Sequence control in supramolecular copolymers is limited by the selectivity of the associating monomer end groups. Here we introduce the use of monomers with amino-pyrimidinone and amino-hydroxy-naphthyridine quadruple hydrogen bonding end groups, which both homodimerize, but form even stronger heterodimers. These features allow the formation of supramolecular copolymers with a tunable composition and a preference for alternating sequences.

More than 20 years after the introduction of the term supramolecular polymer, the field continues to develop rapidly.\textsuperscript{1,2} Applications such as biomedical materials\textsuperscript{3} and self-healing materials\textsuperscript{3} are being explored, and the details of supramolecular polymerization processes have become a subject of detailed study.\textsuperscript{4} However, in at least one aspect supramolecular polymers remain behind their covalent counterparts, viz. in control over monomer sequences in copolymers. The use of well-designed multiple hydrogen bonding units potentially provides the selectivity and strength to create the desired control. Self-complementary quadruple hydrogen bonding motifs\textsuperscript{5} have been shown to be useful in the formation of supramolecular homopolymers. In addition, a variety of complementary hydrogen bonding motifs has been reported,\textsuperscript{6} as well as the possibility to exploit these to form supramolecular copolymers with highly alternating structures in mixtures with a strict 1:1 stoichiometry.\textsuperscript{7} Another approach toward these highly alternating structures relies on self-sorting in mixtures of two AB-type heteroditopic monomers.\textsuperscript{8}

Multiple hydrogen bonding units that are able to switch from self-complementary to complementary modes of complexation would allow the formation of alternating copolymers with tunable composition and a degree of alternation that depends on the selectivity of heterocomplexation.\textsuperscript{9} Here we describe the combination of two quadruple hydrogen bonding units, amino-pyrimidinones (AminoUPy) and amino-hydroxy-naphthyridines (NaPyO), in which this capability is inherently present. Monomers functionalized with two of these units form supramolecular polymers. The selectivity for heterocomplexation results in the formation of copolymers with tunable composition and a preference for alternating sequences when the monomers are mixed in solution.

In supramolecular polymers, extensive use has been made of the strong self-association\textsuperscript{10} \((K_{\text{dim}} = 6 \times 10^7 \text{ M}^{-1})\) of the 2-ureido-4\-[\text{1H}]pyrimidinone (UPy) unit via a DDAA motif of hydrogen bonding sites. UPy's are also able to form heterodimers with 2,7-diamido-1,8-naphthyridine (NaPy).\textsuperscript{11} They do so with high selectivity via a complementary ADDA-DAAD motif upon their tautomerization into the 6\-[\text{1H}]form \((K_{\text{ass}} = 5 \times 10^6 \text{ M}^{-1})\) in CHCl\textsubscript{3}). UPy-NaPy hetero-complexation has been used to form supramolecular copolymers from bifunctional bisUPy and bisNaPy monomers.\textsuperscript{11b} Alternating copolymers are formed over a broad composition range. However, the incapability of the NaPy unit to form homodimers means that the NaPy monomers act as end-cappers of the supramolecular polymer when they are present in excess to the bis-UPy monomers (Fig. 1a).

In order to obtain a system that maintains a high degree of polymerization (DP) over the whole composition range, both hydrogen bonding units must have the capability to self-associate (Fig. 1b). The NaPyO binding unit is capable of forming a homodimeric complex \textit{via} the formation of quadruple hydrogen bonds \textit{via} linear acceptor–donor–acceptor–donor (ADAD) arrays,\textsuperscript{12} UPy's with electron donating substituents at the 6-position are present in the enol-tautomeric form and are also able to dimerize using ADAD hydrogen bonding arrays.\textsuperscript{13} Consequently, a combination of both dimers is expected to result in the formation of a heterodimer (Scheme 1).

Monofunctional NaPyO binding units 1 and 2 and the bifunctional derivative 4 (Chart 1) were prepared on a multigram scale in high yields using a straightforward procedure from...
1,8-naphthyridin-2(1H)-one by reaction with aliphatic acyl chlorides (see ESI†). Naphthyridines 1 and 2 and AminoUpy 3 served as model compounds to investigate the strength and selectivity of binding. Bifunctional derivatives NaPyO 4 (NaPyO end-group functionalization >99%) having a polymeric spacer of pTHF2000 (Mn = 2000) and bisUpy 5 containing a short aliphatic spacer group were prepared to study the formation of NaPyO–Upy supramolecular copolymers.

Homodimerization constants Kdim of the NaPyO model compounds 1 and 2 were determined through fitting of concentration dependent NMR chemical shift data (CDCl3, 25 °C) and were determined to be Kdim(1) = 6 ± 1 \times 10^3 \text{ M}^{-1} (\Delta G^\circ = -21.6 \text{ kJ mol}^{-1}) and Kdim(2) = 8 ± 4 \times 10^4 \text{ M}^{-1} (\Delta G^\circ = -22.3 \text{ kJ mol}^{-1}) respectively. The dimerization constant of AminoUpy 3 (Chart 1) was reported earlier13b and has a value of Kdim(3) = 9.0 \times 10^5 \text{ M}^{-1} (\Delta G^\circ = -34.0 \text{ kJ mol}^{-1}). Hetero-complexation of AminoUpy–NaPyO was determined utilizing compounds 1, 2 and 3 by UV/Vis titration experiments in CHCl3 at a constant concentration of naphthyridine, [NaPyO] = 2.5 \times 10^{-4} \text{ M} (see ESI†). \(K_{ass}\) was obtained by appropriate fitting of the received binding curves to a model describing homodimerization of both components as well as heteroaassocation between the components. The heteroaassociation constants of the complexes were determined to be \(K_{ass}(1-3) = 5.3 \pm 0.3 \times 10^3 \text{ M}^{-1}\) (\(\Delta G^\circ = -32.5 \text{ kJ mol}^{-1}\)) and \(K_{ass}(2-3) = 2.7 \pm 0.2 \times 10^5 \text{ M}^{-1}\) (\(\Delta G^\circ = -31.0 \text{ kJ mol}^{-1}\)). Based on the free energy change obtained for the individual binding events, the free energy change for the formation of heterocomplexes from homocomplexes is calculated to be negative (\(\Delta G^\circ = -9.4 \text{ kJ mol}^{-1}\) for complex 1.3 and \(\Delta G^\circ = -5.7 \text{ kJ mol}^{-1}\) for complex 2.3) and therefore the heterocomplex is favored over the homocomplexes in equimolar mixtures of the components (Table 1).

\(^1\)H-NMR spectroscopy was also used to study the preference for hetero-complexation. However, spectra from equimolar mixtures (10 mM, CDCl3) of NaPyO 1 and Upy 3 at 298 K exhibit broadened signals particularly in the aromatic region (see ESI†). Therefore, the measurements were also performed at lower temperatures where sharpening and splitting of the peaks occurred. The recorded low temperature NMR spectra showed multiple sets of signals, which were assigned to the homo- and heterodimeric species in solution. Upon integration of the respective signals, the selectivity of the heterocomplex 1.3 was determined to be 73% at 263 K. Further lowering of the temperature led to an increased selectivity of 79% at 248 K.

Bis-functionalized derivatives 4 and 5 (Chart 1) form supramolecular homopolymers in chloroform, as shown by the concentration dependence of the specific viscosities (\(\eta_{sp}\)) which

**Table 1.** Hetero-complexation selectivity for quadruple hydrogen bonding units

<table>
<thead>
<tr>
<th>Equilibrium</th>
<th>[Heterodimer]/[homodimer]</th>
<th>298 K (UV)</th>
<th>248 K (NMR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (\rightarrow) 3 (\rightarrow) 2 (\rightarrow) 1</td>
<td>3.6</td>
<td>3.8</td>
<td></td>
</tr>
<tr>
<td>2 (\rightarrow) 3 (\rightarrow) 2</td>
<td>3.7</td>
<td>n.d.</td>
<td></td>
</tr>
</tbody>
</table>
that the degree of alternation in radical polymerizations is determined by kinetics, while in the supramolecular polymers it is determined by a ratio of equilibrium constants.

Further improvement in the system may therefore be achieved by increasing the selectivity of heterocomplexation. The origin of heteroselectivity in the NaPyO–UPy system appears not to be related to improved steric complementarity in the heterodimer, since crystal structures and energy minimized structures of the DADA arrays in both components show that they are linear within 0.1 Å.130,134 Therefore, we propose that electronic complementarity, i.e. matching of the strongest acceptor and donor sites is responsible for the observed selectivity. Current efforts are focused on improving the selectivity in donor–acceptor arrays optimized for electronic complementarity.

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Notes and references


