Construction of polyrotaxanes *via* reversible chain exchange between acylhydrazone bonds†

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By simply heating mixtures of α-cyclodextrins and dumbbell-like poly(ethylene glycol) derivatives at 120 °C, polyrotaxanes form spontaneously *via* reversible chain exchange between acylhydrazone bonds, which have been proven by analyses of diffusion-ordered NMR, WAXD, ^{1}H NMR, solid-state ^{13}C CP/MAS NMR, DSC and UV-Vis together.

Polyrotaxanes, with unique structures and diverse potential applications, have attracted great interest in recent years.[1] Essentially, polyrotaxanes are a kind of interlocked supramolecular structure formed by threading many cyclic molecules onto the polymer chain, either forming main-chain polyrotaxanes or side-chain polyrotaxanes.[2] Many cyclic molecules, such as cyclodextrins,[3] crown ethers[4] and cucurbiturils,[5] are incorporated into the polymer chain to construct polyrotaxanes. Generally, there are two methods to prepare polyrotaxanes: (1) threading the cyclic molecules onto the polymer chain and then end-capping bulky groups to the polymer ends; (2) polymerization of bifunctional pseudorotaxanes, and then terminating with big stoppers if necessary.[2,6]

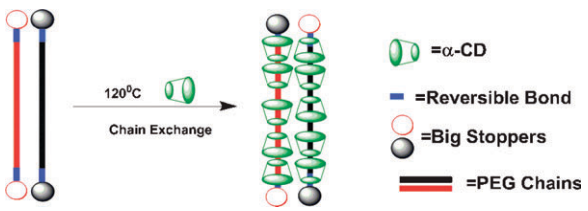
The formation of pseudorotaxanes or polypseudorotaxanes is a prerequisite to prepare polyrotaxane in both aforementioned approaches. Currently, the boom of the dynamic combinatorial chemistry[7] (DCC) provides a brand-new way to construct polyrotaxanes. Many reversible covalent bonds, which are a fundamental concept in DCC, have been introduced and widely investigated.[8,9] Such reversible bonds, differing from traditional covalent bonds, exhibit tunable properties under mild conditions. On the other hand, they are much more stable than non-covalent bonds. Among the known reversible covalent bonds, acylhydrazone bonds, formed by acylhydrazides and aldehydes or ketones in neutral or alkaline condition, can be tunably hydrolyzed in acidic conditions, and furthermore, undergo reorganization in the solid state at high temperature.[10] Based on this concept, the formation of polyrotaxanes might be implemented during a dynamic chain-exchanging process. With the trigger of high temperature, the solid blending of cyclic molecules and dumbbell-like polymers with reversible covalent bonds forms polyrotaxanes *in situ*. Hence, the preparation of pseudorotaxanes or polypseudorotaxanes would not be a necessary step.

Herein the novel method to construct polyrotaxanes with α-CDs and poly(ethylene glycol) (PEG2k, M_n = 2000) terminated with different bulky stoppers (2,4-dinitrobenzaldehyde and 9-anthraldehyde) *via* acylhydrazone bonds at high temperature is studied. The mechanism is described in Scheme 1. We suggest that α-CDs slip into the melted PEG chain during the dynamic exchanging process between the reversible covalent bonds at high temperature, which leads ultimately to the formation of polyrotaxanes.

The synthesis of dumbbell-like PEG2k derivatives with acylhydrazone bonds (bis (2,4-dinitrophenyl)-PEG2k (PEG2k-2DNBA) and bis(9-anthracene)-PEG2k (PEG2k-2AD)) was accomplished by the condensation of PEG2k acylhydrazide derivative with 2,4-dinitrobenzaldehyde and 9-anthraldehyde, respectively. Detailed synthesis information and the corresponding characterizations have been listed in the ESI.†

Mixtures of dumbbell-like PEG2k derivatives and α-CDs with different molar ratio (ethylene glycol units (PEG repeat units)/α-CDs) were fully ground before filling in the standard X-ray sample containers. The sample container was flattened and then placed in the oven at 120 °C. Wide-angle X-ray diffraction (WAXD) scans were carried out for the desired heating time. After heating for 32 h, the mixtures were washed with methanol (twice), deionized water (three times) and diethyl ether (three times) to remove free α-CDs and PEG; yellow products were obtained.

A clear proof of the polyrotaxane formation is given by comparing the diffusion coefficients (D) of the molecules in the samples before and after heating, as shown in the NMR



Scheme 1 Mechanism of constructing polyrotaxanes through reversible chain exchange at high temperature.

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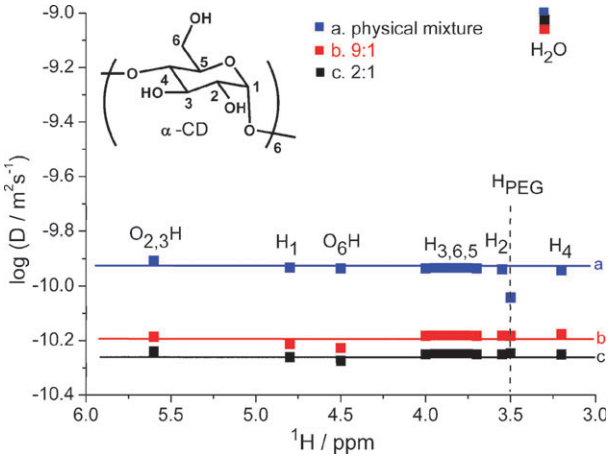

Fig. 1 2D DOSY spectra of (a) physical mixture of PEG2k-2DNBA and α-CD (ethylene glycol units : α-CDs = 2 : 1), stored at room temperature, (b) purified product from mixture of PEG2k-2DNBA and α-CD (ethylene glycol units : α-CDs = 9 : 1) kept at 120 °C for 32 h, and (c) purified product from mixture of PEG2k-2DNBA and α-CD (ethylene glycol units : α-CDs = 2 : 1) kept at 120 °C for 32 h (solvent: DMSO-d_6; calculation error of D: ±5%)

diffusion-ordered spectroscopy (DOSY) spectra in Fig. 1. In the mixture of PEG2k-2DNBA and α-CDs stored at room temperature, all α-CD peaks exhibit similar diffusion coefficients around 1.15×10^{-10} m^2 s^{-1}, while the PEG peaks (backbone) are associated with a different diffusion coefficient of 9.05×10^{-11} m^2 s^{-1}, suggesting that the PEG2k-2DNBA and α-CD in this case are two uncoupled species. In case of purified samples, however, the diffusion coefficients of PEG2k-2DNBA and α-CD are equivalent and nearly two times smaller, that is, around 6.5×10^{-11} m^2 s^{-1} for the mixture with the molar ratio of 9 : 1 and 5.6×10^{-11} m^2 s^{-1} for the mixture with the molar ratio of 2 : 1, as shown in Fig. 1(b) and (c). The equivalent diffusion coefficient of PEG2k-2DNBA and α-CD in this case indicates that the two components are moving together in solution, as required by the formation of the rotaxanated structure. The reduction of *D* may be attributed to an increase in the hydrodynamic volume of the polymer due to the presence of threaded cyclodextrins and an increase in the weight of the moving particle as well.[11]

Fig. 2 shows the ^{1}H NMR spectra of PEG2k-2DNBA and α-CD mixtures before and after heating treatment. The acylhydrazone signals are around 11.9 and 8.35 ppm, respectively, in DMSO-d_6. After keeping at 120 °C for 32 h, no signals assigned to aldehyde (around 10.3 ppm) and acylhydrazide (around 8.8 ppm) appear. More importantly, the integral area of acylhydrazone signal (around 11.9 ppm) and H-1, OH-6, OH-2 and OH-3 signals of α-CD (around 4.8, 4.5, 5.4 and 5.5 ppm, respectively) remains almost unchanged after heating. This evidence proves that the acylhydrazone bonds are still fixed in the PEG ends after heating treatment.

The number of α-CDs in the polyrotaxane can be calculated from ^{1}H NMR of purified products in DMSO-d_6. As shown in Fig. 3, when the sample with the molar ratio of 1 : 1 is heated, the maximal number of α-CDs included in the polyrotaxane is nineteen, with the coverage of 83% to the PEG chain. The calculated molar ratio of ethylene glycol units : α-CDs is

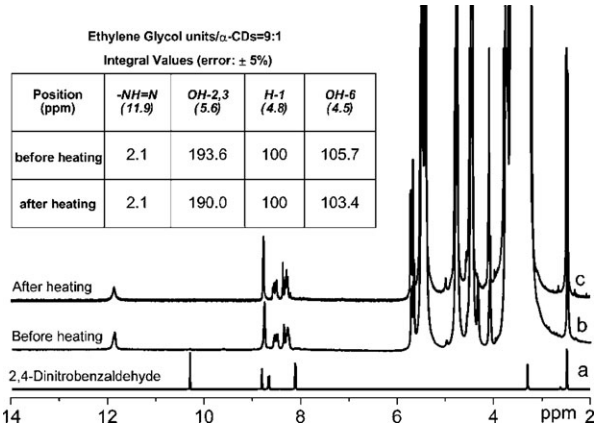

Fig. 2 ^{1}H NMR spectra of PEG2k-2DNBA and α-CD mixtures (ethylene glycol units : α-CDs = 9 : 1) in DMSO-d_6: (a) pure 2,4-dinitrobenzaldehyde, (b) mixture before heating, and (c) mixture after keeping at 120 °C for 32 h (concentration: 600 mg ml^{-1}; integral error: ±5%).

2.36 : 1, much larger than the value reported by Harada and co-workers.[12] The bulky stoppers prevent α-CDs from fully incorporating into the PEG chain during reversible chain exchange, so it is higher than the theoretical value (2 : 1) in the presence of excess α-CDs in the heating mixtures.

WAXD spectra of the purified products obtained from mixtures of PEG2k-2DNBA and α-CDs heated at 120 °C for 32 h are shown in Fig. 4. The pure α-CD crystals are piled up as a "cage-like" structure, with its characteristic diffraction peaks around 12.3 and 13.2°. In the WAXD spectra of the purified products, the appearance of the strong diffraction around 20° indicates the crystal structure changing from "cage-like" to "channel-like".[12,13] It proves that the α-CDs are threaded onto the PEG chain during the heating process. Moreover, the solid-state ^{13}C CP/MAS NMR, DSC and UV-Vis experiments in the ESI† also confirm the formation of α-CD based polyrotaxane.[13]

The 9-anthracene end group is frequently used as a big stopper for β-CD based polyrotaxane. We find that polyrotaxanes can also be constructed by heating mixtures of α-CDs and bis(9-anthracene)-PEG2k with acylhydrazone bonds

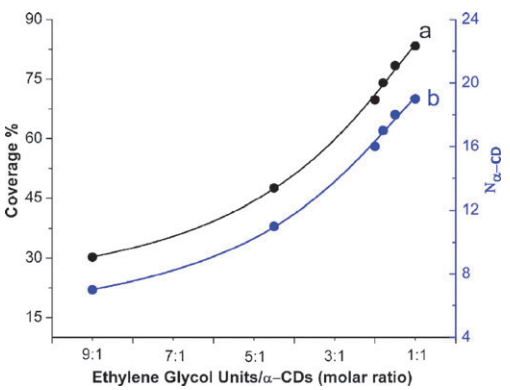

Fig. 3 Stoichiometry calculation of α-CDs in the polyrotaxane: (a) coverage of α-CDs in the polyrotaxane (coverage = 2 (α-CD per chain)/(PEG repeat units)), and (b) the number of α-CDs in the purified products from different samples kept at 120 °C for 32 h (calculation error: ±8%).

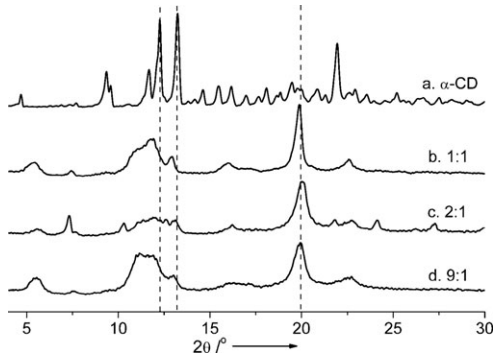

Fig. 4 WAXD spectra of (a) pure α-CD, (b) purified product of PEG2k-2DNBA/α-CD (ethylene glycol units : α-CDs = 1 : 1), (c) purified product of PEG2k-2DNBA/α-CD (ethylene glycol units : α-CDs = 2 : 1) and (d) purified product of PEG2k-2DNBA/α-CD (ethylene glycol units : α-CDs = 9 : 1).

(PEG2k-2AD) at 120 °C. On the other hand, no inclusion complexes form when heating mixtures of α-CDs and PEG2k-2DNFB (2,4-dinitrofluorobenzene modified PEG2k without reversible bonds) at 120 °C for 32 h, illustrating that 2,4-dinitrophenyl is bulky enough to prevent the slipping of α-CDs in the PEG chain. Therefore, it can be inferred that the formation of inclusion complexes between α-CDs and PEG2k-2DNBA results from the reversible chain exchange of acylhydrazone bonds.

In conclusion, a novel method to construct polyrotaxanes *via* reversible chain exchange has been developed. Mixing α-CDs with dumbbell-like PEG derivatives with reversible covalent bonds at 120 °C, the PEG crystals melt. Meanwhile, the reversible chain exchange between acylhydrazone bonds occurs, which would be the chance for α-CDs slipping into the PEG chain. Considering the strong complexation ability between linear PEG and α-CDs, more and more α-CDs are threaded onto the PEG2k-2DNBA chain. Thus, polyrotaxane forms.

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