Supramolecular Polymers

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Amplification of Chirality by Supramolecular Polymerization of Pyrene Oligomers**

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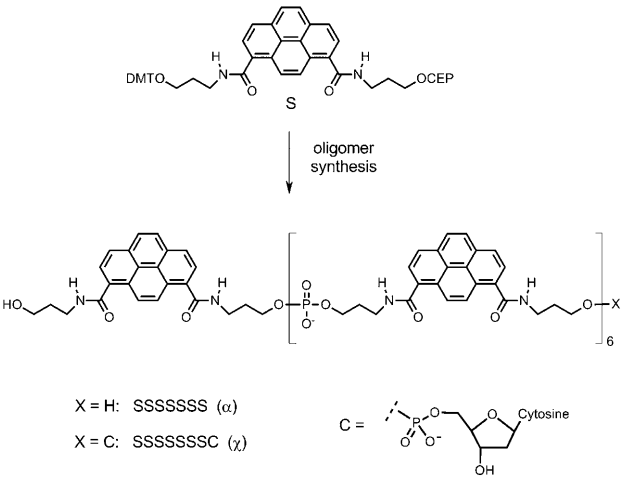
Over the past two decades, the field of supramolecular polymers[1–3] has emerged as a separate area of materials research. As in other areas of supramolecular chemistry,[4,5] the structural and functional properties of supramolecular polymers largely depend on the nature of the noncovalent interactions between the individual units.[6–9] Therefore, the macroscopic properties of the system are strongly dependent on the supramolecular organization and not solely defined by the properties of the molecular components.[10–16] While the formation of supramolecular polymers by hydrogen bonding has been explored rather intensively, systems based on aromatic stacking have been reported to a lesser extent.[17–22] The reason for this may be partly found in the limited directionality of aromatic stacking interactions compared to hydrogen bonding.[15,19,23,24] Strength and directionality of aromatic interactions may be significantly enhanced by using templates[25–29] or by applying geometrical restrictions to preorganize the individual aromatic units, thus reducing unfavorable entropic terms of the assembly process.[24,30–35] A further approach consists in the covalent linking of individual units to oligomeric building blocks. Herein we present that short oligomers of pyrenes connected by flexible phosphodiester linkers show strong amplification of chirality, which is explained by the formation of supramolecular polymers in aqueous environment. To the best of our knowledge, this is the first example of supramolecular polymerization observed with oligomeric building blocks that are not preorganized.

The synthesis of the oligomers is shown in Scheme 1. Using phosphoramidite (S),[36–41] oligomers α (achiral) and χ (chiral, as it contains a terminally attached 2′-deoxycytidine C) were assembled on a pyrene-derived polystyrene solid support by automated phosphoramidite chemistry.[42] The choice of the number of pyrene units was based on our previous studies showing that sections of seven pyrenes lead to helically organized structures in a DNA framework.[43–46]



Scheme 1. Synthesis of oligomeric pyrene strands α (achiral) and χ (chiral, bearing a 2′-deoxycytidine unit). CEP = 2-cyanoethyl-*N*,*N*-diisopropylphosphoramidite, DMT = 4,4′-dimethoxytrityl.

Investigation by UV/Vis and fluorescence spectroscopy (Figure 1) showed that a high salt concentration has a significant influence on the stacking of the pyrene residues of oligomer α, as indicated by a pronounced hyperchromicity, the appearance of vibronic structures in UV/Vis spectra (I_{355}/I_{345}, I_{280}/I_{270}, I_{245}/I_{235}) and also in the excitation spectrum (Supporting Information), and a shift in the excimer fluorescence ($\Delta\lambda_{em} = -12$ nm). Upon increasing the temperature, these effects disappear (Figure 1c,d < xfigr1, indicating a significant loss of stacking interactions between pyrenes at high temperature. Thus, under conditions of high ionic strength, oligomer α adopts a structure in which the pyrene units are conformationally restricted and twisted.[41,47–51] It is noteworthy that the vibronic structures in the UV/Vis spectra are more pronounced for the achiral oligomer α than for the chiral oligomer χ (Supporting Information). This result suggests a degree of stacking in α.

CD spectroscopy reveals no distinct signals for either of the two oligomers alone (Figure 2a). However, if α and χ are mixed in a 1:1 ratio, a non-racemic, helical structure is formed, as indicated by the appearance of strong Cotton effects. This observation can only be explained by the interaction between strands of α and χ, or in other words, the formation of mixed aggregates of the two types of strands. The CD signals disappear with increasing temperature (Figure 2b).

The appearance of a CD-active structure formed by a 1:1-mixture of α and χ prompted us to investigate the behavior of

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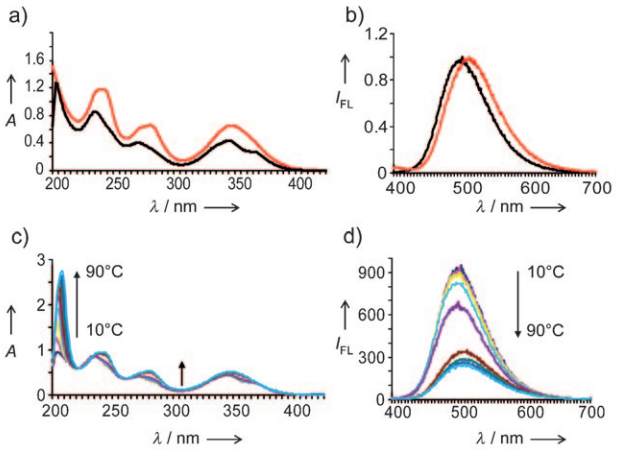


Figure 1. Absorbance and fluorescence spectra of oligomer α. a) UV/Vis, showing the influence of NaCl. Red curve: no NaCl, black: 1 M NaCl. Hyperchromicities: $H_{245}=31\%$, $H_{284}=43\%$, $H_{354}=32\%$. b) Normalized fluorescence spectra; $\lambda_{max}=512$ nm (red curve, no NaCl), 500 nm (black, 1 M NaCl). c) Variable-temperature UV/Vis spectra. d) Variable-temperature fluorescence spectra. C conditions (unless otherwise indicated): pH 7.0, phosphate buffer, 1 M NaCl, 20 °C; 5 μM oligomer concentration.

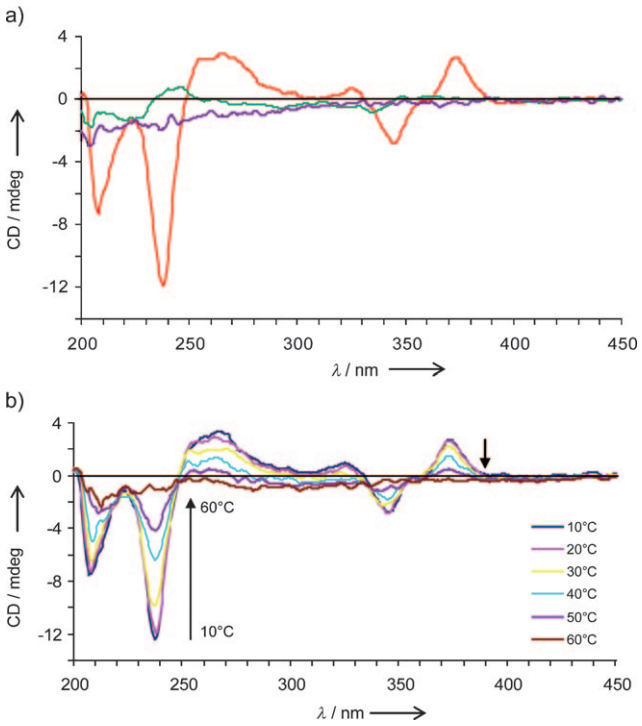


Figure 2. CD spectra of oligomers α and χ. a) α (purple) and χ (green) alone and as a 1:1 mixture (red) at 20 °C. b) Variable-temperature CD spectra of a 1:1 mixture of α and χ (1 M NaCl, pH 7.0 phosphate buffer; 5 μM total oligomer concentration).

different ratios of the two oligomers. Figure 3 shows the CD spectra obtained with various compositions of the two oligomers.

Development of the observed anisotropy is a relatively slow process, as maximum signal intensity is obtained over a

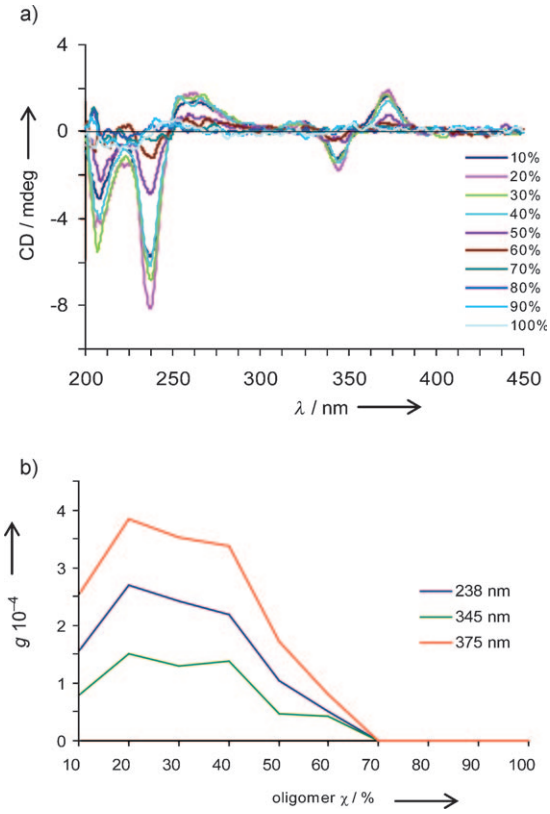
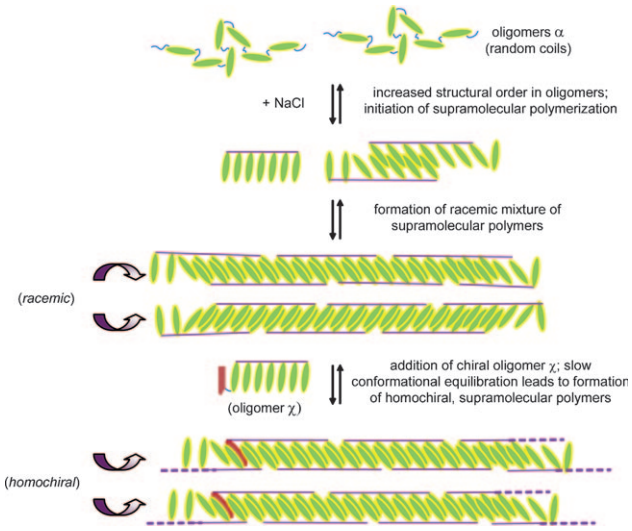


Figure 3. a) CD spectra obtained with various ratios of the two oligomers α and χ. Total oligomer concentration: 2.5 μM. b) Data presented as the anisotropy *g* factor at different wavelengths.

time range of several days (Supporting Information). The rather slow kinetics observed for the present system are a result of slow conformational changes of the extended polymers and are not surprising in view of the slow processes reported for supramolecular systems that are primarily based on aromatic stacking and/or hydrophobic interactions.[24,52]

The observed amplification of chirality[53–58] is compatible with the formation of supramolecular polymers[59] from individual pyrene oligomers. The high degree of anisotropy cannot be the result of formation of heterodimeric complexes (that is, a duplex formed by one α and one χ), because in this case, the effect should increase with the concentration of the chiral oligomer, which is opposite to our observations. The findings are in agreement with the formation of supramolecular polymers obeying the "sergeants and soldiers" rules,[60–63] as illustrated in Scheme 2. High ionic strength favors aromatic stacking between pyrene units, both intra- and intermolecularly. Intermolecular stacking leads to formation of extended aggregates of the oligomers. In the absence of chiral information, that is, in a solution containing only oligomer α, a racemic mixture of helical, supramolecular polymers (*P* and *M*)[64–66] are formed. Upon addition of small amounts of χ, the chiral oligomer is integrated into the dynamic polymers and the solution slowly equilibrates, eventually resulting in an excess of the thermodynamically favored supramolecular helices (*P* helix; see Figure 2 and Figure 3).

Agarose gel electrophoresis provided support for formation of extended aggregates. Oligopyrene α forms large



Scheme 2. Supramolecular polymer formation. High ionic strength is accompanied by pyrene stacking and interaction between individual achiral oligomers α, which leads to a racemic mixture of supramolecular helical polymers. Addition of a small quantity of a chiral inductor shifts the equilibrium in favor of the thermodynamically preferred *P* helix.

aggregates that possess approximately the same migration velocity as double-stranded DNA of approximately 500 base pairs in length (Supporting Information). Even if a direct correlation between the migration velocities of DNA and the phosphodiester-linked pyrene oligomers is not possible, this is clear evidence that α forms aggregates of dozens of oligomers. Further support for suprapolymer formation was obtained by transmission electron microscopy (TEM; Figure 4a), which revealed extended structures of a relatively uniform thickness (4–6 nm) and variable length (up to 200 nm). Furthermore, electron spectroscopic imaging (Figure 4b) showed that the linear structures possess phosphorus content, providing substantial evidence that the observed structures are aggregates of the phosphodiester-linked pyrene oligomers. In Figure 4c, the phosphorus signal is overlaid with the bright-field TEM image.

As described, the chiral induction does not grow linearly with the molar fraction of chiral oligomer, which is in contrast to previous examples of chiral amplification.[54–56] Remarkably, a gradual reduction of the fraction of chiral oligomer led to an increase of the CD signals. The highest anisotropy factor (*g* value) was reached with a 80:20 mixture of (achiral) α and (chiral) χ, which is unexpected in view of previously described systems.[55,56,61,67,68] Temperature-dependent analysis (UV absorption, Figure 5 and excimer fluorescence, Supporting Information) shows that the polymerization of α proceeds in a nucleated process, whereas aggregation of χ follows an isodesmic pattern.[69] Whereas assembly of α is cooperative, the cytidine-bearing χ behaves in a noncooperative way, preventing formation of long polymers. This explains why smaller fractions of χ lead to a higher degree of anisotropy: when only χ is present, the formation of long, conformationally defined polymers is not possible. In contrast, α alone forms long, but racemic supramolecular polymers (*M*-type and *P*-type). Mixtures of the two oligomers with a ratio of less than 70% χ lead to the formation of supramolecular polymers with a preferred helical sense (*P*-type). Larger amounts of χ (>70%) prevent the formation of nuclei of appropriate length, thereby suppressing supramolecular polymerization. Another possibility may reside in the induction of helical reversals,[60,70] by χ which would be observed as an overall racemization at high fractions of this oligomer.

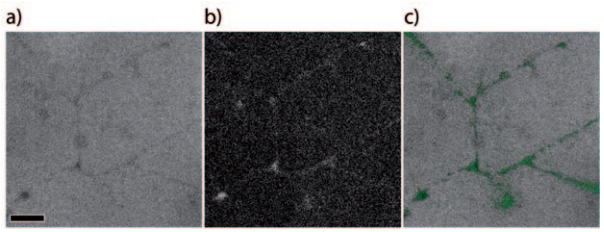


Figure 4. Transmission electron microscopy (TEM) of equilibrated solutions of oligomer α (1 M NaCl; 5 μM total oligomer concentration, no phosphate buffer). a) Bright-field TEM image; b) phosphorus map; c) overlay of phosphorus map with bright-field image. Scale bar: 50 nm.

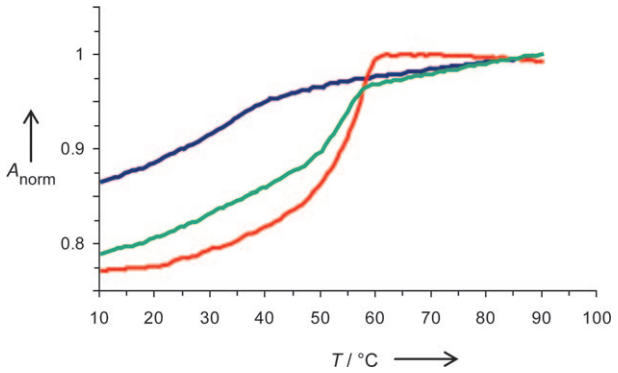


Figure 5. Cooling curves (90 to 10 °C) for cooperative (α; red) and non-cooperative (χ; blue) aggregation behavior of the two oligomers and their 1:1 mixture (green). Absorbance was measured at 354 nm.

In conclusion, chiral amplification was observed with short pyrene oligomers containing a flexible phosphodiester backbone. Highest anisotropy factors were found in the presence of lesser quantities of the chiral inductor, a pyrene oligomer containing a single 2′-deoxycytidine. Data obtained from optical spectroscopy, gel mobility experiments, and electron microscopy support a model in which pyrene oligomers form helical, supramolecular polymers through interstrand stacking interactions. The oligomers described herein are a new type of oligomeric building blocks that form supramolecular polymers under aqueous conditions.

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