VIP Supramolecular Chirality

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Helicity Induction and Amplification in an Oligo(*p*-phenylenevinylene) Assembly through Hydrogen-Bonded Chiral Acids**

Subi J. George, Željko Tomović, Maarten M. J. Smulders, Tom F. A. de Greef, Philippe E. L. G. Leclère, E. W. Meijer, and Albertus P. H. J. Schenning**

Synthetic polymeric and supramolecular helical systems are a topic of great current interest because of their chirotechnological applications in sensors, optoelectronic, and photochromic materials.[1] Mechanistic insight into the chiral amplification of these synthetic systems will provide a better understanding on the origin of homochirality of biological macromolecules and spontaneous resolution on crystallization.[2–4] In most cases, helicity has been achieved by the use of chiral monomers.[3,5] However, tedious asymmetric synthesis and lack of control over the chirality outcome make the design of chiral monomers a challenging task. A different approach towards helical systems is to exploit host–guest chemistry to induce tunable chirality to the achiral host by specific recognition of appropriate chiral guest molecules that are easy accessible. Although this strategy has been well studied in polymeric systems,[1b,3e] the extension of this concept to self-assembled systems is seldom reported,[5a,6] as the guest recognition through additional functional-group interactions may interfere with the stability of the supramolecular receptors themselves and hence a careful design is needed. Herein we use chiral acids as supramolecular chiral regulators, which bind to the periphery of the self-assemblies through hydrogen-bonded interactions and thereby induce tunable chiroptical properties. Spectroscopic probing of the helical self-assembly of optically sensitive π-conjugated chromophores sheds further light into the mechanistic pathways of chiral induction. We also demonstrate the chiral amplification with guest molecules.

The supramolecular system consists of an achiral oligo(*p*-phenylenevinylene) (OPV) π-conjugated host (A-OPVUT) capped with a mono-ureidotriazine (UT) motif designed for self-complementary quadruple hydrogen-bonding interactions (Scheme 1a). The free amine proton Ha and the triazine-ring nitrogen atom of the UT motif between the OPV group and the amine (see Figure 1a) can be used for additional two-point hydrogen bonding. Therefore, we chose complementary homochiral citronellic acid (*R*- or *S*-CA) as a chiral regulator (Scheme 1b).[7] A-OPVUT, carrying the achiral butyloxy side chains, was synthesized according to the reported procedure for chiral analogues with *S*-methylbutyloxy side chains.[8,9] The ^{1}H NMR spectrum of A-OPVUT in [D_8]toluene has NH signals at $\delta = 9.87$ (Hb) and $\delta = 10.49$ ppm (Hc) typical for dimeric quadruple hydrogen-bonded ureido-*s*-triazine species (Figure 1).[8]

We investigated the complexation of *R*-CA with A-OPVUT in [D_8]toluene, a good solvent for OPVs, by performing NMR spectroscopy titration experiments with a constant concentration of A-OPVUT (1 mM) and with increasing concentrations of acid guests. Since all OPV molecules are present as dimers at this concentration,[10] any further changes in NH-resonances of the UT motif in the presence of the acid would give clear information about the mode of binding. The Ha proton of A-OPVUT, which is not involved in the quadruple hydrogen bonding, showed a noticeable downfield shift in presence of the acid, which is definitive proof for hydrogen-bonding interactions between the acid and UT motifs (Figure 1). Nonlinear curve fitting of the chemical shift using a modified 1:1 binding model gave a K_a value of $(31 \pm 6)\ M^{-1}$.[11] The other two NH protons (Hb and Hc) involved in the quadruple hydrogen bonding are affected very weakly by complexation and showed only a small upfield shift, indicating that the dimeric form of OPV is not affected by guest binding (Figure 1).[9] These observations support the structure of the 1:1 A-OPVUT-citronellic acid complex as shown in Scheme 1b, where the acid binds to the ureidotriazine moiety of OPV through orthogonal two-point hydrogen bonding interactions.

We studied the self-assembly of host A-OPVUT (1×10^{-5} M) into supramolecular stacks in methyl cyclohexane (MCH), a poor solvent for the OPV backbone. Spectroscopic data showed characteristic features of the self-assembled OPV chromophores, such as a strong vibronic absorption at 505 nm ($\lambda_{max} = 435$ nm) and a red-shifted broad emission with a maximum at 610 nm ($\lambda_{ex} = 400$ nm).[9] At high temperature, disassembly of A-OPVUT leads to spectral features similar to those observed in chloroform, such as an absorption maximum at 431 nm and a structured emission spectrum with maxima at 501 and 533 nm, and an increased quantum yield.[9] To characterize the spectral changes during the self-assembly and to investigate its mechanism we performed temperature-

[*] Dr. S. J. George, Dr. Ž. Tomović, M. M. J. Smulders, T. F. A. de Greef, Dr. P. E. L. G. Leclère,[+] Prof. Dr. E. W. Meijer, Dr. A. P. H. J. Schenning
Laboratory for Macromolecular and Organic Chemistry
Eindhoven University of Technology
PO Box 513, 5600MB Eindhoven (The Netherlands)
Fax: (+31) 40-245-1036
E-mail: e.w.meijer@tue.nl
a.p.h.j.schenning@tue.nl

[+] Also at:
Université de Mons-Hainaut
Place du Parc, 20, 7000 Mons (Belgium)

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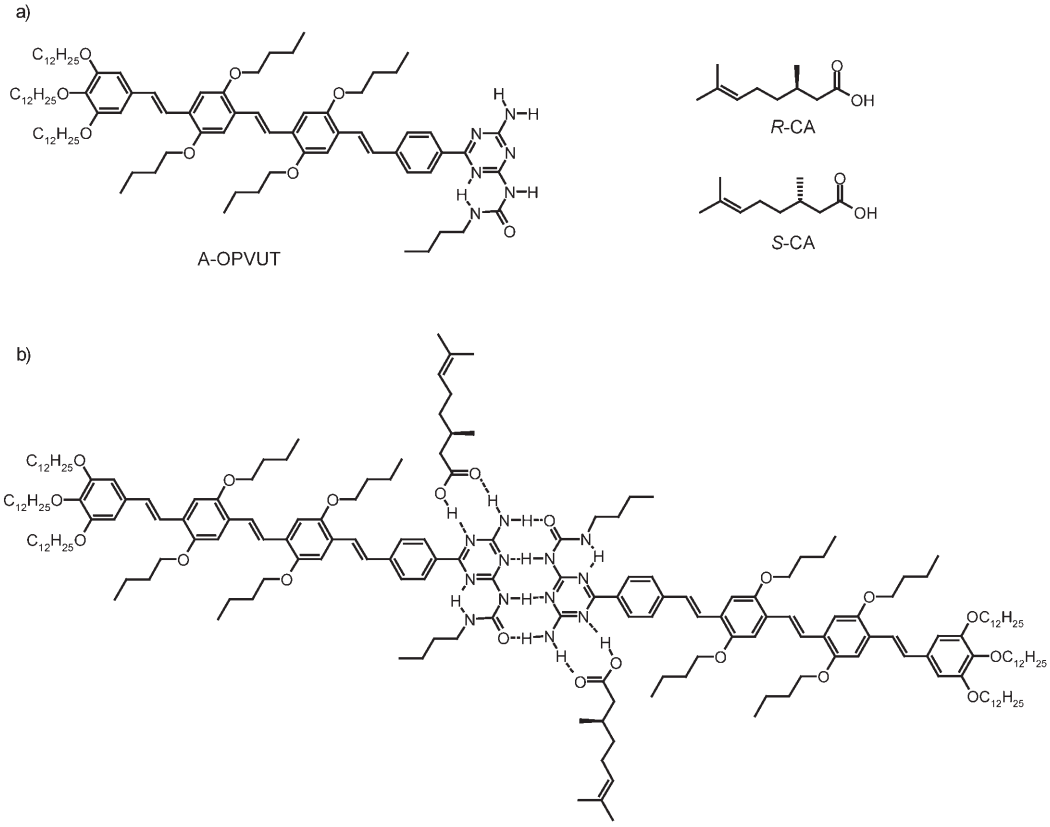
Supporting Information for this article is available on the WWW under http://www.angewandte.org or from the author.



Scheme 1. a) Molecular structures of achiral OPV host A-OPVUT and *R*-(+)- and *S*-(−)-citronellic acid (*R*-CA and *S*-CA, respectively) guests. b) Proposed hydrogen-bonded structure of the A-OPVUT–acid 1:1 host–guest complex (the 2:2 host–guest complex is considered here as a 1:1 complex since the binding sites are independent).

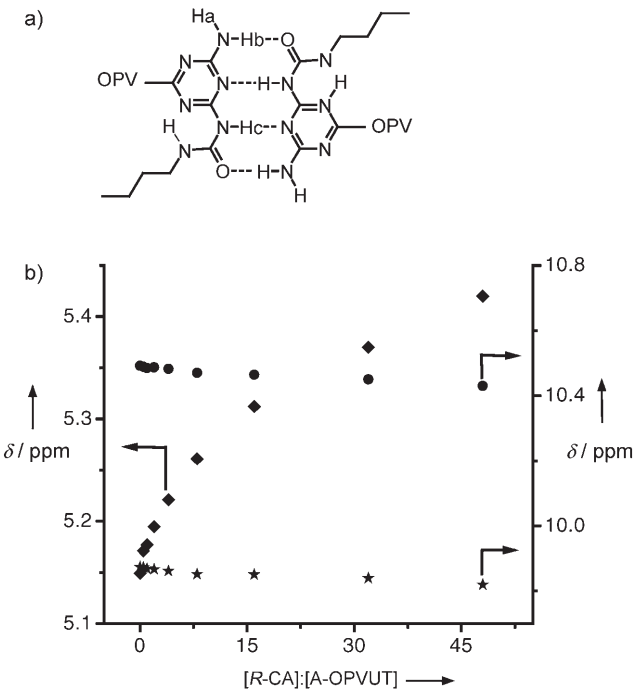


Figure 1. a) The quadruple hydrogen-bonding pattern of UTs. b) Chemical shifts of the NHa (◆), NHb (⋆), and NHc (●) protons of the A-OPVUT dimer (1.0 mM) in the ^{1}H NMR spectra (400 MHz) on complexation with *R*-CA (0–48 equivalents) in [D_8]toluene.

dependent studies under thermodynamic control by slowly cooling the solution from 363 K to 293 K at a rate of 60 K h^{-1}.[9,12] Analysis of the cooling curve obtained by monitoring the vibronic absorption at 505 nm (indicative of π–π stacking) revealed a highly cooperative nucleation-growth pathway for the self-assembly of A-OPVUT similar to that observed for reported chiral analogues: discrete monomeric or hydrogen-bonded dimeric species at high temperatures and π-stacked assemblies at lower temperatures.[8,9] The temperature at which the elongation of the A-OPVUT assembly sets in (T_e, 324 K, 1×10^{-5} M) is noticeably higher than that of the corresponding chiral derivative (313 K), indicating more stable π stacking for these achiral molecules.[9] Atomic force microscopy (AFM) analysis of a dropcasted MCH solution of A-OPVUT on mica showed micrometer long fibers of about 6-nm width that bundled at higher concentration to form gels.[9,13]

We further investigated the chiral induction in the self-assembly of A-OPVUT by the complexation of *R*-(+) or *S*-(−)-citronellic acid guest molecules in MCH. In order to self-assemble the host–guest complexes under thermodynamic control, mixtures of A-OPVUT (2×10^{-4} M) and chiral acid (4×10^{-4} M) in MCH were heated above T_e and cooled slowly (see below). Circular dichroism (CD) studies of A-OPVUT in the presence of *R*-CA or *S*-CA showed very strong mirror-image Cotton effects, indicating that the chiral guest induces a

preferred handedness in the self-assembled helical stacks of achiral OPV molecules (Figure 2a). Binding of *R*-CA gave a bisignated CD spectrum similar to that reported for the homochiral analogues: positive at high energy (λ_{max} = 420 nm) and negative at low energy (λ_{max} = 460 nm), with a zero crossing at 440 nm which is close to the wavelength of the absorption maximum characteristic of exciton-coupled helically ordered chromophores.[8] To follow the saturation of CD effects and to confirm the binding mode of chiral acids to A-OPVUT, we used the chiroptical properties as a marker and performed titration experiments. CD titration with a fixed concentration (2×10^{-4} M) of A-OPVUT in MCH but changing the concentration of the acid guests ($0-4\times10^{-4}$ M) showed a gradual increase of CD signal through an isodichroic point at the zero crossing for both *R*- and *S*-enantiomers of the citronellic acid (Figure 2a,b). The titration curve could be fitted to a 1:1 binding model, in which each OPV behaves as an independent binding site, giving an apparent association constant of $(20\pm3)\times10^{3}\,M^{-1}$ in MCH.[14] Apparently, the complex nature of the various processes occurring during self-assembly (see below) can be fitted to a simple model. No indications for significant chiral amplification during titration are observed, possibly because at low guest concentrations the unoccupied binding sites of the OPV stacks cannot be helically directed. The 1:1 stoichiometry of the A-OPVUT–acid complex is further confirmed by Job plot experiments, whereby the CD intensity was monitored (460 nm) against the mole fraction of A-OPVUT ($\chi_{A\text{-}OPVUT}$), which showed a maximum when the mole fraction of OPV was 0.5 (Figure 2c).[15]

All the normalized CD titration cooling curves (monitored at 460 nm) are fitted well by the nucleation-growth model, revealing in all cases a constant T_e of (341.4 ± 0.1) K and a constant H_e (enthalpy of elongation) of (140 ± 5) kJ mol^{-1} (Figure 2d).[9,12] Remarkably, this T_e value is similar for A-OPVUT itself (341.7 K at 2×10^{-4} M), indicating that chiral acid binding hardly affects the self-assembly and that A-OPVUT in MCH exists as a racemic mixture of *P*- (right handed) and *M*- (left handed) helices, the ratio of which is affected by the chiral guests. This result is further supported by the absorption spectrum of A-OPVUT, which does not change upon acid binding. AFM analysis of the co-assembled OPV-acid solution in MCH does not show significant changes in the morphologies of the aggregated stacks with and without acids.[9] We have taken extra care for linear dichroism (LD) artifacts in the CD measurements as a result of convective flow induced alignment of the long fibrous assemblies.[16] No LD is observed for A-OPVUT stacks during the cooling experiments in MCH in the elongation regime.[9] However, deviation of the CD data from the fit after reaching a critical stack length at low temperatures (approx. 313 K) is due to the contribution of LD from the clustering and alignment of fibers.[17]

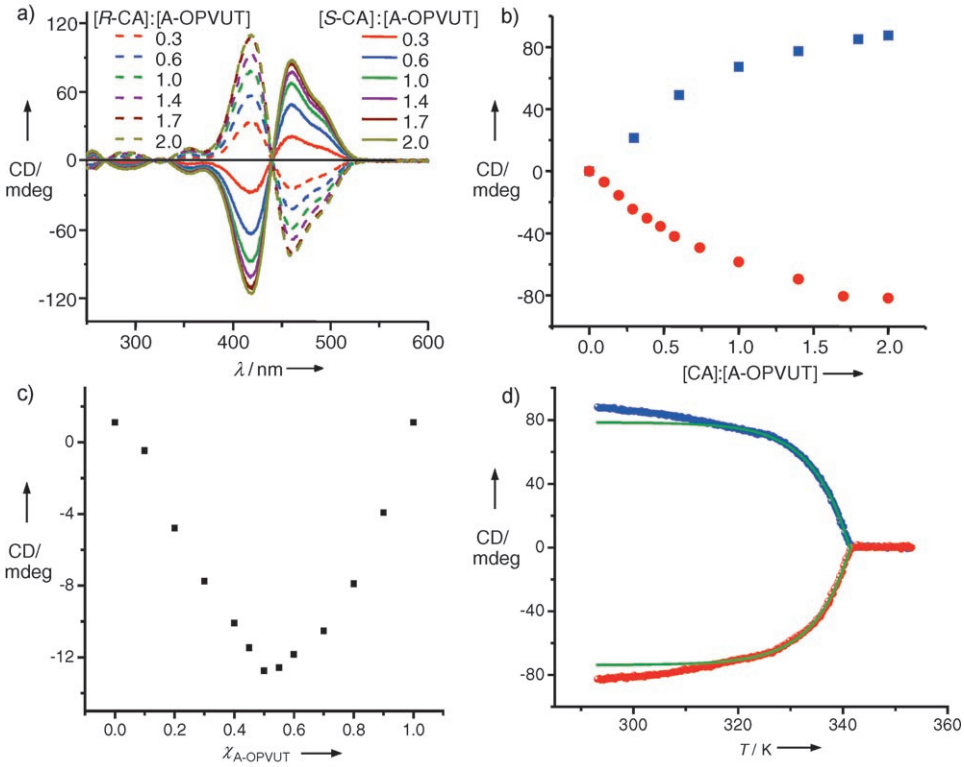


Figure 2. CD titration of *R*-CA and *S*-CA with A-OPVUT (2×10^{-4} M) in MCH; a) mirror-image CD spectra and b) plot of CD intensity at 460 nm versus equivalents of chiral acid; *S*-CA (■) and *R*-CA (●). c) Job plot of the mole fraction of A-OPVUT versus CD intensity at 460 nm; the sum of the concentration of A-OPVUT and *R*-CA is kept constant at 3×10^{-4} M. d) CD cooling curves (red and blue symbols for *R*- and *S*-acid (4×10^{-4} M) respectively) obtained by monitoring the CD intensity at 460 nm. The fits (green lines) are for one-dimensional growth ($dT/dt = -60\,K\,h^{-1}$, l = 1 mm).

Remarkably, when two equivalents of *R*-CA were added to a preassembled MCH solution of A-OPVUT at room temperature, no chiral induction was observed. To gain more insight into this observation, this solution was slowly heated (6 K h^{-1}) (Figure 3a), which showed the appearance and a gradual increase of induced CD signal above 313 K and subsequent disappearance at 343 K on transition to molecularly dissolved species. The temperature at which the CD effect appears (313 K) is close to the critical stack length of the OPVs, where the

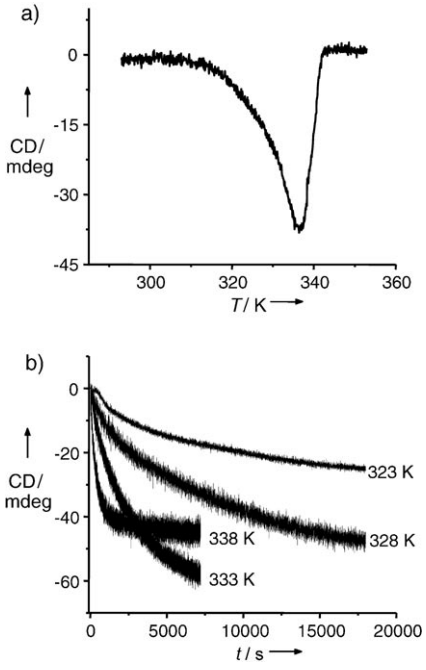


Figure 3. a) Heating curve ($dT/dt = 6\,K\,h^{-1}$) of A-OPVUT in MCH (2×10^{-4} M, $l = 1$ mm) with *R*-CA (4×10^{-4} M) by monitoring the CD intensity at 460 nm. b) Time-dependent growth of CD intensity at 460 nm for A-OPVUT in MCH at different temperatures in the elongation regime on the addition of twoequivalents of *R*-CA.

elongation process deviates from the one-dimensional growth model (Figure 2d). These data suggest that chiral induction only occurs at certain stages of the self-assembly process, where the stacks are dynamic enough for reorganization upon guest binding. To study the kinetics of chiral induction, two equivalents of *R*-CA were added to a preassembled A-OPVUT solution at different temperatures. The induction rate is faster at higher temperatures (Figure 3b). The exact mechanism of the helix reversal is not clear, as it could be helix reorganization similar to that observed in polymers and/or through an equilibrium between monomers and stacks. We have not yet analyzed the kinetic data.

All of the data presented on chiral induction is visualized in Figure 4. The self-assembly of A-OPVUT–citronellic acid complexes into helical stacks through π–π interactions follows a nucleation-growth mechanism, the handedness of which is biased by the remote molecular chirality of the hydrogen-bonded acids. However, chiral induction in a racemic mixture of *P*- and *M*-helical stacks of A-OPVUT in MCH by chiral acids is possible only in a certain temperature range. Although the OPV molecules are not able to reorganize for the helix reversal at low temperatures, the acid–guest binding could still be at equilibrium, as reported for polymeric systems.[18]

We studied the possibility of chiral amplification in the self-assembly of A-OPVUT (2.4×10^{-4} M) by varying the enantiomeric excess (*ee*) of the supramolecular chiral regulators (the total concentration of the acid is kept constant at two equivalents). The plot of CD intensity at 460 nm showed nonlinear behavior of the optical purity for the chiral acids, indicating that the major enantiomer of the guest molecules controls the helical sense of the OPV stacks (Figure 5a). In contrast to the titration experiments, the chiral amplification in the A-OPVUT self-assembly by varying the enantiomeric excess (*ee*) of acids is possible, as the total concentration of the acid is constant. Therefore, at high temperature, mainly host–guest complexes exist, in which the chiral acids are able to amplify the chirality upon self-assembly. Although the so-called "majority rules" principle, coined by Green and coworkers,[19] has been recently extended to noncovalent systems by varying the ratio of enantiomeric chiral monomers,[20] the amplification of chirality by the transfer of chiral information from the supramolecular chiral regulators to the achiral self-assembly is an unique observation. "Sergeant and soldiers" experiments with a mixture of *S*-CA and achiral octanoic acid further showed the chiral amplification in A-OPVUT supramolecular stacks upon guest binding (Figure 5b).

In conclusion, we have demonstrated the tunable chiral induction and amplification in achiral OPV assemblies by hydrogen-bond-assisted chiral-guest recognition. Furthermore, detailed investigation of the chiroptical properties sheds light onto the mechanistic pathways of chiral induction and shows that chirality induction is feasible only at certain stages of the self-assembly process. As the stability of the self-assembly is not affected by the chiral guests, they can be

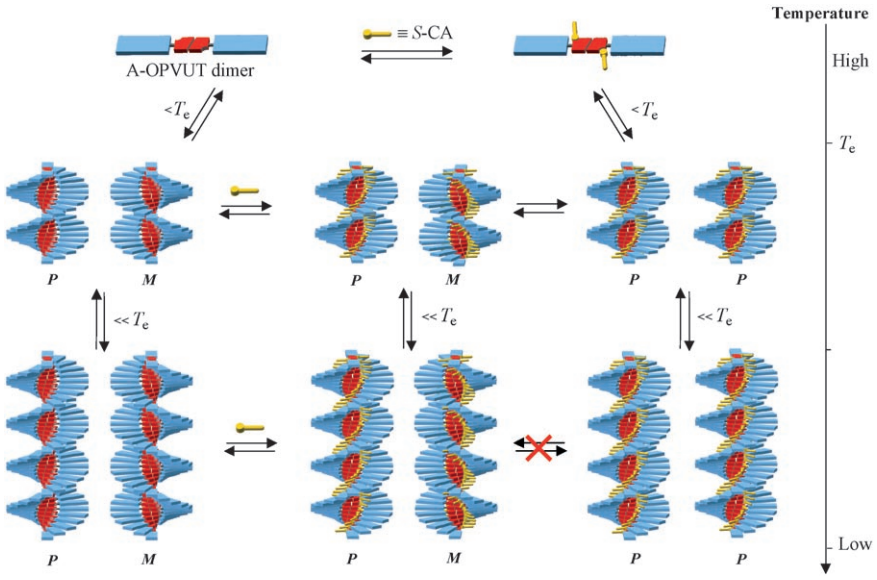


Figure 4. Schematic representation of the chiral induction in A-OPVUT stacks with chiral acid guests.

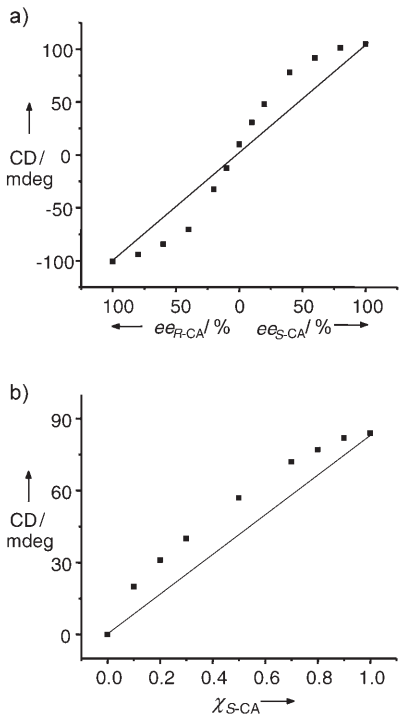


Figure 5. a) CD intensity of A-OPVUT (2.4×10^{-4} M) in MCH for mixtures of *R*-CA and *S*-CA. b) CD intensity of A-OPVUT (2×10^{-4} M) in MCH for mixtures of *S*-CA and achiral octanoic acid. In both cases the total concentration of the acid mixtures are kept constant at two equivalents and the CD intensity monitored at 460 nm. Straight lines show the situation for no amplification.

modified further to introduce interesting functional properties to the π-conjugated stacks.

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[9] See Supporting Information for details.

[10] Based on the association constant ($2\times10^4\,M^{-1}$) of the chiral analogues in chloroform, we propose that A-OPVUT, in toluene at 1 mM concentration and at room temperature, exists as hydrogen-bonded dimers.

[11] We assume the dimerization constant of *R*-CA in toluene is approximately $k_d = 446\,M^{-1}$; see: Y. Fujii, H. Yamada, M. Mizuta, *J. Phys. Chem.* **1988**, *92*, 6768. A-OPVUT exists fully as dimers ($k_d = 2\times10^4\,M^{-1}$) with two independent binding sites. See Supporting Information for details.

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[13] Critical gelator concentrations of A-OPVUT in MCH and toluene were determined to be 1 mM and 2 mM, respectively.

[14] Best fits (based on residual analysis) were obtained by assuming the dimerization constant of acid is zero, which is based on the preparation method of the complexes. *R*-CA is already hydrogen-bonded to the OPV dimers at high temperatures, and upon cooling, the CD signal appears owing to the stacking of this supramolecular complex. See Supporting Information for details.

[15] *S* or *R*-citronellol can also induce a preference for homochiral stacks. However more than 500 equivalents of chiral alcohol is required for the saturation of chirality, suggesting that the interaction between alcohol and OPV is less strong compared to the chiral acid guest (See Supporting Information). No chiral induction occurs when *R*-2,6-dimethyl octane is added.

[16] Surprisingly, we have observed a remarkable linear-dichroism effect in dodecane upon cooling the sample slowly for similar achiral OPV derivatives even in dilute solution, as a result of convective flow and resultant alignment of fibers in the cuvette (10^{-5} M). M. Wolffs, S. J. George, Ž. Tomović, S. C. J. Meskers, A. P. H. J. Schenning, E. W. Meijer, *Angew. Chem.* **2007**, *119*, 8351 – 8353; *Angew. Chem. Int. Ed.* **2007**, *46*, 8203 – 8205.
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