E. W. Meijer and A. R. A. Palmans

DOI: 10.1002/anie.200701285

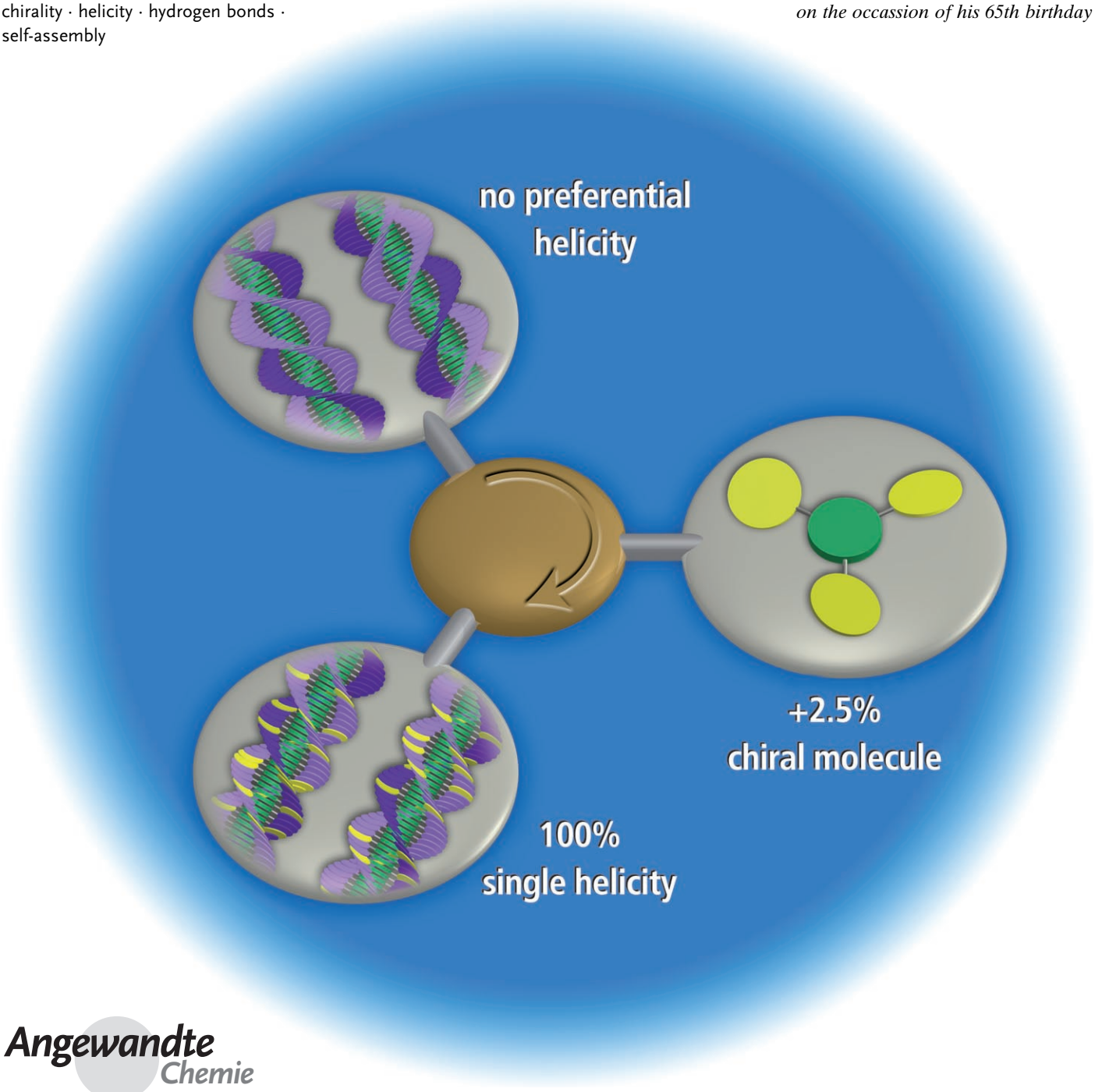
Chirality Amplification

Amplification of Chirality in Dynamic Supramolecular Aggregates

*Anja R. A. Palmans and E. W. Meijer**

Keywords:
chirality · helicity · hydrogen bonds · self-assembly

Dedicated to Professor David N. Reinhoudt on the occassion of his 65th birthday



The quest to understand the origin of chirality in biological systems has evoked an intense search for nonlinear effects in catalysis and pathways to amplify slight enantiomeric excesses in racemates to give optically pure molecules. The amplification of chirality in polymeric systems as a result of cooperative processes has been intensely investigated. Ten years ago, this effect was shown for the first time in noncovalent dynamic supramolecular systems. Since then, it has become clear that a subtle interplay of noncovalent interactions such as hydrogen-bonding, π–π stacking, and hydrophobic interactions is also sufficient to observe amplification of chirality in small molecules. Here we summarize the results obtained over the past decade and the general guidelines we can deduce from them. Predicting amplification of chirality is still impossible, but it appears to be a balance between different types of interactions, the formation of an intrinsically chiral object, and cooperative aggregation processes.

From the Contents

1. Introduction

The origin of homochirality in biological systems has intrigued scientists for many decades, and will undoubtedly continue to do so for the decades to come.[1,2] The chance creation of minute enantiomeric excesses in racemates may have given rise to an initial asymmetry in the prebiotic world, but this can only lead to high levels of optical purity in biomolecules by coupling such chance events with efficient sequential autocatalytic processes to propagate and amplify the chirality.[3] In the Soai reaction—the alkylation of pyrimidyl aldehydes with diisopropylzinc to give a chiral alcohol—the enantiomer formed in slight excess catalyzes its own production at a much higher rate than that of its enantiomer, which shows that the generation of homochirality from nearly racemic sources is indeed possible.[4] Amplification of chirality, therefore, is key to understanding the origin of chirality in biomolecules.

Polymers which have the ability to adopt a helical conformation have provided valuable insight into cooperative processes and the amplification of chirality in macromolecules.[5] Pioneering studies by Green et al. on the amplification of chirality in polyisocyanates, a class of helical polymers, have led to the discovery that only minute amounts of a chiral seed compound are required to bias one helicity and render the polymer homochiral.[6–8] The amplification of chirality in helical polymers such as poly(phenylacetylene)s, polyisocyanides, and polysilanes has now been well studied—experimentally and theoretically.[9,10] The transfer of chiral information through noncovalent interactions to helical polymers by a so-called memory effect is also well established. Reviews on this subject have appeared elsewhere.[11–13] In view of the relevance of the findings from polyisocyanates for understanding the amplification of chirality in noncovalent systems, and the inspiration this provided for many research groups, this Review will also summarize the most remarkable findings of Green and co-workers.

In the last decade, interest in the amplification of chirality has broadened to include nonhelical polymer systems and even fully noncovalent systems. A recent review by Maeda and Yashima discusses the detection and amplification of chirality in dynamic helical structures, with a focus on helical polymers.[13] Reviews discussing the formation of helicity in supramolecular aggregates and the induction of chirality in mesophases have also appeared.[14–21] Our Review concentrates on studies of noncovalent systems and focuses on the factors that affect the amplification of chirality in these dynamic supramolecular aggregates. We have limited ourselves to molecules that form aggregates in solution that are held together by noncovalent interactions (such as hydrogen bonding or π–π stacking) and/or solvophobic interactions. We will include the amplification of chirality in foldamers, an interesting class of oligomers/polymers that adopt a helical conformation in selected solvents.

An increased understanding of the amplification of chirality in such dynamic aggregates may provide simple mechanistic routes to generate homochiral biopolymers from racemic monomers—or nonracemic monomers of low enantiomeric excess—especially when the monomer undergoing the polymerization is in a well-defined self-assembled state.

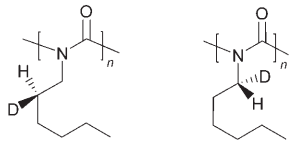
[*] Dr. Ir. A. R. A. Palmans, Prof. Dr. E. W. Meijer
Laboratory of Macromolecular and Organic Chemistry
Eindhoven, University of Technology (The Netherlands)
Fax: (+31) 402451036
E-mail: E.W.Meijer@tue.nl
Homepage: http://www.chem.tue.nl/smo

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

2. Amplification of Chirality in Macromolecules

Pioneering work on the synthesis of stereoregular vinyl polymers from mixtures of achiral and chiral vinyl monomers and mixtures of enantiomers showed there was a nonlinear dependence of the optical activity of the polymers on the enantiomeric excess of the side chain.[5] This remarkable observation was explained by the induction of an excess of one helical conformation of the polymer as a result of the coupling of the asymmetry of the side chain to the helicity of the backbone when there was an enantiomeric excess in the side chains.

In the 1980s, Green et al. started a series of detailed studies on polyisocyanates, a class of stiff polymers with an intrinsically helical conformation. Poly(*n*-hexylisocyanate), a helical polymer that showed no optical activity as a result of equal amounts of *P* and *M* helices, was made optically active by a single stereospecific deuteration at the α or β position of the side chain (Scheme 1).[22] Both polyisocyanates showed



Scheme 1. Structural formulas of specifically deuterated poly(*n*-hexylisocyanate)s.

remarkably large $[\alpha]_D$ values and CD effects, thus pointing to an excess of one helical conformation over the other. Moreover, dissolving poly(*n*-hexylisocyanate) in chiral (*S*)-1-chloro-2-methylbutane resulted in a CD effect for the achiral polymer.[23] The use of a range of chlorinated chiral alkanes as the solvent for poly(*n*-hexylisocyanate) showed that contact of the polymer with the chiral solvent was necessary to cause discrimination between the helical conformations, which was directly responsible for the magnitude of the CD effect.[24]

Interestingly, copolymerization of chiral monomers in poly(*n*-hexylisocyanate) led to the observation that only minute amounts of a chiral seed compound were required to render the polymer homochiral.[25,26] Mixing enantiomeric monomers in different ratios afforded polyisocyanates whose optical activity showed nonlinear effects that were dependent on the enantiomeric excess.[27] The two effects that influenced the amplification of chirality were referred to as the "sergeants-and-soldiers" principle and the "majority-rules" principle. The "sergeants-and-soldiers" principle implies a control of the helicity of large numbers of cooperative achiral units (the soldiers) by a few chiral units (the sergeants) whereas in the "majority-rules" principle a slight excess of one enantiomer leads to a strong bias toward the helicity of that enantiomer. Application of the one-dimensional Ising model to the experimental observations allowed these effects to be quantified.[24] Poly(*n*-hexylisocyanate) consists of left- and right-handed helical regions of variable length which are in equilibrium with each other. The mean length of these regions is determined by the Gibbs free energy for a reversal of helicity. The more free energy involved, the larger the mean distance between the helical reversals. The introduction of a stereocenter into the side chain introduces a bias for one of the helicities (through formation of diastereomers) and an energy difference per monomer residue between the left- and right-handed helices. Fitting the experimental data of deuterated poly(n-hexylisocyanates) to this theory resulted in an energy for helix reversal of 4 kcal mol^{-1} and a chirality-induced energy difference on the order of only 1 cal mol^{-1}. The methods introduced by Green et al. have been used more recently by others to study the intrinsic chirality of a variety of polymers such as poly(phenylacetylene)s, polyisocyanides, and polysilanes.[9]

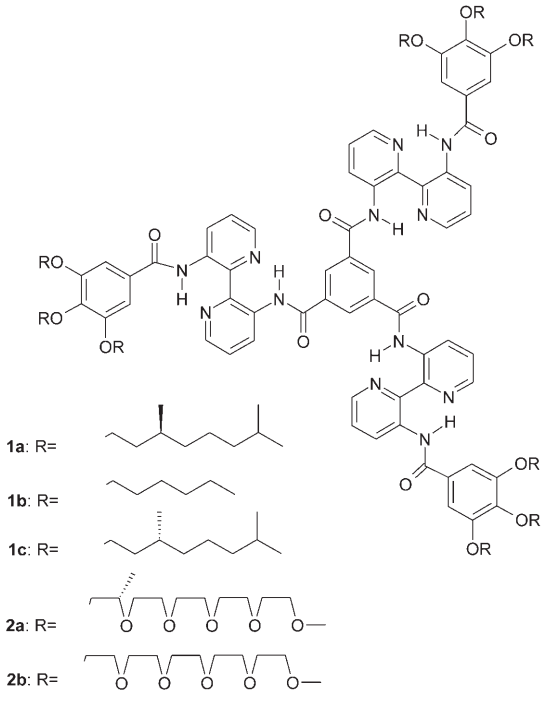
Evidence for chiral amplification is typically obtained by circular dichroism (CD) measurements or optical rotation dispersion (ORD) measurements. Probing the intensity of a CD effect at a certain wavelength or the optical rotation $[\alpha]_D$ as a function of the amount of the chiral entity added should result in a nonlinear response. In the case of the "sergeants-and-soldiers" experiments, chiral compounds are added to nonchiral compounds while in the "majority-rules" experiment enantiomers are mixed in different ratios. Over the past few years, several theoretical models have been developed to quantify the responses, and from these models information on the energy differences involved in the different processes has been extracted.[9,28–33]

Bert Meijer is Distinguished Professor in Molecular Sciences and Professor of Organic Chemistry at the University of Technology in Eindhoven, The Netherlands. After obtaining a PhD in 1982 from the University of Groningen (organic chemistry with Hans Wynberg) he worked for 10 years for Philips and DSM, before becoming head of the Laboratory of Macromolecular and Organic Chemistry at the Eindhoven University of Technology. His research is focused on supramolecular chemistry, functional organic materials, chemical biology, and stereochemistry.

Anja Palmans studied chemical engineering at the University of Technology in Eindhoven and completed her PhD in 1997 in the group of Prof. E. W. Meijer. From 1997 to 1999 she carried out postdoctoral research with Prof. P. Smith at the ETH Zürich. After working in industry (DSM), she became assistant professor at the Laboratory of Macromolecular and Organic Chemistry in Eindhoven in 2002.

3. Amplification of Chirality in C_3-Symmetrical Disc-Shaped Compounds

In the 1990s, we began our studies on disc-shaped C_3-symmetrical molecules based on benzene-1,3,5-tricarboxamide as new ordering moieties for supramolecular chemistry. Compound **1** (Scheme 2) was initially designed to give access to molecules with a large, planar aromatic core that would have liquid-crystalline behavior over a broad temperature range.[34] Inspired by the work of Green et al., and partly out of curiosity, we performed CD experiments by mixing chiral **1a** and achiral **1b** in hexane. Surprisingly, these experiments resulted in the observation of a strong amplification of chirality, and thus a new tool was discovered to study the chiral properties of multicomponent and dynamic supramolecular aggregates. This serendipitous result raised the question of the origin of the effects observed and the energies involved in the assembly process. Subsequently, a series of benzene-1,3,5-tricarboxamide derivatives were synthesized and studied. The most prominent results of these experiments are summarized below, since they form the basis of the now generally accepted concept for studying the cooperative effects involved in the formation of chiral aggregates. We then use this knowledge to review the other systems that have been studied.



Scheme 2. Hydrophobic (**1a–c**) and hydrophilic (**2a,b**) disc-shaped compounds with bipyridine units.

3.1. Disc-Shaped Compounds Based on the 3,3′-Diamino-2,2′-bipyridine Unit

The highly viscous solid compounds **1a** and **1b** (Scheme 2) were designed to show liquid crystallinity. Their structures were studied by polarization optical microscopy (POM), differential scanning calorimetry (DSC), and X-ray diffraction methods. Both derivatives showed thermotropic liquid-crystalline (LC) behavior over a broad temperature range (>300 K), with formation of a columnar, hexagonally ordered (Col_{ho}) phase.[34] The quadruplet splitting reflection observed in the X-ray diffraction measurements of both chiral **1a** and achiral **1b** was attributed to the pitch of a helix present within the columns. Therefore, it was concluded that the supramolecular order of the disc-shaped molecules was intrinsically chiral.

The chiral columnar structure present in the mesophase was retained when the molecules were dissolved in alkane solvents, as evidenced by X-ray diffraction measurements and UV/CD spectroscopy. The significant CD effect in the bipyridine transition of **1a** in hexane suggested that a preferred helicity of the columns was obtained as a result of the diastereomeric relationship of the *P*- and *M*-helical column in **1a** (Figure 1a).[35,36] In contrast, no CD effect was observed in chloroform, a solvent in which **1a** is molecularly dissolved. Sergeants-and-soldiers experiments of **1a** and **1b** in hexane revealed a pronounced nonlinear response of the CD effect when a small amount of chiral **1a** was added to a solution of **1b** (Figure 1b). Fitting the data to a theoretical model developed by Havinga showed an association constant K_{ass} of 5×10^8 L mol^{-1}, and also showed that one molecule of **1a** sufficed to dictate the helical sense of 80 molecules of achiral **1b**.[35]

Majority-rules experiments carried out on mixtures of the enantiomers **1a** and **1c** also showed a nonlinear response of the CD effect on the enantiomeric excess (Figure 2), thus

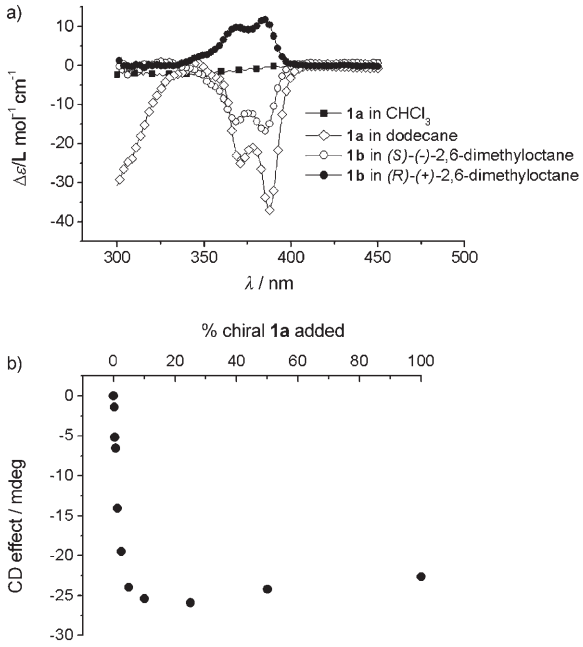


Figure 1. a) CD spectra of chiral compound **1a**, recorded in $CHCl_3$ or dodecane, and achiral compound **1b**, recorded in *(R)*-(−)-2,6-dimethyloctane or *(S)*-(+)-2,6-dimethyloctane. b) Amplification of chirality observed upon mixing solutions of **1a** and **1b** in hexane results in a nonlinear relationship between the CD effect and the amount of chiral **1a** added to achiral **1b**.

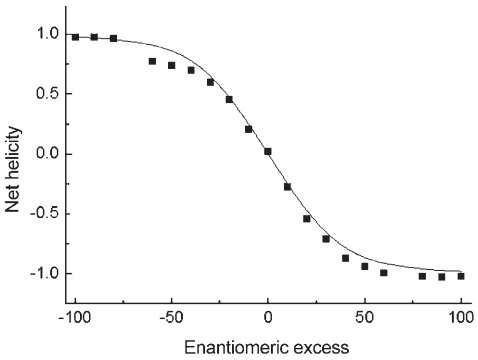


Figure 2. Net helicity as a function of enantiomeric excess measured by CD spectroscopy on mixtures of *(S)*-**1a** and *(R)*-**1c** in *n*-octane at 20 °C. The line indicates the theoretical result that gives the closest agreement with the experiment.

confirming the strong tendency for chiral amplification in these systems.[37] Furthermore, achiral **1b** showed pronounced mirror-image CD effects when dissolved in the chiral alkane solvents (*R*)-(−)- and (*S*)-(+)-2,6-dimethyloctane (Figure 1a). This remarkable observation—since these solvents are barely chiral and do not possess specific functional groups—suggests that the solvent is capable of organizing itself along the peripheral alkoxy chains of the bipyridine-based discs, thereby dictating the sense of the helicity. All of these results—including the preferred chiral solvation—are reminiscent of the behavior of poly(*n*-hexylisocyanate). Hence, it is expected that the theoretical models developed for macromolecules can also be applied to the noncovalent systems, provided the dynamic nature of the supramolecular aggregates is taken into account.

An important prerequisite for amplification of chirality in supramolecular aggregates is an intrinsic conformational chirality of the assembly, irrespective of the presence of a stereocenter in the molecules. The disc-shaped bipyridine compounds **1** were designed to be planar as a result of intramolecular hydrogen bonding between the amide-NH group and an N atom of the bipyridyl moiety in combination with the expected conjugation between the amide group and the aromatic core. However, the above results could only be rationalized by assuming a nonplanar conformation in which the bipyridine wedges are tilted with respect to the central benzene core. In alkane solvents, the packing between the molecules in one stack is optimal when all the wedges are tilted in the same direction, which results in a preferred stable chiral conformation of each individual molecule. This conformation resembles a propeller, which is a chiral object. When the propellers are stacked on top of each other, rotating the first with respect to the next will improve the packing, but will also give rise to a helix (Figure 3). Although no direct evidence was available to confirm this assumption, the stacks were proposed to be stabilized by threefold intermolecular hydrogen bonding between the amide groups of the central benzene ring of neighboring molecules. Equal amounts of *P* and *M* helices are present within the stacks of achiral **1b**, but the addition of one molecule of **1a** (sergeant) can dictate the helical sense of a number of achiral molecules of **1b** (the

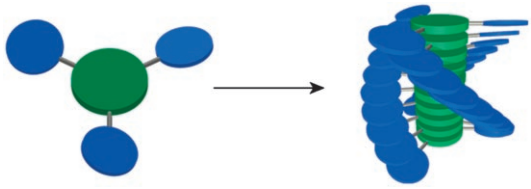


Figure 3. Propeller-like shape of compounds **1** (blue: bipyridine wedges, green: central benzene ring which results in a helical superstructure upon stacking in columns.

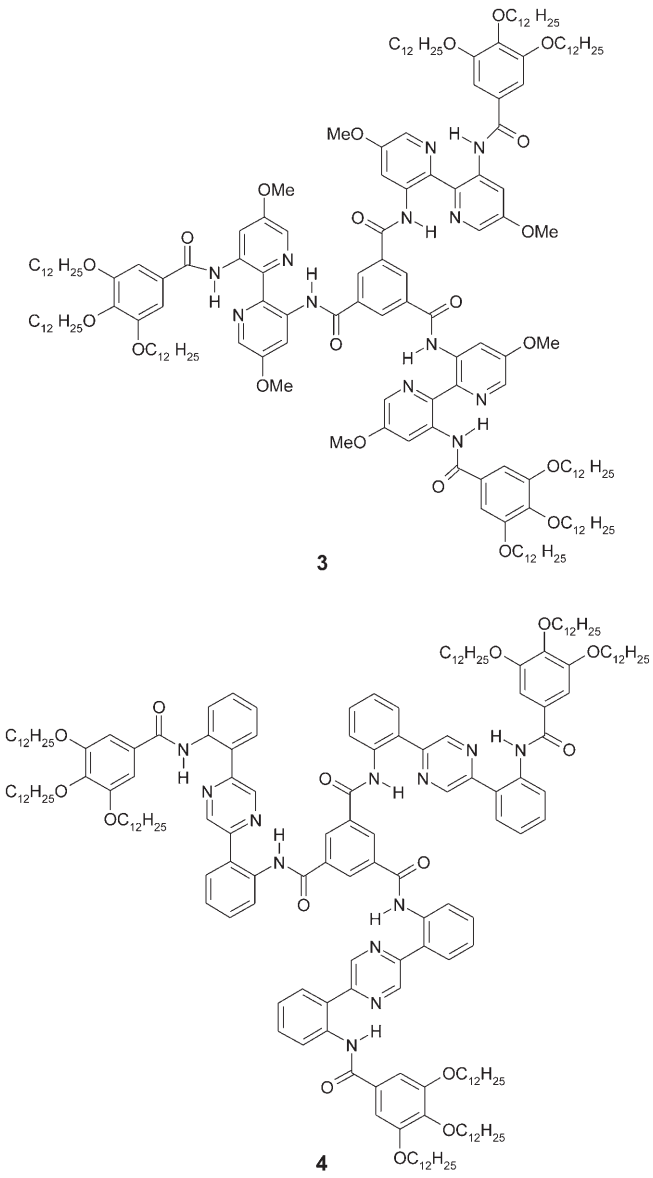
soldiers). This process is highly dynamic since the addition of a small amount of **1a** to achiral **1b** instantly results in a CD effect, which suggests there is a fast exchange between the molecules of different stacks.

The majority-rules experiments were carried out in combination with a theoretical model. Values for the energy penalty of a mismatch (the monomer is present in a helix of its nonpreferred screw sense) and of a helical reversal were obtained by fitting the experimental data with this model.[38] The mismatch penalty (0.94 kJ mol^{-1}) is about eight times lower than the penalty for a reversal of the helicity (7.8 kJ mol^{-1}). Despite the presence of contradictory information at the periphery, the energy gained by aggregation is apparently still larger than the energy lost by a mismatch. This result is rationalized by the fact that the "wrong" enantiomer has a different orientation of a methyl group in the disordered aliphatic part of the molecule. If present in small amounts, this minor enantiomer is unlikely to strongly affect the helicity of the aggregate and will act in accordance with the helicity preferred by the majority in the aggregate.

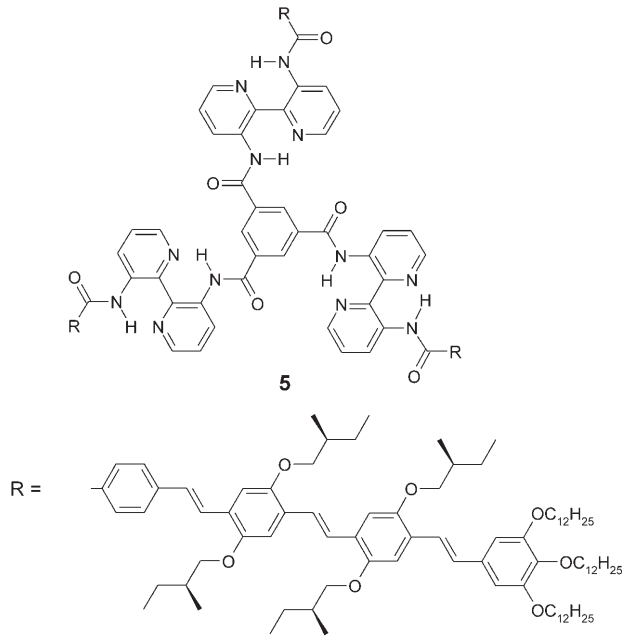
The importance of the careful matching of secondary interactions to obtain a well-defined chiral conformation in the aggregation process was illustrated by studying the aggregation behavior of analogous C_3-symmetrical molecules with additional methoxy substituents on the bipyridine units (**3**) or C_3-symmetrical molecules containing diphenylpyrazine moieties (**4**, Scheme 3).[39] UV measurements revealed a stronger aggregation of **3** and **4**, as expected in view of their stronger π–π stacking interactions. However, they lack any expression of chirality in the chiral solvent (*S*)-(+)-2,6-dimethyloctane.

The periphery of the disc-shaped compounds is also important, as highlighted when the bipyridine moiety was functionalized with chiral oligo(phenylene vinylene) (OPV) side chains (**5**, Scheme 4): Although **5** did form stable aggregates, little chiral ordering was observed. This finding was explained by competing types of π–π stacking interactions that differ in their strength and orientation.[40] Hence, in all of the modified systems evaluated, the ability for amplification of chirality, as observed in **1**, was completely suppressed as a result of an imbalance in the different interactions governing the aggregation process. Therefore, no well-defined chiral object was obtained in which cooperativity could result in an amplification of chirality.

Changing the peripheral alkoxy chains to hydrophilic oligo(ethylene oxide) chains (Scheme 2) allowed the study of the bipyridine-based discs **2** in polar solvents, such as *n*-butanol.[28,41] In contrast to the results of **1a** in hexane, where



Scheme 3. Compounds **3** and **4**, in which the bipyridine moiety was changed to a 5,5′-dimethoxy-2,2′-bypiridine and diphenylpyrazine moiety, respectively.



Scheme 4. OPV-functionalized C_3-symmetrical compound **5** with bipyridine units.

aggregation and expression of chirality are strongly interrelated, **2a** showed a two-step process upon heating in *n*-butanol. The combination of neutron scattering, CD, and fluorescence experiments showed that two different kinds of assemblies of **2a** in *n*-butanol exist: one which expresses chirality at the supramolecular level and one that does not (Figure 4a,b).[41] At low temperatures, rigid helical columns are present which lose their expression of chirality before they disaggregate. This behavior is strongly concentration dependent, as depicted in Figure 4c.

Evidently, *n*-butanol is capable of interfering with the structuring secondary interactions between the molecules that account for the positional order in the self-assembled structure. Nevertheless, a pronounced amplification of chirality was found when **2a** and **2b** were mixed in *n*-butanol at 5 °C in a sergeants-and-soldiers experiment at a concentration of 10^{-4} M.[42] It took only 1 molecule of **2a** to direct the helicity of 400 molecules of achiral **2b**. These sergeants-and-soldiers experiments were characterized by a strong time-dependence: approximately two hours were needed before the CD effect was fully developed after the addition of a small quantity of **2a** to a solution of achiral **2b**, irrespective of the temperature used to mix the compounds. This observation is in sharp to contrast to the mixtures of **1a** and **1b** in hexane where the maximal CD effect was reached instantaneously after mixing. Apparently, the high degree of order within the columns of the polar bipyridine-based discotic molecules **2** makes them reluctant to dissociate but, on the other hand, this stability favors a high degree of amplification of chirality. Similar to the transfer of the chirality from the chiral alkane solvent to achiral **1b**, the chirality of the solvent alcohol solvent (2*S*)-(−)-methyl-1-butanol was also transferred to the helical columns of **2b**.

Surprisingly, the dynamic behavior of **2a**,**b** was retained in water.[43] The maximum expression of chirality was observed when 25–30 mol% of **2a** was added to achiral **2b** at 5 °C in water. The association constant (K_{ass}) was calculated from Havinga's model to be $1\times10^{8}\,\mathrm{L\,mol^{-1}}$, with a homochiral helicity length of **12** molecules. This means that at a concentration of 10^{-4} M, columns with a degree of polymerization as high as 200 are being formed and that 15–20 chiral molecules are needed to form homochiral columns. This is remarkable in an environment were the stabilizing intermolecular interactions, that are responsible for the transfer of chirality, can only exist by means of the hydrophobic microenvironment created by the arene–arene interactions.

The increase in the understanding of the role of the solvent in a nucleation–growth-type aggregation processes, as

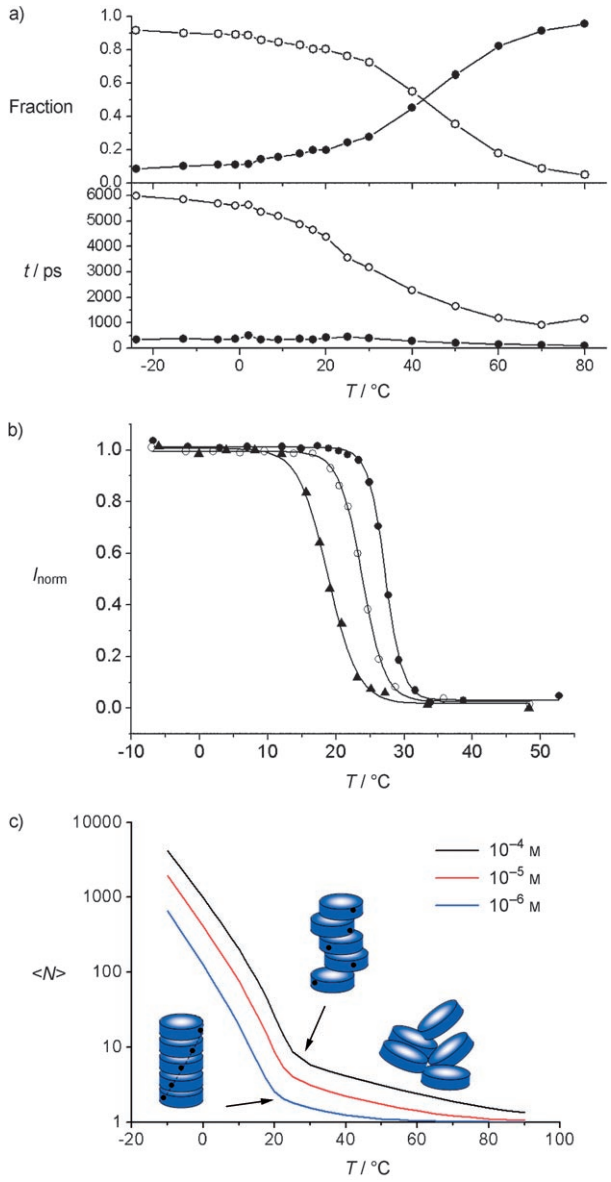


Figure 4. a) Top: Fraction of aggregated molecules (○) and molecularly dissolved molecules (●) in a 10^{-6} M solution of **2a** in *n*-butanol at different temperatures. Bottom: Lifetimes *t* of the two species, aggregated (○) and single molecules (●), as a function of temperature in the same solution. b) Normalized intensities of the CD spectra of **2a** in *n*-butanol at 337 nm at three different concentrations (10^{-6} ▲, 10^{-4} ○, and 10^{-2} M ●). c) Prediction of the average number of molecules participating in one column $\langle N \rangle$ at the three different concentrations as a function of temperature. The arrows mark the transition from achiral to chiral aggregates.

recently discussed for OPV-triazines (see Section 5), holds much promise to further unravel the intriguing helical aggregation of **1** in alkane solvents and of **2** in water and alcohols.[44] Moreover, the combination of quantum chemical calculations and detailed solid-state MAS-NMR experiments will enable direct evidence to be obtained on the presence/absence of the elusive intermolecular hydrogen bonds as well as the relative contributions of the different noncovalent interactions during the aggregation process.[45]

3.2. C_3-Symmetrical Compounds with Urea and Inverted Amide Groups

Apart from the effects of changes in the periphery of disc-shaped compounds on the ability to amplify chirality, changes to the interior of disc-shaped compounds based on the benzene-1,3,5-tricarboxamide core were also studied in detail (Scheme 5).[46,47]

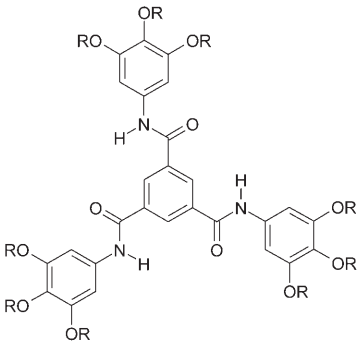
In **6a**, the bipyridine moiety was omitted and the gallic acid moiety was directly added to the central core. Although **6a** shows a columnar liquid-crystalline phase, a complete loss of the columnar structure in apolar solutions was observed. Inverting the three central amide bonds to form trisamides **6b** in which the nitrogen atoms were connected directly to the aromatic ring (Scheme 5) failed to generate a columnar structure in solution.[40,46,47] The columnar structure was restored in alkane solvents by changing the central trisamide to a benzene ring with three urea groups to give **7**.[46] Moreover, amplification of chirality was observed upon mixing compounds **7a** and **7b** in heptane. The effect is much less pronounced than in case of the bipyridine-based discs **1** and **2**: a cooperative length of only two molecules and large hysteresis effects were observed.

The effect of replacing the three central amide groups by three urea groups was also studied for the bipyridine-based discs. Compounds **8a**,**b** showed liquid-crystalline behavior and columnar stacks were present in alkane solvents. However, sergeants-and-soldiers experiments showed a lack of chiral amplification. Apparently, the stronger hydrogen bonds between the urea groups drastically affects the dynamic nature of the supramolecular aggregates. This result confirms that carefully balancing the different types of interactions is the key for a successful amplification of chirality.

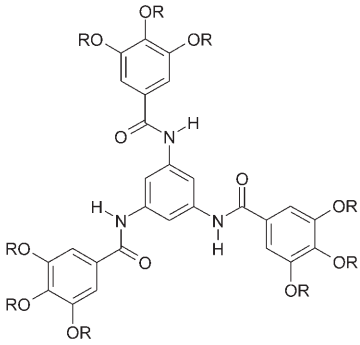
3.3. *N*,*N*′,*N*″-Trialkylbenzene-1,3,5-tricarboxamide Derivatives

The disc-shaped bipyridine compounds are a fascinating class of molecules for studying the factors governing aggregation processes and transfer of chirality, which ultimately may lead to in-depth insight into the amplification of chirality processes in dynamic aggregates. However, because of their complex molecular structure, important questions for explaining the phenomena observed—such as the origin of the CD effects and the importance of hydrogen-bonding interactions during the aggregation process—have remained unanswered. Therefore, we decided to simplify the system and omit the bipyridine section. *N*,*N*′,*N*″-Trialkylbenzene-1,3,5-tricarboxamides, the most basic structure for disc-shaped compounds based on the benzene-1,3,5-tricarboxamide unit, was therefore selected for further detailed investigations.

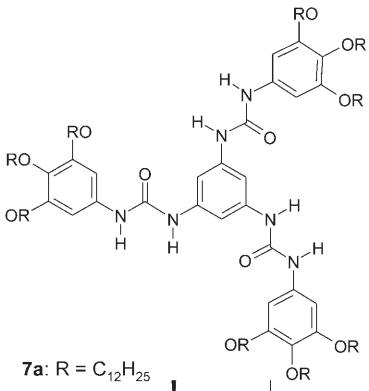
Gratifyingly, *N*,*N*′,*N*″-trialkylbenzene-1,3,5-tricarboxamides also demonstrate pronounced amplification of chirality (Scheme 6) as evidenced by mixing achiral **9a** with chiral **9b** (sergeants-and-soldiers experiment) and mixtures of chiral **9b** and **9c** with achiral **9a** (diluted majority-rules experiment). The energy for helical reversal and mismatch were on the same order of magnitude as observed for the bipyridine-based tricarboxamides, and the mean correlation length



6a: R = $C_{12}H_{25}$



6b: R = $C_{12}H_{25}$



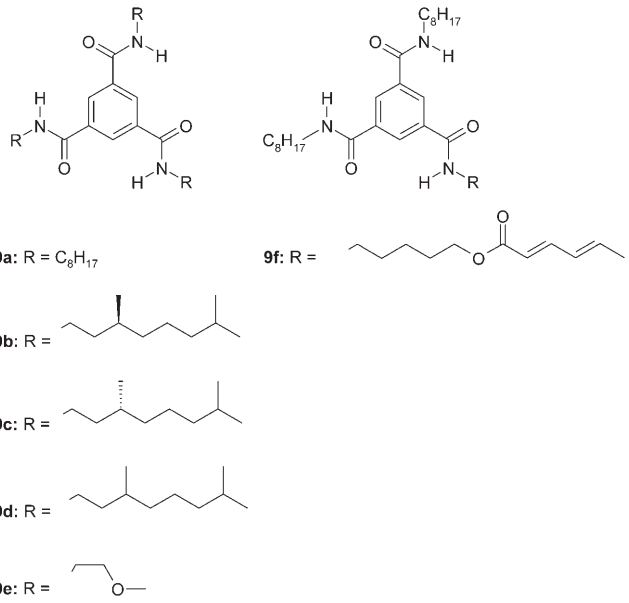
7a: R = $C_{12}H_{25}$

7b: R =

8a: R = $C_{12}H_{25}$

8b: R =

Scheme 5. Disc-shaped compounds **6**–**8** with different cores.



9a: R = C_8H_{17}

9b: R =

9c: R =

9d: R =

9e: R =

9f: R =

Scheme 6. Benzene-1,3,5-tricarboxamide derivatives **9a**–**f**.

between sites of helical reversal was estimated to be 225 monomer units.[48,49] Matsunaga et al. had previously studied these compounds for their thermotropic liquid-crystalline behavior,[50,51] while Hanabusa et al. had observed that they formed organogels in selected solvents.[52,53] The efficiency of gel formation was attributed to a combination of intermolecular hydrogen-bonding and van der Waals interactions between the alkyl side chains. Most importantly, the crystal structure of *N*,*N*′,*N*″-tris(2-methoxyethyl)-benzene-1,3,5-tricarboxamide (**9e**) was reported by Lightfoot et al.[54] The X-ray structure clearly showed the presence of a triple-helical network of hydrogen bonds that resembled the α helix in proteins (Figure 5). The amide moieties were tilted by about 40° with respect to the central benzene core. The proposed propeller shape of the wedges (see Section 3.1) around the central core may therefore indeed be the key for efficient transfer of chirality in all discotic compounds based on benzene-1,3,5-tricarboxamide.

The simple structure of **9** allowed for a detailed study by IR spectroscopy in both the solid state and in solution. The typical NH stretch of the intermolecularly hydrogen-bonded

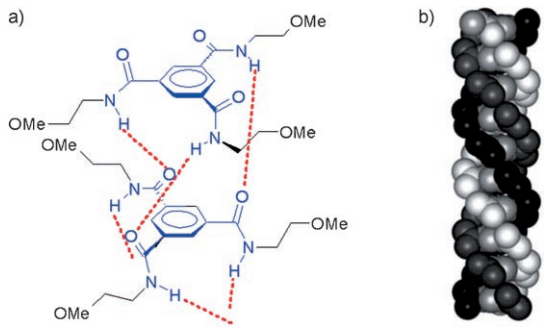
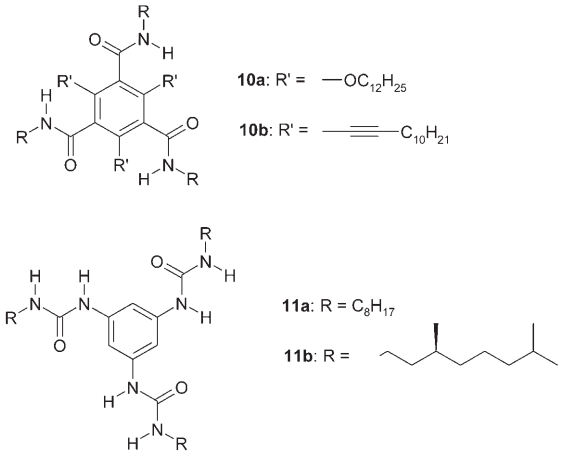


Figure 5. a) Threefold intermolecular hydrogen bonding in molecular stacks of disc-shaped compound **9e**. b) 3D representation of **9e** showing the triple-helical hydrogen-bonding network.

amide group at 3223 cm^{-1} found in the solid state was indeed retained in alkane solution up to high dilutions (10^{-5} M in cyclohexane); this interaction was responsible for stabilizing the columnar structure.[48,49] The viscoelastic behavior of gels based on **9d** was studied in detail by Shikata and co-workers by rheology methods as well as by IR and CD spectroscopy.[55–57] Interestingly, the addition of the chiral *S* enantiomer **9b** increased the amount of hydrogen-bonded amide groups, as evidenced by IR spectroscopy, and an increase in the relaxation time of the system was observed from rheology measurements. Moreover, the formation of an excess of one helicity as a result of the majority-rule effect was found when more **9b** was added to the racemate **9d** (comprised of **9b** and **9c**).[58]

The addition of alkoxy or acetylene substituents at the 2-, 4-, and 6-positions in the-1,3,5-tricarboxamide moiety results in "crowded" aromatic compounds (Scheme 7).[59–64] The



Scheme 7. Crowded benzene-1,3,5-tricarboxamide derivatives **10a,b** and urea derivatives **11a,b**.

alkoxy derivative **10a** self-assembles into columns, and the NH stretch at 3295 cm^{-1} is indicative of intermolecular hydrogen bonding in the mesophase.[62] The introduction of chiral side chains onto the amide groups showed that helicity is also present in these columnar stacks, even in solution.[63] Interestingly, the chiral columnar stacks organize further into superhelices in concentrated solutions which reflect circularly polarized light. Replacing the alkoxy groups with acetylene groups (**10b**) also resulted in the columnar structure remaining intact in the solid state and also in solution.[60,64] It is expected that the study of this highly interesting class of crowded aromatic compounds by using sergeants-and-soldiers and majority-rules experiments will reveal details of the cooperativity of the stacking process and the energies involved.

The introduction of additional hydrogen bonds by replacing the amide group by a urea group afforded compounds **11a** and **11b** (Scheme 7).[46] Although these compounds were thermally too unstable to enable a thorough study of their thermotropic liquid-crystalline behavior, IR spectroscopy showed that hydrogen bonding occured in the ordered (liquid) crystalline phases. The chiral derivative **11b** showed a small CD effect in alkane solution which is indicative of the presence of ordered stacks. The CD effects proved to be unstable over time when 10^{-4} M solutions of **11a** and **11b** were mixed, which suggests that the aggregates formed are not present in a thermodynamically stable state. Mixing solutions of achiral urea **11a** with chiral amide **9b** illustrated the effect of a mismatch of the secondary hydrogen-bonding interactions in these systems: mixing chiral amide **9b** (5–20%) with achiral urea **11a** resulted in amplification of chirality (Figure 6a). However, increasing the amount of chiral amide **9b**

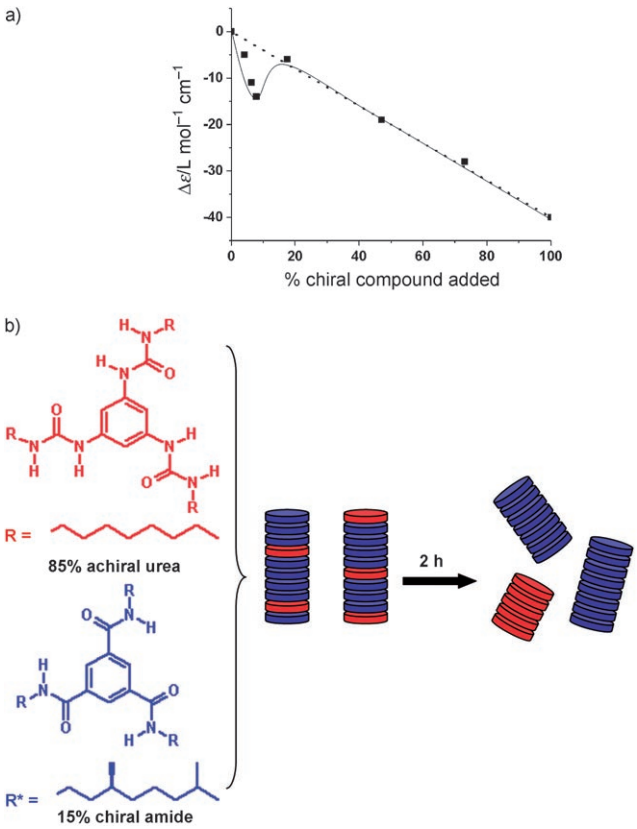


Figure 6. Results of the sergeants-and-soldiers experiments with chiral amide **9b** and achiral urea derivative **11a** in heptane: a) After an initial amplification of chirality when low concentrations of chiral amide **9b** are added, a linear behavior of $\Delta\varepsilon$ as a function of the concentration of **9b** is observed. b) Schematic representation of the phase separation of initially mixed stacks into two different stacks containing only the chiral amide or achiral urea derivative.

resulted in a linear relationship of the CD effect as a function of the amount of chiral **9b** added. Moreover, the CD effect present in the mixture of 15% chiral **9b** and 85% achiral urea **11a** disappeared over time. This result was attributed to a phase separation of the chiral amide and achiral urea molecules in different stacks (Figure 6b).

Currently, we are applying the nucleation-growth self-assembly model, which is established in the self-assembly of OPV-triazines (see Section 5), to a variety of *N,N′,N″*-trialkylbenzene-1,3,5-tricarboxamides.[65] A high cooperativ-

ity is involved in the stacking process, and the degree of cooperativity is more pronounced when chiral molecules are employed. The role of the position of the chiral center as well as the role of the solvent in this self-assembly process is currently under investigation.

3.4. Polymerization of N,N′,N″-Trialkylbenzene-1,3,5-tricarboxamide Derivatives

The efficient helical organization of benzene-1,3,5-tricarboxamide derivatives raised the question as to whether it was possible to retain the columnar structure after polymerization and if chirality can be expressed into a polymer backbone during the polymerization of achiral monomers.[66,67] For this purpose, asymmetrical sorbyl-functionalized compound **9f** was synthesized (Scheme 6). In cyclohexane, **9f** aggregated through its amide bonds into a columnar structure and the sorbyl groups could be readily polymerized with UV light.[67] It appeared that photopolymerization preferentially occurred within the columnar assembly. Mixing polymerizable, achiral **9f** with chiral, nonpolymerizable **9b** in a sergeants-and-soldiers type experiment and subsequent photopolymerization of the sorbyl groups in cyclohexane resulted in a CD effect, after removal of any remaining chiral **9b**.[66] Blending **9f** with the enantiomeric sergeant **9c** resulted in the mirror image CD effect after photopolymerization, as expected. The CD spectra were concentration independent, which suggests that the CD effect is a consequence of the intramolecular organization within the molecularly dissolved polymers: any helical bias present before the poymerization was almost completely retained in the polymer. The CD effect completely disappeared when methanol was added to the solution, but removal of all the solvent and re-dissolution in the original solvent led to a complete recovery of the CD effect. The process amounts to a reversible unfolding/refolding cycle of the polymer and indicates that the helical bias induced by chiral **9b** is locked into the polymer and that the chiral information is encoded in the sorbyl main chain. The complete sequence is shown in Figure 7.

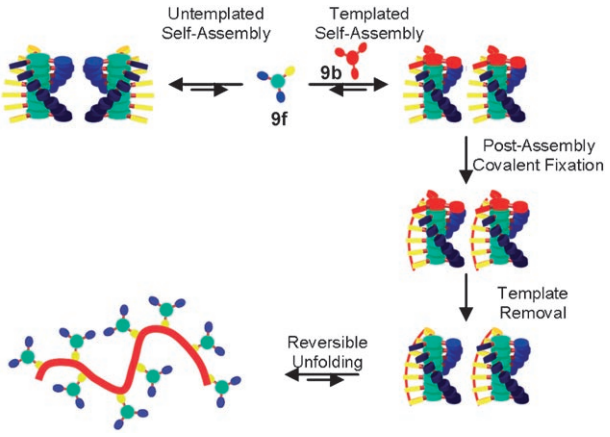


Figure 7. Sequence of events leading to the locking of supramolecular chirality into supramolecular aggregates.

4. Amplification of Chirality in Other Disc-Shaped Molecules

Apart from the 1,3,5-tricarboxamide-based compounds discussed above, there are numerous examples of disc-shaped compounds that exhibit (helical) columnar structures in the solid state and in their mesophases.[17] If the intermolecular interactions are positional and sufficiently strong, the helical superstructure can be expected to be retained in solution, and thus amplification of chirality may occur.

A particularly well-studied class of disc-shaped compounds are the hexa-*peri*-hexabenzocoronenes (HBCs) developed by Müllen and co-workers.[68,69] HBCs with lipophilic alkyl side chains display thermotropic liquid-crystalline behavior over a broad temperature range and form Col_h mesophases. A helical arrangement of the molecules within the columns was observed in the mesophase of a chiral derivative,[70] but no studies on the amplification of chirality in solution were reported. Presumably, the strong π–π stacking interactions are not sufficient to lock the positional information within the columns in solution which results in the loss of helicity upon dilution. Moreover, HBC molecules tend to rotate freely around their columnar axis in solution.[71] Additional specific interactions are required to keep the molecules positionally ordered with respect to each other, as exemplified by complexes of carboxy-substituted HBC with poly(L-lysine), which formed helical superstructures in the mesophase.[72]

To date, amplification of chirality has only been observed in amphiphilic HBC derivatives (Figure 8a).[73] In this case, crystalline bilayer tapes were formed in THF which consisted of two graphitic layers of π-stacked HBC units that were connected by interdigitation of the paraffin side chains (Figure 8b). These layers rolled up in a helical fashion and a mixture of left- and right-handed helical nanotubes resulted when an achiral derivative was used, whereas chiral HBC amphiphile **12** showed a strong amplification of chirality. Majority-rules experiments were conducted, and a nonlinear relationship between the enantiomeric excess and the CD effect was observed. The magnitude of the effect is comparable to that observed with **1**. Compound **13**, which has the stereocenter located in the alkyl substituents, did not show any evidence of chirality amplification—when the chiral center was positioned in the oligo(ethylene oxide) side chain in these systems, a preference for one of the helicities in these systems was observed. This finding was attributed to the fact that the branching methyl group hampers crystallization of the paraffin side chains, thereby preventing the formation of a bilayer.

X-ray diffraction measurements showed that chiral phthalocyanine **14** had a helical superstructure in its columnar mesophase, and Langmuir–Blodget films showed a CD effect (Scheme 8).[74,75] No CD activity was present in solution, which suggests that the intermolecular interactions were too weak. Increasing the intermolecular interactions by the addition of four additional crown ether residues to the phthalocyanine core (**15a**, Scheme 8) resulted in columnar mesophases and long linear aggregates; the latter are indicative of increased intermolecular interactions.[76] A

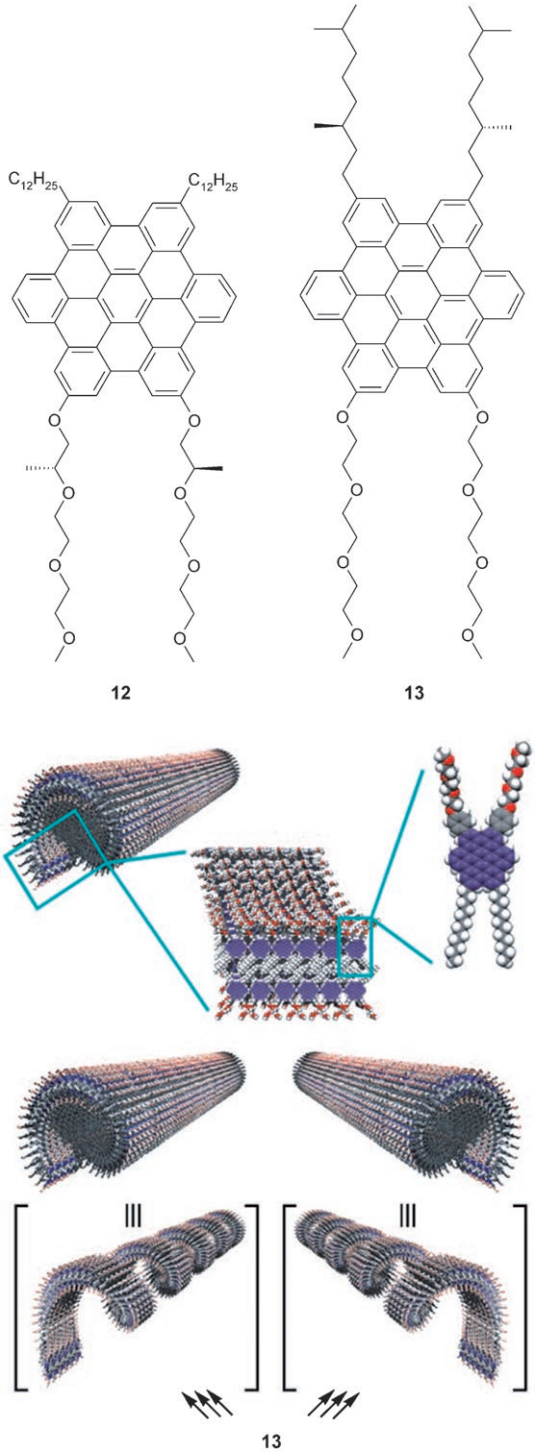
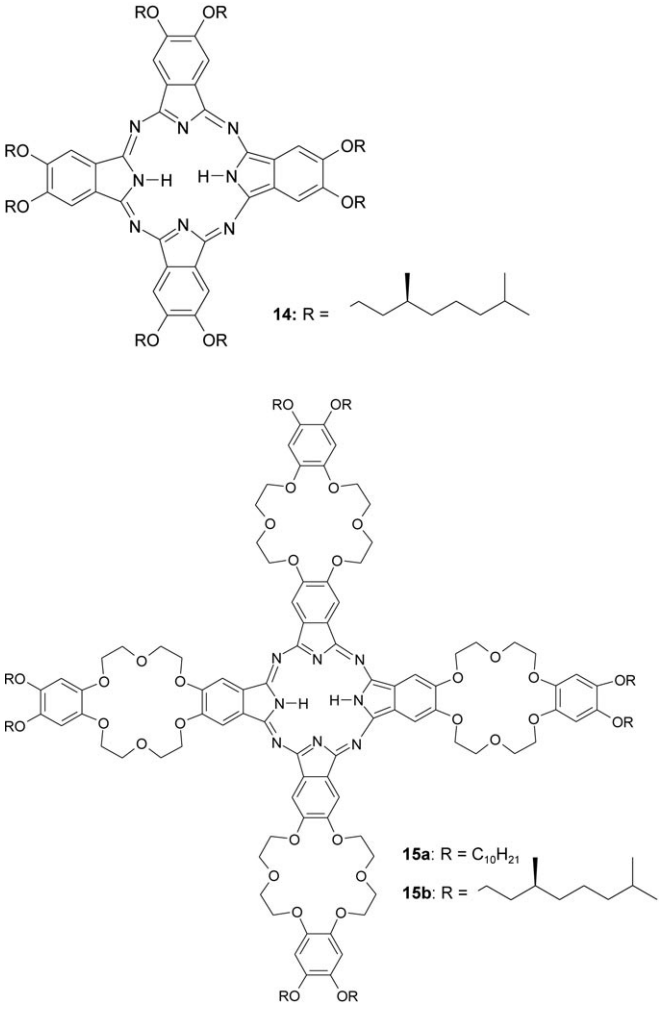


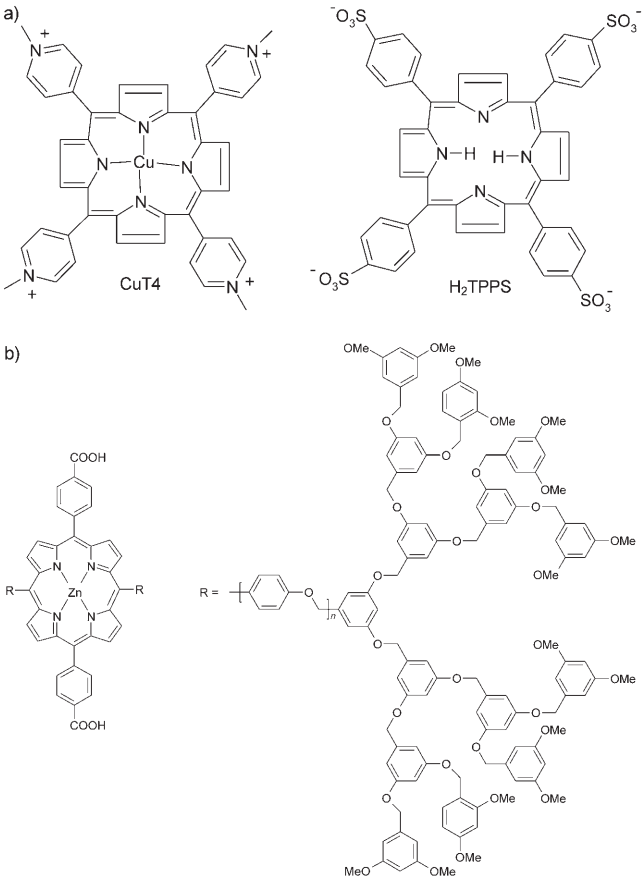
Figure 8. a) Amphiphilic HBC derivatives **12** and **13**. b) Self-assembly of the chiral graphitic nanotubes consisting of the HBC amphiphiles **13**.



Scheme 8. Phthalocyanine derivatives **14** and **15** investigated for their ability to show chiral amplification.

solution of chiral derivative **15b** (Scheme 8) in chloroform/methanol (1/1) showed helicity in solution as evidenced by a CD effect.[77] Sergeants-and-soldiers experiments on mixtures of chiral **15b** and achiral **15a**, however, showed no amplification of chirality.[17] In fact, at least two molecules of the chiral **15b** have to stack next to each other to give rise to a helical packing. This finding suggests that the chiral side chains are necessary to induce chiral perturbations in the stacking of the chiral molecules. Other examples in which an anti-cooperative stacking process in solution resulted in a lack of chirality amplification include the aggregation of hexakis(-porphyrinato)benzenes and complexes of tetrazoles with 1,3,5-tris(4,5-dihydroimidazol-2-yl)benzene.[17,78]

Water-soluble, achiral porphyrins were found to show hierarchical, helical self-assembly in water when a ternary complex was prepared from an achiral CuT4 tetracation, a H_2TPPS tetraanion, and the helical anionic poly(L-glutamate) (Scheme 9a).[79,80] The formation of such a complex was made possible by the shielding effect of the cationic units, which minimize the electrostatic repulsion between the two anionic components. These complexes were remarkably stable, which allowed them to "memorize" the chiral information imprinted by the template, poly(L-glutamate). After a pH-induced helix-to-coil transition of poly(L-glutamate), the CD effects remained unchanged, thus proving the stability of the complex. This evidence strongly suggests that the porphyrin heteroaggregates initially adopt the chirality from the template and then, because of their kinetic inertness, memorize the helicity and become themselves intrinsically chiral. In

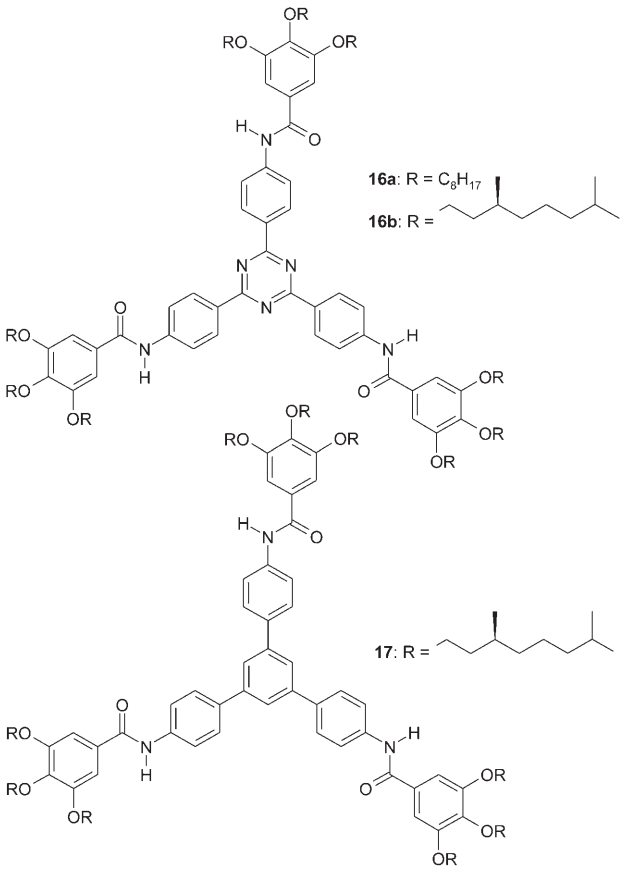


Scheme 9. a) Water-soluble porphyrin derivatives that form chiral aggregates when templated with poly(L-glutamate). b) Hydrogen-bonded dendritic zinc porphyrin J aggregate that has a chiroptical memory for spin-coating directions.

fact, they are perfectly capable of acting as templates for the amplification of their own structure: the addition of CuT4 and H_2TPPS to the imprinted assemblies lead to a proportional increase in the CD effect, which shows that the growth process is completely enantiospecific.

An interesting and still not fully understood example of transfer of chirality from the macroscale to the nanoscale was recently described by Aida and co-workers for a porphyrin-based system,[81] following the pioneering work of Ribo et al.[82] An achiral dendritic zinc porphyrin (Scheme 9b) gave rise to optically active films after spin coating. Although the zinc porphyrines studied were achiral, J aggregates can be formed in solution which may adopt a chiral conformation by twisting the stack. Either of the two enantiomeric forms could be selected by choice of the spinning direction during the spin-coating process, as evidenced by the mirror-image CD spectra of the films obtained after clockwise and counter-clockwise spinning. Interestingly, esterification of the acid groups of the porphyrin or spin coating from a solvent in which the porphyrin was molecularly dissolved resulted in the absence of CD effects after spin coating. This remarkable transformation of a macroscopic spinning direction into a stable supramolecular chirality led to the suggestion that macroscopic mechanical forces are also capable of transfering chirality to a nanoscale object. A similar result, but without studying the amplification of chirality, was found by Li and co-workers when they observed the spontaneous formation of optically active monolayers of chiral porphyrins as a consequence of the formation of a statistical imbalance between right- and left-handed aggregates.[83] They found that sampling the aggregates of multiple experiments resulted in an equal number of left- and right-handed aggregates. These results hint at the intrinsic chirality of the aggregates, even in the absence of a stereocenter and hence these systems should be capable of showing sergeants-and-soldiers effects.

Ishi-i et al. recently introduced benzene- and triazine-based discotic compounds **16** and **17** (Scheme 10)[84] which form stable gels in a variety of solvents. IR spectroscopic



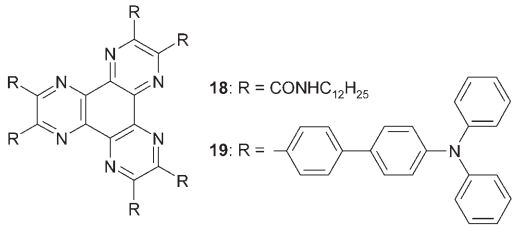
Scheme 10. Disc-shaped compounds **16** and **17** with central triazine and benzene rings, respectively.

studies showed the presence of intermolecular hydrogen bonds. As seen in Section 3, a columnar aggregate structure stabilized by cooperative π–π stacking, hydrogen-bonding, and van der Waals interactions is a good indication of the successful transfer of chirality. The π–π stacking of the central triazine moieties results in a one-dimensional aggregate in which a triple-helical network of hydrogen bonds between the amide groups propagates along the aggregate axis and enforces a helical structure. A bias for one helicity is observed by introducing a chiral center in to the alkyl substituent. Sergeants-and-soldiers experiments between chiral **16b** and achiral **16a** revealed a strong amplification of chirality: the

addition of only 1 mol% of chiral **16b** to achiral **16a** resulted in a CD spectrum having the intensity of pure chiral **16b**. Changing the central triazine ring to a benzene ring resulted in the complete loss of the CD effect in chiral derivative **17**, even in nonpolar solvents. This result was explained by the fact that the benzene derivative can only stack through hydrogen-bonding interactions between the amide groups, while ordered π–π stacking is hampered because of its nonplanar structure, and thus a less-ordered aggregate is formed.

Interestingly, the helicity in **16** can be preserved by ring-closing metathesis polymerization mediated by the Grubbs catalyst when an achiral component with terminal olefinic groups forms the pseudoenantiomeric aggregate in the presence of a tiny amount of the chiral **16b**.[84] In the absence of a chiral center, and after polymerization and removal of the chiral component, optically active objects with extremely high stabilities result. It is interesting to note that a small change in the molecular design—removing the benzamide and directly coupling the 3,4,5-trialkoxybenzene moiety to the triazine core—results in columnar mesophases, but no CD effect is observed in solution.[85]

Although no data are published on the presence of amplification of chirality, aliphatic derivatives of triphenylenes, hexathiotriphenylenes, and hexaazatriphenylenes have all been extensively evaluated for their ability to form columnar mesophases. Helicity in the columnar structure was observed in the case of hexathiotriphenylene.[17] Typically, the intermolecular interactions are weak and columnar order is lost upon the addition of solvent. A notable exception may be hexaazatriphenylene **18** (Scheme 11), where the presence

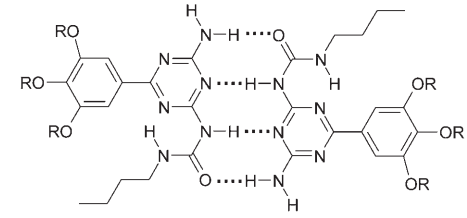


Scheme 11. Hexaazatriphenylene derivatives **18** and **19**.

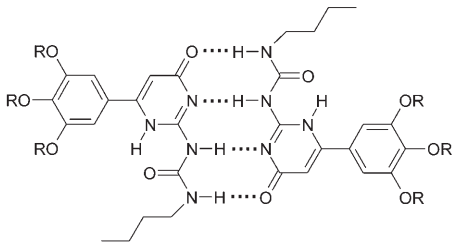
of six amide bonds resulted in the smallest interdisc distance (3.18 Å) found in discotic molecules.[86] The amide clamps between the adjacent molecules in the stacks must lead to a dramatic increase in the columnar stability, but no data on the solution characteristics of the system have been reported. Hexaazatriphenylene (HAT) **19**, on the other hand, not only shows a columnar mesophase, but is also capable of gelating a variety of solvents. Interestingly, strong mirror-image CD effects are observed when **19** is dissolved in (*R*)- and (*S*)-1-phenylethanol. These CD effects in the HAT chromophore region are attributed to the formation of ordered chiral aggregates in the gel phase, presumably as a result of a helical packing of the molecules. These observations show that the chiral information present in the solvent can be transferred to the self-assembled stack.[87]

5. Cooperative Stacking in Helical Self-Assembled Ureidopyrimidinone and Ureidotriazine Polymers

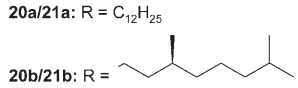
Self-complementary ureidopyrimidinone and ureidotriazine units have been well studied as building blocks for supramolecular polymers (Scheme 12).[88–93] Strong cooperative fourfold hydrogen bonding in a DDAA or DADA array (D = donor and A = acceptor), respectively, gives rise to strong dimers in the solid state and in solution. The association constants measured for the ureidopyrimidinone



20



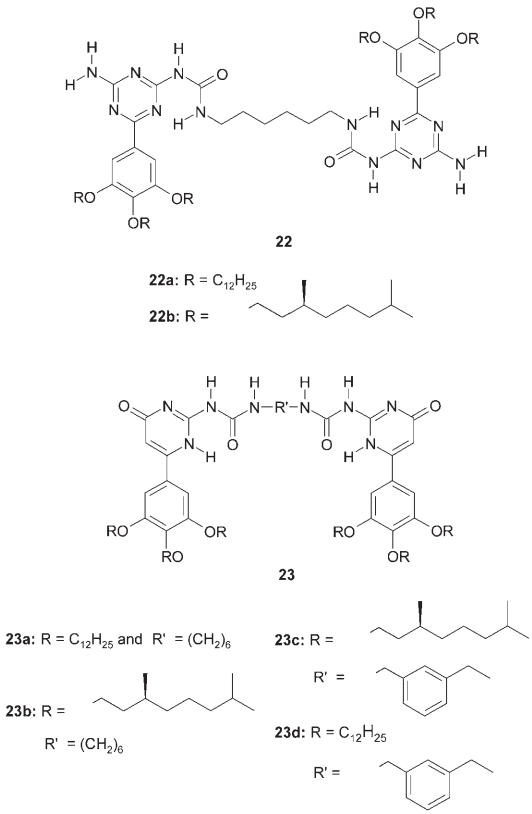
21



Scheme 12. Self-complementary ureidopyrimidinone and ureidotriazine units **20** and **21**, respectively.

and ureidotriazine units in chloroform are around 10^7 and $10^4\,M^{-1}$, respectively. A large and planar aromatic core is formed through the dimerization (Scheme 12). Compounds such as **20** and **21** with flexible side chains lead to columnar mesophases. Ureidotriazine derivatives were elaborately studied by small angle neutron scattering, CD spectroscopy, and NMR spectroscopy. A solvent such as dodecane, in which the dimers are unable to dissolve, leads to the formation of columnar aggregates, although no CD effects were observed for **20b** because of free rotation of the dimers in the columnar structure.[89] The difunctional species **22** (Scheme 13) also formed a columnar structure in dodecane; in this case a pronounced CD effect in the π–π transition of the ureidotriazine unit pointed to the presence of helicity in these columns.[89] Apparently, the hexamethylene linker restricts the rotation and locks the relative orientation of the difunctional derivatives in **22b** so that peripheral chiral information can be transferred into a preferred helicity of the columnar aggregate.

Changing the ureidotriazine unit to the more easy to dimerize ureidopyrimidinone unit highlighted the subtleties



Scheme 13. Difunctional ureidotriazine and ureidopyrimidinone **22** and **23**.

involved in the aggregation pocessess. In this case, monofunctional compound **21b** did not show a CD effect in dodecane, while difunctional derivative **23b** did.[92] However, the importance of the balance between the different interactions for inducing a chiral columnar structure was revealed when the hexamethylene spacer in the chiral difunctional compound **23b** was increased in length. No CD effects were present in the CD spectra of compounds with C_7- and C_8-methylene spacers, which suggests that the helical columnar structure is lost. A clear CD effect in dodecane was found for the difunctional ureidopyrimidinone **23c** with a *meta*-phenyl spacer.[92] Interestingly, mixing chiral **23c** with achiral **23d** in a sergeants-and-soldiers experiment resulted in strong amplification of chirality, whereas this was not the case for mixtures of **23a** and **23b** with the flexible hexamethylene spacer. This result suggests that helical polymeric aggregates are formed in stacks of **23c/d** in dodecane, while **23a/b** probably consists of stacked dimers.[92] The exact reason for these remarkable differences is not completely understood, but evidently small changes in the molecular design results in dramatic changes in the aggregation behavior.

One of the most remarkable amplifications of chirality was observed in mixing experiments of achiral difunctional **22a** with chiral monofunctional **20b**.[94] Whereas **22a** alone gave equal amounts of *P* and *M* helices and the stacks of **20b** were not chiral, because of free rotation of the discs in the stack, a mixture of **22a** and **20b** gave a strong nonlinear optical activity. Hence, mixing the two optically inactive solutions resulted in the formation of an optically active solution. It is proposed that **20b** acts as a chiral end stopper for supramolecular polymer **22a**, thus making both helices of **22a** diastereomeric. The difference in energy and the dynamics of the systems results in an excess of one helix over the other. The maximum optically activity was found for a 10% solution of **20b** with 0.02 wt% **22a**.

Ureidotriazine derivatives were also equipped with polar chiral penta(ethylene oxide) side chains instead of the lipophilic alkyl chains to study their aggregation behavior in water.[90] Although the monofunctional derivatives did not stack in water, the difunctional derivatives did. This stacking finds its origin in the high local concentration of hydrophobic units as a consequence of the hexamethylene linker. A hydrophobic stacking at 10^{-5} M preceded the dimerization. A pronounced CD effect of the chiral difuntional derivatives at concentrations of 10^{-4} M suggested a preferred organization in a supramolecular chiral aggregate. Chiral amplification was observed by mixing a chiral monofunctional ureidotriazine with an achiral difunctional triazine, both with water-soluble oligo(ethylene oxide) side chains, albeit at the slightly higher concentration (10^{-3} M).

To investigate the influence of additional π–π stacking interactions, ureidotriazine derivatives with chiral OPV moieties were synthesized.[95] A combination of CD, UV, and fluorescence spectroscopy leads to the conclusion that these molecules stack in a helical fashion, reminiscent of a helical stairway (Figure 9). The aggregation process was found to occur through a nucleation and growth type of self-assembly, which is characterized by a size-dependent association constant that gives rise to cooperative kinetics.[44] The self-assembly process depended strongly on the solvent,

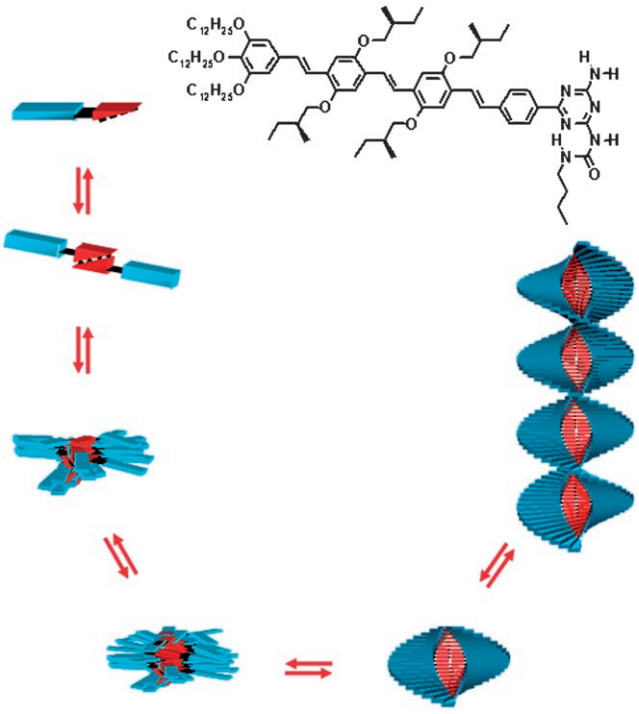


Figure 9. A ureidotriazine (red) with chiral OPV side chains (blue) that dimerizes and subsequently polymerizes into a helical stairway.

which suggests that an organized shell of solvent molecules plays an explicit role in rigidifying the aggregates and guiding them into higher order assembled structures. Surprisingly, preliminary sergeants-and-soldiers experiments of the chiral OPV-triazine derivative (Figure 9) with an achiral tetrabutyloxy analogue did not show amplification of chirality, even though all the prerequisites are there: dimerization of the triazine moieties through fourfold hydrogen bonding, π–π stacking through an extended π system, phase separation between the lipophilic alkyl tails and the aromatic core, and the formation of an intrinsically chiral object. However, phase separation between the chiral and achiral OPV-triazine moieties seemed to dominate the aggregation process at low concentrations, which resulted in a lack of mixing between the different helical stacks.[96]

6. Chiral Amplification in Dynamic Hydrogen-Bonded Aggregates

Reinhoudt and co-workers performed detailed studies on the transfer of chirality in hydrogen-bonded aggregates with a rosette motif.[97,98] Calix[4]arene dimelamines and chiral 5,5-diethylbarbituric acid derivatives were found to assemble diastereoselectively into a chiral hydrogen-bonded structure.[99] The driving force for the assembly process is the formation of 36 hydrogen bonds between the complementary bonding arrays of the 9 components.[100] The chirality in the self-assembled system results from the helical twist between the two rosette motifs, which can be either left- (*M*) or right-handed (*P*; Figure 10). A preferred helicity arises by adding a chiral barbiturate. Interestingly, the chiral barbiturate can be substituted by an achiral cyanurate, as cyanurates form stronger hydrogen bonds with melamines than barbiturates.[101] The newly formed aggregate showed a very pronounced CD effect, despite the lack of a stereocenter. Clearly, this system has a memory for chirality. The resultant chiral structures were very stable, as exemplified by a half-life of racemization of over four days at room temperature in solution. The amplification of chirality in these dynamic aggregates was then investigated by the sergeants-and-soldiers technique.[102] Either chiral melamine derivatives or chiral cyanurate derivatives were added to the dynamic hydrogen-bonded aggregates. Large nonlinear effects were observed, and the chiral response was different depending on the nature of the chiral seed compound used (melamine or cyanurate). Kinetic models were successfully developed to fit the experimental data.

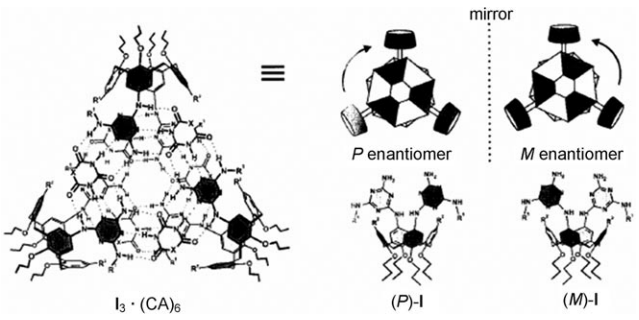


Figure 10. Melamine-cyanurate complexes $I_3 \cdot (CA)_6$ [CA = cyanurate (X = NR^3)] self-assemble into an object that is intrinsically chiral. The use of achiral building blocks leads to the both *P* and *M* enantiomers in soluition.

Increasing the level of complexity resulted in the synthesis and study of tetrarosette aggregates.[103] These larger structures can be considered as two double rosette aggregates linked covalently. The dissociation of one tetramelamine building block required the breaking of 24 hydrogen bonds, and therefore a smaller dissociation rate constant than the double rosette assembly was expected, which would give rise to a system with a more pronounced amplification of chirality. The results indeed show a high degree of amplification of chirality under thermodynamically controlled conditions, that is, the degree of chiral amplification is not influenced by the method by which the system is formed.

Several other elegant examples have been reported that take advantage of the formation of dynamic complexes or macrocycles in solution as a result of multiple hydrogen-bonding interactions.[104–109] Helical rosette nanotubes with tunable chiroptical properties were reported by Fenniri et al.[105,110,111] In fact, this appears to be the first example in which the majority-rules principle was found to be operative in a supramolecular system.[105] Compound **24** self-assembles into hexameric macrocycles that stack into nanotubes in a methanolic solution (Figure 11).

An induced CD effect was expected to arise when a chiral amino acid in its zwitterionic form was added to the prochiral compound **24**. Indeed, the addition of L-alanine and D-alanine, respectively, to a solution of **24** resulted in mirror-image CD spectra, thus confirming that the chirality of the guest (promotor) was transferred to the supramolecular assembly. The inducing power of alanine was expected to be proportional to its enantiomeric excess but, instead, the addition of a slight excess of D-alanine resulted in a non-proportional response of the CD effect. This result suggests that the major enantiomer of the amino acid present in excess not only binds to the nanotubes but apparently promotes the binding of its congeners and dictates the induced chirality and its extent (dominant promotor), while the enantiomer present in lower concentration does not express its chirality at the supramolecular level (recessive promotor). Indeed, this is a classical example of the majority-rules principle, here observed in a supramolecular aggregate.

An elegant example of the transfer of chiral information through molecular assembly was shown by Rebek co-workers.[104,112] A calix[4]arene substituted with urea groups on the upper rim was reported to form dimers in solution that were held together by 16 hydrogen bonds and could accommodate small guest molecules in its interior.[112] A stereocenter introduced next to the urea group served as a chirality element, and heterodimerziation occured exclusively with a single-handed direction of the urea bonds. The resulting capsules were nonracemic and were capable of discriminating between enantiomers of guest molecules.

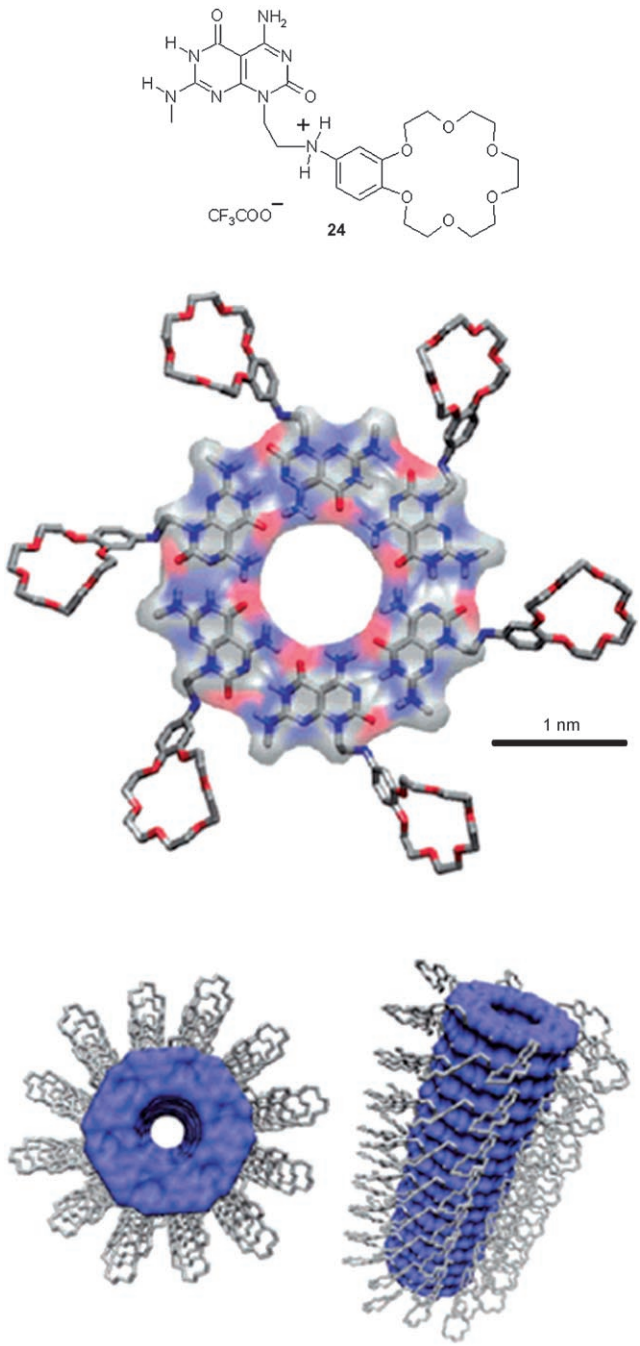
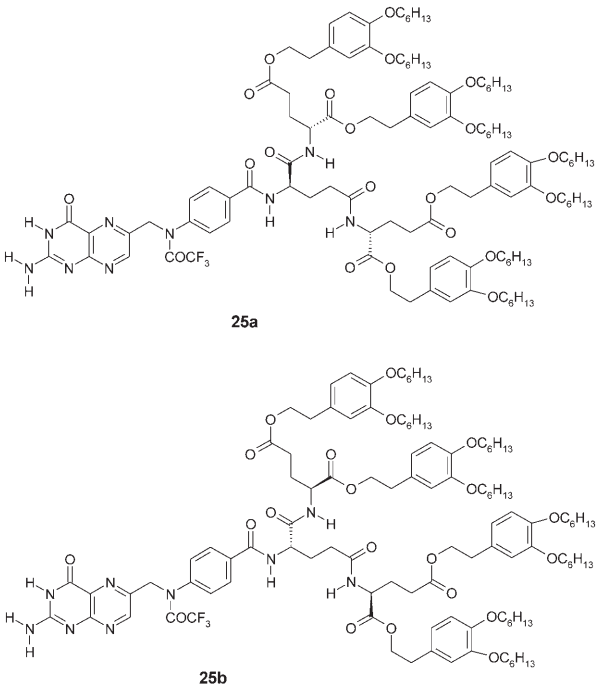


Figure 11. Helical rosette nanotubes based on **24**; blue N, red O, gray C.



Scheme 14. Lipophilic folic acid derivatives **25** derived from D- or L-glutamic acid.

Folic acid aggregates **25** (Scheme 14) have been studied by Kato and co-workers for their ability to form cyclic tetramers through the formation of intermolecular hydrogen bonds of the pterine rings to afford a disclike structure.[113] In the solid state, the stacked tetramers form thermotropic hexagonal columnar mesophases over wide temperature ranges. The addition of alkali-metal salts induces the chirality in the columnar phases: In dilute chloroform solution, the folic acid derivatives form nonchiral self-assembled structures, but the addition of sodium triflate results in chiral columnar structures, as evidenced by the occurrence of CD effects. Interestingly, a racemic mixture of equimolar amounts of **25a** and **25b** showed no CD effects, while nonracemic mixtures of **25a** and **25b** in the presence of sodium triflate showed CD effects with an intensity proportional to the enantiomeric excess; this result indicates that no specific cooperative interactions are occurring. However, the use of dodecane as the solvent resulted in strong mirror-image CD spectra for **25a** and **25b** in the absence of sodium triflate. Apparently, in a lipophilic environment, where phase separation at the nanometer level induces self-assembly that results in π–π interactions between the pterine rings, supramolecular chirality is induced without the need for an ion. Unfortunately, nonracemic mixtures of chiral **25a** and **25b** were not reported for solutions in dodecane, so the question of chirality amplification in this interesting system remains unanswered.

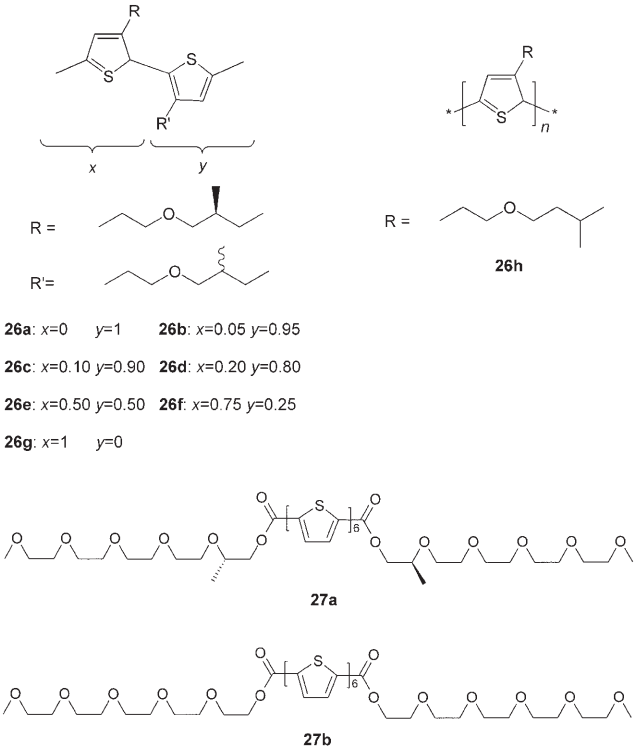
Gottarelli and co-workers evaluated the self-assembly of guanosine derivatives into columnar aggregates in water as well as in apolar solvents.[108,114] The hierarchical self-assembly of oligomeric deoxyguanosines in water through hydrogen bonding is initiated by the formation of cyclic tetramers, which stack into a columnar superstructure. Above a certain concentration, lyotropic LC phases were observed to evolve into a cholesteric phase at even higher concentrations.[114] In a similar approach, apolar lipophilic guanosine complexes were prepared and studied in apolar solvents. In the presence of alkali-metal ions, these guanosine derivatives form polymeric tubular structures.[108] Amplification of chirality was not studied in these aggregates.

An interesting variation on the sergeants-and-soldiers theme was recently described. In this case, conformational effects were employed to induce structural changes in the polymers.[115,116] The incorporation of a single conformationally locked monomer could force a folded block copolymer

into an alternate topology. McQuade and co-workers demonstrated that the presence of conformational-biased monomers (the sergeants) in a sequence of flexible monomers (the soldiers) yielded an oligonucleotide block copolymer that folds into two topologies with competitive free energies and activation barriers.[116]

7. Miscellaneous

In many of the above presented examples, the formation of hydrogen bonds is an important driving force in the assembly process and is largely responsible for the ability of a system to amplify chirality. There are a number of examples where amplification of chirality is observed which results predominantly from chiral stacking of the molecules through π–π interactions. Chiral polythiophenes are such a case that have been well-studied, experimentally and theoretically. The chiroptical effects observed in these polymers are not connected to a helical conformation of the backbone, but arise from the organization of the polymer chains into a chiral aggregate in so-called "bad solvents".[117,118] The polymers **26a**–**h** (Scheme 15) were synthesised to study the operativity of the majority-rules and sergeants-and-soldiers principles. A nonlinear response of the anisotropy value *g* as a function of the enantiomeric excess of the monomer was observed in polymers **26a**–**g**; this result is indicative of the presence of a majority-rules effect. Moreover, the intensity of the CD effect of nonracemic mixtures of chiral **26a** and achiral **26h** also showed a small but pronounced deviation from linearity as a function of the percentage of chiral **26a** added; this result is suggestive of the sergeants-and-soldiers effect. Cooperative interactions between the chiral and achiral side chains of polythiophene **26** clearly affected the optical activity of the polythiophene aggregates in a nonlinear fashion and all the evidence suggested that the aggregation of π-conjugated polymers is a multichain event, even in dilute solutions.

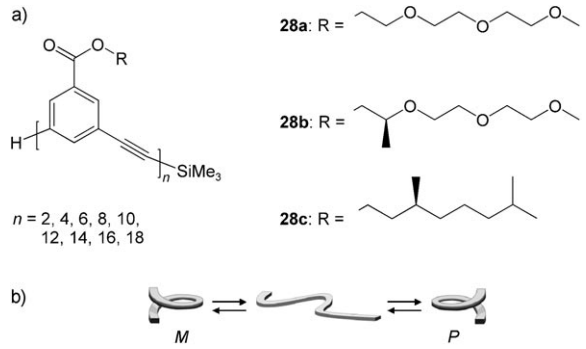


Scheme 15. Poly- and oligothiophenes **26** and **27** employed in chirality amplification studies.

In an extension of this work, well-defined α-α′-disubstituted sexithiophenes **27** were substituted with chiral and achiral oligo(ethylene oxide) chains (Scheme 15).[119] Both compounds showed thermotropic liquid-crystalline behavior. The presence of chirality in the aggregates was unambiguously shown by CD spectroscopy in combination with atomic force microscopy (AFM) and scanning tunneling microscopy (STM) measurements. These well-defined oligothiophenes showed amplification of chirality in polar solvents, such as *n*-butanol, as evidenced by the nonlinear response of the CD effect on the enantiomeric excess of mixtures of chiral **27a** and achiral **27b**. However, both the above examples require careful preparation of the aggregates: a simple mixing of the different compounds did not result in amplification of chirality, and the fast cooling of mixed aggregates resulted in CD spectra which were the inverse of the spectra obtained by slow cooling. This observation suggests that kinetic effects are operative which interfere with the generation of a thermodynamically stable aggregate.

A related example involves the amplification of chirality in a hydroxy-terminated OPV derivative.[120–122] These compounds form organogels in a variety of solvents and, interestingly, mixtures of chiral and achiral derivatives in dodecane resulted in the observation of the sergeants-and-soldiers effect. In the present case, however, combined studies of AFM and CD suggested that individual nonhelical stacks of the nonchiral OPV derivative, left-handed stacks of the chiral OPV derivative, and right-handed coaggregates of chiral and nonchiral OPV derivatives are formed initially which, at a later stage, self-associate and fuse into superstructures. This situation led to a significant reduction of the CD effect after the addition of more than 23 mol% of the chiral OPV derivative, and is indicative of the occurrence of stacks of opposite helicity. Such an inversion of helicity has also been observed in other systems, such as for merocyanine dyes, which highlight the importance of conducting amplification of chirality experiments in thermodynamically stable systems.[123]

Foldamers, an interesting class of oligomers/polymers, usually behave as random polymer coils in solution but under the right conditions preferred helical orientations may result. Subsequent stacking of the oligomers affords columnar structures.[124–130] Ray and Moore showed that achiral *m*-phenylene ethynylene (*m*-PPE) oligomers (Scheme 16a) could fold into left- or right-handed helices (Scheme 16b).[131] The addition of a peripheral chiral side chain (**28b**) led to the bias of one helicity and a chiral columnar superstructure, as evidenced by CD measurements. Solvent denaturation studies revealed that the helix was formed by a hierarchical growth process, in which a well-defined architecture is first formed, and then these helices stack into columns.[127,129] The stacking is a cooperative process, as evidenced by the

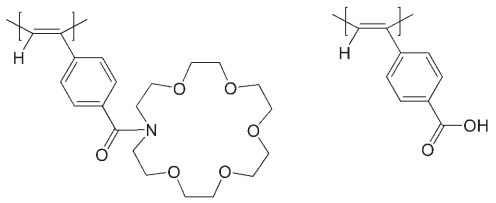


Scheme 16. a) Polar and apolar oligo-*m*-PPE derivative **28**. b) In a "good" solvent, a random coil is observed while in a "bad" solvent, the molecules adopt a helical conformation and subsequently stack into a columnar superstructure.

sergeants-and-soldiers experiments with mixtures of **28a** and **28b**: helically folded oligomers of one helicity create a platform onto which the achiral molecules can dock, and in this way the chirality is transferred to the achiral oligomer.[127,131] Lipophilic *m*-PPE oligomers **28c** were also found to adopt a helical conformation with a large bias of the twist sense in heptane. In this case, the strong twist sense was highly time dependent, which was partially attributed to an intermolecular aggregation process.[128]

A related example is helicene, an intrinsically helical molecule that self-assembles into columns in apolar solutions when enantiomerically pure.[132,133] As a result of its structure, the chiral helicene cannot rotate within the columns, which is a prerequisite for chirality amplification in columnar stacks. Unfortunately, it was observed that the racemic helicene was much less soluble in dodecane than the pure enantiomer and did not form fibers under identical conditions.[132] The implication is that long columns form and assemble into fibrous structures only if the molecules have the same helicity. Although not reported, amplification of chirality in this promising system does not seem to be viable.

Finally, an interesting variation on the amplification of chirality is the transfer of chiral information from nonracemic guest molecules to achiral helical macromolecules through noncovalent interactions. This concept is commonly known as chirality induction or chirality sensing.[11] Poly(phenylacetylene)s, for example, have been intensively studied by the research groups of Yashima and Masuda for their ability to form helical polymers.[11,134–139] poly(phenyacetylene)s with crown ethers (**29** Scheme 17) or acid groups (**30**, Scheme 17) induced a CD effect after the addition of chiral amino acids or chiral amines, respectively.[140] This induced CD effect was indicative of the formation of a preferred helicity along the polymer backbone. A remarkable memory for the induced helicity was observed in the case of polymer **30**: after completely replacing the chiral amine by an achiral amine, the macromolecular helicity was retained and stable for a very long time. Moreover, the detection of very small enantiomeric excesses in α-amino acids by **29** was indicative of a strong amplification of chirality, with cooperative noncovalent interactions between the crown ether pendants.[136]



Scheme 17. Substituted poly(phenyacetylene)s **29** and **30** used in chirality sensing.

8. Conclusions and Outlook

The exponential increase in examples showing amplification of chirality in noncovalent systems over the last decade may eventually lead to an increased understanding of the factors responsible. Although it is too early to formulate general guidelines to predict whether amplification of chirality will occur, we can summarize a number of features that appear to reoccur in the different examples discussed:

1) The ability of a molecule to form an intrinsic chiral object (such as the propeller shape of trisamide discs), a helical object (*m*-PPE foldamers), or a chiral distortion in the complex (hydrogen-bond structures based on the rosette motif) is a prerequisite for the transfer of chirality since it creates a chiral platform onto or into which the achiral molecules can dock.
2) In all the systems reported that show amplification of chirality, different noncovalent interactions are operative—for example, intermolecular hydrogen bonding in combination with π–π stacking interactions and microphase separation (trisamide discs, triazine based discs) or π–π stacking in combination with solvophobic interactions (oligo- and polyhiophene as well as *m*-PPE foldamers). However, there must be a balance between the different interactions: if one is out of proportion with the other, chirality may be observed in the liquid-crystalline state, but is usually not transferred when the molecules are brought into solution.
3) The presence of thermotropic and lyotropic mesomorphism, preferably both, in combination with positional locking of the molecules within the columnar structure, is usually a good indicator of a successful amplification of chirality (trisamide discs, difunctional ureidotriazines and ureidopyrimidinones). Moreover, strong and cooperative aggregation of the molecules in solution (porphyrins, trisamide discs) is a prerequisite for amplification of chirality.

The detailed study of the existence of chirality amplification in dynamic systems is, however, sensitive to many factors. Currently, most supramolecular chemistry is performed within the concept of systems under thermodynamic equilibrium and the formation of systems that are energetically most stable. Recent investigations to unravel the mechanism of formation (by an isodesmic or a nucleation–elongation mechanism) and to identify the different substates in a complex energy landscape of kinetically trapped metastable

states have highlighted the power of the amplification of chirality in dynamic supramolecular systems. For example, if the thermodynamically most stable species is not immediately formed, as was shown in the disc-shaped molecules with urea groups and by oligothiophenes, complicated CD spectra arise and experiments with mixed chiral and achiral compounds are difficult to interpret. In fact, in many of the examples discussed, the exact origin of the CD effect is often not very well understood. The integration of a theoretical approach with experimental work to determine the origin of CD effects in assemblies of molecules would be highly beneficial and help elucidate many of the unanswered questions. Moreover, theoretical models to quantify the energies involved in the amplification of chirality contribute greatly to a deeper understanding of the subtleties involved in these processes. Only then, can the lessons we learn from studies on the amplification of chirality in dynamic systems be fully exploited to help elucidate the elusive omnipresence of chirality in nature.

We would like to thank Jef Vekemans for his continuous support, Martijn Veld for help with the art work, and the NWO (Council of Chemical Sciences) for financial support.

Received: March 23, 2007
Published online: October 12, 2007

[1] I. Weissbuch, L. Leiserowitz, M. Lahav, *Top. Curr. Chem.* **2005**, *259*, 123.
[2] W. A. Bonner, *Origins Life Evol. Biosphere* **1991**, *21*, 59.
[3] P. L. Luisi, *The Emergence of Life: From Chemical Origins to Synthetic Biology*, Cambridge University Press, Cambridge, **2006**.
[4] K. Soai, T. Shibata, H. Morioka, K. Choji, *Nature* **1995**, *378*, 767.
[5] M. M. Green, S. K. Jha, *Chirality* **1997**, *9*, 424.
[6] M. M. Green in *Circular Dichroism: Principles and Applications* (Eds.: N. Berova, K. Nakanishi, R. W. Woody), Wiley-VCH, New York, **2000**, pp. 491 – 520.
[7] M. M. Green, K.-S. Cheon, S.-Y. Yang, J.-W. Park, S. Swansburg, W. Liu, *Acc. Chem. Res.* **2001**, *34*, 672.
[8] M. M. Green, J.-W. Park, T. Sato, A. Teramoto, S. Lifson, R. L. B. Selinger, J. V. Selinger, *Angew. Chem.* **1999**, *111*, 3328; *Angew. Chem. Int. Ed.* **1999**, *38*, 3139.
[9] A. Teramoto, *Prog. Polym. Sci.* **2001**, *26*, 667.
[10] F. Takei, K. Yanai, K. Onitsuka, S. Takahashi, *Chem. Eur. J.* **2000**, *6*, 983.
[11] E. Yashima, K. Maeda, T. Nishimura, *Chem. Eur. J.* **2004**, *10*, 42.
[12] E. Yashima, N. Okamoto in *Circular Dichroism: Principles and Applications* (Eds.: N. Berova, K. Nakanishi, R. W. Woody), Wiley-VCH, New York, **2000**, pp. 521 – 546.
[13] K. Maeda, E. Yashima, *Top. Curr. Chem.* **2006**, *265*, 47.
[14] C. Schmuck, *Angew. Chem.* **2003**, *115*, 2552; *Angew. Chem. Int. Ed.* **2003**, *42*, 2448.
[15] R. Eelkema, B. L. Feringa, *Org. Biomol. Chem.* **2006**, *4*, 3729.
[16] A. Brizard, R. Oda, I. Huc, *Top. Curr. Chem.* **2005**, *256*, 167.
[17] L. Brunsveld, E. W. Meijer, A. E. Rowan, R. J. M. Nolte, *Top. Stereochem.* **2003**, *24*, 373.
[18] M. A. Mateos-Timoneda, M. Crego-Calama, D. N. Reinhoudt, *Chem. Soc. Rev.* **2004**, *33*, 363.
[19] J. J. L. M. Cornelissen, A. E. Rowan, R. J. M. Nolte, N. A. J. M. Sommerdijk, *Chem. Rev.* **2001**, *101*, 4039.
[20] J. L. Serrano, T. Sierra, *Coord. Chem. Rev.* **2003**, *242*, 73.
[21] A. E. Rowan, R. J. M. Nolte, *Angew. Chem.* **1998**, *110*, 65; *Angew. Chem. Int. Ed.* **1998**, *37*, 63.
[22] M. M. Green, C. Andreola, B. Munoz, M. P. Reidy, K. Zero, *J. Am. Chem. Soc.* **1988**, *110*, 4063.
[23] M. M. Green, C. Khatri, N. C. Peterson, *J. Am. Chem. Soc.* **1993**, *115*, 4941.
[24] M. M. Green, N. C. Peterson, T. Sato, A. Teramoto, R. Cook, S. Lifson, *Science* **1995**, *268*, 1860.
[25] H. Gu, Y. Nakamura, T. Sato, A. Teramoto, M. M. Green, S. K. Jha, C. Andreola, M. P. Reidy, *Macromolecules* **1998**, *31*, 6362.
[26] M. M. Green, M. P. Reidy, R. D. Johnson, G. Darling, D. J. O'Leary, G. Willson, *J. Am. Chem. Soc.* **1989**, *111*, 6452.
[27] M. M. Green, B. A. Garetz, B. Munoz, H. Chang, S. Hoke, R. G. Cooks, *J. Am. Chem. Soc.* **1995**, *117*, 4181.
[28] P. van der Schoot, M. A. J. Michels, L. Brunsveld, R. P. Sijbesma, A. Ramzi, *Langmuir* **2000**, *16*, 10076.
[29] J. van Gestel, P. van der Schoot, M. A. J. Michels, *J. Chem. Phys.* **2004**, *120*, 8253.
[30] J. van Gestel, P. van der Schoot, M. A. J. Michels, *Langmuir* **2003**, *19*, 1375.
[31] J. van Gestel, P. van der Schoot, M. A. J. Michels, *J. Phys. Chem. B* **2001**, *105*, 10691.
[32] J. van Gestel, P. van der Schoot, M. A. J. Michels, *Macromolecules* **2003**, *36*, 6668.
[33] F. Tanaka, *Macromolecules* **2004**, *37*, 605.
[34] A. R. A. Palmans, J. A. J. M. Vekemans, H. Fischer, R. A. Hikmet, E. W. Meijer, *Chem. Eur. J.* **1997**, *3*, 300.
[35] A. R. A. Palmans, J. A. J. M. Vekemans, E. E. Havinga, E. W. Meijer, *Angew. Chem.* **1997**, *109*, 2763; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2648.
[36] A. R. A. Palmans, J. A. J. M. Vekemans, R. A. Hikmet, H. Fischer, E. W. Meijer, *Adv. Mater.* **1998**, *10*, 873.
[37] J. van Gestel, A. R. A. Palmans, B. Titulaer, J. A. J. M. Vekemans, E. W. Meijer, *J. Am. Chem. Soc.* **2005**, *127*, 5490.
[38] J. van Gestel, *Macromolecules* **2004**, *37*, 3894.
[39] E. W. Meijer, J. A. J. M. Vekemans, A. R. A. Palmans, P. Breure, J. De Kraker, L. Brunsveld, *Polym. Prepr. Am. Chem. Soc. Div. Polym. Chem.* **2000**, *41*, 902.
[40] J. van Herrikhuyzen, P. Jonkheijm, A. P. H. J. Schenning, E. W. Meijer, *Org. Biomol. Chem.* **2006**, *4*, 1539.
[41] L. Brunsveld, H. Zhang, M. Glasbeek, J. A. J. M. Vekemans, E. W. Meijer, *J. Am. Chem. Soc.* **2000**, *122*, 6175.
[42] L. Brunsveld, B. G. G. Lohmeijer, J. A. J. M. Vekemans, E. W. Meijer, *J. Inclusion Phenom. Macrocyclic Chem.* **2001**, *41*, 61.
[43] L. Brunsveld, B. G. G. Lohmeijer, J. A. J. M. Vekemans, E. W. Meijer, *Chem. Commun.* **2000**, 2305.
[44] P. Jonkheijm, P. van der Schoot, A. P. H. J. Schenning, E. W. Meijer, *Science* **2006**, *313*, 80.
[45] T. Metzroth, A. Hoffmann, A. Rapp, E. W. Meijer, H. W. Spiess, I. Schnell, J. Gauss, unpublished results.
[46] J. J. van Gorp, J. A. J. M. Vekemans, E. W. Meijer, *J. Am. Chem. Soc.* **2002**, *124*, 14759.
[47] J. J. van Gorp, J. A. J. M. Vekemans, E. W. Meijer, *Mol. Cryst. Liq. Cryst.* **2003**, *397*, 191.
[48] L. Brunsveld, A. P. H. J. Schenning, M. A. C. Broeren, H. M. Janssen, J. A. J. M. Vekemans, E. W. Meijer, *Chem. Lett.* **2000**, 292.
[49] A. J. Wilson, J. van Gestel, R. P. Sijbesma, E. W. Meijer, *Chem. Commun.* **2006**, 4404.
[50] Y. Matsunaga, Y. Nakayasu, S. Sakai, M. Yonenaga, *Mol. Cryst. Liq. Cryst.* **1986**, *141*, 327.
[51] Y. Matsunaga, N. Miyajima, Y. Nakayasu, S. Sakai, M. Yonenaga, *Bull. Chem. Soc. Jpn.* **1988**, *61*, 207.
[52] K. Hanabusa, C. Koto, M. Kimura, H. Shirai, A. Kakehi, *Chem. Lett.* **1997**, 429.
[53] K. Hanabusa, A. Kawakami, M. Kimura, H. Shirai, *Chem. Lett.* **1997**, 191.

[54] M. P. Lightfoot, F. S. Mair, R. G. Pritchard, J. E. Warren, *Chem. Commun.* **1999**, 1945.
[55] A. Sakamoto, D. Ogata, T. Shikata, O. Urakawa, K. Hanabusa, *Polymer* **2006**, *47*, 956.
[56] A. Sakamoto, D. Ogata, T. Shikata, K. Hanabusa, *Macromolecules* **2005**, *38*, 8983.
[57] T. Shikata, D. Ogata, K. Hanabusa, *J. Phys. Chem. B* **2004**, *108*, 508.
[58] D. Ogata, T. Shikata, K. Hanabusa, *J. Phys. Chem. B* **2004**, *108*, 15503.
[59] M. L. Bushey, T.-Q. Nguyen, W. Zhang, D. Horoszewski, C. Nuckolls, *Angew. Chem.* **2004**, *116*, 5562; *Angew. Chem. Int. Ed.* **2004**, *43*, 5446.
[60] G. S. Tulevski, M. L. Bushey, J. L. Kosky, S. J. T. Ruter, C. Nuckolls, *Angew. Chem.* **2004**, *116*, 1872; *Angew. Chem. Int. Ed.* **2004**, *43*, 1836.
[61] T.-Q. Nguyen, R. Martel, P. Avouris, M. L. Bushey, L. Brus, C. Nuckolls, *J. Am. Chem. Soc.* **2004**, *126*, 5234.
[62] M. L. Bushey, A. Hwang, P. W. Stephens, C. Nuckolls, *J. Am. Chem. Soc.* **2001**, *123*, 8157.
[63] M. L. Bushey, A. Hwang, P. W. Stephens, C. Nuckolls, *Angew. Chem.* **2002**, *114*, 2952; *Angew. Chem. Int. Ed.* **2002**, *41*, 2828.
[64] M. L. Bushey, T.-Q. Nguyen, C. Nuckolls, *J. Am. Chem. Soc.* **2003**, *125*, 8264.
[65] M. M. J. Smulders, A. P. H. J. Schenning, E. W. Meijer, *J. Am. Chem. Soc.*, submitted.
[66] A. J. Wilson, M. Masuda, R. P. Sijbesma, E. W. Meijer, *Angew. Chem.* **2005**, *117*, 2315; *Angew. Chem. Int. Ed.* **2005**, *44*, 2275.
[67] M. Masuda, P. Jonkheijm, R. P. Sijbesma, E. W. Meijer, *J. Am. Chem. Soc.* **2003**, *125*, 15935.
[68] P. Herwig, C. W. Kayser, K. Müllen, H. W. Spiess, *Adv. Mater.* **1996**, *8*, 510.
[69] M. D. Watson, A. Fechtenkoetter, K. Müllen, *Chem. Rev.* **2001**, *101*, 1267.
[70] A. Fechtenkötter, N. Tchebotareva, M. Watson, K. Müllen, *Tetrahedron* **2001**, *57*, 3769.
[71] A. J. Fleming, J. N. Coleman, A. B. Dalton, A. Fechtenkoetter, M. D. Watson, K. Müllen, H. J. Byrne, W. J. Blau, *J. Phys. Chem. B* **2003**, *107*, 37.
[72] A. F. Thunemann, S. Kubowicz, C. Burger, M. D. Watson, N. Tchebotareva, K. Müllen, *J. Am. Chem. Soc.* **2003**, *125*, 352.
[73] W. Jin, T. Fukushima, M. Niki, A. Kosaka, N. Ishii, T. Aida, *Proc. Natl. Acad. Sci. USA* **2005**, *102*, 10801.
[74] C. F. van Nostrum, A. W. Bosman, G. H. Gelinck, S. J. Picken, P. G. Schouten, J. M. Warman, A. J. Schouten, R. J. M. Nolte, *J. Chem. Soc. Chem. Commun.* **1993**, 1120.
[75] C. F. van Nostrum, A. W. Bosman, G. H. Gelinck, P. G. Schouten, J. M. Warman, A. P. M. Kentgens, M. A. C. Devillers, A. Meijerink, S. J. Picken, U. Sohling, A.-J. Schouten, R. J. M. Nolte, *Chem. Eur. J.* **1995**, *1*, 171.
[76] C. F. van Nostrum, S. J. Picken, A.-J. Schouten, R. J. M. Nolte, *J. Am. Chem. Soc.* **1995**, *117*, 9957.
[77] H. Engelkamp, S. Middelbeek, R. J. M. Nolte, *Science* **1999**, *284*, 785.
[78] A. Kraft, F. Osterod, R. Fröhlich, *J. Org. Chem.* **1999**, *64*, 6425.
[79] R. Lauceri, M. De Napoli, A. Mammana, S. Nardis, A. Romeo, R. Purrello, *Synth. Met.* **2004**, *147*, 49.
[80] R. Lauceri, R. Purrello, *Supramol. Chem.* **2005**, *17*, 61.
[81] T. Yamaguchi, T. Kimura, H. Matsuda, T. Aida, *Angew. Chem.* **2004**, *116*, 6510; *Angew. Chem. Int. Ed.* **2004**, *43*, 6350.
[82] J. M. Ribo, J. Crusats, F. Sagues, J. Claret, R. Rubires, *Science* **2001**, *292*, 2063.
[83] P. Chen, X. Ma, P. Dua, M. Liu, *ChemPhysChem* **2006**, *7*, 2419.
[84] T. Ishi-i, R. Kuwahara, A. Takata, Y. Jeong, K. Sakurai, S. Mataka, *Chem. Eur. J.* **2006**, *12*, 763.
[85] H. Lee, D. Kim, H.-K. Lee, W. Qiu, N.-K. Oh, W.-C. Zin, K. Kim, *Tetrahedron Lett.* **2004**, *45*.
[86] R. I. Gearba, M. Lehmann, J. Levin, D. Ivanov, M. H. J. Koch, J. Barberá, M. G. Debije, J. Piris, Y. H. Geerts, *Adv. Mater.* **2003**, *15*, 1614.
[87] T. Ishi-i, T. Hirayama, K.-i. Murakami, H. Tashiro, T. Thiemann, K. Kubo, A. Mori, S. Yamasaki, T. Akao, A. Tsuboyama, T. Mukaide, K. Ueno, S. Mataka, *Langmuir* **2005**, *21*, 1261.
[88] L. Brunsveld, B. J. B. Folmer, E. W. Meijer, R. P. Sijbesma, *Chem. Rev.* **2001**, *101*, 4071.
[89] J. H. K. K. Hirschberg, L. Brunsveld, A. Ramzi, J. A. J. M. Vekemans, R. P. Sijbesma, E. W. Meijer, *Nature* **2000**, *407*, 167.
[90] L. Brunsveld, J. A. J. M. Vekemans, J. H. K. K. Hirschberg, R. P. Sijbesma, E. W. Meijer, *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 4977.
[91] R. P. Sijbesma, F. H. Beijer, L. Brunsveld, B. J. Folmer, J. H. Hirschberg, R. F. Lange, J. K. Lowe, E. W. Meijer, *Science* **1997**, *278*, 1601.
[92] J. H. K. K. Hirschberg, R. A. Koevoets, R. P. Sijbesma, E. W. Meijer, *Chem. Eur. J.* **2003**, *9*, 4222.
[93] A. W. Bosnian, L. Brunsveld, B. J. B. Folmer, R. P. Sijbesma, E. W. Meijer, *Macromol. Symp.* **2003**, *201*, 143.
[94] J. H. Hirschberg, L. Brunsveld, A. Ramzi, J. A. Vekemans, R. P. Sijbesma, E. W. Meijer, *Nature* **2000**, *407*, 167.
[95] A. P. H. J. Schenning, P. Jonkheijm, E. Peeters, E. W. Meijer, *J. Am. Chem. Soc.* **2001**, *123*, 409.
[96] Z. Tomovic, A. P. H. J. Schenning, E. W. Meijer, unpublished results.
[97] M. A. Mateos-Timoneda, M. Crego-Calama, D. N. Reinhoudt, *Supramol. Chem.* **2005**, *17*, 67.
[98] M. Crego-Calama, D. N. Reinhoudt, G. J. ten Cate Mattijs, *Top. Curr. Chem.* **2005**, *249*, 285.
[99] L. J. Prins, J. Huskens, F. De Jong, P. Timmerman, D. N. Reinhoudt, *Nature* **1999**, *398*, 498.
[100] G. M. Whitesides, E. E. Simanek, J. P. Mathias, C. T. Seto, D. Chin, M. Mammen, D. M. Gordon, *Acc. Chem. Res.* **1995**, *28*, 37.
[101] L. J. Prins, F. De Jong, P. Timmerman, D. N. Reinhoudt, *Nature* **2000**, *408*, 181.
[102] L. J. Prins, P. Timmerman, D. N. Reinhoudt, *J. Am. Chem. Soc.* **2001**, *123*, 10153.
[103] M. A. Mateos-Timoneda, M. Crego-Calama, D. N. Reinhoudt, *Chem. Eur. J.* **2006**, *12*, 2630.
[104] J. M. Rivera, S. L. Craig, T. Martin, J. Rebek, Jr., *Angew. Chem.* **2000**, *112*, 2214; *Angew. Chem. Int. Ed.* **2000**, *39*, 2130.
[105] H. Fenniri, B.-L. Deng, A. E. Ribbe, *J. Am. Chem. Soc.* **2002**, *124*, 11064.
[106] T. Kato, T. Matsuoka, M. Nishii, Y. Kamikawa, K. Kanie, T. Nishimura, E. Yashima, S. Ujiie, *Angew. Chem.* **2004**, *116*, 2003; *Angew. Chem. Int. Ed.* **2004**, *43*, 1969.
[107] S. Yagai, T. Nakajima, K. Kishikawa, S. Kohmoto, T. Karatsu, A. Kitamura, *J. Am. Chem. Soc.* **2005**, *127*, 11134.
[108] E. Mezzina, P. Mariani, R. Itri, S. Masiero, S. Pieraccini, G. P. Spada, F. Spinozzi, J. T. Davis, G. Gottarelli, *Chem. Eur. J.* **2001**, *7*, 388.
[109] C. Thalacker, F. Würthner, *Adv. Funct. Mater.* **2002**, *12*, 209.
[110] H. Fenniri, B.-L. Deng, A. E. Ribbe, K. Hallenga, J. Jacob, P. Thiyagarajan, *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 6487.
[111] H. Fenniri, P. Mathivanan, K. L. Vidale, K. Sherman, K. Hallenga, K. V. Wood, J. G. Stowell, *J. Am. Chem. Soc.* **2001**, *123*, 3854.
[112] R. K. Castellano, C. Nuckolls, J. Rebek, Jr., *J. Am. Chem. Soc.* **1999**, *121*, 11156.
[113] Y. Kamikawa, M. Nishii, T. Kato, *Chem. Eur. J.* **2004**, *10*, 5942.
[114] S. Bonazzi, M. Capobianco, M. M. De Morais, A. Garbesi, G. Gottarelli, P. Mariani, M. G. Ponzi Bossi, G. P. Spada, L. Tondelli, *J. Am. Chem. Soc.* **1991**, *113*, 5809.
[115] P. K. Dominick, M. B. Jarstfer, *J. Am. Chem. Soc.* **2004**, *126*, 5050.

[116] J.-I. Park, S. L. Roth, K. E. Price, D. T. McQuade, *J. Polym. Sci. Part A* **2006**, *44*, 3271.
[117] B. M. W. Langeveld-Voss, R. A. J. Janssen, E. W. Meijer, *J. Mol. Struct.* **2000**, *521*, 285.
[118] B. M. W. Langeveld-Voss, D. Beljonne, Z. Shuai, R. A. J. Janssen, S. C. J. Meskers, E. W. Meijer, J.-L. Bredas, *Adv. Mater.* **1998**, *10*, 1343.
[119] A. P. H. J. Schenning, A. F. M. Kilbinger, F. Biscarini, M. Cavallini, H. J. Cooper, P. J. Derrick, W. J. Feast, R. Lazzaroni, P. Leclere, L. A. McDonell, E. W. Meijer, S. C. J. Meskers, *J. Am. Chem. Soc.* **2002**, *124*, 1269.
[120] A. Ajayaghosh, R. Varghese, S. J. George, C. Vijayakumar, *Angew. Chem.* **2006**, *118*, 1159; *Angew. Chem. Int. Ed.* **2006**, *45*, 1141.
[121] S. J. George, A. Ajayaghosh, P. Jonkheijm, A. P. H. J. Schenning, E. W. Meijer, *Angew. Chem.* **2004**, *116*, 3504; *Angew. Chem. Int. Ed.* **2004**, *43*, 3422.
[122] A. Ajayaghosh, R. Varghese, S. Mahesh, V. K. Praveen, *Angew. Chem.* **2006**, *118*, 7893; *Angew. Chem. Int. Ed.* **2006**, *45*, 7729.
[123] A. Lohr, A. Lysetska, F. Würthner, *Angew. Chem.* **2005**, *117*, 5199; *Angew. Chem. Int. Ed.* **2005**, *44*, 5071.
[124] J.-L. Hou, H.-P. Yi, X.-B. Shao, C. Li, Z.-Q. Wu, X.-K. Jiang, L.-Z. Wu, C.-H. Tung, Z.-T. Li, *Angew. Chem.* **2006**, *118*, 810; *Angew. Chem. Int. Ed.* **2006**, *45*, 796.
[125] J. J. van Gorp, J. A. J. M. Vekemans, E. W. Meijer, *Chem. Commun.* **2004**, 60.
[126] R. B. Prince, J. S. Moore, L. Brunsveld, E. W. Meijer, *Chem. Eur. J.* **2001**, *7*, 4150.
[127] L. Brunsveld, E. W. Meijer, R. B. Prince, J. S. Moore, *J. Am. Chem. Soc.* **2001**, *123*, 7978.
[128] L. Brunsveld, R. B. Prince, E. W. Meijer, J. S. Moore, *Org. Lett.* **2000**, *2*, 1525.
[129] R. B. Prince, L. Brunsveld, E. W. Meijer, J. S. Moore, *Angew. Chem.* **2000**, *112*, 234; *Angew. Chem. Int. Ed.* **2000**, *39*, 228.
[130] R. W. Sinkeldam, M. H. C. J. van Houtem, G. Koeckelberghs, J. A. J. M. Vekemans, E. W. Meijer, *Org. Lett.* **2006**, *8*, 383.
[131] C. R. Ray, J. S. Moore, *Adv. Polym. Sci.* **2005**, *177*, 91.
[132] C. Nuckolls, T. J. Katz, G. Katz, P. J. Collings, L. Castellanos, *J. Am. Chem. Soc.* **1999**, *121*, 79.
[133] C. Nuckolls, T. J. Katz, *J. Am. Chem. Soc.* **1998**, *120*, 9541.
[134] H. Goto, H. Q. Zhang, E. Yashima, *J. Am. Chem. Soc.* **2003**, *125*, 2516.
[135] G. Kwak, T. Masuda, *J. Polym. Sci. Part A* **2001**, *39*, 71.
[136] R. Nonokawa, E. Yashima, *J. Am. Chem. Soc.* **2003**, *125*, 1278.
[137] J. Tabei, R. Nomura, M. Shiotsuki, F. Sanda, T. Masuda, *Macromol. Chem. Phys.* **2005**, *206*, 323.
[138] J. Tabei, R. Nomura, F. Sanda, T. Masuda, *Macromolecules* **2004**, *37*, 1175.
[139] J. Tabei, R. Nomura, F. Sanda, T. Masuda, *Macromolecules* **2003**, *36*, 8603.
[140] H. Goto, Q. Zhang Hao, E. Yashima, *J. Am. Chem. Soc.* **2003**, *125*, 2516.

