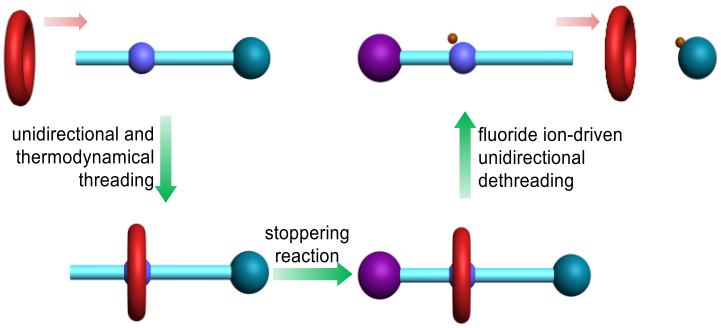
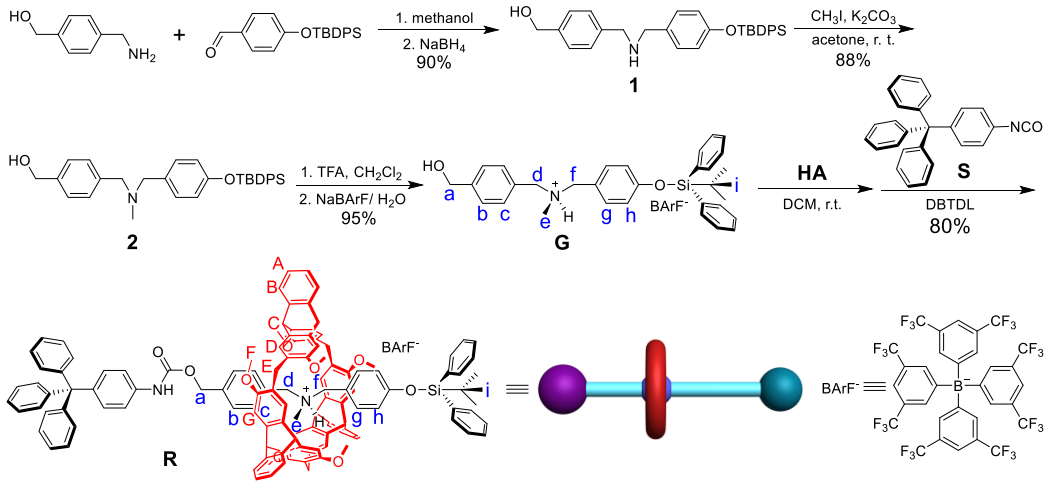


Figure 1. Cartoon representations of directional macrocycle transportation system.

As shown in Scheme 1, a semidumbbell axle **G** which incorporated protonated tertiary ammonium as a binding site, bulkier *tert*-butyldiphenylsilyl at one side and a

terminal hydroxyl group at the other side was designed and synthesized. Due to the steric interaction, the threading process of **HA** exclusively occurred from the open terminus of the axle. We firstly investigated the complexation between **HA** and **G** by ^{1}H NMR spectroscopy. The ^{1}H NMR spectrum of 1:1 solution of **HA** and **G** showed an obvious difference compared to the spectra of the uncomplexed species, which clearly demonstrated the formation of the complex (Figure S15). And the electrospray ionization mass spectra (ESI-MS) also confirmed the formation of 1:1 complex between **HA** and **G** (Figure S16). According to the ^{1}H NMR spectroscopic titration experiments, the association constant (K_a) of the complex in CD_2Cl_2 solution was determined to be 3317±254 M^{-1} using the nonlinear curve-fitting method.[23]

Scheme 1. Synthesis of [2]Rotaxane R.



Based on the 1:1 complexation mode between **HA** and **G**, we obtained the [2]rotaxane **R** (Scheme 1). The macrocycle **HA** was firstly mixed with three equiv of **G** in dry CH_2Cl_2 for the formation of pseudorotaxane. To the above solution was then added a catalytic amount of dibutyltin dilaurate (DBTDL) and slight excess bulky

isocyanate stopper **S**. After the solution was stirred under room temperature for eight hours, the [2]rotaxane **R** was isolated by column chromatography in a yield of 80% as a white solid. Then the structure of **R** was identified by NMR spectroscopy. As shown in Figure 2a, the strong upfield shifts were observed for protons H_e in the ammonium unit and the contiguous methylene protons H_d and H_f. Especially, the signal of proton H_e appeared at −0.80 ppm, implying that the ammonium unit was combined with macrocycle. The ROESY spectrum of **R** in CD_2Cl_2 showed clear cross peak between the protons of **HA** and the protons related to the ammonium unit (Figure S14), firmly supporting the host-guest interactions. Moreover, the HR-ESI mass spectrum of **R** gave intense peak at m/z 1835.8037, corresponding to $[R\text{-}BArF]^+$ (calcd. m/z 1835.8053).

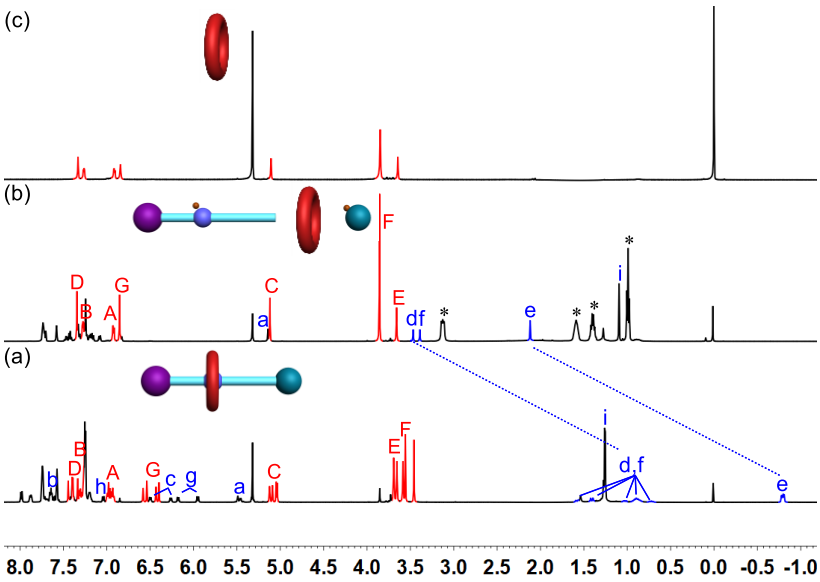


Figure 2. ^1H NMR spectra (500 MHz, 5 mM, 298 K, CD_2Cl_2) of (a) **R**, (b) the solution obtained after adding 3.6 equiv of TBAF to **R**, (c) **HA**. ∗ denotes TBAF.

To promote the unidirectional dethreading process of **HA** we used fluoride ions. They could be a strong hydrogen-bond acceptor that destroyed the host-guest

interaction between **HA** and protonated tertiary ammonium.[20b] Subsequently, the silyl stopper could be removed, giving rise to dethreading of helic[6]arene from the other side. The unidirectional dethreading process was indeed verified through NMR and mass spectrum. When 3.6 equiv of tetrabutylammonium fluoride (TBAF) were added into **R** in CD_2Cl_2, the ^1H NMR spectra clearly displayed the separate components (Figure 2b). The proton signals of **HA** were consistent to those shown in Figure 2c. And the signals of protons H_d, H_e and H_f related to the ammonium unit drastically shifted downfield owing to their disassociation with macrocycle. The ^{19}F NMR spectrum also revealed two additional signals that were different from free fluoride ions in TBAF (Figure S19), which was in accordance with the dual role of fluoride ions. Moreover, the atmospheric pressure chemical ionization mass spectra (APCI-MS) also gave a strong peak at m/z 979.3985 corresponding to dethreaded helic[6]arene $[\mathbf{HA}+H]^+$ (calcd. m/z 979.3920), m/z 619.2944 corresponding to the detached axle (calcd. m/z 619.2955) (Figure S20). These results unambiguously demonstrated that **HA** was completely released from **R** in a directed path.

The ^1H NMR kinetic experiments were carried out to investigate the rate of macrocycle release in the presence of various amount of TBAF. The concentration changes versus time (min) for dethreaded **HA** were recorded by the integrals of proton signals of H_F (see Supporting Information). As shown in Figure 3, it was found that 1.2 equiv of TBAF was enough to thoroughly release **HA**. With the increase of concentration of TBAF, the rate of macrocycle release showed an increasing trend. After 3.6 equiv of TBAF was added to **R** (5 mM, CD_2Cl_2), the dethreading process of

HA could be completed within a few minutes.

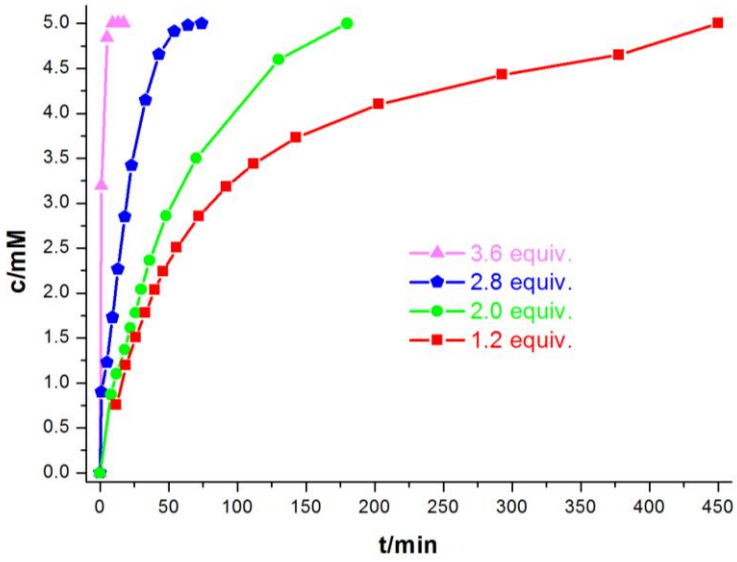


Figure 3. The concentration of dethreaded **HA** with the time after the addition of 1.2−3.6 equiv of TBAF to **R** (5 mM, CD_2Cl_2, 298 K).

Taking into consideration of the whole process, we could achieve the directional transportation of a helic[6]arene along a nonsymmetric molecular axle. Moreover, the whole process could be conducted in dichloromethane without isolating the rotaxane, which was clearly demonstrated by ^{1}H NMR spectra (Figure S29). This unidirectional threading and dethreading process was a typical energy ratchet. An essential feature of these systems is their ability to modulate both of the depths of energy wells and the heights of energy barriers.[24] Firstly, **HA** was directionally combined with protonated tertiary ammonium site to complex formation under thermodynamical control, corresponding to the particles in the energy well (Figure 4). Then, **HA** was covalently captured by stoppering the terminal primary hydroxyl group that prevents dethreading for kinetic factors, corresponding to elevating the heights of energy barriers at the left

side. When fluoride ions were added, the direction-biased movement was attained by raising the energy well and synchronously lowering the energy barriers at the right side.

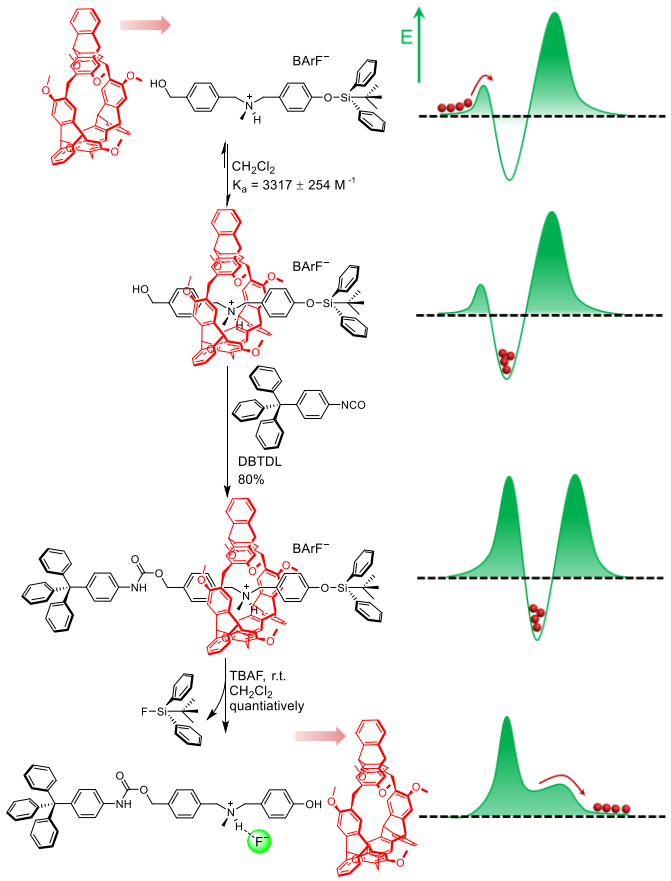


Figure 4. Chemical drawing and energy profiles of directional transportation of a helic[6]arene along a nonsymmetric molecular axle through an energy ratchet mechanism.

In conclusion, we have constructed a directional macrocycle transportation system driven by stopper reaction and subsequent addition of fluoride ions. Fluoride ions could act as a versatile stimulus to directionally release the helic[6]arene from a rotaxane. **HA** was initially threaded onto a semidumbbell axle from the open side and subsequently was covalently captured by stoppering reaction, affording to a

nonsymmetric [2]rotaxane. The directional dethreading process of **HA** could be triggered by the addition of fluoride ions without any additional intervention, which destroyed the host-guest interaction and removed the silyl stopper. The dethreading rate could be tuned by varying the amounts of TBAF. As a result, the directional transportation of a helic[6]arene along a nonsymmetric molecular axle in dichloromethane was achieved through an energy ratchet mechanism. We believe that this system would not only provide a facile and effective way to molecular machines with directional motion, but also find potential applications in design and construction of functional materials.

EXPERIMENTAL SECTION

General Information. All reagents were commercially available and used without further purification. Helic[6]arenes (**HA**),[18b] (4-(aminomethyl)phenyl)methanol,[25] 4-((*tert*-butyldiphenylsilyl)oxy)benzaldehyde,[26] ((4-isocyanatophenyl)methanetriyl)tribenzene[27] were synthesized according to the literature procedures.

*(4-(((4-((tert-Butyldiphenylsilyl)oxy)benzyl)amino)methyl)phenyl)methanol (**1**).* A solution of (4-(aminomethyl)phenyl)methanol (0.21 g, 1.53 mmol) and 4-((*tert*-butyldiphenylsilyl)oxy)benzaldehyde (0.55 g, 1.53 mmol) in 20 mL of CH_3OH was stirred at room temperature for 4 h, and then was added 0.12 g (3.16 mmol) of $NaBH_4$ in small portions. After the reaction mixture was stirred for 2 h, water was slowly added to quench the reaction, and the mixture was partitioned between water and CH_2Cl_2 (80 mL). The organic extract was washed with water (20

mL × 3), and then dried over anhydrous magnesium sulfate. The solvent was evaporated, and the reside was purified by column chromatography (CH_2Cl_2/methanol 20:1 v/v) to afford compound **1** as colorless sticky oil (0.66 g, 90%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.72–7.69 (m, 4H), 7.41–7.33 (m, 6H), 7.28–7.25 (m, 4H), 7.04 (d, J = 8.1 Hz, 2H), 6.72 (d, J = 8.0 Hz, 2H), 4.64 (s, 2H), 3.73 (s, 2H), 3.64 (s, 2H), 1.09 (s, 9H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 154.6, 139.7, 139.4, 135.5, 133.0, 132.3, 129.8, 129.1, 128.4, 127.7, 127.1, 119.6, 65.1, 52.6, 52.4, 26.5, 19.5. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{31}H_{36}NO_2Si$ 482.2515; Found 482.2504.

*(4-(((4-((tert-Butyldiphenylsilyl)oxy)benzyl)(methyl)amino)methyl)phenyl)methanol (**2**).* Compound **1** (0.59 g, 1.23 mmol) and K_2CO_3 (0.17 g, 1.23 mmol) were mixed in acetone (20 mL). Then, iodomethane (0.1 mL, 1.62 mmol) was added and the mixture was stirred at room temperature for 30 min. The reaction mixture was filtrated, and the filtered cake was washed with CH_2Cl_2. The filtrate was collected and concentrated under reduced pressure to give a residue, which was purified by silica-gel column chromatography (CH_2Cl_2/methanol 40:1 v/v) to give compound **2** (0.53 g, 88%) as a colorless oily liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.80–7.64 (m, 4H), 7.41–7.30 (m, 6H), 7.28–7.25 (m, 4H), 7.05 (d, J = 8.1 Hz, 2H), 6.71 (d, J = 8.0 Hz, 2H), 4.66 (s, 2H), 3.45 (s, 2H), 3.37 (s, 2H), 2.11 (s, 3H), 1.09 (s, 9H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ = 154.6, 139.5, 138.8, 135.5, 135.5, 133.0, 129.9, 129.8, 129.2, 128.8, 127.7, 127.0, 119.4, 115.5, 65.2, 61.3, 61.1, 42.0, 26.5, 19.5. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{32}H_{38}NO_2Si$ 496.2672; Found 496.2661.

N-(4-((tert-Butyldiphenylsilyl)oxy)benzyl)-1-(4-(hydroxymethyl)phenyl)-N-methylmeth

*anaminium tetrakis(3,5-bis(trifluoromethyl)phenyl)borate (**G**).* Trifluoroacetic acid (0.067 mL, 0.86 mmol) was added to the solution of **2** (0.40 g, 0.80 mmol) in CH_2Cl_2 (20 mL). The solution was stirred at room temperature for 1 h, concentrated in vacuo to give a residue. Then the residue was dispersed in CH_2Cl_2/H_2O with sodium tetrakis[3,5-bis(trifluoromethyl)phenyl] borate (NaBArF) (0.72 g, 0.81 mmol). After the mixture had been stirred overnight, the organic layer was separated, washed with water three times, and dried with anhydrous $MgSO_4$. The organic layer was evaporated under vacuum to afford **G** (1.04 g, 95%) as a white solid. M.p.: 70–72 ℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.83–7.67 (m, 12H), 7.57–7.55 (m, 6H), 7.50–7.40 (m, 6H), 7.32 (d, J = 7.9 Hz, 2H), 7.13 (d, J = 8.2 Hz, 2H), 6.96 (d, J = 8.1 Hz, 2H), 4.79 (s, 2H), 4.51–4.29 (m, 2H), 4.18–4.07 (m, 2H), 2.84 (d, J = 5.1 Hz, 3H), 1.14 (s, 9H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ = 162.3, 158.5, 145.2, 135.4, 134.8, 131.8, 131.8, 131.7, 130.3, 130.3, 129.0, 128.9, 128.7, 128.7, 128.7, 128.5, 128.3, 127.9, 127.82, 125.8, 125.7, 123.5, 121.6, 121.3, 119.1, 117.5, 117.5, 117.4, 63.9, 61.5, 61.3, 40.3, 26.0, 19.2. HRMS (ESI) *m/z*: $[M–BArF]^+$ Calcd for $C_{32}H_{38}NO_2Si$ 496.2666; Found 496.2665.

*[2]Rotaxane (**R**).* **G** (0.25 g, 0.18 mmol) and **HA** (0.06 g, 0.06 mmol) were dispersed in dry CH_2Cl_2 (2 mL). The mixture was stirred at room temperature for 4 h. Then ((4-isocyanatophenyl)methanetriyl)tribenzene (0.07 g, 0.19 mmol) and two drops of dibutyltin dilaurate (DBTDL) were added into the above solution. The mixture was further stirred at room temperature for 8 h, and then purified by column chromatography (CH_2Cl_2) to give **R** as white powder (0.13 g, 80%). M.p.: 170–

172 ℃. ^{1}H NMR (500 MHz, CD_2Cl_2) δ = 8.02–7.93 (m, 2H), 7.87–7.74 (m, 2H), 7.79–7.66 (m, 9H), 7.66–7.51 (m, 9H), 7.49–7.35 (m, 6H), 7.35–7.13 (m, 25H), 7.03 (d, *J* = 8.2 Hz, 1H), 7.01–6.87 (m, 8H), 6.57–6.55 (m, 3H), 6.49 (d, *J* = 7.5 Hz, 1H), 6.43–6.41 (m, 3H), 6.25 (d, *J* = 7.6 Hz, 1H), 6.17 (d, *J* = 8.2 Hz, 1H), 5.94 (d, *J* = 8.2 Hz, 1H), 5.51–5.42 (m, 2H), 5.12–5.10 (m 3H), 5.04–5.03 (m, 3H), 3.68 (d, *J* = 3.0 Hz, 5H), 3.65 (s, 4H), 3.58–3.56 (m, 9H), 3.45 (s, 4H), 1.42–1.39 (m, 2H), 1.26–1.24 (m, 10H), 1.02–1.00 (m, 1H), 0.95–0.77 (m, 3H), 0.74–0.69 (m, 1H), -0.79–-0.82 (m, 3H). ^{13}C{^{1}H} NMR (125 MHz, CD_2Cl_2) δ = 163.6, 163.3, 162.9, 162.5, 155.3, 155.2, 155.2, 155.2, 148.1, 146.4, 146.3, 146.2, 146.2, 146.2, 144.1, 139.1 138.9, 138.8, 138.7, 137.1, 137.0, 136.9, 136.9, 136.1, 133.2, 133.2, 133.1, 133.0, 132.4, 132.2, 132.0, 131.5, 130.6, 130.3, 130.3, 130.1, 130.0, 129.7, 129.7, 129.5, 129.5, 129.2, 128.9, 128.8, 128.6, 128.4, 128.3, 127.3, 127.2, 127.2, 127.2, 127.1, 127.0, 126.7, 126.6, 124.8, 124.6, 124.5, 122.7, 122.0, 121.9, 119.1, 118.8, 118.7, 109.5, 109.4, 109.1, 109.1, 67.1, 65.9, 61.6, 61.0, 60.4 57.7, 57.6, 57.4, 57.3, 54.2, 54.2, 35.3, 35.2, 31.0, 29.5, 29.4, 27.6, 27.5, 20.7, 20.6. HRMS (ESI) *m/z*: $[M–BArF]^+$ Calcd for $C_{127}H_{111}N_2O_9Si$ 1835.8053; Found 1835.8037.

ASSOCIATED CONTENT

Supporting Information

NMR and MS spectra of new compounds, determination of the association constants of **HA** and **G**, NMR kinetic experiments for the dethreading process. The Supporting Information is available free of charge on the ACS Publications website.

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Notes

The authors declare no competing financial interest.

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