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EDGE ARTICLE

A solvent-driven molecular spring†

Zibin Zhang, Chengyou Han, Guocan Yu and Feihe Huang*

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A solvent-driven doubly threaded rotaxane dimer based on an amino-modified copillar[5]arene was prepared using bis(trifluoromethyl)phenyl isocyanate as stoppers. By comparison of proton NMR spectra of the rotaxane dimer and the control compound, the inclusion-induced shielding effects of the decyl protons of the dumbbell compound were estimated. From the crystal structures of previously reported analogous pillar[5]arene/alkane pseudorotaxanes, we know that four methylenes can be totally encapsulated in the pillar[5]arene cavity. When a pillar[5]arene is swaying along a guest with a long linear alkyl chain (more than four methylenes), its cavity statistically locates on the four methylenes whose protons showed relatively larger upfield shifts. Based on this, the length of the rotaxane dimer can be estimated. In $CDCl_3$, it was in a contracted state with a length of 31 Å. In DMSO-d_6, it was in a extended state with a length of 37 Å. Moreover, as the polarity of the solvent is changing, the length of the rotaxane dimer can change continuously as the contraction/stretching systems work in living organisms. Therefore, we can control the length of this molecular spring as needed.

Introduction

A spring is an elastic device that can change its shape and/or length continuously by compression or stretching. Therefore, a molecular spring can be considered as a single molecule or a part of a biological system that can change its shape or length continuously caused by external stimulus. Some spring-like devices play very important roles in living organisms.[1] For example, titin is a giant sarcomeric protein found in cardiac and skeletal muscles with a wide range of cellular functions, including providing muscle cells with elasticity. It works like a spring whose length is controlled by the calcium responsive conformational changes.[2] The first step of vision is also a compression of a molecular spring by a minor change of its nuclear coordinates the strain of which can be released by altering the protein environment.[3] Artificial molecular machines that exhibit nanoscale motions have recently experienced a remarkable development.[4] Among them, those with contraction/stretching properties are usually based on multi-stable rotaxanes. They were composed of two ring-shaped hosts and at least two kinds of different binding sites with adjustable host–guest binding abilities in the thread-like components (Fig. 1). When an external stimulus, such as a chemical,[5] electrical[6] or optical stimulus,[7] was added, the host parts tended to complex the other guest moieties, which further caused the relative linear translocation of the ring parts. For instance, Coutrot *et al.* reported a molecular muscle that can accurately change its length between half-contracted and contracted co-conformation depending on solvent polarity.[5h] However, to the best of our knowledge, all of the reported artificial contraction/stretching molecules can only change their lengths stepwise caused by translocation of the ring parts between different guest moieties. They cannot change their lengths continuously like the real self-stretchable system in living organisms. To mimic the unique spring-like function of biological systems, we prepared a molecular device based on a copillar[5]arene without different guest moieties in the thread component. We can control the length of this molecule continuously just by changing the solvent polarity, which is quite similar to the process by which we control the length of a spring by adjusting the external forces.

Copillar[5]arene is a kind of pillar[5]arene[8] with different repeating units. We prepared the very first copillar[5]arene from

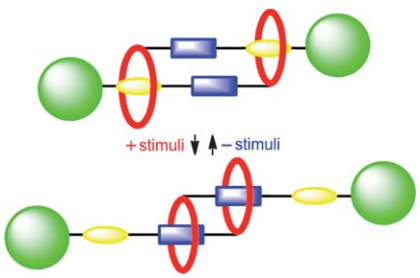

Fig. 1 A schematic presentation of a bistable doubly threaded rotaxane dimer with two kinds of guest moieties in the thread-like components.

Department of Chemistry, Zhejiang University, Hangzhou 310027, P. R. China. E-mail: fhuang@zju.edu.cn; Fax: +86 571 8795 3189; Tel: +86 571 8795 3189

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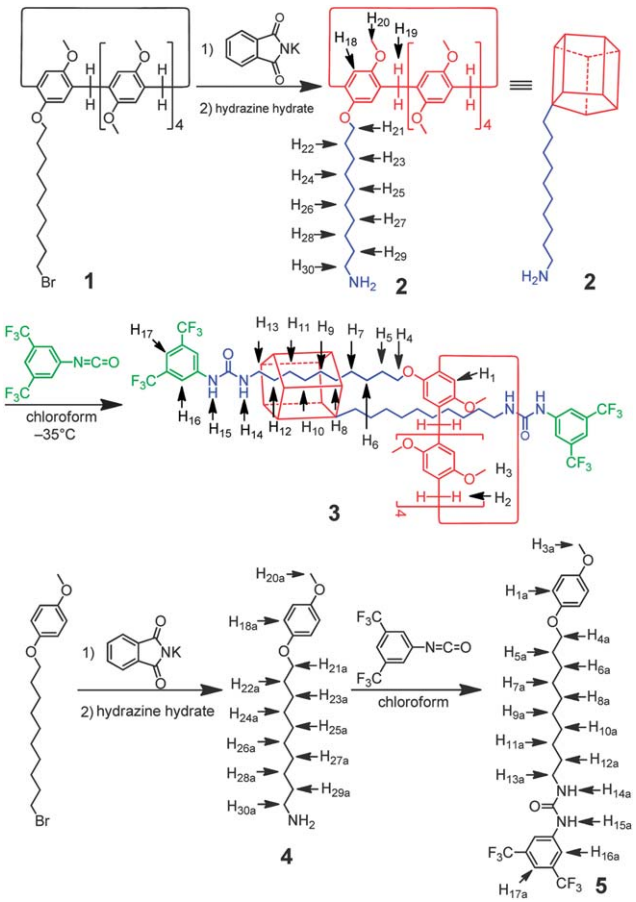
one pot co-oligomerization of different monomers.[9] In the same paper, we found that there were quadruple CH···π interactions between the guest and the host from the crystal structure of the complex of DBpillar[5]arene with *n*-hexane.[9] Later, many neutral molecules,[10] organic cations[11] and organic anions[12] with long linear alkyl groups have been discovered that can complex with pillar[5]arenes, copillar[5]arenes and also pillar[5]arene dimers in different solvent systems. Furthermore, supramolecular polymers based on copillar[5]arenes were constructed using a similar host–guest system.[13,14] In our recent work, we found that if the linear alkyl group on a copillar[5]arene is long enough (at least ten carbon atoms) and with a bromo atom at the end of the alkyl chain, the copillar[5]arene could self-assemble into cyclic dimers both in solution and in the solid state.[14] From single crystal X-ray analysis, we found that the dimerization was caused by van der Waals forces (mainly dispersion force) between the *exo* cavity parts of the decyl groups.[14] Here, we capped this kind of cyclic dimer with suitable stoppers and obtained a doubly threaded rotaxane dimer. By adjusting the competition of dispersion force (between the linear alkyl groups) and interactions between the rotaxane dimer and the solvent molecules, we demonstrated that this interlocked molecule could work as a molecular spring that could change its length continuously instead of step-by-step.

Results and discussion

To make the capping process mild and efficient, we converted bromo-containing copillar[5]arene **1** (ref. 14) to an amino-modified copillar[5]arene **2** *via* the Gabriel synthesis method (Scheme 1). To investigate the self-complexation of **2**, we synthesized **4** as a control compound. From the ^{1}H NMR spectrum of **2** in chloroform-*d* (Fig. S2 and S15†), we found that signals from the bridging protons H_{19} and methoxy protons H_{20} of **2** are significantly overlapped and couldn't be identified clearly. In addition, there were two broad peaks below zero. These observations indicated the self-complexation of **2** in chloroform-*d*.[14] From the 2D ^{1}H–^{1}H COSY spectrum of **2** (Fig. S14†) and comparison of ^{1}H NMR spectra of **2** and **4** (Fig. S15†), self-complexation-induced chemical shifts of the decyl protons can be estimated (Table S1†). Protons H_{27}, H_{28}, H_{29} and H_{30} on the four methylenes next to the amino group showed larger upfield chemical shifts than the other protons on the decyl chain (Fig. 2).

From the crystal structures of previously reported pillar[5]arene/alkane pseudorotaxanes,[9,10b,10d,10g,10h,13,14] we know that in the solid state there are four methylenes on an alkyl chain that can be totally encapsulated in the aromatic cavity of pillar[5]arenes. Therefore, a symmetric guest that contains a linear alkyl chain with four methylenes usually showed a bigger binding constant with pillar[5]arenes in solution than similar compounds with longer or shorter alkyl chains. Li *et al.* have done some pretty convincing work about this recently.[8d,10b,10g,10h,11b] For a pillar[5]arene complex with guests with a linear alkyl chain with more than four methylenes, the cavity still can only encapsulate four methylenes (Fig. 3a). However, the pillar-shaped cavity can vibrate along the alkyl chain, which will cause upfield shifts of protons on more methylenes (Fig. 3d). For example, protons on twelve methylenes of icosanedioic acid shifted upfield in D_2O caused by inclusion of the aromatic cavity of decaamine pillar[5]arene.[10a] We can estimate the extent of the shielding effect by comparing the ^{1}H NMR signals of the encapsulated protons with those of the free ones. Therefore, we can conclude that when a pillar[5]arene is swaying along a guest with a long linear alkyl chain, the cavity statistically located on the four methylenes whose protons showed relatively bigger upfield shifts in solution (Fig. 3d). In all reported pillar[5]arene based host–guest systems with long alkyl guests, this conclusion is in accordance with their crystal structures.[10d,11e,13,14] For copillar[5]arene **2**, the aromatic cavity mainly covered the four methylenes next to the amino



Scheme 1 Syntheses of **2**, **3**, **4** and **5**.

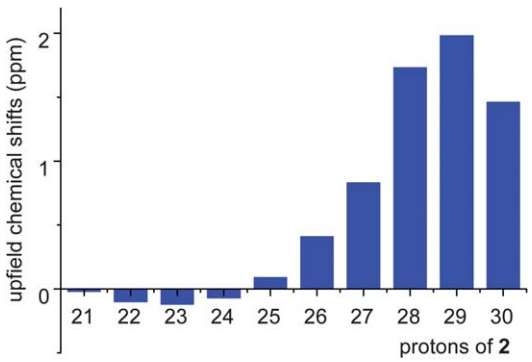


Fig. 2 Upfield chemical shifts of the decyl protons on **2** caused by the self-complexation in chloroform-*d*.

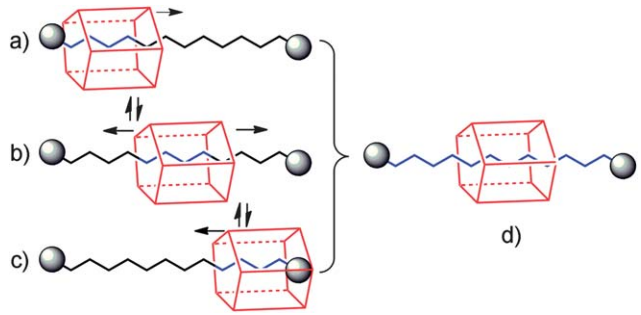


Fig. 3 A schematic presentation of the vibration of a pillar[5]arene along a guest with a long linear alkyl chain.

group and left the other methylenes out of the cavity as **1** did in $CDCl_3$.[14] Driven by the dispersion force between the *exo* cavity parts of the alkyl groups, **2** may also form cyclic dimers in $CDCl_3$.

To strengthen the self-complexation of **2** and increase the yield of the capping process, a mixture of 3,5-bis(trifluoromethyl) phenyl isocyanate (0.71 g, 2.8 mmol) and **2** (0.60 g, 0.67 mmol) in 10 mL of chloroform was stirred at −35 °C for 3 days. After purification by column chromatography using petroleum ether/dichloromethane (1 : 3) as the eluent, the main product was isolated in 30% yield. From its MALDI-TOF mass spectrum (Fig. S7†) we can conclude that it should be a singly threaded or a doubly threaded rotaxane dimer (Fig. S16†). The proton NMR spectrum of **3** (Fig. S5†) in chloroform-*d* showed that, like copillar[5]arenes **1** and **2**, there were also broad peaks located below zero. Peaks from free decyl groups were not observed. Therefore, **3** should not be a singly threaded rotaxane but a doubly threaded rotaxane dimer. Moreover, we found that signals from the bridging protons H_2 and methoxy protons H_3 of **3** were overlapped, which also indicated the complexation of the decyl chain in the aromatic cavity (Fig. 6b). From 2D ^1H–^1H COSY experiments of **3** (Fig. S19†) and **5** (Fig. S17†) in chloroform-*d*, the signals from the decyl protons can be identified, respectively. From comparison of ^1H NMR spectra of **5** and **3** (Fig. 6a and b) in chloroform-*d*, the chemical shift changes of the decyl protons caused by threading through the electron-rich copillar[5]arene cavity can be estimated. The protons H_{11}, H_{12}, H_{13} and H_{14} of **3** showed much larger upfield chemical shift changes than other protons (Fig. 4).[14] The shape of peaks from H_{11}, H_{12}, H_{13} and H_{14} are also quite different from other ones. Signals from H_{12} and H_{13} are all broad peaks. Either of the two signals from H_{11} and H_{14} almost split into two peaks (Fig. 6b). From the 2D NOESY NMR spectrum of **3** in chloroform-*d* (Fig. S19†), we found that strong correlations were observed between all of the decyl protons H_{5-14} and the bridging methylene protons (H_2). Also, NOEs were found between H_{9-14} and the aromatic protons H_1. There were no correlations between H_5, H_6, H_7 and H_8 on the decyl group and the aromatic protons H_1. These phenomena indicated that the decyl group was threaded into the copillar[5]arene cavity with protons H_{11}, H_{12}, H_{13} and H_{14} right located in the cavity statistically. From molecular model studies (Fig. 7a),[15] we concluded that **3** was in a contracted state in chloroform-*d* with a length of about 31 Å. The cavity can vibrate a little to the centre and encapsulate protons H_9 and H_{10} sometimes (Fig. 4). This vibration is somewhat slow on the NMR time scale. In addition, we thought that the broad peaks of H_{12} and H_{13} and split of H_{11} and H_{14} were also caused by the vibration of the cavity.

At first, we thought that the contracted state of **3** in chloroform was caused by the stronger NH···π interactions compared with CH···π interactions, which drag the urea groups into the copillar[5]arene cavity. Therefore, we tried to use trifluoroacetate anion to complex the urea group and cut off the NH···π interactions. However, the proton NMR spectrum of **3** did not change much after we added 4 equiv. of triethylammonium trifluoroacetate into a chloroform-*d* solution of **3** (Fig. S24†). Therefore, we believed that the dispersion forces between *exo* cavity parts of the decyl groups are the main driving forces for the contracted state in chloroform. If we add a polar solvent to this solution, introduction forces between **3** and the polar solvent molecules can be introduced. When the introduction forces are stronger than the dispersion forces between *exo* cavity parts of the decyl groups, the rotaxane dimer **3** will be stretched. Because the solubility of **3** in acetone and acetonitrile is too bad, we did not use them for our proton NMR studies. Instead, we chose DMSO-d_6 as the polar solvent because it has high polarity and dimer **3** has good solubility in it. From the proton NMR spectrum of **3** in DMSO-d_6 (spectrum i in Fig. 6), we could also find broad peaks below zero, but quite different from that in $CDCl_3$ (spectrum a in Fig. 7). From the 2D ^1H–^1H COSY NMR in DMSO-d_6 (Fig. S23†), the signals from the decyl protons could be identified clearly. From comparison of ^1H NMR spectra of **3** and **5** (spectra i and j in Fig. 6) in DMSO-d_6, the chemical shift changes of the decyl protons could be calculated.[16] The protons H_7, H_8, H_9 and H_{10} of **3** showed larger upfield chemical shifts than other protons (Fig. 5). Therefore, **3** was in an extended state in DMSO-d_6 with a length of 37 Å calculated from molecular modeling when H_7, H_8, H_9 and H_{10} were located in the copillar[5]arene cavity statistically (Fig. 7c). The length is evaluated from the most stretched state, due to the flexibility of the alkyl chains. Except for H_4, all of the protons on the decyl group showed upfield chemical shifts, which indicated that the vibration of the cavity is stronger in DMSO-d_6 than in chloroform-*d*.

In biological systems, the contraction/stretching process is caused by the conformational change of proteins, which means that the variation must be continuous. We could mimic this unique spring-like function using **3** by gradually changing the polarity of the solvent. Hence, we changed the volume ratio of chloroform-*d* and DMSO-d_6 to adjust the solvent polarity. We found that as the solvent polarity changed, the proton NMR spectrum of **3** changed correspondingly. From several 2D ^1H–^1H COSY spectra of **3** in different solvent mixtures (Fig. S20–22†), we could clearly assign peaks for all protons. From ^1H NMR of **3** in different solvent mixtures (Fig. 6), we found that as the solvent polarity increased, signals from H_{11}, H_{12}, H_{13} and H_{14} (the blue peaks) of **3** shifted downfield. These observations indicated that as the solvent polarity increased, H_{11}, H_{12}, H_{13} and H_{14} were moving out of the cavity gradually. On the contrary, signals from H_7, H_8, H_9 and H_{10} (the red peaks) shifted upfield, indicating that they were gradually moving into the cavities. Signals from the two stoppers (H_{16} and H_{17}) and the two cavities (H_1, H_2 and H_3) did not shift much. However, the two sets of peaks from H_1 gradually became one set of peaks as the polarity of the solvent

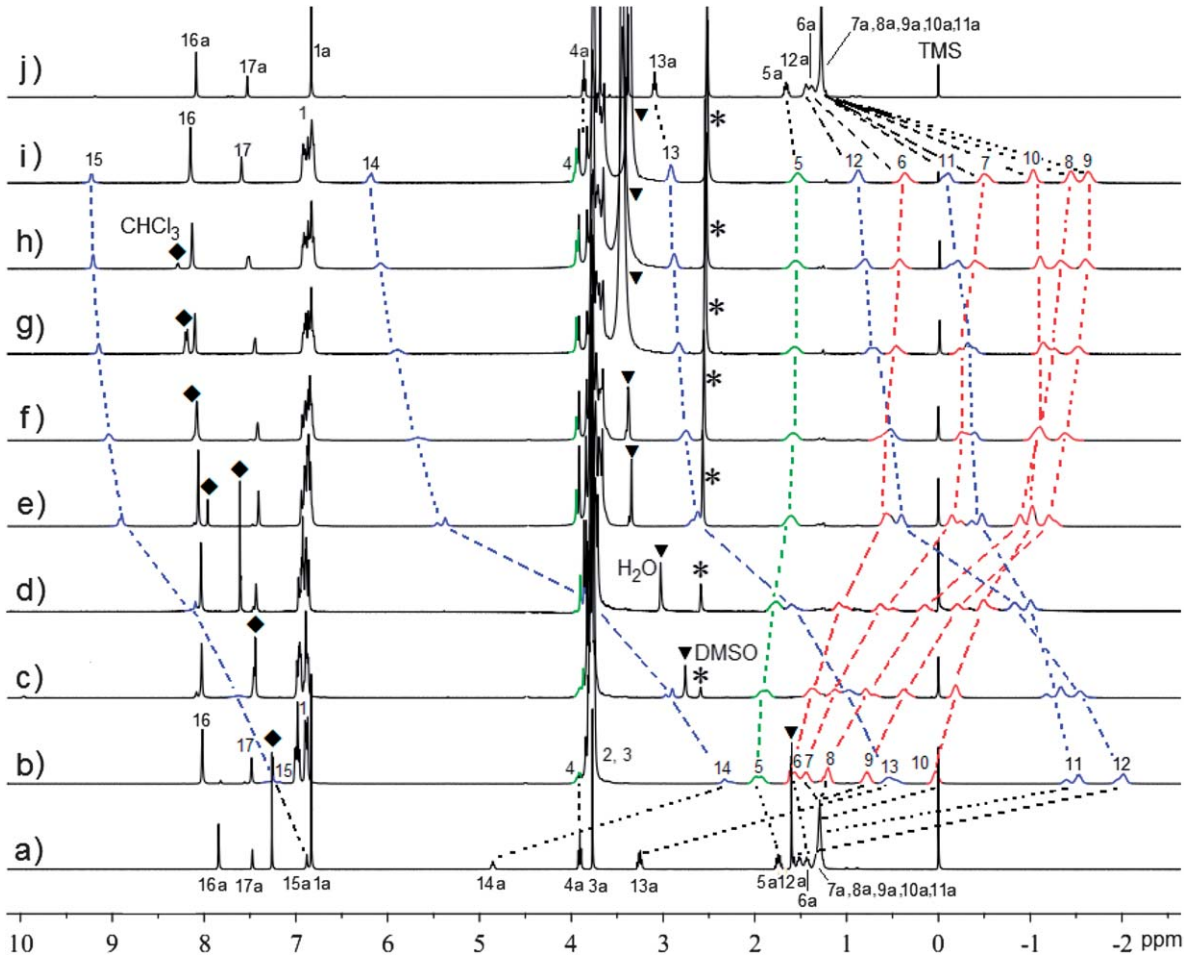


Fig. 6 [1]H NMR spectra (400 MHz, 25 °C) of (a) **5** in chloroform-*d*; (b) **3** in chloroform-*d*; (c) **3** in 10 : 1 (*v*/*v*) chloroform-d/DMSO-d_6; (d) **3** in 5 : 1 chloroform-*d*/DMSO-d_6; (e) **3** in 2 : 1 chloroform-*d*/DMSO-d_6; (f) **3** in 1 : 1 chloroform-*d*/DMSO-d_6; (g) **3** in 1 : 2 chloroform-*d*/DMSO-d_6; (h) **3** in 1 : 4 chloroform-*d*/DMSO-d_6; (i) **3** in DMSO-d_6; (j) **5** in DMSO-d_6. The numbers correspond to the proton assignments indicated in Scheme 1.

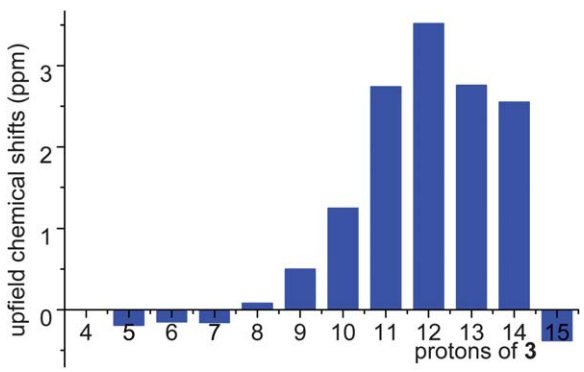


Fig. 4 Upfield chemical shifts of the decyl protons on **3** caused by inclusion in the aromatic cavity in chloroform-*d*.

increased. When **3** was in $CDCl_3$, the outer side of the cavity located partly on the urea group and the inner side located on the decyl group. When it was in DMSO-d_6, both sides of the cavity located on the decyl group, which made the signal of H_1 become one set of peaks (Fig. 7a and c). Using the same method, we calculated the chemical shift changes between **5** and **3** in different solvent systems (Table S3†).[16] We determined four protons that

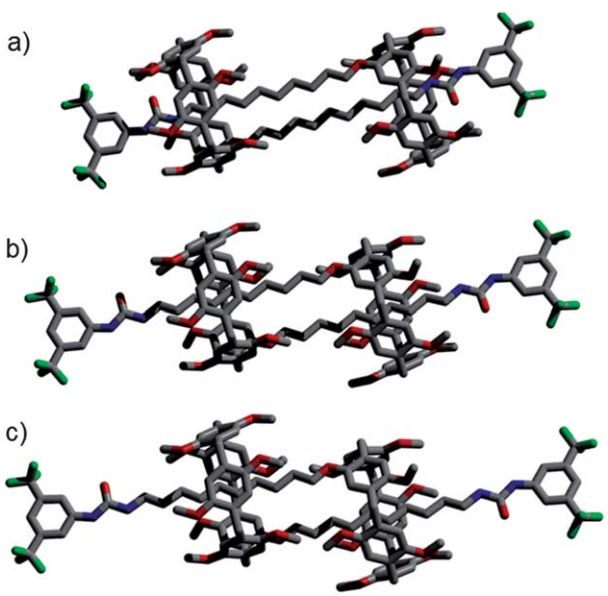


Fig. 7 The length variation of **3** in different solvents: (a) chloroform-*d*; (b) chloroform-*d*:DMSO-d_6 (2 : 1, *v*/*v*); (c) DMSO-d_6.

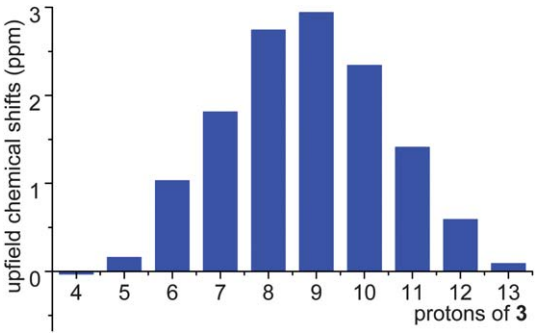


Fig. 5 Upfield chemical shifts of the decyl protons on **3** caused by inclusion in the aromatic cavity in DMSO-d_6.

showed upfield shifts more than the other methylene protons in different solvent mixtures (Fig. S26†) and estimated the length of **3** in the same way. For instance, when **3** is in chloroform-*d*:DMSO-d_6 (10 : 1, *v*/*v*), H_{10}, H_{11}, H_{12} and H_{13} are located in the cavities statistically (Fig. S26a†) with a length of 33 Å. When **3** is in chloroform-*d*:DMSO-d_6 (2 : 1, *v*/*v*), its molecular length is about 35 Å with H_8, H_9, H_{10} and H_{11} encapsulated in the copillar[5]arene cavity (Fig. S26c and 7b†). These observations indicate that **3** can work as a molecular spring. As the polarity of the solvent is changing, the statistical length of **3** is changing continuously.

Conclusions

In conclusion, using bis(trifluoromethyl)phenyl isocyanate as the stopper, we successfully prepared a solvent-driven doubly threaded rotaxane dimer from an amino-modified copillar[5]arene. From the comparison of ^{1}H NMR spectra of the molecular spring **3** and control compound **5**, the shielding effect of protons on the decyl chain caused by encapsulation in the aromatic cavity were estimated. The cavity statistically located at the four methylenes whose protons shifted more. From this method, the length of this molecular spring was calculated. In $CDCl_3$, it was in a contracted state with a length of about 31 Å. In DMSO-d_6, it was in an extended state with a length of 37 Å. As the polarity of the solvent is changing, its length can change continuously as a spring, which is quite like the contraction/stretching process in living organisms. As we know, the continuous length change of **3** is different from the reported molecular devices that can change their length only step-by-step. The present study not only provides a useful method to investigate the relative motion of a pillararene-based molecular switch, but also offers a basis for the construction of an environment responsive interlocked polymer that can mimic the biologic contraction/stretching process.

Acknowledgements

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15 There should be three different supramolecular stereoisomers including a "meso" supramolecular S_2-symmetric stereoisomer and a "threo" supramolecular racemic C_2-symmetric mixture. Here we used the meso stereoisomer as the model in Fig. 7. See ref. 5*g*.

16 We didn't calculate the chemical shifts of H_{14} and H_{15} in DMSO-d_6 because signals from H_{14a} and H_{15a} of **5** cannot be found from its proton NMR spectrum in DMSO-d_6.