Communication

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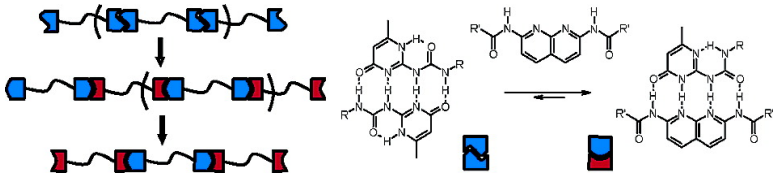

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Complementary Quadruple Hydrogen Bonding in Supramolecular Copolymers

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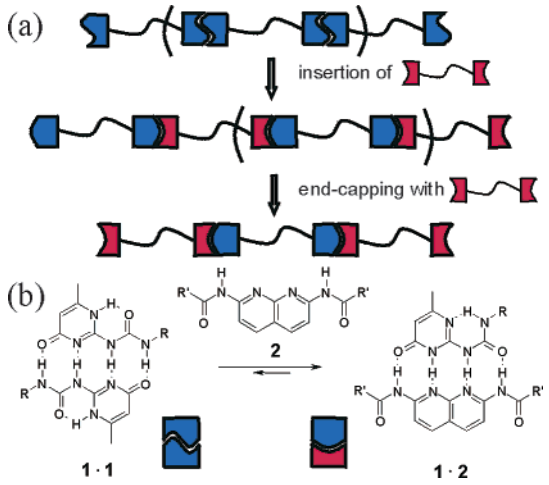
This paper describes a supramolecular copolymer with continuously tunable composition from pure homopolymeric to strictly alternating, based on a combination of complementary and self-complementary hydrogen-bonding units (Scheme 1a). Due to the high binding strength of quadruple hydrogen-bonding motifs, high degrees of polymerization are obtained. Furthermore, simply mixing components in solution results in different degrees of comonomer incorporation.

Scheme 1



Among several noncovalent interactions used in the self-assembly of polymers,[1] multiple hydrogen bonds have taken a prominent position.[2] The first supramolecular polymers, as well as more recent examples, are based on complementary hydrogen-bonding units,[3,4] while complementarity and self-complementarity were combined in calixarene urea-based polymers.[5] Supramolecular polymers based on self-complementary 2-ureido-4[1*H*]-pyrimidinone (UPy) units, **1**, were shown to have high degrees of polymerization (DP) in bulk as well as in solution,[6] due to the very high binding strength (K_{dim} = 6 × 10^7 M^{-1} in $CDCl_3$).[7]

Recently, Li and co-workers[8] have reported the strong and selective complexation of the 6[1*H*] tautomeric form of **1** with 2,7-diamido-1,8-naphthyridines,[9] **2** (Napy), via quadruple hydrogen bonds between ADDA and DAAD arrays (Scheme 1b). One equivalent of Napy in $CDCl_3$ disrupts the UPy dimers. The high selectivity and strength render the UPy−Napy heterodimer very attractive for constructing complementary supramolecular copolymers. Therefore, we decided to study heterodimerization between bifunctional molecules in more detail.

The study of UPy−Napy supramolecular copolymers required the synthesis of bifunctional Napy derivatives on a multigram scale. To this end, an efficient route based on Buchwald amidation[10] of 2-amido-7-chloro-1,8-naphthyridine with hexanedioic amide was developed to obtain bifunctional Napy derivative **3**, which contains 2-ethylhexamido substituents for added solubility.

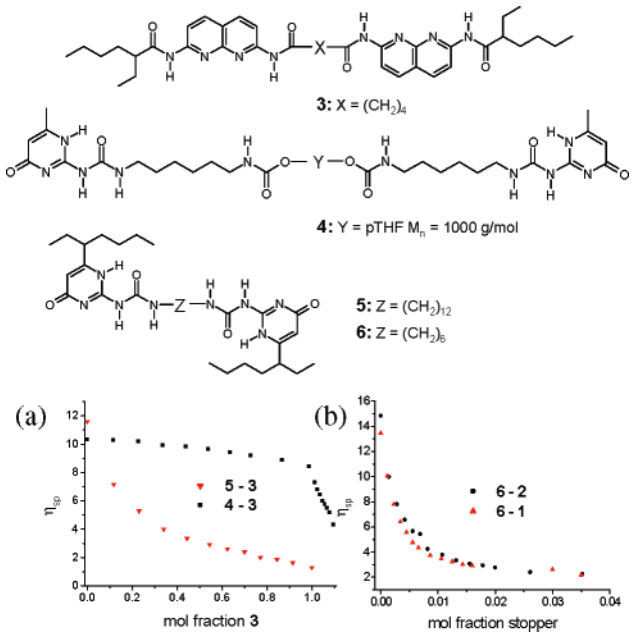


Figure 1. (a) (■, black): Specific viscosity of 25 mM *p*-THF1000bisUPy **4** in chloroform as a function of added bisNapy **3**. (▼, red): Specific viscosity of 40 mM bisUPy **5** in chloroform as a function of added bisNapy **3**. (b): Specific viscosity of 40 mM bisUPy **6** in chloroform as a function of added monofunctional Napy **2** (●, black) and UPy **1** (▲, red).

Subsequently, UPy−Napy complexation in supramolecular polymers was studied using **3** and bifunctional UPy derivatives **4**−**6**. Titration of a 25 mM solution of UPy telechelic polytetrahydrofuran[11] **4** (M_n = 10^3 g/mol; UPy end-group functionality > 1.98)[12] with **3** resulted in a viscosity plot with two distinct regions (Figure 1a). Upon addition of <1 equiv of **3**, only a small decrease in viscosity was observed, changing from η_{sp} = 10.4 for the pure solution of **4** to η_{sp} = 8.5 in the presence of 0.99 equiv of **3**. However, when a further 0.1 equiv of **3** was added, η_{sp} suddenly dropped to 4.3. In contrast to the behavior of macromonomer **4**, titration of a 40 mM solution of short bifunctional UPy **5** or **6** with **3** gave the strongest decrease in viscosity in the initial part of the titration (Figure 1a).

The results obtained for systems **4**−**3** and **5**−**3** can be rationalized considering the combined effects of selective heterocomplexation and different propensities of short and large monomers to form cyclic dimers.

Upon titration of macromonomer **4** with **3**, only a limited amount of cyclic heterodimer is formed. Instead, **3** is incorporated in the supramolecular polymer chain until a strictly alternating copolymer is obtained at a 1:1 ratio of monomers. When the equivalence point is exceeded, however, additional molecules of **3** can no longer be incorporated into the polymer chains. They therefore act as end-cappers, and the length of the alternating copolymer is progressively reduced. The observed effect in the second stage of the titration is

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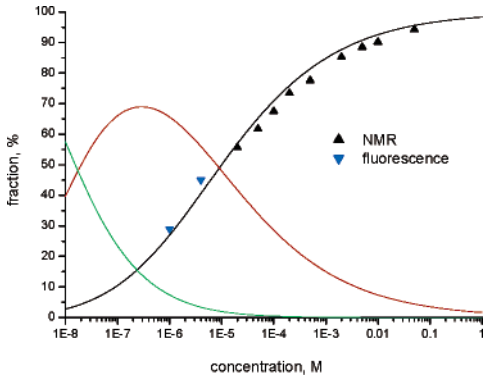

Figure 2. Measured fractions of UPy present in UPy−Napy heterodimer determined by NMR (▲) and fluorescence (▼). Calculated (see Supporting Information) fractions of UPy in UPy−Napy (black), UPy_2 (red), and free UPy (green) as a function of concentration (M) in a 1:1 mixture of UPy and Napy. K_{dim}(UPy) = 6 × 10^7 M^{-1}, K_a(UPy−Napy) = 5 × 10^6 M^{-1}.

analogous to the effect of adding monofunctional UPy[6a] (**1**, R = *n*-butyl) or monofunctional Napy (**2**, R′ = undecyl) to a solution of bifunctional UPy **6** in $CHCl_3$ (Figure 1b).

Cycle formation from short monomers **5** and **3** is anticipated to be significant. The extent to which this occurs in the titration may be probed by comparing the effects of *adding* **3** and *removing* **5** from a solution of **5**. The changes in viscosity are remarkably similar. For example, when 4.7 mM **3** was added to a 40 mM solution of **5** (η_{sp} = 11.6), η_{sp} decreased to 7.2, while a value of 7.4 was observed when the concentration of **5** was reduced by 5 mM. Ring-chain equilibria are characterized by a critical concentration,[13,14] below which only cyclic species are present, and the viscosity data strongly suggest the quantitative formation of cyclic heterodimers **5**−**3**. Cycle formation in this system is further supported by the high relative diffusion constant of complexed **3** observed in diffusion-ordered NMR experiments (see Supporting Information).

Selective formation of an alternating copolymer as described above requires very selective heterocomplex formation. The position of the equilibrium, UPy_2 + 2 Napy ⇆ 2 UPy·Napy (Scheme 1), and hence the selectivity of heterocomplexation are expected to be concentration dependent due to mass-action. Therefore, selectivity was measured upon dilution of a 1:1 mixture of **1** (R = *n*-butyl) and **2** (R′ = undecyl). As UPy_2 and UPy−Napy dimers are in slow exchange on the ^{1}H NMR time scale, separate signals for both UPy_2 and Napy-bound UPy can be seen. At concentrations as low as 2 × 10^{-5} M, the corresponding signals in 1:1 mixtures of **1** and **2** could be integrated. Dilution from 5 × 10^{-2} to 2 × 10^{-5} M resulted in a decrease in selectivity from 93 to 56% heterocomplexation.

Below concentrations of 10^{-5} M, where the sensitivity of NMR is insufficient, selective heterodimerization was studied by fluorescence spectroscopy (see Supporting Information).[15] The combined ^{1}H NMR and fluorescence data are in very good agreement with selectivities calculated for K_a(UPy−Napy) = 5(±2) × 10^6 M^{-1} and K_{dim}(UPy) = 6 × 10^7 M^{-1} (Figure 2). The observed selectivities are in disagreement with the reported value of K_a(UPy−Napy) = 1.5 × 10^9 M^{-1}, which was determined using a competitive binding model, without noting the concentration dependency.[8b]

In conclusion, we have shown that the relative values of K_{dim}(UPy) and K_a(UPy−Napy) (6 × 10^7 and 5 × 10^6 M^{-1}, respectively) lead to concentration-dependent selectivity, favoring the heterodimer above 10^{-5} M. The selectivity at higher concentrations induces the formation of cyclic heterodimers in mixtures of bifunctional UPy and Napy derivatives with short linkers, whereas polymeric linkers lead to alternating supramolecular copolymers. In contrast to polymer systems solely based on complementary hydrogen-bonding units, these polymers retain a high DP over a broad composition range. A large diversity of supramolecular copolymers can now be obtained by variation of the nature of linker units X and Y in monomers **3** and **4**.

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Supporting Information Available: Synthesis and characterization of compounds **2**−**6**. Derivation of equilibrium equations. Experimental data of NMR and viscometry measurements. This material is available free of charge via the Internet at http://pubs.acs.org.

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