Amplification of Chirality in Helical Supramolecular Columns

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Abstract

Strong amplification of chirality occurs in dynamic, but highly ordered, helical columns in *n*-butanol, for which one chiral seed molecule suffices to render a column of 400 molecules to become homochiral. The chiral columns are formed in a thermally dependent stepwise process. The transition from achiral stacks to helical columns is highly cooperative owing to well-defined intermolecular interactions. 'Sergeant and Soldiers' measurements allow for the calculation of the association constant and cooperativity length of the homochiral segments. The 'Sergeant and Soldiers' data on the number of molecules within a column show a strikingly good match with data obtained from a theoretical model describing the self-assembly of the discotic molecules as a function of temperature and concentration.

Introduction

Strong amplification of chirality for the generation of homochiral molecules or architectures is a fascinating aspect of life that has inspired chemists repeatedly [1, 2]. Approaches to create such systems have ranged from crystallization-induced resolution to asymmetric synthesis. Copolymers made from chiral and achiral monomers have been shown to possess a positive, non-linear dependence of the specific rotation [3]. The work of Green and co-workers on polyisocyanates is seeding in this field and their 'Sergeant and Soldiers' and 'Majority Rules' principles have confirmed the importance of cooperativity for the amplification of chirality [4, 5]. Recently we have shown that impressive amplification of chirality also occurs in well-defined aggregates of self-assembled molecules [6, 7]. The amplification of chirality in self-assembled architectures is increasingly gaining interest and the results obtained from the systems studied may aid in the elucidation of the self-assembly processes in Nature and, particularly, the chirality involved [6–12]. The results show that cooperative interactions within the self-assembly are a prerequisite for strong amplification of chirality.

Recently, we described the self-assembly of chiral discotic **1** in *n*-butanol and showed the occurrence of a highly cooperative transition from achiral stacks of molecules to chiral helical columns upon cooling solutions of **1** in alcohols [13]. The cooperative formation of the chiral architecture renders this system very attractive for generating a strong amplification of chirality. To investigate this, 'Sergeant and Soldiers' [5] measurements were performed on mixtures of **1** and **2**. In this article we will first briefly explain the self-assembly process of compound **1** and the cooperativity involved in the formation of the helical columns, and then we will address the phenomenon of amplification of chirality in the columns composed of **1** and **2**. The results will be correlated with a model describing the helicity and size of the columns as a function of temperature [14]. Finally, we will discuss the transfer of chirality in *n*-butanol from one chiral seed molecule to 400 achiral molecules within a helical column; an unprecedented amplification of chirality for self-assembled supramolecular architectures under reversible conditions.

Chiral discotic **1** has a threefold symmetry axis and is molecularly dissolved in chloroform, consequently no Cotton effect is observed in the circular dichroism spectra recorded in this solvent: the flexible chiral side-chains do not influence the also freely moving wedges of the aromatic core. The large aromatic core, however, aggregates in polar solvents such as water, methanol and *n*-butanol. Several techniques have been used to characterize the columnar aggregates in these solvents: upon aggregation a red-shift occurs in the UV-Vis spectra with respect to those recorded in chloroform, upon cooling broadening of signals occurs in ^{1}H-NMR spectra and the life-time of the fluorescence strongly increases and finally neutron scattering experiments have elucidated the columnar shape of the aggregates [13, 14]. In *n*-butanol at high temperatures the molecules are molecularly dissolved. Lowering of the temperature initially accounts for non-cooperative linear aggregation via solvophobic interactions. In those aggregates the molecules can still rotate and hence they lack mesoscopic chirality. Further cooling results in a very cooperative ($\sigma = 0.02$) transition (~25 °C) during which the three wedges of the discotic arrange themselves in a propeller like order and stacking
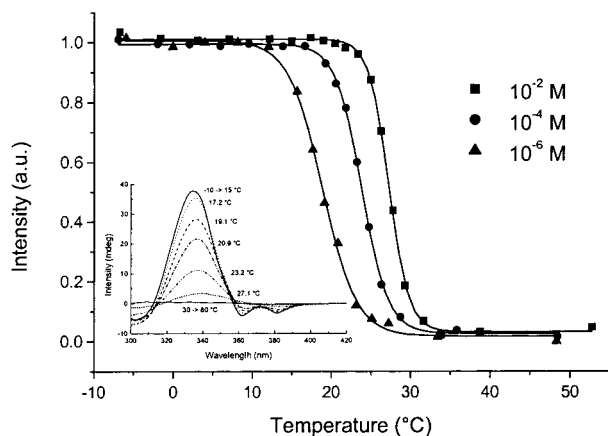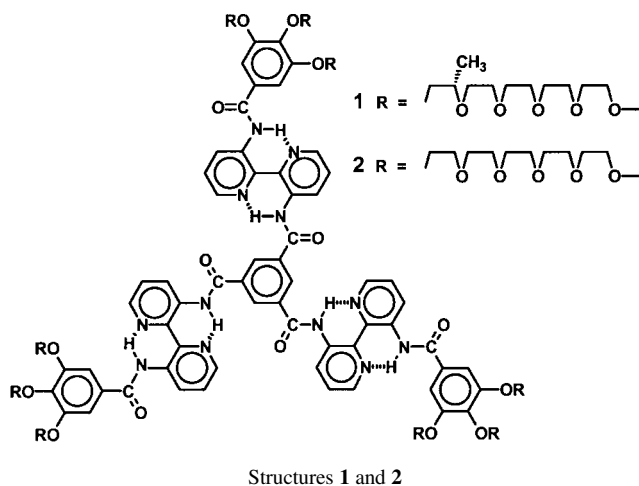
Figure 1. Normalized intensities of the CD-spectra of **1** in *n*-butanol at 337 nm at three concentrations (10^{-6}, 10^{-4} and 10^{-2} M). The cooperative transition lies around 25 °C, slightly depending on the concentration. The inset shows the temperature dependent CD spectra of **1** in *n*-butanol at 10^{-5} M.

Figure 2. Dependence of the overall chirality on the mole fraction of chiral **1** in *n*-butanol at 5 °C, expressed in terms of the g-value measured at the maximum of the Cotton effect at 341 nm. Measurements were recorded at 10^{-5} M in a 1 cm cell (circles) and at 10^{-4} M in a 1 mm cell (squares). The solid lines represent the best fit to the data using a uniform helicity length of 400 molecules and a K of 5×10^8 L mol^{-1}.

of the propellers by intramolecular hydrogen bonding affords chiral supramolecular columns (Figure 1). Below this transition temperature a strong and constant Cotton effect ($g_{abs} = 3 \times 10^{-3}$), in the chromophores corresponding to the aromatic core, can be observed. The presence of a Cotton effect implies that the molecules are positionally ordered in the columns, a prerequisite for transfer of chirality from the side-chains into the columns, to generate a helix. The cooperative transition and the high and constant degree of order of the molecules in the helical columns suggest that strong amplification of chirality can occur.

Structures **1** and **2**

Results

We have now synthesized **2**, the achiral analogue of chiral **1** and studied self-assemblies made out of **1** and **2** and investigated the amplification of chirality of **1** (the sergeant) into **2** (the soldiers). Obviously, achiral **2** does not show any optical activity in *n*-butanol, but the aggregation behaviour is similar to that of **1** and hence equal amounts of *P* and *M* helices are formed. The 'Sergeant and Soldiers' [5] experiments on **2/1** mixtures in *n*-butanol were conducted at
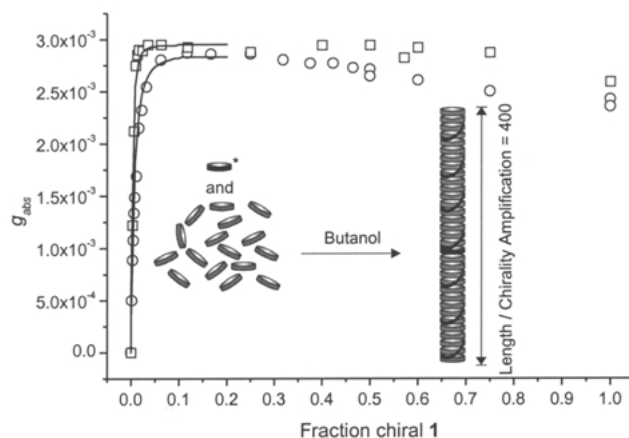
two concentrations at 5 °C (Figure 2) and the intensity of the Cotton effect divided by the absorption (g_{abs}) was monitored as a function of mole percent sergeant added. A very strong amplification was observed at a concentration of 10^{-4} M; the maximal Cotton effect was reached already after addition of only one percent chiral **1**, implying an extremely large cooperativity within the helical columns. The amplification of chirality at 10^{-5} M appeared to be significantly smaller, since over five percent of sergeant was needed to achieve full bias of helicity. Apparently, at this tenfold lower concentration a substantial smaller number of achiral molecules is subject to amplification of chirality. The 'Sergeant and Soldiers' data were fitted to the model derived by Havinga [6] to determine the association constant and the strength of the chirality amplification, i.e., the number of soldiers forming one unit of uniform helicity within one column. The length over which one single chiral seed molecule can amplify its chirality, the length of uniform helicity within one column, was calculated to slightly exceed 400 molecules and the association constant K was determined to be approximately 5×10^8 L mol^{-1} at 5 °C.

In addition, these 'Sergeant and Soldiers' experiments were characterized by a strong time-dependence. After the addition of a small aliquot of chiral **1** to a solution of achiral **2** it took approximately 2 hours before full amplification of chirality was reached. This process was independent of the temperature at which the compounds were mixed. Apparently, the high degree of order within the kinetically formed non-biased helical columns makes them somewhat reluctant to dissociation. This high stability on the other hand favours a high degree of amplification of chirality in the thermodynamically favoured homochiral aggregates.

Even though highly ordered columns are formed, the interactions accounting for the chirality transfer are subtle and involve an interplay between the supramolecular architecture and the solvent. Thus, achiral **2** was dissolved in the chiral solvent (2*S*)-(−)-methyl-1-butanol. UV-Vis and fluorescence spectroscopy measurements indicated that also
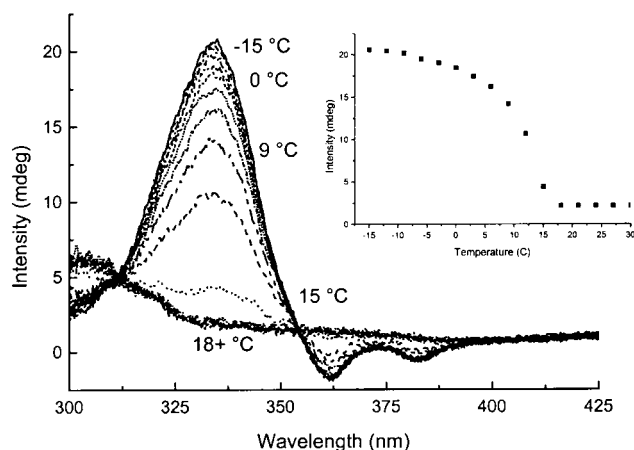
Figure 3. CD-spectra of **2** in (2*S*)-(−)-methyl-1-butanol at 10^{-5} M at different temperatures. The UV-Vis insensitive chiral solvent induces helicity in the columns built up from **2**, resulting in a Cotton effect in the chromophores of **2**. The inset shows the maxima of the Cotton effect as a function of temperature.

Figure 4. Prediction for the average number of molecules participating in one column, $\langle N \rangle$, at three different concentrations as a function of temperature. The arrows mark the transition form achiral to chiral aggregates.

in this solvent aggregation takes place upon cooling and the Cotton effect at temperatures below 10 °C indicated that the chirality of the solvent is transferred to the helical columns. Similar to solutions of chiral **1** in achiral alcohols, the achiral columns formed in (2*S*)-(−)-methyl-1-butanol become chiral at a defined temperature (∼15 °C) (Figure 3). A Cotton effect comparable in shape and intensity (g_{abs} = 2×10^{-3}) to that of **1** in *n*-butanol can be observed. The transition from achiral to chiral columns is again relatively sharp and cooperative.

Discussion

The 'Sergeant and Soldiers' experiments on **2/1** mixtures have revealed a high association constant (5×10^8 L × mol^{-1} at 5 °C) and a cooperativity length of over 400 molecules. The assembly in columns yields supramolecular rod-like polymers with an average degree of polymerisation (DP) depending on temperature and concentration, as also revealed by SANS studies [14]. The association constant K allows for calculation of the number average degree of polymerisation using the formula DP = $2 \times \sqrt{(K \times \text{concentration})}$. At a concentration of 10^{-4} M the length of the columns is approximately 450 molecules and at 10^{-5} M 140 molecules. These results thus reveal that at 10^{-5} M the column length (∼140) is the limiting factor in the amplification of chirality. Even though the cooperativity/persistence length of uniform chiral domains is theoretically 400 molecules, the small 'platoons' of 140 soldiers limit the influence of the sergeants. At 10^{-4} M the two variables are comparable, both around 400. At this concentration the helical columns represent a (virtual) molecular weight as high as 1.4×10^6 Da and a length of ∼140 nm (400 × 0.35 nm). Impressively, only one chiral seed molecule with a thickness of 3.5 Å is needed to render these long columns diastereomerically pure. It should be noted, however, that due to a statistical location of the chiral seeds within the columns more than
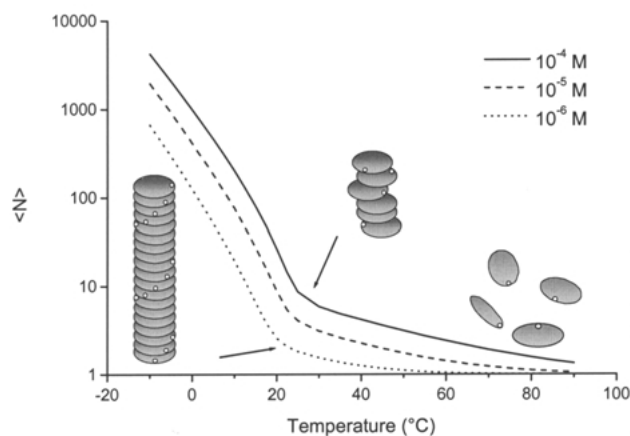
0.25% seed molecules are required. The experiments have shown that approximately 1% is necessary. Furthermore, the persistence length of the homochiral segments is constantly 'moving' over the columns, while thermal motion disconnects different segments.

The columns assemble in a hierarchical fashion in *n*-butanol, as discussed in the introduction. Recently van der Schoot *et al.* formulated a model rationalising these experimentally observed self-assembly data [14]. In this model, the standard theory of linear self-assembly was modified by adopting a two-state model for the molecules in the aggregates, to account for the cooperative transition. The theory allows for the calculation of the average number of molecules in the columns at any concentration and temperature. The theory predicted an average size of the aggregates at 5 °C of 160 molecules at 10^{-5} M and 440 at 10^{-4} M. These numbers are in excellent agreement with the 'Sergeant and Soldiers' experiments that yielded calculated column lengths at 5 °C of 140 and 450 molecules at 10^{-5} and 10^{-4} M, respectively. This is a remarkably close match, when one considers that the column lengths were obtained via totally different and independent experiments and calculations. Figure 4 shows the calculated column lengths, on the bases of the model by van der Schoot, as a function of temperature at three different concentrations. Clearly visible is the small aggregate size at high temperatures and the rapid increase of the size at temperatures below the achiral-chiral transition around 30 °C.

In conclusion, very strong amplification of chirality in *n*-butanol rationalizes why columns consisting of achiral molecules can be made homochiral by only one chiral seed molecule per 400 achiral molecules. The high cooperativity and the time dependence for full expression of chirality demonstrate the high degree of order in the assembly. The calculated column lengths based on the 'Sergeant and Soldiers' measurements nicely match data obtained using a model for the two-step cooperative self-assembly in columns. The results presented here show that for a strong amplification of chirality within self-assembled aggregates,

cooperative interactions are essential, together with large aggregate sizes.

Experimental procedures

UV-Vis spectra were recorded on a Perkin Elmer Lambda 900 UV/VIS/NIR spectrometer. CD spectra were recorded on a Jasco J-600 spectropolarimeter. All measurements were performed after reaching equilibrium.

Acknowledgements

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