ORGANIC
LETTERS

2012
Vol. 14, No. 18
4826–4829

Novel Pillar[5]arene-Based Dynamic Polyrotaxanes Interlocked by the Quadruple Hydrogen Bonding Ureidopyrimidinone Motif

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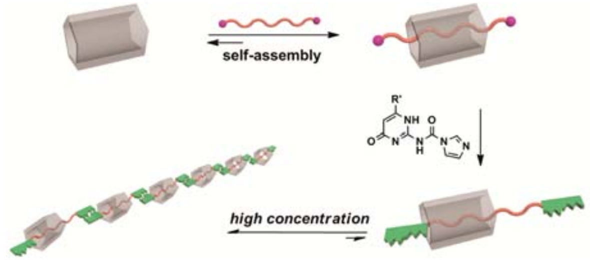
Received August 3, 2012

ABSTRACT



Novel dynamic polyrotaxanes constructed from pillar[5]arenes as wheels and diamines as axles have been successfully synthesized in good yield using quadruple hydrogen bonding ureidopyrimidinone (UPy) motifs, which play a dual role as the end-capping and interlocking units. The present study is the first example of noncovalent bonded dynamic polyrotaxanes constructed by multiple hydrogen bonding interactions.

Polyrotaxanes[1,2] are constructed simply by incorporating rotaxane moieties into supramolecular polymers, which have attracted increasing attention in the past two decades for their unique structural features and wide potential applications in the preparation of smart materials in a relatively simple way.[3] The reported polyrotaxanes usually use one covalent polymer as axles, in which the threading efficiency of macrocycles to the covalent polymers is relatively low and is significantly influenced by many intrinsic and extrinsic factors such as chain length, concentration, and temperature etc.[4] However, the synthesis of well-defined, homogeneous, dynamic supramolecular polyrotaxanes assisted by noncovalent interactions as the polymeric backbones is relatively less common, although they might have excellent mechanical properties and good processability. Hitherto, there are only a few reports on the formation of polyrotaxanes constructed by noncovalent interactions, which mainly focused on dynamic metal–ligand coordination or hydrophobic interactions.[5,6] Herein, we report for the first time a novel type of pillar[5]arene-based dynamic polyrotaxanes interlocked

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Published on Web 09/04/2012

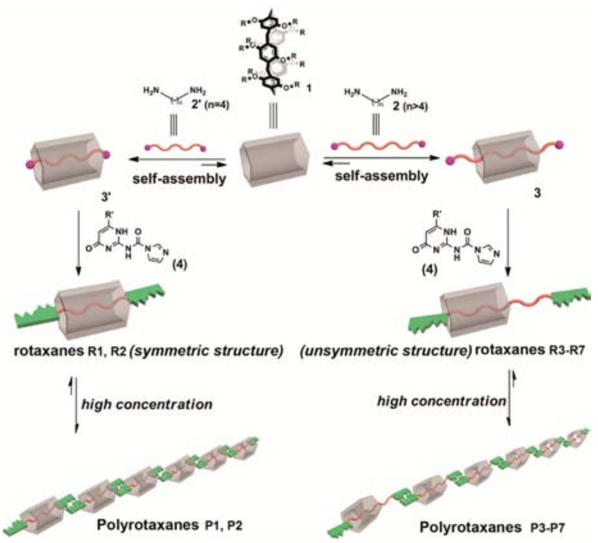

Figure 1. Graphical representation of the construction of dynamic polyrotaxanes.

by two orthogonal noncovalent interactions: quadruple H-bonding and host−guest interaction, in which the ureidopyrimidinone (**UPy**) motifs play quite important roles as the end-capping and interlocking units in the supramolecular polymerizations (Figure 1).

Pillar[5]arene with interesting properties in the host−guest chemistry[7,8] has considerable interest in the creation of (poly)rotaxanes.[9,10] Particularly, Stoddart successfully synthesized a novel pillar[5]arene-based[2]rotaxane using 1,8-octanediamine as the axle;[11] more recently, Huang et al. reported a solvent-driven doubly threaded rotaxane dimer based on an amino-modified copillar[5]arene;[12] To our knowledge, reversible pillararene-based polyrotaxane constructed by noncovalent interactions have not been reported yet. While exploring novel dynamic [2]catenanes interlocked by the quadruple H-bonding **UPy** motif,[13] and supramolecular polymers based on the pillar[5]arene in our group,[10c] we envisioned that if an appropriate diamine guest could thread into the cavity of pillar[5]arene to form a pseudorotaxane-type inclusion complex (**3** and **3′**),[11] two **UPy** groups then could be incorporated into each end of the diamine axle to obtain [2]rotaxanes (**R1**−**R7**) end-capped with **UPy** units and further to form the dynamic supramolecular polyrotaxanes (**P1**−**P7**) at high concentration (Figure 1) based on the high directionality and strong association constant of the quadruple H-bonding **UPy** motifs. In other words, **UPy**, which is connected at both ends of the flexible axle, could play a dual role, acting not only as a large end-capping group but also as a reversible linker to control the conformation of the dynamic supramolecular polyrotaxanes.

Using the strategy “diamine threading followed by end-capping with **UPy** units”, imidazolide (**4**) was added to the solution of 1 equiv of 1,8-octanediamine ($NH_2(CH_2)_nNH_2$, $n = 8$) and 4 equiv of DMPillar[5]arene (**DMP5**, **1**) in dry $CHCl_3$, and the resulting mixture was stirred at 65 °C for 48 h. Pure [2]rotaxane **R4** was isolated in 32% yield using silica-gel flash column chromatography. Similarly, when 1,4-butanediamine ($NH_2(CH_2)_nNH_2$, $n = 4$) was used as the axle, [2]rotaxane **R1** was obtained in 65% isolated yield. Compared with **R4**, the high yield of **R1** might be attributed to the relatively higher association interaction between 1,4-butanediamine and **DMP5** (see Supporting Information (SI), Figure S38).

The structures of **R1** and **R4** were initially investigated by a ^{1}H NMR experiment (Figure 2a and c). The ^{1}H NMR spectrum of **R4** in $CDCl_3$ with the aid of its 2D H−H COSY spectrum (Figure S25) and NOESY NMR spectrum (Figure S31) showed that three signals below 0 ppm (δ: −0.09, −1.78, and −2.23 ppm) were observed, indicating 1,8-octanediamine threaded into the cavity of **DMP5**. It was interesting that the methylene protons on 1,8-octanediamine were split into eight dissimilar peaks, indicating the unsymmetrical threading structure of **R4**. Moreover, the **UPy** N−H signals on **R4** in $CDCl_3$ were also unsymmetric and showed six different peaks, in which five N−H signals showed large downfield shifts together with a lower intensity (between 8.5 and 13.0 ppm), due to the dimerization of **UPy** units. Notably, one of the N−H signals of **UPy** unit on **R4** was in the upfield region (δ: 2.82, H_3), which is probably because it was encapsulated in the cavity of **DMP5** (shielding effect) and H_3 could form stable multiple N−H···O hydrogen bonds with the methoxy group on **DMP5**,[11] which possibly weakens the association interaction between the two **UPy** units. The above results clearly demonstrated that the unsymmetrical threading structure of **R4** was formed in $CDCl_3$. With respect to **R1** (Figure 2c), ^{1}H NMR spectrum showed the symmetrical threading structure, which might be due to the

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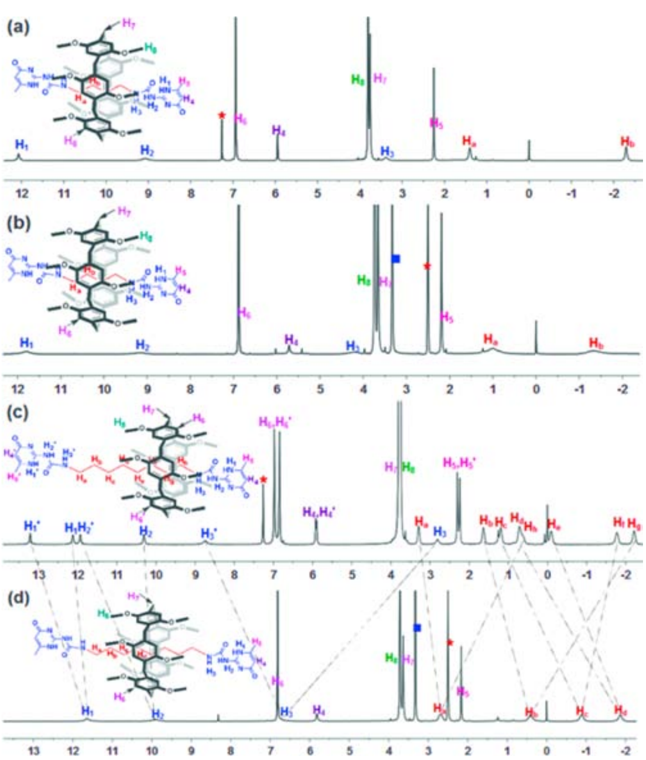

Figure 2. ^1H NMR spectra of **R1** and **R4** (400 MHz, 298 K, 10 mM): (a) **R1** in $CDCl_3$, (b) **R1** in DMSO-d_6, (c) **R4** in $CDCl_3$, (d) **R4** in DMSO-d_6. The asterisk symbols (*) indicate solvent peaks and the blue squares (■) in (b) and (d) stand for water peaks.

formation of two such stable N−H···O hydrogen bonds at each end of the axle in **R1**.

To investigate the solvent effect on the above N−H···O hydrogen bond, **R1** and **R4** were then investigated in polar solvent DMSO-d_6 by ^1H NMR, respectively (Figure 2b and d). When **R4** was dissolved in DMSO-d_6, the threading structure becomes completely symmetrical, indicating that such a stable N−H···O hydrogen bond was destroyed by a polar solvent and the diamine axle symmetrically threaded into the cavity of **DMP5**. Moreover, we also gradually changed the polarity of the solvent to investigate the sliding process of the threading structure of **R4** (Figure S35). It was found that, with the solvent polarity increased by adding DMSO-d_6 into the $CDCl_3$ solution gradually, signals from H_a, H_b, H_c, and H_d of **R4** shifted upfield; conversely, signals from H_e, H_f, H_g, and H_h shifted downfield, and the eight sets of peaks from 1,8-octanediamine gradually became four sets of symmetric peaks. This observation indicated that the **DMP5** wheel gradually moved into the middle position of the 1,8-octanediamine axle from one side as the polarity of the solvent increased. Variable temperature ^1H NMR was also used to further investigate the dynamic properties of the polyrotaxanes (Figure S36). It was found that the stable N−H···O hydrogen bond could not be destroyed with the temperature rising to 393 K, and the unsymmetrical structure of **R4** still was retained.

Two-dimensional diffusion-ordered ^1H NMR spectroscopy (DOSY), a convenient and reliable method to test the dimensions of supramolecular aggregates, was usually applied to study the quadruple H-bonded supramolecular polymers.[14] Thus we also measured the DOSY NMR spectra of **R1** and **R4** in $CDCl_3$ to investigate the conformation of the aggregates at different concentrations. As shown in Figure 3, the average measured diffusion constant of **R4** decreased from 3.49×10^{-10} m^2 s^{-1} at 5 mM to 1.38×10^{-10} m^2 s^{-1} at 150 mM, which indicates the formation of much larger aggregates (**P4**) at "higher" concentrations. As the concentration of **R1** increased from 5 to 300 mM, the average measured diffusion constant decreased from 5.28×10^{-10} to 1.36×10^{-10} m^2 s^{-1}, also indicating the concentration dependence of the supramolecular polymerization of **R1** to form polyrotaxane **P1**. Based on previous reports, it is well-known that a high degree of polymerization for the repeat unit usually leads to a sharp decrease of the diffusion constant.[14b,c] Therefore, the above results clearly indicate the formation of high-molecular-weight polymeric structures. Viscometry is a convenient method to test the polymerization property of polymer molecules. As presented in Figure 4a, the aggregates assembled from [2]rotaxane **R4** presented a viscosity transition. At the low concentration region, the curve slope is 1.05, which indicates the predominance of cyclic oligomers in dilute solutions. When the concentration increased above the critical polymerization concentration (CPC, 50 mM), an obvious increase of the viscosity was observed (slope = 2.01), indicating a transition from the small size of oligomers to supramolecular polymers with an increasing size of assembly. With respect to **P1**, it also exhibited a viscosity transition with a dramatic change of the slope at 100 mM, indicating progress from the presence of the small size of oligomers (slope = 1.03) to supramolecular polymers with the longer polymeric chain (slope = 2.07). Both of the slope values for **P1** and **P4** in the high concentration region is lower than that of the

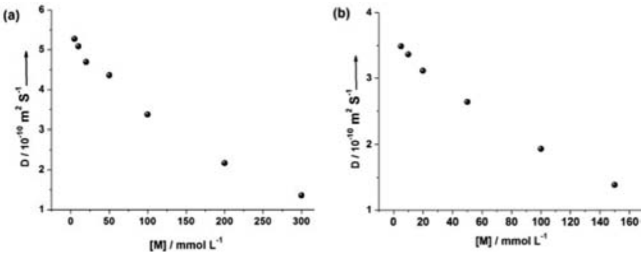

Figure 3. Concentration dependence of diffusion coefficient D (400 MHz, $CDCl_3$, 298 K) of **P1** (a) and **P4** (b) (when the systems have different assemblies, we chose the larger one).

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UPy-based self-assembling systems reported by Meijer et al. (slopes = 3−6),[15] implying that there should be some degree of disruption in association between the two **UPy** moieties in solution in our case.

We also conducted the dynamic light scattering (DLS) measurements of **P1** and **P4** in chloroform, respectively, to investigate the size of the supramolecular aggregates (Figure 4b). The aggregate of **R1** (160 mM) shows the average hydrodynamic radius (R_h) values of 249 nm, and the aggregate of **R4** (120 mM) shows the average R_h values of 488 nm. The results obtained were in accordance with those of the DOSY experiments and also supported the formation of the supramolecular polymer. Furthermore, transmission electron microscopy (TEM) was also used to provide further insight into the size and shape of the aggregates.[5,16] Representative TEM images of **P1** and **P4** formed in chloroform are shown in Figure 5 (for details, see SI).

To expand the applicability of this method, we synthesized a series of polyrotaxanes with different ‘wheels’ and ‘axles’ (Table S1). Both **DMP5** and 1,4-bis(butoxy)pillar[5]arene could be used as the macrocyclic wheels to form the target [2]pseudorotaxane with diamines of different chain lengths (axles), and then methyl- or tertiary heptyl-substituted **UPy** units could be used as the end-capping and interlocking groups in the formation of the dynamic polyrotaxanes. When 1,4- butanediamine was used as the axle, the obtained polyrotaxanes **P2**, like **P1**, also showed a completely symmetrical threading structure; however, with respect to the longer alkyl-chain diamine, the threading structure of the corresponding polyrotaxanes (**P3**−**P7**) became unsymmetric, which could probably be attributed to the presence of the stable N−H···O hydrogen bond between pillararene and one of the **UPy** N−H bonds.

In summary, we have reported a highly efficient synthetic method for the construction of pillararene-based dynamic polyrotaxanes interlocked by two orthogonal noncovalent interactions: quadruple H-bonding and host−guest interactions through the “diamine threading followed by end-capping with **UPy** units” approach. In such novel dynamic polyrotaxanes, the **UPy** motifs particularly play quite important roles in the reversible formation of main-chain backbones of supramolecular polymers. The stepwise and one-pot strategies used in the preparation of the dynamically reversible polyrotaxanes based on quadruple H-bonding provide a novel and efficient methodology for the smart design and construction of new types of higher-ordered architectures and sophisticated molecular devices. In particular, the dynamic nature of supramolecular polymers also creates a unique possibility to fabricate self-healing bioactive materials. The construction of more complicated supramolecular polyrotaxane networks based on quadruple H-bonding interactions and its biomedical applications are in progress in our lab.

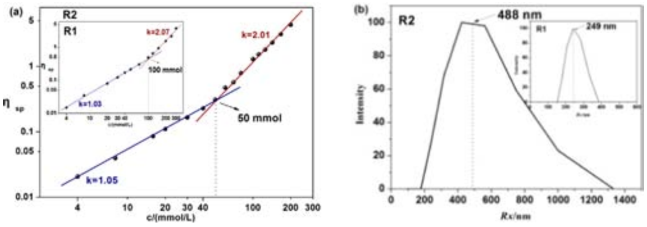

Figure 4. (a) Specific viscosity of chloroform solutions of **R1** (inset) and **R4** at 298 K. (b) Distribution of the hydrodynamic diameter of **R1** (160 mM, inset) and **R4** (120 mM) in chloroform at 298 K.

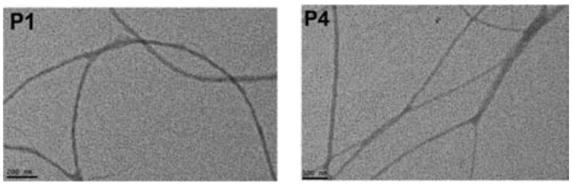

Figure 5. TEM mcicrograph of **P1** and **P4** (samples were prepared by placing one drop of the chloroform solution of the polyrotaxanes onto a carbon-coated copper grid).

Acknowledgment. We gratefully thank the financial support of the National Natural Science Foundation of China (Nos. 20932004, 21072093), National Basic Research Program of China (2011CB808600), and the Natural Science Foundation of Jiangsu (BK2011055).

Supporting Information Available. Synthesis and characterization of all the compounds, results of NMR and DLS experiments. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

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