Chiral Amplification in the Transcription of Supramolecular Helicity into a Polymer Backbone**

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*Dedicated to Professor Roeland Nolte
on the occasion of his 60th birthday*

Herein, we describe the expression of chirality into a polymer backbone during the photopolymerization of achiral monomers. The monomers are brought into a chiral self-organized supramolecular structure by using an enantiomerically pure structure-directing agent. The polymer obtained, despite incomplete tacticity, holds enough chiral information to fold itself into an almost homochiral, helical structure. In reporting this system we outline the first example of a chiral supramolecular "sergeant"[1] that affects backbone stereochemistry during a polymerization process by controlling the intrinsic helicity of self-assembled achiral monomers. It implies that self-organization[2–5] can play a critical role in amplifying the enantiomeric purity of the monomeric constituents of polymers.[6]

Cooperative expression and amplification of chirality present in the monomeric components of biopolymers is central to biological function, particularly with respect to folding and hierarchical self-assembly of large functional nanoscale ensembles. For synthetic chiral polymers, asymmetric synthesis of the polymer backbone with chiral monomers, catalysts, initiators, and solvents is well established.[7,8] However, in investigating why biopolymers are composed of enantiomerically pure monomers, it is useful to consider mechanisms[9,10] through which small unbalances in enantiomeric excess[11] are amplified.[12] In synthetic polymers without stereocenters, the latent helical conformation of polyisocyanates,[13] polyisocyanides,[14,15] and polysilanes[16] can be expressed by using small quantities of chiral monomer, chiral

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catalysts, and/or chiral solvents during polymerization. Similarly, noncovalent interaction of chiral molecules with the backbone of an achiral polymer can bias and express a preferred helical conformation,[17] while subsequent exchange for achiral guests results in a chiral memory effect.[18] Wholly self-organizing systems take advantage of cooperative noncovalent interactions to elicit so-called supramolecular induction of chirality[1,19] and supramolecular memory of chirality.[20] However, the kinetic lability of self-assembled architectures renders them subject to environmental stress. Recently, Feringa and co-workers used labile supramolecular chirality to enhance significantly the asymmetric induction in a photochemical ring closure.[21]

We propose herein the use of covalent fixation after self-assembly[22] as a means of obtaining kinetically robust chiral nanoscale architectures, as an extension of our previously described self-assembly and polymerization of achiral discotic **1** in apolar solvents (Scheme 1 and Figure 1).[23] By introducing an enantiomerically pure structure-directing agent, we found one handedness of the helix only. After polymerization and removal of the structure-directing agent, the polymer obtained from achiral monomers is chiral and folds into a preferred helical superstructure. Surprisingly, the folding process is more directed by the supramolecular interactions than by the tacticity of the polymer backbone.

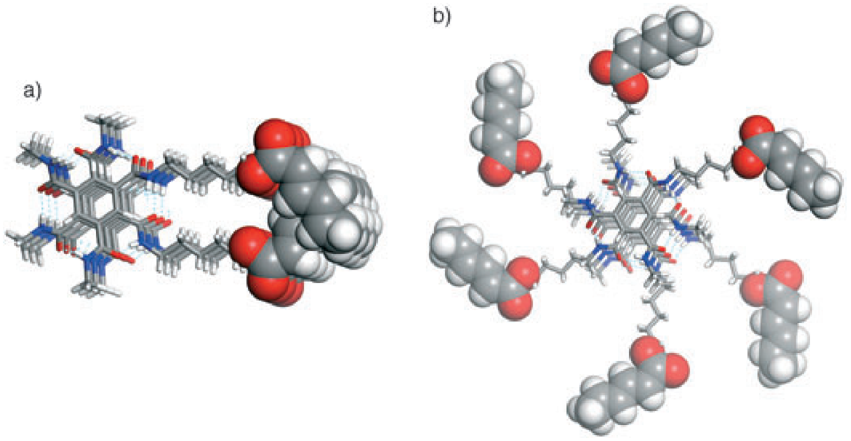
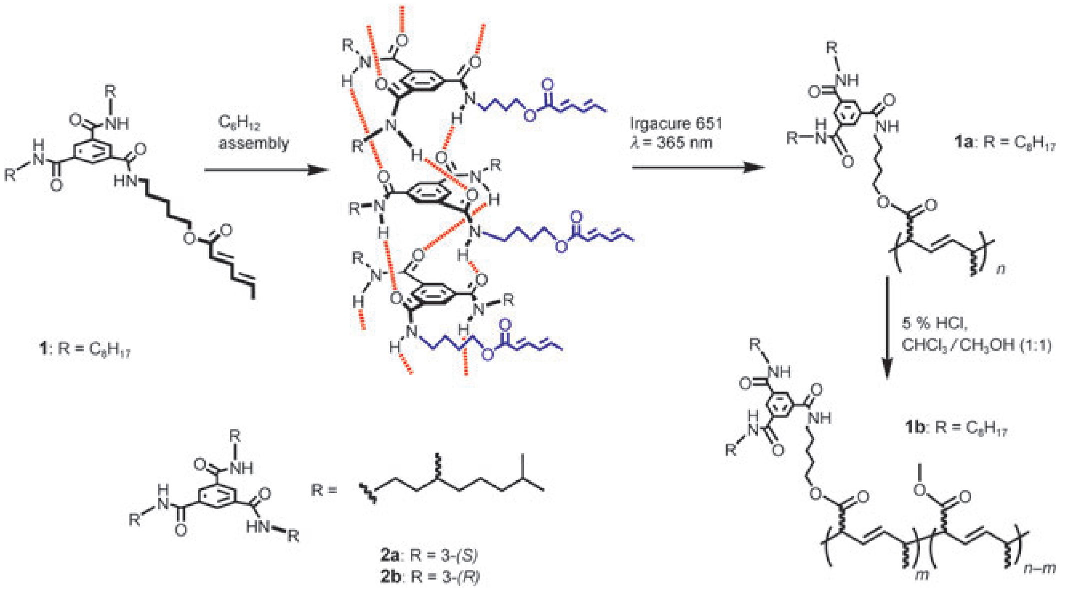


Figure 1. Representation of regular conformations of polymerizable self-assembled columns of **1**, based on the crystal structure of a benzene tricarboxamide.[24] Octyl side chains have been omitted for clarity. a) "Zigzag" conformation of sorbyl-containing side chains to give an achiral polysorbyl backbone. b) Helical conformation of sorbyl-containing side chains to give a chiral polysorbyl backbone.

Self-assembly of **1** in cyclohexane (10^{-5}–10^{-2} M) occurs through cooperative hydrogen bonding, aromatic stacking, and van der Waals interactions as proposed in Figure 1. The proposed mode of assembly results in the cooperative formation of a triple helical seam of hydrogen bonds down the axis of the column[1,24–28] with equal probabilities of left- and right-handed helices in the absence of further sources of chirality. This proposal for the structure of **1** is based on the single-crystal structure of another substituted benzene-1,3,5-tricarboxamide.[24] It is therefore important to explore the effect of the supramolecular sergeants-and-soldiers experiment[1,25] during polymerization because it results in the formation of two new chiral centers per discotic **1**. As has been observed in several other systems,[1,25,27,28] in the absence of any chiral additives equal quantities of left- and right-handed helices composed of discotic **1** are present in solution (0.8×10^{-3} M, cyclohexane). However, in the presence of chiral discotic **2a** a large negative circular dichroism (CD) effect is observed (Figure 2). The CD effect is induced by a supramolecular sergeant-and-soldiers effect as the spectrum reflects the absorption spectrum of monomer **1**, while its



Scheme 1. Self-assembly and polymerization of discotic **1**.

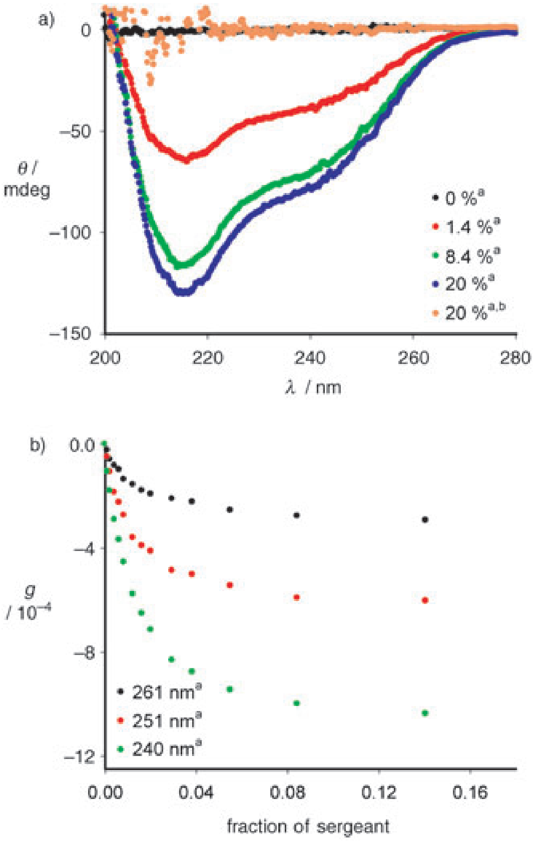


Figure 2. a) CD spectra of monomer **1** in the presence of different amounts of sergeant **2a** and b) anisotropy factor of monomer **1** as a function of added sergeant **2a**. [a] [**1**] = 8.1×10^{-4} M, cyclohexane, 0.1 cm pathlength. [b] [**1**] = 8.1×10^{-4} M, 95:4.5:0.5 C_6H_{12}/$CHCl_3$/CH_3OH, 0.1 cm path length.

magnitude increases nonlinearly with the quantity of added "sergeant" **2a** (leveling off at around 10%). The effect is completely lost upon increasing the solvent polarity (C_6H_{12}/$CHCl_3$/CH_3OH 95:4.5:0.5). Gratifyingly, the use of a mirror image "sergeant" **2b** with opposite chirality results in an induced CD signal of opposite and similar magnitude (see ESI).

We next investigated whether the chirality induced by sergeant **2a** was retained upon polymerization of monomer **1** in the presence of varying amounts of sergeant **2a**. As reported previously by us,[23] 1,4-polymerization of the sorbyl moiety in **1** provides sufficient distance to bridge stacked aromatics. Photoinitiated polymerization (365 nm) of the self-assembled stacks (1×10^{-2} M solution in cyclohexane) of **1**, in the presence of 2,2-dimethoxyphenylacetophenone as initiator, furnishes columnar polymers **1a**. Full analysis of the polymers requires careful removal of monomer **1** and structure-directing agent **2a** by Soxhlet extraction followed by methanolysis of the polymer formed[29] to detach most of the trimesic amide moieties from the polysorbyl backbone. The highly soluble and non-aggregating polymethyl sorbate **1b** can be analyzed by ^1H NMR, ^{13}C NMR, and size-exclusion chromatography (SEC). The latter analysis shows that the photopolymerization results in polymers with DPs of 50–130 and polydispersities of ≈1.7, while no signals of remaining **1** or **2a**, nor products thereof are detected. Importantly, the presence of varying amounts of **2a** does not significantly affect these parameters through radical C–H abstraction mechanisms, that is, the sergeant does not act as a chain stopper. (Table 1)

Table 1: Conversion, degree of polymerization (DP), and polydispersity index (PDI) of photoinitiated polymerization of **1** in the presence of varying amounts of sergeant **2a**.

2a [%]	Conversion [%]	DP	PDI
0	58	58	1.76
0	51	110	2.1
0	50	103	1.53
10	56	130	1.68
10	47	63	1.2
15	50	100	1.7
20	50	54	1.57
20	45	77	1.6

Induced chirality was studied by CD spectroscopy on **1a** after careful removal of unconverted monomer and sergeant **2a** by exhaustive Soxhlet extraction with diethyl ether. ^{13}C NMR spectroscopy of a methanolyzed sample demonstrated the absence of any sergeant (incorporation at a level below 0.3 molecules of **2a** per polymer chain, see ESI). CD spectra were recorded in C_6H_{12}/$CHCl_3$/CH_3OH (95:4.5:0.5), a solvent combination in which the polymer has sufficient solubility and in which monomer and sergeant **2a** do not form columnar stacks as outlined above. Remarkably, the polymers still display optical activity in the CD spectrum (Figure 3) despite the complete removal of chiral sergeant **2a** from the product. The CD spectra were concentration independent between 10^{-3} and 10^{-4} M (see ESI) which suggests that the signal is a consequence of intramolecular organization within molecularly dissolved polymers. If the variation in the magnitude of the CD spectrum is plotted against the fraction of sergeant **2a** present during the polymerization, almost complete induction of helicity is observed at around 10% of added sergeant **2a** (once again the use of sergeant **2b** produces an opposite response of equal intensity, see ESI). The shape of the curve matches that observed during the self-assembling sergeants-and-soldiers experiment and the anisotropy value is of similar magnitude, suggesting that the helical bias present before polymerization is almost completely (>80%) retained in the polymer. The Cotton effect completely disappears when the methanol content is increased to 1.5%. Removal of all solvent and redissolution in the original solvent mixture leads to complete recovery of the original Cotton effect. The process can be repeated several times without significant loss of CD signal. The process amounts to an unfolding–refolding cycle of the polymer and indicates that the helical bias induced by sergeant **2a** in self-assembled stacks of monomer **1** is locked in the polymer and that the chiral information is encoded in the stereochemistry of the sorbyl main chain. The complete sequence of assembly, fixation, sergeant removal, and reversible unfolding is summarized in Figure 4.

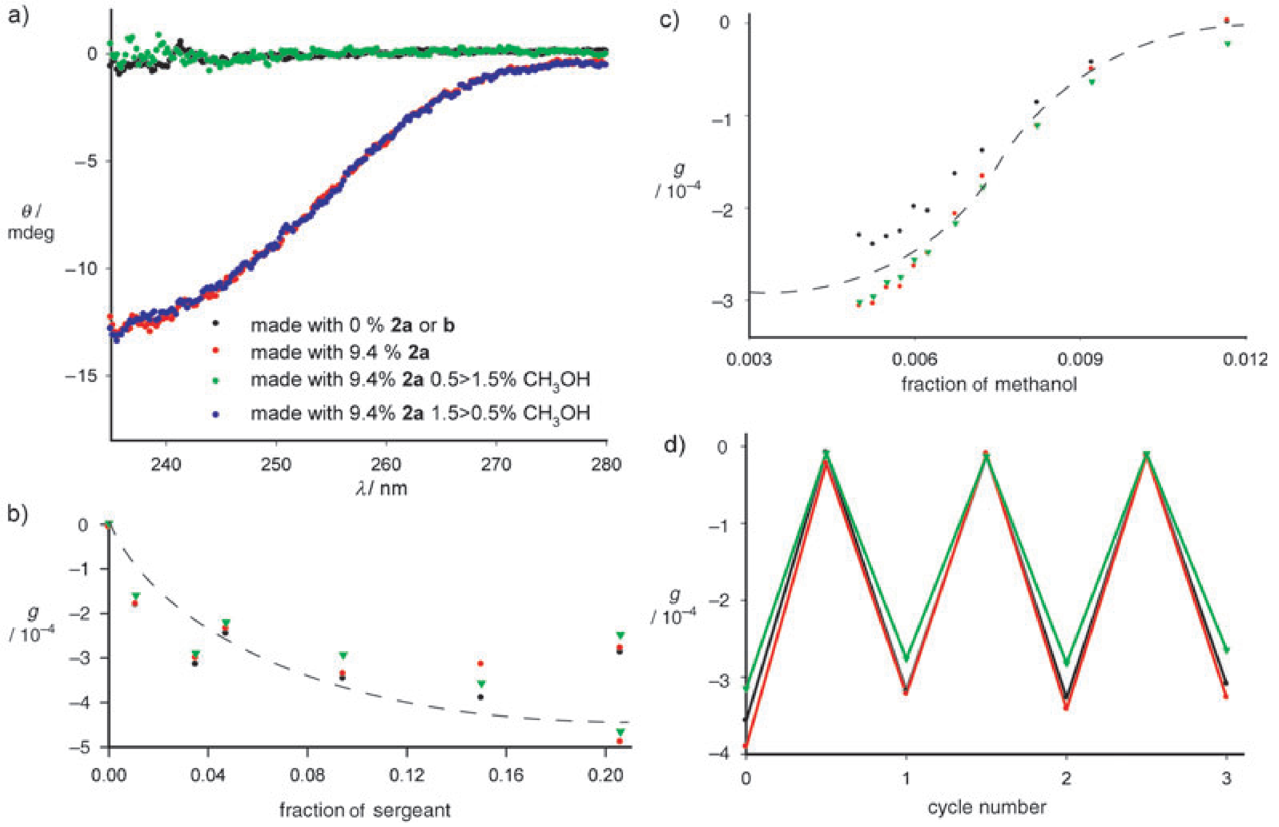


Figure 3. CD spectroscopy of polymer **1a** made in the presence and absence of sergeant **2a** (0.1 cm path length, 95:4.5:0.5 C_6H_{12}/$CHCl_3$/CH_3OH). a) CD spectra of polymer **1a** (9.5×10^{-4} M). b) Variation in the anisotropy factor *g* of the polymer **1a** as a function of sergeant **2a** present during polymerization. c) Variation in the anisotropy factor *g* as a function of added methanol (polymer **1a** with 9.4% sergeant **2a** present during the polymerization). d) Folding and unfolding behavior (as shown by g value) upon addition and removal of methanol (polymer **1b** made with 15% sergeant **2a** present during the polymerization).

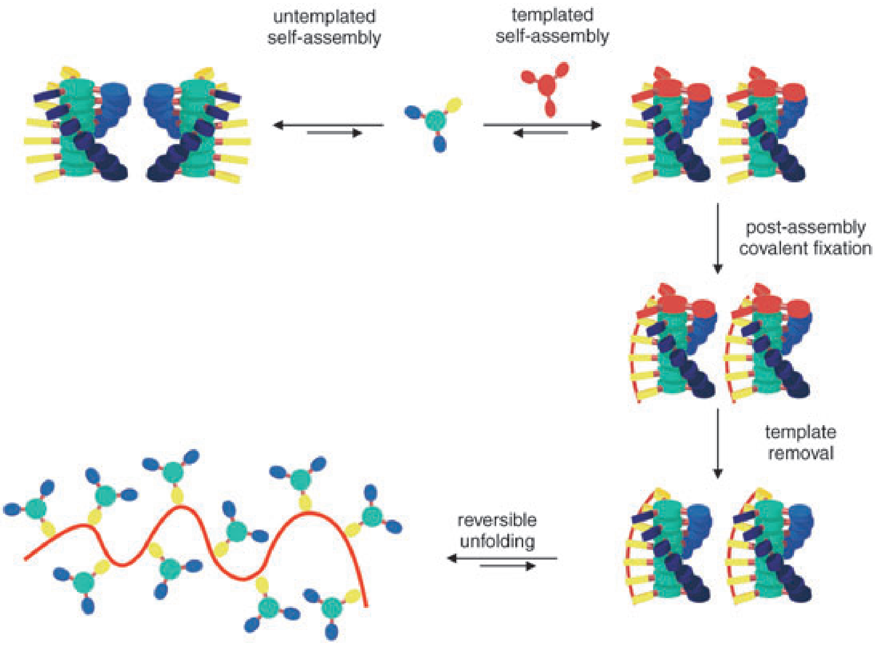


Figure 4. Sequence of events leading to locking of supramolecular chirality into columnar self-assemblies of **1**.

Deeper understanding of the structural details responsible for the chiral amplification effect required a more detailed analysis of the polymer backbone. This was achieved with transesterified polymer **1b**, which has higher mobility relative to **1a** resulting in higher-quality ^{13}C- and ^{1}H-correlated spectra. ^{1}H,^{1}H COSY of **1b** reveals the interconnection along the backbone and is entirely consistent with a 1,4-*trans* polymerization (confirmed with ^{13}C NMR spectroscopy) in which both *erthyro* and *threo* stereocoupled centers are formed.[30,31] The addition of sergeant **2a** or **2b** to a solution of the self-assembled stack prior to polymerization has very little effect on the NMR spectrum of the polymer. However, the unfolding–refolding experiments show that the helical bias is strongly retained in the backbone of the polymer. This implies that despite the fact that the polymer has a mixed microstructure, at least part of the polysorbyl backbone has been formed with asymmetric preference. It is highly surprising that the mixed microstructure results in a very high stereoselectivity in the folding process. It can be rationalized with the notion that the polymer backbone is formed in a perfect helical assembly and that the backbone, despite its mixed microstructure, fits perfectly into the refolded helical polymer. Notably, order in polymer backbones lowers chirality, and disorder enhances chirality, as beautifully shown by Green and Garetz for polystyrene.[32]

We made several models to rationalize these observations further. The *trans*-1,4-polymerization of (*E*,*E*)-sorbyl esters in the preferred transoid conformation fixes the relative stereochemistry of methyl and ester groups on each side of the double bond to *rel-(R,S)*. But the relative stereochemistry of adjacent methyl and ester groups in the polymer is determined by the relative orientation of the sorbyl groups during polymerization (see ESI). In all cases in which the polymerization proceeds in a zig-zag fashion down the column from sorbyl-containing side chains alternating in orientation by +30° and −30° (Figure 2a), no net chirality results. When sorbyl-containing side chains follow the seam of hydrogen bonds, a chiral polymer results, but the increased distance between consecutive monomeric units results in the accumulation of strain in the polymer (Figure 2b). Therefore, a mixed microstructure, resulting from polymerization switching between zig-zag and helical propagation is in line with both NMR and CD spectral evidence. In the presence of **2a** or **2b** there is no change in tacticity of the polymerization;[33,34] rather it introduces a bias of the absolute stereochemistry with which the helical propagation proceeds. Therefore it resembles in many aspects the "majority rules" principle pioneered by Green.[13]

In summary, we have shown that it is possible to exploit noncovalent interactions to first assemble and then transfer chiral information to a well-defined, kinetically inert, columnar architecture by using a chiral structure-directing agent. Even though the polysorbate backbone is not completely stereoregular, it is capable of storing complete stereochemical information. The observation of the remarkable chiral memory effect opens up the possibility of using noncovalent interactions to amplify and transfer chiral information to structurally robust nanoscale architectures.

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