Amplification of chirality in *N*,*N*′-1,2-ethanediylbisbenzamides: from planar sheets to twisted ribbons†

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A remarkable sergeants-and-soldiers effect is observed in the coassembly of *N*,*N*′-1,2-ethanediylbisbenzamides onto surfaces that experience an amplification of chirality able to transform flat lamellae into twisted ribbons.

DNA helices and amyloid or cellulose fibrils are examples of natural helical structures with specific functions. The helical morphology of such biomolecules expresses the chirality of their components and demonstrates the direct relationship between the molecular and the supramolecular chirality.[1] Man-made chiral structures are being amply utilized in asymmetric chemical synthesis and catalysis,[2] liquid crystals,[3] and conductive materials.[4] However, a very intriguing question around chirality is the origin of homochirality, that is, how Nature utilized minute enantiomeric excesses to convert racemates into enantiomerically enriched mixtures. Despite the relatively high number of examples reported on the amplification of chirality in solution,[5] less efforts have been made to amplify the chirality onto surfaces thus generating aggregates with high aspect ratios.[6]

In our laboratory, self-assembly of a variety of non-ionic amphiphiles is being studied in solution and onto surfaces.[7] We report herein on the spectacular chirality amplification process of very simple *N*,*N*′-1,2-ethanediylbisbenzamides[8,9] with the transformation of flat sheets from achiral **1a** into twisted ribbons in the sergeants-and-soldiers[10] coassembly of achiral **1a** and chiral **1b** (Fig. 1).

The synthesis of compounds **1a** and **1b** starts with the preparation of the peripheral wedges **4a** and **4b** by reacting the commercially available 3-chloro-2-chloromethyl-1-propene (**2**) and the corresponding alcohol (1-decanol or (*S*)-3,7-dimethyloctanol). The subsequent hydroboration of the olefin, and Mitsunobu's reaction of the resulting alcohol (**4a,b**) with ethyl 4-hydroxybenzoate yields esters **5a,b**. Finally, the acidic hydrolysis of these esters, followed by the formation *in situ* of the corresponding acid chloride derivatives by treatment with oxalyl chloride and the reaction with ethylenediamine yields the target *N*,*N*′-1,2-ethanediylbisbenzamides with yields of 82 and 71%, respectively (Scheme 1). The chemical structure of all the new reported compounds has been confirmed by NMR, FT-IR, and MALDI-TOF techniques (see Supporting Information).

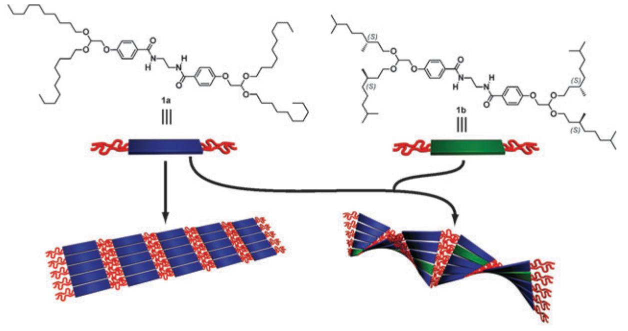
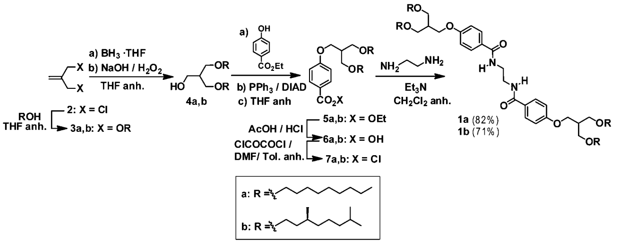


Fig. 1 Chemical structure of bisamides **1a** and **1b** (top) and schematic illustration of the self-assembly of **1a** into sheets and the coassembly of **1a** and **1b** into twisted ribbons.

The self-assembly of bis-benzamides **1a** and **1b** has been investigated by a number of techniques. Firstly, the aggregation of these amides in solution has been confirmed by concentration-dependent ^{1}H NMR experiments in deuterated chloroform (Fig. 2 and S1).[11] This solvent is well-known to stabilize H-bonded arrays although it is a bad solvent to detect π–π stacking. These studies reveal a clear deshielding of the N–H protons (resonances in red in Fig. 2 and S1) with increasing concentration, diagnostic of the intermolecular interaction of



Scheme 1 Synthesis of *N*,*N*′-1,2-ethanediylbisbenzamides **1a** and **1b**.

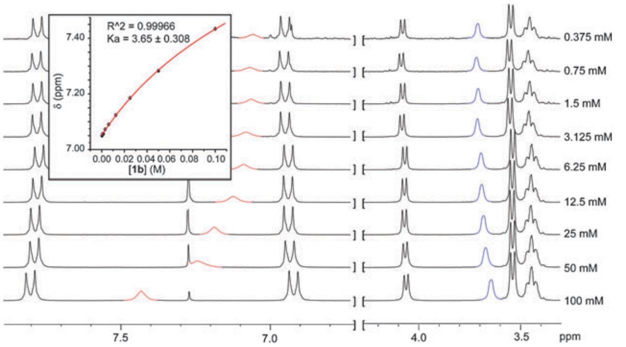


Fig. 2 Partial ^{1}H NMR spectra (300 MHz, 298 K) of **1b** at different concentrations in $CDCl_3$. The inset depicts the variation of the N–H resonance with concentration and the fit to eqn (1). The resonances in red and in blue correspond to the N–H and ethylene bridge protons, respectively.

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the bis-benzamides by H-bonding. Plotting the variation of the chemical shift against concentration shows a non-linear behaviour that can be fitted to eqn (1) that corresponds to an isodesmic or equal-K aggregation behaviour. c and K_a are concentration of amide and the binding constant, respectively.[12,13]

$$\delta = \Delta\delta_{\max} + (\delta_{\text{aggr}} - \Delta\delta_{\max}) \frac{1 + 1 - \sqrt{4cK_a}}{2cK_a} \qquad (1)$$

The calculated K_a values for amides **1a** and **1b** applying eqn (1) are rather low (2.88 and 3.65 M^{-1} for **1a** and **1b**, respectively) suggesting that the presence of only two H-bonding amide units is not sufficient to create highly stabilized aggregates in solution. The concentration-dependent ^{1}H NMR experiments also demonstrate the very weak interaction between the benzene units by π–π stacking. However, a small interaction involving the ethylene spacer linking the two benzamide moieties is noticeable (resonances in blue in Fig. 2 and S1). This effect is indicative of the close proximity of the protons of this spacer in the aggregated species.

The participation of different forces in the aggregation of amides **1a** and **1b** changes drastically in the neat state as demonstrated by the corresponding FTIR spectra (Fig. S2). The broad wave at 3330 cm^{-1} is ascribable to bounded N–H stretches and confirms the contribution of the amide groups in H-bonded arrays.[14] In addition, the amide I and amide II bands at 1637 and 1545 cm^{-1}, respectively, corroborate the H-bonded C=O stretching and the N–H bending modes.[15] Finally, the stretching bands at ν 2925 and 2865 cm^{-1} suggest the peripheral CH_2 groups are not in a crystalline state. Nonetheless, the band at around 1464 cm^{-1} is indicative of the interdigitation of these paraffinic substituents.[16,17]

The morphology of the supramolecular structures formed from amide **1a** has been investigated by utilizing field-emission scanning electron microscopy (SEM) onto a glass substrate. Initially, we prepared a suspension of **1a** in acetonitrile (1×10^{-3} M) that was subsequently deposited onto the glass substrate. The SEM images of this suspension exhibit big flake-like objects (Fig. 3a and S3). The SEM images of a more diluted suspension of **1a** in acetonitrile (1×10^{-4} M) show stratified clusters of microcrystalline lamellae formed upon the superimposition of thinner sheets (Fig. 3b and S4). These lamellae are formed by the synergy of π–π stacking between the phenyl rings, the H-bonding of the amide groups and the van der Waals interactions between the peripheral wedges. π-Stacking induces the formation of one-dimensional aggregates that are able to propagate along the aggregate axis by H-bonding. The further interdigitation of the paraffinic chains finally gives rise to the bidimensional structures.

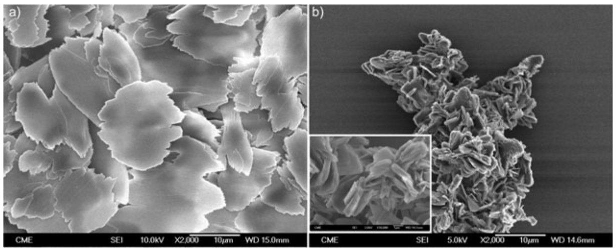

Fig. 3 SEM images of the microcrystalline flat sheets formed by the self-assembly of bis-amide **1a** in acetonitrile at 1×10^{-3} M (a) and at 1×10^{-4} M (b). For an enlarged view of the inset in (b), see Fig. S4.

The incorporation of stereogenic centres at the peripheral chains in bis-amide **1b** should induce the self-assembly of this compound into helical supramolecular structures.[5,6] The first approach to demonstrate the helical character of the aggregates formed by the association of amide **1b** was circular dichroism (CD) in methylcyclohexane (MCH), an apolar solvent in which the stabilization of the H-bonding and the π–π stacking should be maximized. The CD spectrum of **1b** at 1×10^{-3} M exhibits a weak bisignated Cotton effect with a zero crossing of CD signal at the frequency of the absorption maximum (250 nm) and with negative and positive waves at 248 and 253 nm (Fig. S5). This CD response is too weak to perform an accurate study of the self-assembly mechanism and also to investigate the possible sergeants-and-soldiers behaviour in solution.

Unexpectedly, SEM images of chiral bis-amide **1b** do not show any organized supramolecular structure most probably due to the low binding constant determined by the concentration-dependent ^{1}H NMR studies.[18] The situation is different when achiral **1a** soldiers and chiral **1b** sergeants are coassembled in acetonitrile (1×10^{-4} M) and deposited onto a glass substrate. The presence of only 5 mol% of the sergeant **1b** is able to transfer the chirality embedded in the peripheral chains to the remaining 95% of **1a** soldiers as revealed by the corresponding SEM images (Fig. 4a and b and S6). The transfer of chirality transforms the lamellae observed for **1a** into micrometre long twisted ribbons of high aspect ratio. Similarly to achiral **1a**, the synergy of π–π, H-bonds and van der Waals interactions forms bidimensional supramolecular structures. However, the presence of stereogenic centres in the coassembly of achiral **1a** with chiral **1b** provokes the chiral propagation of the H-bonding of the amide functionalities reinforcing the formation of twisted ribbons.

The formation of twisted ribbons by increasing the percentage of chiral sergeant **1b** in the coassembly of **1a** and **1b**

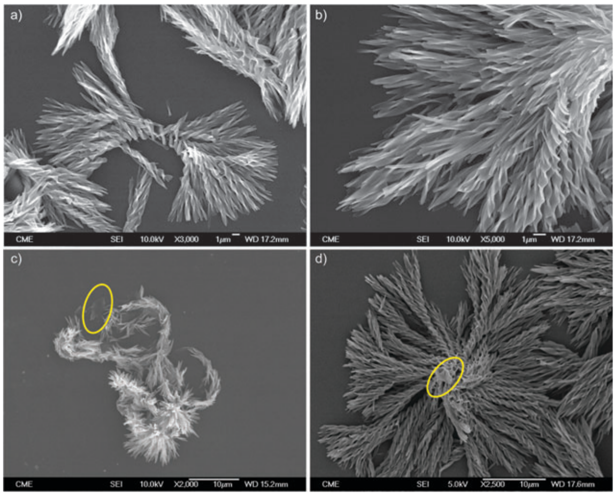

Fig. 4 SEM images (298 K, 1×10^{-4} M in acetonitrile, glass substrate) of twisted ribbons formed by the coassembly of the achiral soldier **1a** and chiral sergeant **1b** at different percentages of chiral component: 95/5 (a and b), 90/10 (c), and 85/15 (d). The yellow ellipses in (c) and (d) highlight amorphous material.

is also observed (Fig. 4c and d, S7 and S8). When a 10% or 15% molar ratio of chiral **1b** is added to **1a**, twisted ribbons are again clearly visible in SEM images. In both cases, unorganized material appears in the SEM images together with twisted ribbons which implies that only a minute amount of chiral sergeant (5% molar ratio) is capable to dictate the chirality to the whole coassembled structures. In all the tested cases, the chiral twisted ribbons appear spirally entangled to form pillars of chiral structures (Fig. 4a and d, S6, and S8).

To summarize, we have demonstrated that it is possible to apply the sergeants-and-soldiers principle, and therefore an amplification of chirality, to the self-assembly of very simple *N*,*N*′-1,2-ethanediylbisbenzamides despite these compounds exhibiting a low binding constant and also a negligible dichroic response in solution. The self-assembly of achiral bis-amide **1a** forms microcrystalline lamellae due to the synergy of H-bonding, π–π stacking and van der Waals interactions. The addition of **1b**, which acts as chiral sergeant in the coassembly of both bis-amides, provokes the transcription of the chirality embedded in the stereogenic centres at the peripheral chains generating the formation of twisted ribbons of high aspect ratio. The results presented herein represent an excellent example of the study of homochirality onto surfaces and, at the same time, contribute to increasing the knowledge about the set of rules governing the generation of chiral objects that hold a great potential for the development of supramolecular devices.

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