

Supporting Information

Amplification of Chirality in Benzene Tricarboxamide Helical Supramolecular Polymers

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SYNTHESIS

All solvents were purchased from Biosolve and all reagents were purchased from Aldrich unless otherwise stated and were used without further purification. Yields are not optimized. Purification by column chromatography was carried out using Merk Kieselgel 60 silica gel. Analytical thin layer chromatography (TLC) was conducted using Merck Kieselgel .25mm silica gel pre-coated glass plates with fluorescent indicator active at UV₂₄₅. NMR spectra were acquired on *Varian Inova500*, *Mercury400*, *Gemini300* or *Mercury200* spectrometers; ¹H at 500, 400, 300 or 200 MHz and ¹³C 125, 100, 75 or 50 MHz, respectively. Chemical shifts are expressed as parts per million downfield of TMS as a standard and coupling constants are expressed in Hz. The following abbreviations are used: s for singlet, d for doublet, t for triplet, q for quartet, m for multiplet and br for broad. MALDI-TOF MS were acquired using a PerSeptive Biosystems Voyager-DE PRO spectrometer. CHN analyses were performed on a *Perkin Elmer 2400 series II CHNS/O Analyzer*. Optical properties and melting points (uncorrected) were obtained using a *Jeneval Polarisation Microscope* with cross polarizers fitted with a *Linkam THMS600* heating device. DSC spectra were obtained using a *Perkin Elmer Pyris 1 DSC*. IR Spectra were obtained using a *Perkin Elmer Spectrum One* and unless otherwise stated using a *Universal ATR*. UV spectra were measured using a *Perkin Elmer Lambda 40 UV/vis* spectrophotometer. CD spectra were obtained using a *Jasco J-600 Spectropolarimeter* equipped with a *PTC-348WI* peltier temperature controller.

(*S*)-1-Amino-3,7-dimethyloctane, (*R*)-1-Amino-3,7-dimethyloctane, 3,5-bis(methoxycarbonyl)benzoic acid, 1-carboxy-*N,N'*-di(*n*-octyl)benzene-3,5-dicarboxamide, *N,N',N''*-Tris((*S*)-3,7-dimethyloctyl) benzene -1,3-5-tricarboxamide **2a**, *N,N',N''*-Tris((*R*)-3,7-dimethyloctyl) benzene- 1,3-5-tricarboxamide **2b** and *N*- (1-sorbyl-5-aminopentyl)- *N',N''*- di(*n*-octyl) benzene-1,3,5-tricarboxamide **1**, have all been previously described elsewhere.^{S1}

5-methoxycarbonyl isophthalic acid Trimesic acid trimethyl ester (2.4 g, 9.5 mmol) and sodium hydroxide (0.64 g, 19 mmol) in methanol (150 mL) were stirred under reflux for 18 hours. The reaction mixture was then poured into 300 mL water and acidified with HCL to pH ~ 1. The solution was extracted with ether (3 x 100 mL) dried over anhydrous magnesium sulphate, filtered and concentrated to leave a white residue. This was recrystallised from 50 mL ethyl acetate to yield 0.4 g of a mixture of the title compound and 3,5-bis(methoxycarbonyl)benzoic acid in a 1:2 ratio. This was used in subsequent reactions without further purification or characterization.

***N*-((S)-3,7-dimethyloctyl)-3,5-bis(methoxycarbonyl)benzamide and *N,N'*-bis((S)-3,7-dimethyloctyl)-5-methoxycarbonyl benzamide.** To a stirred solution (S)-1-Amino-3,7-dimethyloctane (0.329 g, 2.099 mmol), DMAP (0.256 g, 2.099 mmol), 5-methoxycarbonyl isophthalic acid (0.215 g, 0.954 mmol), in chloroform (15 mL) at 0°C under an atmosphere of argon was added EDCI (0.456 g, 2.380 mmol). The reaction mixture was allowed to warm to room temperature and stir overnight then diluted with chloroform (50 mL) and washed successively with hydrochloric acid (1N, 30 mL) saturated sodium bicarbonate (30 mL) and saturated sodium chloride solution (30 mL). The organic layer was dried over Na₂SO₄, filtered, concentrated and subjected to column chromatography (dichloromethane/ ethyl acetate, 9:1 v/v) to yield two fractions the first as a white solid *N*-((S)-3,7-dimethyloctyl)-3,5-bis(methoxycarbonyl)benzamide (0.232 g, 64 %); mp 64.3-66.2°C; ¹H NMR (300 MHz, CDCl₃) δ 0.86 (6H, d, *J* = 6.6 Hz, CH(CH₃)₂), 0.95 (3H, d, *J* = 6.6 Hz, CH₃), 1.16 (4H, m, alkyl), 1.30 (4H, m, alkyl), 1.52 (3H, m, CH and CH₂), 1.66 (1H, m, CH), 3.51 (2H, m, CONHCH₂), 3.96 (6H, s, OCH₃), 6.37 (1H, t, *J* = 5.5 Hz, NH), 8.60 (2H, s, ArCH), 8.76 (1H, s, ArCH); ¹³C NMR (75 MHz, CDCl₃) δ 19.56, 22.55, 22.67, 24.57, 27.95, 30.84, 36.62, 37.10, 38.97, 39.18, 52.52, 131.13, 131.99, 132.98, 135.63, 165.36, 167.57; IR ν (cm⁻¹) 3283 (NH stretch), 1733 (C=O ester) 1637 (amide I), 1546 (amide II); Found: C, 66.54; H, 8.26; N, 3.57. C₂₁H₃₁NO₅ requires: C, 66.82; H, 8.28; N, 3.71 %; *m/z* (GC-MS single peak) 377 (M⁺), and the second as a white solid *N,N'*-bis((S)-3,7-dimethyloctyl)-5-methoxycarbonyl benzamide (0.119 g, 25 %); mp 89.7-91.6°C; ¹H NMR (300 MHz, CDCl₃) δ 0.86 (12H, d, *J* = 6.6 Hz, CH(CH₃)₂), 0.94 (6H, d, *J* = 6.0 Hz, CH₃), 1.15 (8H, m, alkyl), 1.31 (8H, m, alkyl), 1.52 (6H, m, CH and CH₂), 1.64 (2H, m, CH), 3.49 (4H, m, CONHCH₂), 3.95 (3H, s, OCH₃), 6.41 (1H, t, *J* = 5.0 Hz, NH), 8.40 (1H, s, ArCH), 8.52 (2H, s, ArCH); ¹³C NMR (100

MHz, CDCl₃) δ 19.51, 22.56, 22.70, 24.64, 27.45, 30.79, 36.65, 37.12, 38.56, 39.18, 52.63, 129.73, 130.23, 131.10, 135.59, 165.47, 165.85; IR ν (cm⁻¹) 3262 (NH stretch), 1728 (C=O ester) 1630 (amide I), 1556 (amide II); Found: C, 70.48; H, 9.68; N, 5.20. C₃₀H₅₀N₂O₄ requires: C, 71.67; H, 10.02; N, 5.57 %; *m/z* (MALDI-TOF α -cyano-4-hydroxycinnamic acid matrix) 503 (M+H⁺).

***N*-((S)-3,7-dimethyloctyl)-3,5-bis(carboxy)benzamide.** To a stirred solution of *N*-((S)-3,7-dimethyloctyl)-3,5-bis(methoxycarbonyl) benzamide (0.107 g, 0.284 mmol) in THF/ Water/ Ethanol 10:2:10 v:v:v (10 mL) was added sodium hydroxide (1N, 1 mL, 1 mmol). The reaction mixture was allowed to stir overnight and then acidified (pH ~1) with HCl (1N). The reaction mixture was then poured into water (20 mL) and extracted with chloroform: ethyl acetate 1:1 v:v (2 x 30 mL). The combined organic extract was dried over anhydrous sodium sulphate, filtered and then dried thoroughly in vacuo to yield the title compound (0.0845 g, 85 %) as a white solid; mp 274.2-275.9°C; ¹H NMR (200 MHz, DMSO-d₆) δ 0.83 (6H, d, *J* = 6.2 Hz, CH(CH₃)₂), 0.90 (3H, d, *J* = 6.2 Hz, CH₃), 1.20 (7H, m, alkyl), 1.50 (3H, m, alkyl), 3.30 (4H, m, CONHCH₂), 8.57 (1H, s, ArCH), 8.63 (2H, s, ArCH), 8.84 (1H, t, *J* = 5.5 Hz, NH); ¹³C NMR (125 MHz, DMSO-d₆) δ 19.5, 22.3, 22.5, 23.9, 27.3, 29.8, 35.8, 36.4, 37.3, 38.6, 131.5, 131.8, 131.9, 135.4, 164.2, 166.1; IR ν (cm⁻¹) 3314 (NH stretch), 1691 (ν C=O of acid), 1637 (amide I), 1536 (amide II); Found: C, 65.12; H, 7.60; N, 3.88. C₁₉H₂₇NO₅ requires: C, 65.31; H, 7.79; N, 4.01 %; *m/z* (MALDI-TOF α -cyano-4-hydroxycinnamic acid matrix) 348 (M-H⁻).

***N*-((S)-3,7-dimethyloctyl)-*N',N''*-bis(octyl)benzene-1,3,5-tricarboxamide 3**

To a stirred solution of *N*-((S)-3,7-dimethyloctyl)-3,5-bis(carboxy)benzamide (0.0250 g, 0.072 mmol), DMAP (0.0193 g, 0.158 mmol), and *n*-octylamine (0.0201 mL, 0.158 mmol) in chloroform (30 mL) at 0°C under an atmosphere of argon was added EDCI (0.0302 g, 0.158 mmol). The reaction mixture was allowed to warm to room temperature and stir overnight then diluted with chloroform (50 mL) and washed successively with hydrochloric acid (1N, 20 mL) saturated sodium bicarbonate solution (20 mL) and saturated sodium chloride solution (20 mL). The organic layer was dried over Na₂SO₄, filtered, concentrated and subjected to column chromatography (ethyl acetate/ chloroform, 1:4 v/v) to leave the title compound as a white sticky solid (0.023 g, 56 %); DSC 223.20 °C (22.27 kJ mol⁻¹); ¹H NMR (300 MHz, CDCl₃) δ 0.87 (12H, m, 4 x CH₃), 0.94 (3H, d, *J* = 6.6 Hz, CH₃), 1.15 (m, 3H,

alkyl), 1.27 (18H, brm, alkyl), 1.55 (6H, m, alkyl), 3.45 (6H, m, NHCH_2CH_2), 6.69 (3H, m, NH), 8.30 (3H, s, ArCH); ^{13}C NMR (75 MHz, CDCl_3) δ 14.1, 19.4, 22.6, 24.6, 26.9, 27.0, 27.9, 28.4, 29.0, 29.2, 29.3, 29.5, 31.8, 36.6, 37.1, 38.5, 39.2, 40.4, 127.8, 135.3, 165.9; IR ν (cm^{-1}) 3240 (NH stretch), 1639 (amide I), 1559 (amide II); m/z (MALDI-TOF α -cyano-4-hydroxycinnamic acid matrix) 573 ($\text{M}+\text{H}^+$).

SELF-ASSEMBLY AND CHIRAL INDUCTION

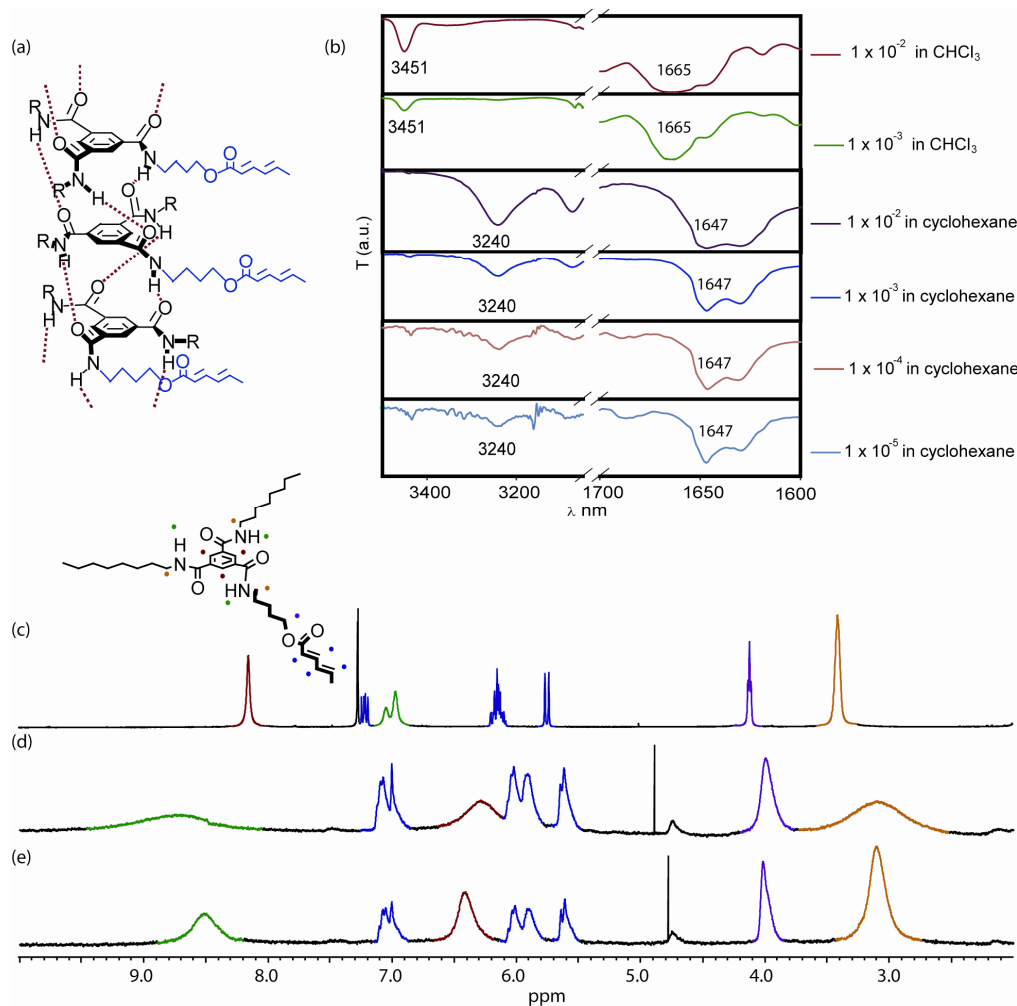


Figure S1. (a) proposed mode of self-assembly for discotics **1-3** (b) IR spectra of **1** (0.1 cm pathlength) (c) ^1H NMR spectrum of **1** (500 MHz, CDCl_3 , 25°C, 1×10^{-3} M), (d) ^1H NMR spectrum of **2** (500 MHz, C_6D_{12} , 25°C, 1×10^{-3} M), (e) ^1H NMR spectrum of **1** (500 MHz, C_6D_{12} , 65°C, 1×10^{-3} M)

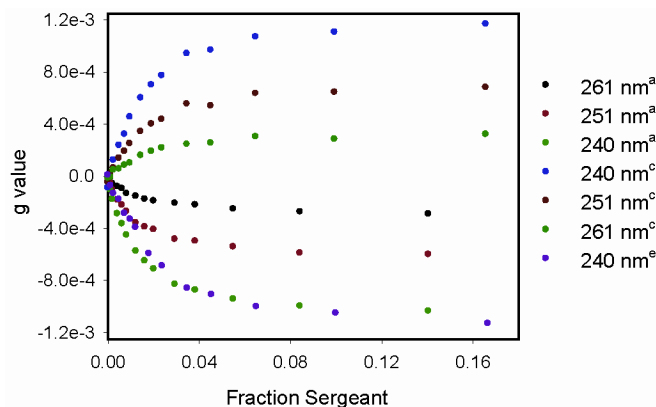


Figure S2. Anisotropy factor (g) of discotic **1** as a function of added sergeant **2a** or **2b** (cyclohexane, 0.1 cm pathlength). ^a 8.1×10^{-4} M **1** ^c 9.3×10^{-4} M **2** ^e1 cm pathlength 2×10^{-5} M **2**

CURVE FITTING

In order to gain a deeper insight into the mechanism behind the observed chirality amplification, the experimental results were compared to those of a recent theory describing the amplification of chirality in solutions containing achiral monomers, as well as both enantiomeric forms of chiral monomers^{S2}. This theory introduces two free-energy parameters, the penalty on a helix reversal along the chain and the so-called mismatch penalty, which is incurred if a chiral monomer is present in a helix of non-preferred handedness. Values for these parameters were obtained by performing a curve fitting procedure on the experimental results summarized in Figure 3, and those shown in Figure 2ii. This means that the same theory was used to describe both the sergeants-and-soldiers case and the diluted majority-rules case. While it is possible to describe the sergeants-and-soldiers effect with a single parameter,^{S3} an effective helix reversal penalty, in this case sufficient independent experimental data was available to obtain both parameters from a curve fit. Note that the theory as presented in reference S2 is only applicable if the aggregates are long, i.e., if the mean aggregation number exceeds the mean number of monomers that are influenced by a single sergeant molecule. This means that only experiments in which the chirality amplification is

independent of the overall monomer concentration can be described by this theory. For concentration-dependent data, finite-size effects need to be explicitly taken into account.^{S4}

To compare theory and experiment, The experimental CD signal intensities were converted to net helicities, defined as the fraction of bonds with one particular helical screw sense minus the fraction of bonds with the opposite screw sense. To this end, the point where the measured Cotton effect saturates was located and the CD signal at this point was equated to a net helicity of unity. As can be seen in Figure 2, for the system currently being studied, this is not straightforward, as the CD signal does not reach a plateau value, but instead keeps increasing with increasing fraction of “sergeants”. It was therefore necessary to estimate the saturation point of the graph. This was done by extrapolation of the curves at all three wave lengths; the saturation point was set at a fraction of sergeant of 0.2 for the mixture of monomers **2a** and **1** (black curve) and 0.4 for the mixture of monomers **3** and **1** (red curve). If $x=0.3$ or $x=0.5$ was chosen as the saturation point for the latter curve, good agreement between theory and experiment was obtained with similar values for the energetic parameters. Apparently, the energetic parameters are relatively insensitive to a change in the value of x at saturation. The lack of a plateau in the curve indicates that the chiral monomers have a larger contribution to the optical effect than do the achiral ones. This is likely related to the packing of the different types of monomer inside an aggregate.^{S3} To account for this, a parameter γ was introduced which measures the relative contributions of both monomer types to the net optical activity of the solution. Likewise, a constant of proportionality α was introduced, which connects the theoretical and the experimental optical effects. Both these parameters have been described previously in some detail.^{S3} Values for γ and α were obtained by fitting the

regime in Figure 2ii where the fraction of sergeants is high, and the values found ($\gamma = 1.3$ and $\alpha = 0.94$) were used in comparison to all experiments .

When comparing the theory to the measurements of the optical effect in solutions containing compounds **1** and **2a/2b**, it is expected that both the sergeants-and- soldiers results and the diluted-majority-rules results can be described with the same values for the free-energy parameters. This is because the only significant difference between the solutions is the amount of compound **2b** that is present, and because the values of the free-energy parameters do not depend on the handedness of the chiral monomers. Using a two-parameter least-squares-type fitting procedure, it was indeed found that the data of Figure 3 and that of Figure 2 (the black symbols) can be described with values of the helix reversal penalty and the mismatch energy of 5.4 and 0.48 $k_B T$. This corresponds to 13.5 and 1.2 kJ/mole at a temperature of 300 K.

A curve fit was also performed on the red symbols of Figure 2, corresponding to experimental CD data on solutions containing compounds **1** and **3**. Naturally, because a different sergeant was used here, the same parameter values cannot be expected to again yield a good agreement between theory and experiment. However, the value of the helix reversal penalty is expected to be close to that of the case described above, because the number of sergeants is small in both experiments, and the helix reversal penalty for these aggregates is in both cases likely close to that of aggregates consisting entirely of achiral monomers. Indeed, a value quite close to that of the black curve was found, 5.2 $k_B T$ instead of 5.4. (Although it is in fact possible to take the contributions of the achiral and chiral units to the helix reversal penalty into account explicitly,^{S2} this was not done, as it would introduce another parameter to the theoretical description.) The value of the mismatch penalty, on the other hand, was expected to be different from that of the solution containing **1** and **2a/2b**, since it

strongly depends on the molecular architecture of the sergeant molecules. Indeed, good agreement was found between these measurements and the theory for a value of $0.095 k_B T$, compared to 0.48 for the black curve.

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