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Selective Formation of Cyclic Dimers in Solutions of Reversible Supramolecular Polymers

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Supramolecular polymers[1−21] are chains of molecules, reversibly connected through noncovalent interactions; the reversibility allows these polymers to respond strongly to environmental changes. We have shown that quadruple hydrogen bonding between 2-ureido-4[1*H*]-pyrimidinone units[22−24] (Figure 1), with an association constant of 6×10^7 L mol^{-1} in chloroform,[25] can serve as a strong, directional, and reversible bond for the construction of supramolecular polymers with high degrees of polymerization.[13] These polymers[26−28] and other hydrogen-bonded supramolecular polymers[29] show pronounced viscoelastic behavior, while the concentration-dependent viscosity in solution is in accordance with Cates' model[30−32] for reversible polymers. We also observed that monomers containing strongly preorganized spacers selectively form cyclic dimers.[33] The equilibrium between rings and chains in reversible polymers has been mainly restricted to theoretical studies,[34−37] because it is not possible to isolate rings from linear chains in an equilibrium system. Recently, cyclization in associated acid-terminated poly(dimethylsiloxanes) has been inferred from quantitative IR measurements of the terminal acid groups and solution viscosimetry.[38] In the condensation polymerization[39] of covalent polymers,[40−42] cyclization is a well-studied issue, both theoretically and experimentally. An intriguing phenomenon in these polymerizations is the occurrence of a critical monomer concentration, below which virtually no polymer is produced and cycles are the main species formed. Above this concentration, the concentration of cyclic product is constant. Here we present direct experimental confirmation of a critical monomer concentration in solutions of bifunctional 2-ureido-4[1*H*]-pyrimidinone (UPy) derivatives, which have a favorable structure to selectively form cyclic heterodimers. Molecular models show that bifunctional UPy derivatives of type **1**, with short alkyl spacers (shorter than 14 carbon atoms), cannot cyclize intramolecularly, while the formation of cyclic dimers is strongly restricted. Since the UPy units associate in an antiparallel fashion, linear dimers **1·1** (Figure 1) can only cyclize when the two free UPy units fold back and stack on top of the dimerized units. Similar conformational restrictions apply to cyclic dimers **2·2**, in which the alkyl spacers are connected at the 6-position of the UPy moieties. It

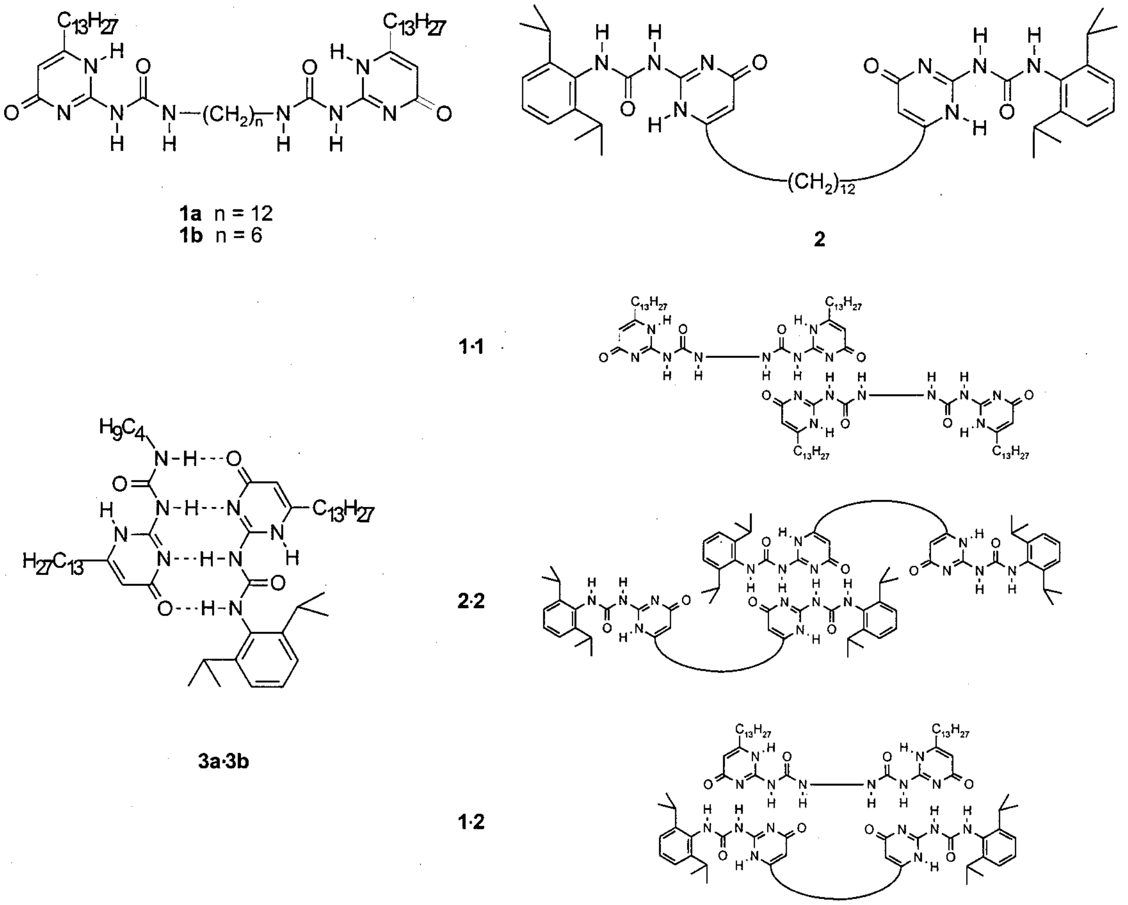

Figure 1. Bifunctional 2-ureido-4[1*H*]pyrimidinone derivatives **1** and **2**. Dimer of monofunctional compounds **3a** and **3b**. Homo- and heterodimers of **1** and **2**.

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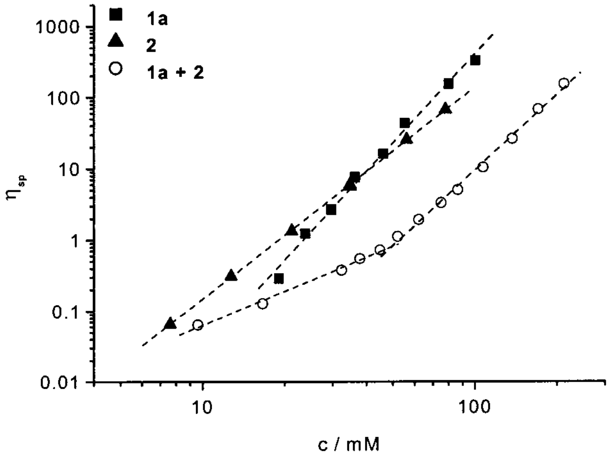

Figure 2. Specific viscosity of chloroform solutions of compounds **1a** and **2** and of equimolar mixtures as a function of concentration.

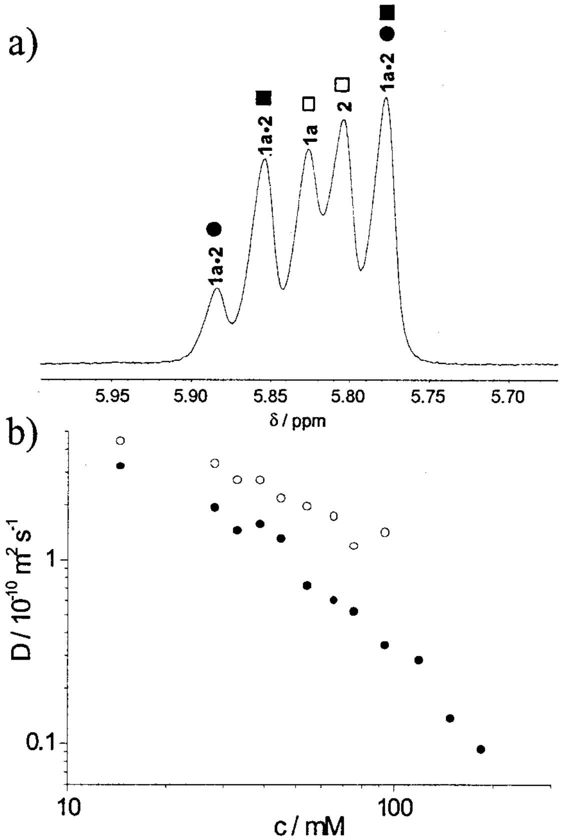

Figure 3. (a) Alkylidene region of a 500 MHz ^{1}H NMR spectrum of an equimolar mixture of the bifunctional 2-ureido-4[1*H*]pyrimidinone monomers **1a** and **2** at 60 mM in CDCl$_3$: (●) signals of cyclic heterodimers; (■) signals of heteroassociated units in oligomeric cycles and polymers; (□) signals of homoassociated units in oligomeric cycles and polymers. (b) Apparent self-diffusion coefficients of the species resonating at 5.88 ppm and the averaged value of the species resonating at 5.80, 5.82, and 5.85 ppm. The relative intensity of the peak at 5.88 ppm is sufficient only below a total concentration of 110 mM to evaluate the diffusion coefficient reliably.

is evident from Figure 1 that a much larger range of conformations of dimers **1·2** can cyclize, because an antiparallel arrangement of the two free UPy units is imposed by the topology of the linear heterodimer. Cyclization of **1**, of **2**, and of their equimolar mixtures was studied using (Ubbelohde) viscosimetry, ^{1}H nuclear magnetic resonance, and ^{1}H NMR diffusion measurements in chloroform solution. The 2,6-diisopropylphenyl derivative **2** was used because the phenyl groups are forced to be perpendicular to the UPy unit to which they are connected and thus hamper formation of cyclic dimers with stacked UPy groups. The chemical shift anisotropy of the phenyl groups in **2** also facilitates spectroscopic characterization of complexes, because it induces distinct shift differences in ^{1}H NMR between homo- and heteroassociated units, as was employed earlier in the study of monofunctional UPy analogues.[25]

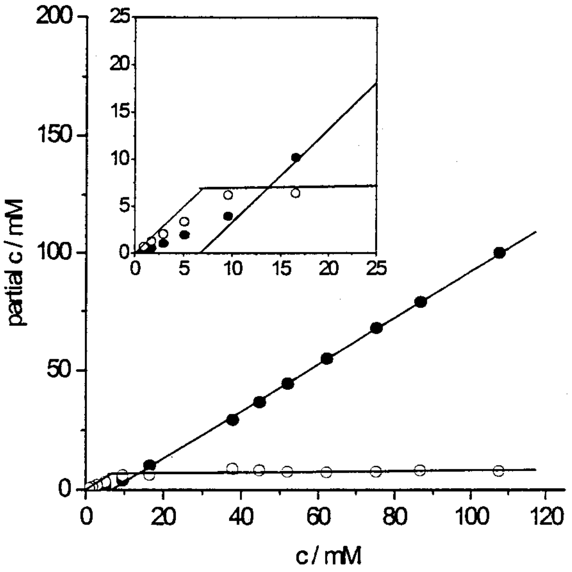

Figure 4. Partial concentrations as a function of overall concentration of a stoichiometric mixture of bifunctional monomers **1a** and **2** in CDCl$_3$: (○) population of cyclic heterodimers; (●) oligomeric cycles and polymers. Lines indicate predicted partial concentrations in the absence of oligomeric cycles.

The concentration dependence of the solution viscosity gives important information on the aggregation behavior of compounds **1** and **2**. Double-logarithmic plots of the specific viscosity (η_{sp}) vs concentration of **1a** and **2** have slopes of 4.1 and 3.0, respectively, in chloroform (Figure 2). The strong concentration dependence indicates that entangled aggregates of increasing size are formed.[30−32] When the viscosity of equimolar mixtures of **1a** and **2** was studied, a completely different concentration-dependent viscosity was observed. While at concentrations above 50 mM an intermediate slope of 3.5 was found, although at a specific viscosity which is approximately 1 order of magnitude lower than for the separate components, the slope of η_{sp} vs concentration decreases toward much lower values below 50 mM. This indicates that much smaller aggregates predominate. Since the high dimerization constant ($K_{dim} = 6 \times 10^7$ L mol^{-1}) of the 2-ureido-4[1*H*]pyrimidinone group in CDCl$_3$ does not allow the presence of a high concentration of free end groups, these aggregates must be cyclic.

^{1}H NMR spectra of the equimolar mixtures of **1a** and **2** (at 293 K) were measured at concentrations varying from 0.96 to 185 mM overall concentration. At high concentrations, four peaks of comparable intensity were observed at 5.78, 5.80, 5.82, and 5.85 ppm for the pyrimidinone alkylidene CH protons of **1a** and **2**. The same number of peaks, with equal intensities and at practically identical positions (5.77, 5.80, 5.82, and 5.85 ppm), was observed in an equimolar mixture of monofunctional derivatives **3a** and **3b**, which strongly suggests that at high concentrations **1a** and **2** form a statistical copolymer and that the number of peaks is due to shift differences between homo- and heteroassociated units in the polymer. The signals at 5.80 and 5.82 ppm correspond to peak positions of the homoassociated UPy groups of **1a** and **2**, respectively, while the two remaining peaks are assigned to heteroassociated linear units. At low concentrations, only two signals of equal intensity are observed in the mixture (5.88 and 5.78 ppm), which are absent in dilute solutions of the separate compounds. This leads us to conclude that in the small cyclic aggregates selective heteroassociation between **1a** and **2** takes place. The generality of the selective heteroassociation is supported by the fact that very similar spectra with identical peak positions are observed for dilute equimolar solutions of **1b** and **2**. At intermediate concentrations, a combination of the two subspectra is observed, the peak at 5.78 ppm consisting of two coinciding signals. A section of the NMR spectrum of a 60 mM solution of **1a** and **2** is shown in Figure 3. The relative sizes of these spectroscopically distinguishable aggregates in the mixtures were probed by determining their apparent self-diffusion coefficients with ^{1}H NMR[43,44] using the BPP-LED pulse sequence proposed by Johnson[45] (Figure 3). Over the whole concentration range, the diffusion coefficient of the aggregate with a peak at 5.88 ppm is significantly higher than that of the other aggregates, confirming its smaller size. The heteroassociated cyclic aggregate can be a dimer or it may be a larger even-membered ring. On the basis of its ring size (it contains 26 single bonds and two partly flexible quadruple hydrogen bonds), the cyclic heterodimer **1·2** is expected to be virtually strainless.[46] The theory of Jacobsen and Stockmayer[40] predicts that the equilibrium concentration of unstrained rings decreases with the $^5/_2$ power of their size and that cyclic tetramers consequently have a concentration that is approximately 5.7 times lower than the cyclic dimer. We therefore conclude that the spectroscopically distinguishable cyclic aggregate observed in mixtures of **1** and **2** is the cyclic heterodimer and that other cyclic species (homodimers and larger homo- or heteroassociated cycles) either resonate at a different position in the NMR spectrum or have a low abundance.

The concentration of molecules present in the cyclic heterodimers and in the remaining aggregates (other cycles and polymers) was determined quantitatively by deconvolution of the peaks in the alkylidene region of the ^{1}H NMR spectrum and is plotted against the total concentration of bifunctional molecules in Figure 4. It is immediately clear that these populations have completely different concentration dependence. At low concentration, the cyclic heterodimer predominates, and the population of all other species is low. Above an overall concentration of about 7 mM, the concentration of molecules residing in cyclic heterodimers is constant at a value of 7 mM, while the concentration of the other species increases linearly. Theories of ring–chain equilibria[35,40] predict that up to the critical concentration, where the concentration of all cycles becomes constant, the concentration of polymer is vanishingly small, and all aggregates are cyclic. The inset in Figure 4 shows that below 9 mM a small fraction of material is present outside the cyclic heterodimer. We propose that this material mainly consists of oligomeric cycles, which are spectroscopically indistinguishable from linear polymer.

In summary, we have shown that specific formation of cyclic heterodimers results in a strong shift of the ring–chain equilibrium in equimolar mixtures of **1** and **2** compared to solutions of the separate compounds. Using the spectroscopic differences between cycles and chains, and between homoassociated and heteroassociated UPy units, the equilibrium was investigated quantitatively. The presence of a critical concentration, above which the concentration of cycles is constant, has been confirmed experimentally in a reversible system. We are now focusing our attention on using the cyclizaton in solution to form polymer blends in the solid state and on studying the effect of the ring–chain equilibrium on phase separation in supramolecular polymers.

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Supporting Information Available: Synthesis of compounds **1**–**3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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