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A Supramolecular Multi-Block Copolymer with a High Propensity for Alternation

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Within the area of supramolecular polymer chemistry, there is considerable interest in alternating[1] block copolymers.[2] In mixing oligomers or polymers with complementary recognition units at both pairs of chain ends, several superstructures might form. Figure 1 shows three limiting cases. If the recognition unit in A self-associates, A can form homopolymer A_n. If B binds A, but not itself, addition of B to A leads to chain lengthening when $[B] < [A]$ but shortening when $[B] > [A]$ as the B unit acts as a chain stopper (upper path Figure 1a). This scenario was recently described by Meijer, Sijbesma, and their co-workers, along with cyclization in the $[B] < [A]$ regime.[3] If however, A and B bind each other as strongly as they self-associate, addition of A to B_n or B to A_n leads to chain extension and random copolymers (lower path Figure 1a). In short, the strength and fidelity with which the recognition units in A and B bind one another dictates the structure formed and its properties. Fidelity becomes a special concern when A and B contain polymers with different physical properties because the drive for phase separation may dominate the equilibria in Figure 1.

We recently reported that recognition unit **1** (UG) and **2** (DAN) form complex **1·2**, with exceptional stability (Figure 2a) and fidelity of pairing (**1**, $K_{\text{dimer}} = 200\ \text{M}^{-1}$; **2**, $K_{\text{dimer}} < 10\ \text{M}^{-1}$).[4,5] Indeed, both the pairing stability and fidelity greatly exceed that of DNA base pairs.[6] We report herein that these properties are useful in creating the limiting supramolecular copolymer represented in Figure 1b, a linear multi-block copolymer where blocks of poly(butyl methacrylate) (PBMA) have a high propensity to alternate with poly(ethylene glycol) (PEG) segments.

The oligomers and polymers, end-functionalized with UG or DAN (**3**−**6**), were prepared by standard methods as described in the Supporting Information. The MW of PBMA **3** determined by dynamic light scattering was 100 kDa. Combining this value with the ratio of ^{1}H NMR integrals for the aromatic protons of DAN ($\delta = 8.2-8.6$ ppm) and the methylene protons of the main backbone ($\delta = 4.0$ ppm) indicated that at least 95% of the ends of **3** contained DAN.[7]

Supramolecular polymers from mixtures of **3** and **5** could be observed by viscometry.[8] Thus, as shown in Figure 3a, addition of **5** to a solution of **3** gradually increased the viscosity up to one equivalent where η_{SP} levels off. Additionally, as seen in Figure 3b, the viscosity of the mixture at this composition exhibited a significantly larger increase with concentration than did **3** or **5** alone, or a mixture of **3** with PEG (2 kD)[7] where no significant entanglements were observed. Additionally, η_{sp} of a mixture of **3** with PEG (5 kD) bearing a UG unit at one end, where formation of a triblock is expected, exhibited a η_{sp} versus concentration profile very similar to that of **3** (see Figure S4).[7] Combined with ^{1}H NMR data for **3·5** ($CDCl_3$) showing UG·DAN heterocomplexation, these data are consistent with alternating chain growth as the concentration of **3·5** is increased and as the stoichiometry approaches 1:1.

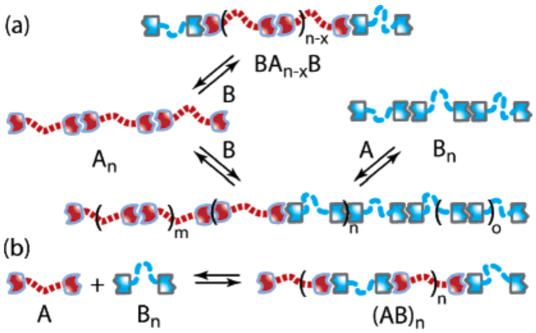

Figure 1. (a) Two examples of how addition of B to A_n will affect chain length and structure. (b) Strictly alternating, block copolymer.

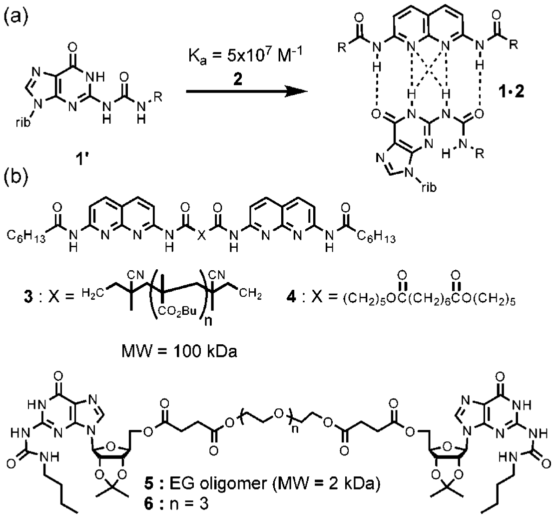

Figure 2. (a) Strong UG·DAN heterocomplex (**1·2**). (b) Structure of bifunctional polymers and oligomers **3**−**6**.

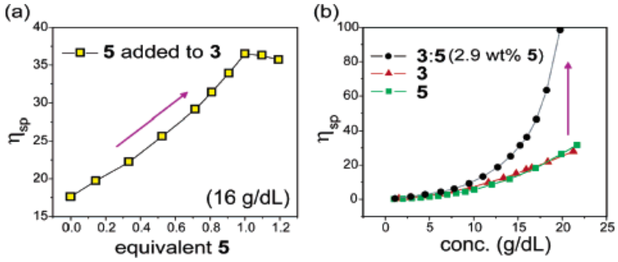

Figure 3. (a) Specific viscosity (η_{sp}) at 26 °C of 16 g/dL (1.6 mM) **3** in $CHCl_3$ with **5** added. The 1:1 equivalence point is at ca. 2.9 wt. (b) Specific viscosity (η_{sp}) of $CHCl_3$ solutions of **3** (red), **5** (green), and their mixture (2.9 wt % **5**) (black) versus concentration.

Unlike supramolecular network polymers,[4c] the SEC of **3·5**[7] failed to show assembly, possibly as a result of the dissociation of units,[9] unfavorable interactions between the PEG and PBMA blocks,

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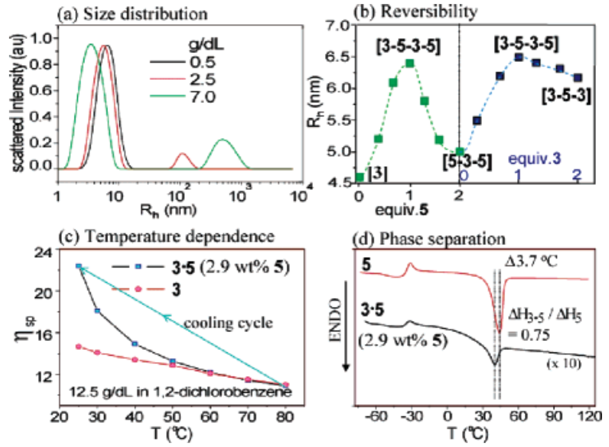

Figure 4. (a) Hydrodynamic radius (R_h) of **3·5** measured by DLS at three concentrations. (b) R_h at various ratios of **3** and **5** at C^* (0.05 mM, 0.5 g/dL). Titration of **3** with 2 equiv of **5** followed by titration with **3**. Brackets indicate composition of copolymers. (c) Dependence of specific viscosity (η_{sp}) of **3·5** and **3** as a function of temperature in 1,2-dichlorobenzene. (d) DSC thermograms (second heating) of **3·5** and **5**.[7] T_m and ΔH_m of PEG unit in **3·5** are 3.7 °C and 25% lower than for **5**.

or steric inaccessibility of the recognition units. In contrast, **4·6** exhibits the sharpest peak with the shortest retention time when the recognition units are in a 1:1 ratio. The MW determined both by SEC and VPO suggested formation of, on average, a 3:3 aggregate, presumably cyclic.[3,7] The **4·6** mixture was not extensively studied because of its higher propensity for cyclization.

To examine the **3·5** structure in more detail, its hydrodynamic radius (R_h) was measured in chloroform by dynamic light scattering (DLS). The concentration of the 1:1 complex (ratio of UG to DAN units) was limited by the high viscosity above 10 g/dL. As seen in Figure 4a, at 0.5 g/dL, a small, oligomeric species is present which can be estimated to have an average structure of $(\mathbf{3})_2(\mathbf{5})_2$. As the concentration is increased, a much larger particle grows both in size and intensity, along with a reduced R_h for the smaller particles due to increased hydrodynamic repulsive forces between particles.[7] At 7 g/dL, the larger particle has a MW > 10^7 Da. Although at this concentration it represents a very minor component, it is possible that this species contributes to the dramatic increase in viscosity. It is possible that a kinetic barrier separates the small and large aggregates and, indeed, there is some increase in intensity of the large aggregate over time.

Because the ^{1}H NMR spectrum does not show UG and DAN units bound and free (chain ends),[7] either they are in fast exchange or the aggregates are cyclic despite the polymeric structure separating the chain ends.[11] The formation of the larger particles above the overlap concentration (C^*) must occur by agglomeration or incorporation of smaller aggregates into larger ones.

The reversibility, qualitative rate of mixing and exchange, and alternation of the oligomeric species were examined by a double titration experiment of **3** and **5** at C^*. As shown in Figure 4b, addition of **5** to **3** within seconds induced an increase in R_h. A maximum size of ca. 6.5 nm (approximate structure: **3**−**5**−**3**−**5**) was reached at 1 equiv, whereupon addition of **5** resulted in a decrease in R_h as **5** began to act as a chain stopper. Subsequent addition of 1.0 equiv of **3** reversibly formed the tetramer. Further addition of **3** reduced the R_h but less dramatically than did **5**, probably because the UG unit in **3** weakly self-associates. These data indicate ready subunit exchange in a kinetically reversible superstructure with a high propensity for alternation.

A key feature of supramolecular polymers is reversibility induced by external stimuli. As shown in Figure 4c, a 12.5 g/dL solution of **3** alone and with 2.9 wt % **5** in 1,2-dichlorobenzene exhibited identical η_{sp} values at 80 °C but upon cooling **3·5** shows a significant increase in viscosity. Interestingly, the DSC of **3·5** exhibits a distinct T_m that is 25% lower than that seen in **3** (Figure 4d). The measurement of a T_m with only 2.9 wt % **5** indicates phase separation of the PEG blocks. In covalently alternating block copolymers with a low mol % of PEG or with a high degree of alternation, no phase separation is observed.[10] This apparent difference between covalent and noncovalent block copolymers may reflect the ability of the latter system to reorganize through dissociation of the recognition units.

In conclusion, we have shown the formation of an alternating, supramolecular multi-block copolymer in which the degree of polymerization depends on the concentration and ratio of the blocks in the mixture. The ability to bring together polymeric blocks of different structure and properties in a precise way is possible because of the high affinity and fidelity inherent in the UG·DAN complex. As the tool kit of recognition units expands, progressively more complex supramolecular polymeric structures will be accessible.

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Supporting Information Available: Detailed synthetic procedures and characterization data for radical initiator and compounds **3**−**6**, and detailed ^{1}H NMR, DLS, VPO, and SEC data. This material is available free of charge via the Internet at http://pubs.acs.org.

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