Chirality amplification in dynamic helical columns in water

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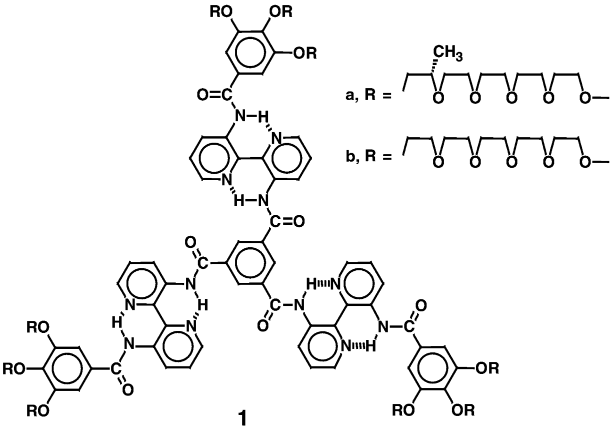
Extended core discotic molecules self-assemble in water by different secondary interactions to give well-defined, helical columns in which the chirality of one chiral molecule is transferred to on average 12 achiral molecules.

Amplification of chirality, generating homochiral molecules or architectures, is one of the fascinating aspects of life that chemists have repeatedly tackled.[1] Approaches have ranged from crystallization-induced resolution to asymmetric synthesis, while Green pioneered the amplification of chirality at helical macromolecular backbones.[2] We have shown that the addition of small amounts of homochiral seed molecules to dynamic, racemic supramolecular architectures of achiral building blocks in solution generates homochiral supramolecular assemblies.[3,4] For well-defined columns formed by *N*-acylated 3,3′-diamino-2,2′-bipyridine based C_3-extended core discotics, we determined that a single chiral molecule imposes its chirality on 80 achiral molecules at rt.[3] In columnar assemblies of alkyl substituted benzene-1,3,5-tricarboxamides, one chiral seed can even direct the chirality of 200 molecules.[4] For aggregates not formed by directional secondary interactions, such as alkoxy substituted polythiophenes, the amplification of chirality was found to be orders of magnitude lower.[5] The solvents used for the study of these architectures, as well as for other chirality transferring supramolecular systems reported so far,[6] are apolar and organic, favouring specific polar secondary interactions. The creation of well-defined chiral supramolecular architectures in water is a subject of increasing importance and one of the goals in bio-inspired supramolecular chemistry.[7]

In the C_3-extended discotic **1**, oligo(ethylene oxide) side chains have been incorporated. The synthesis and the lyotropic behaviour of chiral **1a** in *n*-butanol, have been described elsewhere.[8] Compound **1a** is molecularly dissolved in $CHCl_3$, but is aggregated in *n*-butanol[9] as evidenced by a red-shift in the UV-Vis spectra with respect to those in $CHCl_3$, broad signals in ^1H-NMR spectra and a fluorescent species with a long life time.[8] Furthermore, at low temperatures, the columnar aggregates of **1a** in alcohols are chiral, as evidenced from the appearance of a strong Cotton effect ($g_{abs} = 3 \times 10^{-3}$) in the chromophore corresponding to the aromatic core.[10] We have now synthesized achiral **1b** and studied the self-assembly of **1a**–**1b** mixtures in water. Different interactions are shown to be operative in the self-assembly in water and one chiral molecule is able to induce chirality into 12 achiral molecules at 5 °C.

Compounds **1a**,**b** dissolve in water due to their hydrophilic side chains, but intriguingly, aggregation takes place as evidenced by broad signals in the ^1H-NMR spectra and a red shift of the UV-Vis spectra, and a strong intensity of the luminescence compared to solutions in $CHCl_3$. This aggregation in water resembles that of chromonics that are known to aggregate *via* hydrophobic interactions of their aromatic cores.[11] Remarkably and in contrast to chromonics, the architectures are chiral and well-defined as evidenced by the appearance of a Cotton effect for **1a** at the wavelength corresponding to the aromatic core ($g_{abs} = 1.4 \times 10^{-3}$). Apparently, the arene–arene interactions of the aromatic cores create a hydrophobic micro-environment that allows for structuring *via* the specific, solvent-sensitive interactions.[8] Furthermore, this shows that the peripheral chirality of the individual molecules can be transmitted to the centre of the self-assemblies by cooperative side-chain interactions.



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In order to investigate the self-assembly, we studied the solution of **1a** in water as a function of temperature. Raising the temperature from 0 to 90 °C resulted in gradual changes in the UV (Fig. 1, top) and CD spectra (Fig. 1, bottom) as well as the fluorescence characteristics (not shown). In contrast to the *n*-butanol solutions that showed a highly cooperative loss of chirality around 20 °C,[8] the Cotton effect of the aqueous solutions only decreased slowly from 0 to 70 °C. At temperatures as low as 0 °C the Cotton effect is still temperature-sensitive, suggesting that the individual molecules are not yet fully locked in one defined position. The bandshape characteristics of the UV-spectra and the high luminescence suggest that the molecules remain aggregated at all temperatures. The stacking at high temperatures is in contrast with the behaviour of **1** in *n*-butanol[8] and to that of chromonics in general.[11] We attribute this behaviour to the combination of a large aromatic core, allowing for strong arene–arene interactions, and the

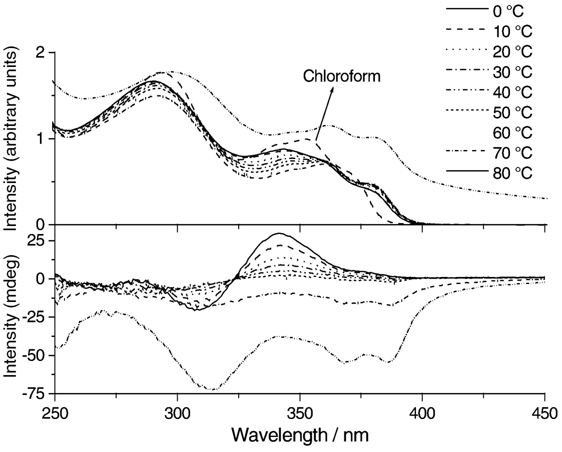

Fig. 1 Temperature dependent UV-Vis (top) and CD (bottom) spectra of **1a** in water (2.6×10^{-5} M). Furthermore, the UV-Vis spectrum of **1a** in chloroform (2.6×10^{-5} M) is shown.

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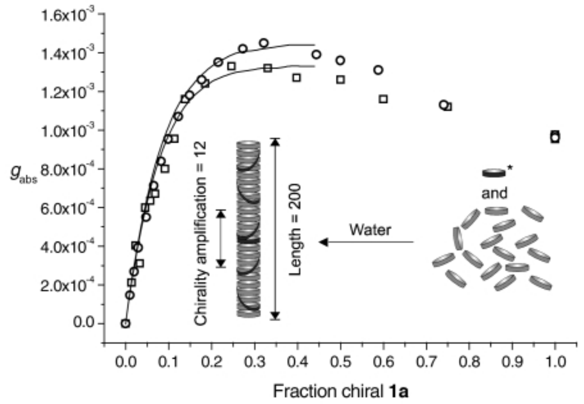

Fig. 2 Dependence of the overall chirality on the mole fraction of chiral **1a** in water at 5 °C, expressed in terms of the *g*-value measured at the maximum of the Cotton effect at 336–341 nm. Measurements were recorded at 10^{-5} M in a 1 cm cell (circles) and at 10^{-4} M in a 1 mm cell (squares). The solid lines represent the best fit to the data using a cooperativity length of 12 molecules and a K_{ass} of 1×10^8 L mol^{-1}.

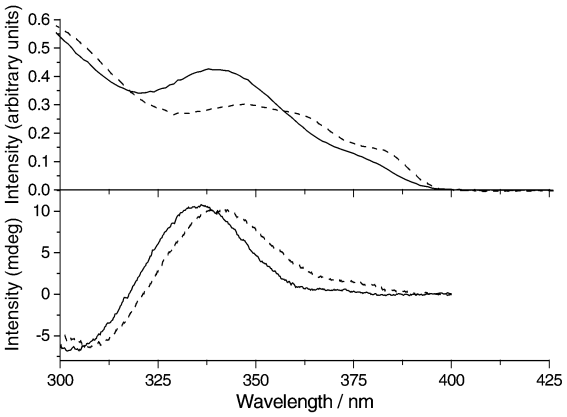

Fig. 3 UV-Vis (top) and CD (bottom) spectra of **1a** (----) and a mixture containing 8% **1a** and 92% **1b** (——) in water at 5 °C at a total constant concentration of 10^{-5} M.

LCST behaviour of oligo(ethylene oxide)s in water. Dilute solutions of **1a**/**b** in water become turbid around 70 °C (Fig. 1). The turbidity is ascribed to the formation of clusters of columns. At 60 °C a Cotton effect with opposite sign appears (Fig. 1 bottom). Whether this ‘inversion’ results from the formation of clusters with super-helical structure, or is simply due to scattering of the large particles is not clear yet.

‘Sergeant and Soldiers’ experiments[12] on **1a**/**1b** mixtures in water were conducted at two different concentrations at 5 °C (Fig. 2) to investigate the possibility of amplification of chirality. Indeed, chirality is amplified in the assembly; the maximal expression of chirality is reached after the addition of 25–30% chiral compound. Adopting the model of Havinga,[3] the association constant (K_{ass}) was calculated to be 1×10^8 L mol^{-1}, with a cooperativity length of 12 molecules. This means that at 10^{-4} M columns with a degree of polymerisation as high as 200 are being formed[13] and that 15–20 chiral molecules are needed to achieve a homochiral column. We are aware of the fact that the model is not exactly suited for the system in water, since it is made for single molecules forming a columnar stack whereas in water non-chiral columns, already present, become chiral. However, to a first approximation the calculated data seem to fit well with the results observed.

The high stability and order of the columns, essential for obtaining chirality amplification, is reflected in a strong time-dependence for the columns to become homochiral; after addition of a small aliquot of chiral **1a** to a solution of achiral **1b** it takes approximately 1.5 h before full amplification of chirality is reached. This phenomenon either results from a diffusion-limited transport of molecules from one stack to the other, or, more likely, is due to an extremely ordered and stable packing of the molecules, both **1a** and **1b**, in the columns.

Fig. 2 clearly shows that in water the intensity of the Cotton effect for particular mixtures is significantly higher than for pure chiral **1a**. In addition, it was established that in water the UV-Vis spectra of **1a** and **1b** differ and as a consequence the CD spectra, for which the maximum has been shifted from 342 nm for pure chiral **1a** to 336 nm for the mixtures with low ‘seed’ content (Fig. 3). These results demonstrate that the efficiency of packing in columns is different for **1a** and **1b**. The stronger Cotton effect of the mixtures suggests the packing of the achiral molecules to be superior. We attribute the differences in packing to the differing hydrophobicities of **1a** and **1b** and the increased steric hindrance in stacks of **1a** caused by the extra nine branching methyl groups.

In conclusion, we have demonstrated the creation of well-defined chiral self-assembled structures in aqueous solutions. Although the aggregation process of **1a** in water has similarities with that in organic solvents,[8] the special behaviour in water and the interaction of water with ethylene oxide side-chains results in striking differences. Currently, we are trying to elucidate the specific role of the water in the formation of the (chiral) supramolecular architectures based on **1a** and **1b**.

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