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Probing the Limits of the Majority-Rules Principle in a Dynamic Supramolecular Polymer

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Abstract: By systematic variation of the chemical structure of benzene-1,3,5-tricarboxamide (BTA) derivatives, the effect of chemical structure on the amplification of chirality was studied and quantified. In combination with temperature-dependent amplification experiments, the limits of the majority-rules principle were also investigated. For all BTA derivatives a high, constant helix reversal penalty was determined, which is related to the intermolecular hydrogen bonds that are present in all studied derivatives. For asymmetrically substituted BTA derivatives an odd−even effect was found in the degree of chiral amplification when changing the position of the stereogenic center with respect to the amide functionality. It was found that the mismatch penalty could be directly related to the number of stereocenters present in the molecules. Increasing this number from one to three resulted in an increase in this energy penalty while leaving the helix reversal penalty unaffected. For the majority-rules principle this implies that a single stereocenter present in the molecule contains sufficient chiral information at the molecular level to result in a chirally amplified state at the supramolecular level. Further evidence that the mismatch penalty is directly related to the number of stereocenters was obtained from mixed majority-rules experiments where two BTA derivatives with different numbers of stereocenters with opposite stereoconfiguration were studied in a majority-rules experiment. Finally, the ultimate limits of chiral amplification for the majority-rules principle were investigated, revealing that, given a certain helix reversal penalty, there is an optimum to which the mismatch penalty can be reduced while also enhancing the degree of chiral amplification. Temperature-dependent majority-rules experiments could indeed confirm these simulations. These findings show the relevance of both energy penalties when trying to enhance the degree of chiral amplification for the majority-rules principle in a one-dimensional helical supramolecular polymer.

Introduction

Minute changes in the molecular structure can have large effects on the supramolecular organization of molecules, as has been observed in liquid crystalline phases and for (supramolecular) polymers in solution. For example, for covalent helical polymers in solution, the effect of small changes in the side-chain structure has been investigated in great detail by the group of Masuda for poly(*N*-propargylamides).[1−5] For these helical poly(*N*-propargylamides) they reported on the so-called *odd−even effect*[6] upon shifting an (*S*)-chiral stereocenter from the carbon atom α with respect to the amide group to the carbon atom at the β position.[3] The odd−even effect was manifested in a reversal of the sign of the Cotton effect upon this shift of the (*S*)-stereocenter, indicative of a reversal of the handedness of the helical polymer. The odd−even effect has also been reported for poly(isocyanides),[7−9] polysilylenes,[10] functionalized polystyrene derivatives,[11] and helical aggregates of oligo- and polythiophenes,[12−14] while it is absent in poly(propiolic ester)s.[15]

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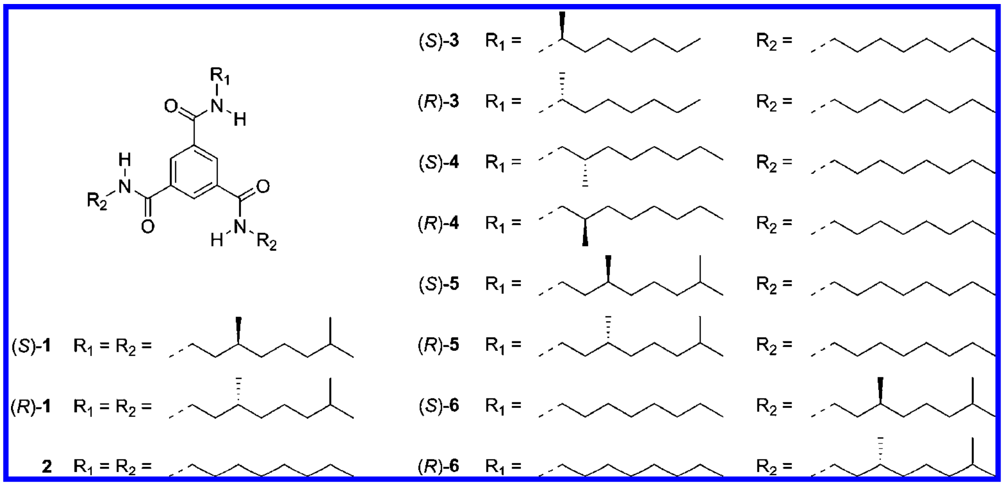
10.1021/ja9080875

Chart 1. Molecular Structure of the Different Symmetrically and Asymmetrically Substituted Discotics



In addition, also in the liquid crystalline state, odd−even effects have been observed for chiral nematic phases.[16−19]

In the preceding contribution (DOI 10.1021/ja908053d), we studied the role of temperature on the chiral amplification behavior in supramolecular polymers comprising C_3-symmetrical alkyl-substituted benzene-1,3,5-tricarboxamides (BTAs, Chart 1). As a result of those investigations we could conclude that the sergeants-and-soldiers phenomenon for the symmetrical derivatives (*S*)-**1**:**2** and the majority-rules phenomenon for the (*S*)-**1**:(*R*)-**1** mixtures are operative and that both phenomena are characterized by a high helix reversal penalty (HRP). This energy penalty is paid when in a helical stack of these discotics the handedness of the stack is reversed, i.e., going from a left-handed to a right-handed helical segment, or *vice versa*. The origin of this high HRP was related to the strong intermolecular hydrogen bonds that, once a handedness is chosen, maintain this handedness throughout the stack. The selection of either of the two helicities was governed by the chirality of the "sergeant" in the case of the sergeants-and-soldiers principle or by the major enantiomer in the case of the majority-rules principle.

Given the high and more or less constant HRP, the extent of chiral amplification was found to be determined by the mismatch penalty (MMP). This second energy penalty is paid when incorporating a chiral disc in a stack of its unpreferred helicity. This MMP was found to be strongly dependent on temperature, and its origin was ascribed to the steric interactions between the alkyl side chains, either equipped with or without the stereogenic centers.

Considering the molecular origin of both the HRP and the MMP, we set out to investigate to what extent relatively small changes in the molecular structure of the BTA derivatives would affect the chiral amplification behavior. In particular we anticipated an effect of the number of stereocenters per molecule, which for the BTA can vary between 0 and 3, as well as an effect of the position of the stereocenter with respect to the amide group, i.e., the odd−even effect. Moreover, reducing the number of stereocenters in a molecule results in less chiral information per monomer, which could result in a system that can no longer reach a fully amplified state.

As each BTA comprises three side groups, also asymmetrically substituted monomers can be synthesized, which enabled us to study the effect of the number of stereocenters on the degree of chiral amplification. The desymmetrization of monomers has already been described for other self-assembling systems, including porphyrins and porphyrazines,[20−24] perylenes,[25−27] dehydrobenzo[18]annulenes,[28] amphiphilic hexa-*peri*-hexabenzocoronenes,[29,30] triphenylenes,[31−36] and bis-urea derivatives.[37] Because of their simple molecular structure, the synthesis of various symmetrically

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or asymmetrically substituted BTA monomers is rather straightforward.[38−41] For example, our group has reported on the post-assembly photopolymerization of asymmetrically substituted BTAs in which one of the side chains was functionalized with a polymerizable sorbyl group.[39−41]

In a previous study we reported the effect of a subtle change in the molecular structure of the BTAs on the supramolecular polymerization behavior in solution and in the liquid crystalline phase.[42] To this end we synthesized asymmetrically substituted discotics equipped with two achiral *n*-octyl chains and one chiral side chain (Chart 1). The stereochemistry and the position of the stereocenter were both varied. We showed that shifting the stereogenic center closer to the aromatic core resulted in a more stable liquid crystalline phase. Also in solution more stable supramolecular polymers were formed when the stereogenic center was shifted closer to the amide moiety. Furthermore, in solution an odd−even effect in the sign of the Cotton effect was observed. This library of symmetrically and asymmetrically substituted BTAs (**1**−**6**, Chart 1) now allows us to study in detail the effect of molecular structure on the chiral amplification phenomena, i.e., the sergeants-and-soldiers and majority-rules principles. In addition, by quantifying the data with the extended chiral amplification model, as originally developed by van Gestel,[43−46] we can also predict the limitations of the degree of chiral amplification in this system, in particular for the majority-rules principle. These findings can help to understand the origin of homochirality observed in Nature,[47,48] i.e., how a small enantiomeric excess (ee), in combination with a set of conditions, can still be amplified to a homochiral state.

Results

Effect of the Position of the Stereogenic Center on the Chiral Amplification in the Benzene-1,3,5-tricarboxamide Derivatives. We first varied the position of the stereogenic center in asymmetrically substituted BTAs (**3**−**5**, Chart 1). The synthesis of these derivatives was reported previously, and in solution an odd−even effect in the sign of the Cotton effect was observed.[42] At room temperature at a concentration of 3.0 × 10^{-5} M in methylcyclohexane (MCH), both sergeants-and-soldiers and majority-rules experiments were performed with one of the enantiomers and achiral discotic **2** or with the two enantiomers, respectively. The results of the sergeants-and-soldiers experiments are shown in Figure 1.

Upon addition of small fractions of “sergeant” for all three different “sergeants”, (*R*)-**3**, (*R*)-**4**, and (*R*)-**5**, a strong increase in the Cotton effect was observed, indicative of a strong sergeants-and-soldiers effect operative in all three mixtures. Considering the sign of the Cotton effect, also in these sergeants-and-soldiers experiments an odd−even effect can be discerned, as for (*R*)-**3** and (*R*)-**5** a positive Cotton effect is observed, while (*R*)-**4** gives a negative Cotton effect. Normalizing the Cotton effect at 223 nm yielded the net helicity as a function of fraction of “sergeant” (Figure 1D).[49] For the (*R*)-**3**:**2** and (*R*)-**5**:**2** mixtures very similar results were obtained; i.e., in both of these systems a net helicity of 1 is obtained at a fraction of “sergeant” of ~0.15. For the (*R*)-**4**:**2** mixture more of the “sergeant” solution needed to be added to obtain a net helicity of 1, i.e., more than 30% “sergeant”.

To fit and quantify the sergeants-and-soldiers data we used our adapted amplification model,[49] originally developed by van Gestel, which was introduced in the preceding contribution. This model describes the chiral amplification phenomena in terms of two free energy penalties, the HRP and the MMP. The former penalizes a helix reversal in a stack, whereas the latter penalizes a mismatch when a chiral monomer is introduced into a stack of its unpreferred helicity.[44] Fitting of the data will yield the dimensionless energy penalties, σ and ω, which are related to the HRP and the MMP via $\sigma = \exp[-2\mathrm{HRP}/RT]$ and $\omega = \exp[-\mathrm{MMP}/RT]$, respectively.[44]

The values of the HRP as well as the MMP, as determined from fitting the sergeants-and-soldiers data, are given in Table 1. For the (*R*)-**3**:**2** and (*R*)-**5**:**2** systems a HRP of 11.2(±1.4) kJ mol^{-1} was found, which is similar to the value of 12.6(±2.0) kJ mol^{-1} previously determined for (*R*)-**1**:**2**. Hence, it can be concluded that moving the stereogenic center closer to the benzene core has no significant effect on the HRP. This confirms our hypothesis that the high HRP is the result of the intermolecular hydrogen bonds, which can be expected to be equally strong for the different “sergeant”:“soldiers” mixtures. For the MMP for the (*R*)-**3**:**2** and (*R*)-**5**:**2** systems only a lower limit of about 0.5 kJ mol^{-1} could be determined. For a more accurate determination the MMP fitting of the majority-rules experiments is required (*vide infra*). For the mixtures of (*R*)-**4**:**2** a considerably weaker sergeants-and-soldiers effect was observed, which could be explained by assuming either a low HRP of about 6−8 kJ mol^{-1} or a MMP as low as 0.3 kJ mol^{-1}. Since the intermolecular hydrogen bonds are expected to be equally strong for the (*R*)-**4**:**2** mixtures, we do not assume that the HRP is reduced in this system. Hence, it was proposed that a low MMP is responsible for the rather weak sergeants-and-soldiers effect. This low MMP is also observed for the majority-rules effect for (*R*)-**4**:(*S*)-**4** mixtures (*vide infra*).

Upon closer inspection of the CD spectra obtained for the (*R*)-**3**:**2** and (*R*)-**5**:**2** mixtures, two different types of CD spectra can be discerned. That is, at low fraction of “sergeant”, up to about 0.25, the CD spectrum has its maximum at 215 nm and a shoulder at ~240 nm (which we refer to as a type I spectrum). At higher fractions of “sergeant”, the CD spectrum resembles the spectrum of pure “sergeant”, with a maximum CD intensity at 223 nm (type II spectrum). For the (*R*)-**4**:**2** mixtures this distinction could not be made, as in this case the CD spectrum of pure “sergeant” is similar to the CD spectrum recorded at low fraction of “sergeant”; i.e., all CD spectra have a maximum in absorption at 217 nm and a shoulder at ~240 nm. As was already discussed in a previous report, the difference in the CD spectra of the pure “sergeants”, (*R*)-**3**, (*R*)-**4**, and (*R*)-**5**, was attributed to a slightly different molecular packing in the helical stacks of (*R*)-**4** as compared to the stacks of (*R*)-**3** or (*R*)-**5**.[42]

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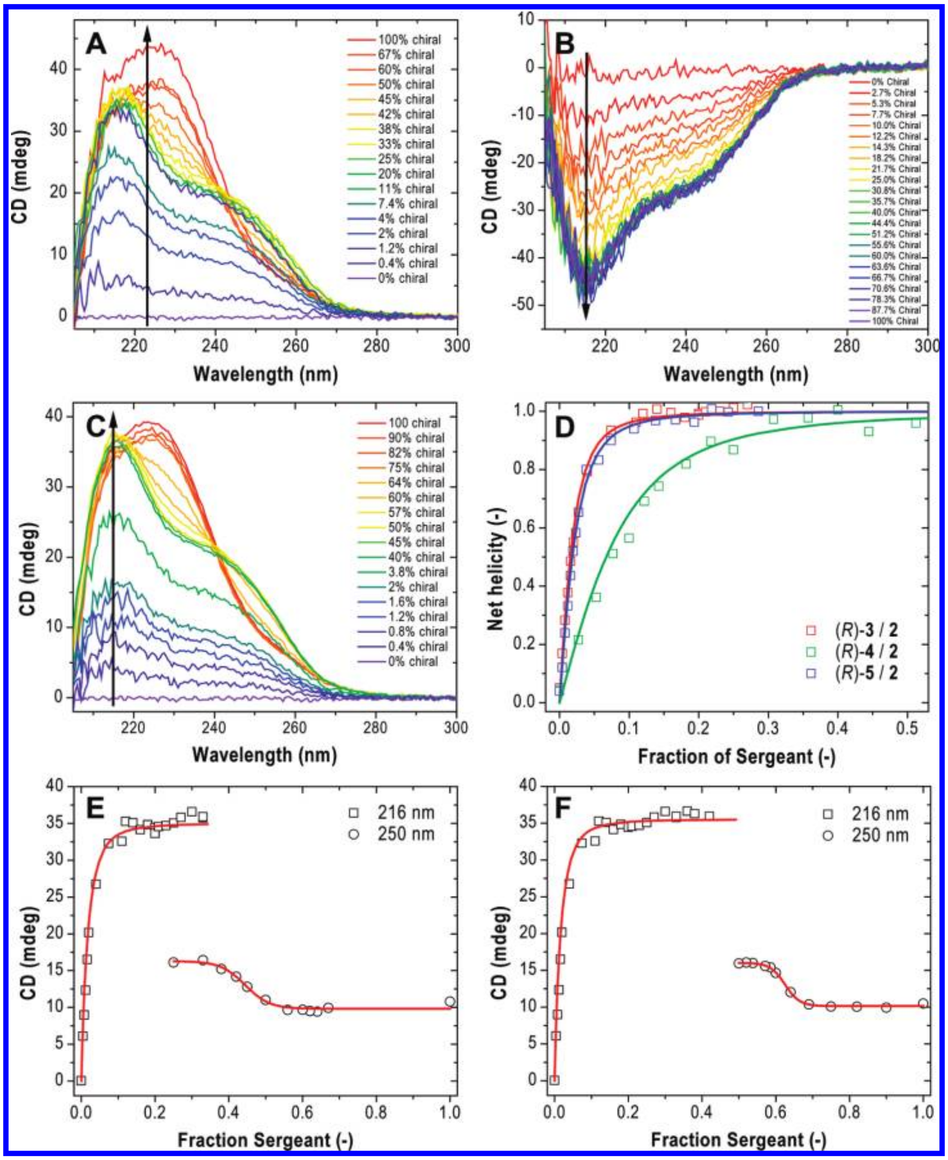

Figure 1. CD spectra of mixtures of (*R*)-**3**:**2** (A), (*R*)-**4**:**2** (B), and (*R*)-**5**:**2** (C). Net helicity versus fraction of "sergeant" for mixtures of (*R*)-**3**:**2**, (*R*)-**4**:**2**, and (*R*)-**5**:**2** (D) with the corresponding fit. Change in CD effect at 216 nm and at 250 nm as a function of fraction of "sergeant" for mixtures of (*R*)-**3**:**2** (E) and (*R*)-**5**:**2** (F). Concentration, 3.0 × 10^{-5} M in MCH; temperature, 20 °C.

Table 1. Energy Penalties (in kJ mol^{-1}) Determined from Fitting the Sergeants-and-Soldiers and the Majority-Rules Data

	sergeants-and-soldiers		majority-rules	
disc	HRP	MMP	HRP	MMP
1	12.6 ± 2.0	>0.5^a	15 ± 4	1.9 ± 0.2
3	11.2 ± 1.4	>0.5^a	15 ± 4	1.0 ± 0.2
4	10.5 ± 3.5	>0.3^a	16 ± 4	0.5 ± 0.2
5	11.2 ± 1.4	>0.5^a	15 ± 4	1.0 ± 0.2
6	n.d.	n.d.	15 ± 4	1.6 ± 0.3

[a] From fitting the sergeants-and-soldiers data it was only possible to determine a lower limit for the value of the mismatch penalty.

For the (*R*)-**3**:**2** and (*R*)-**5**:**2** mixtures the sergeants-and-soldiers effect was equally strong; i.e., the appearance of the type I CD spectrum occurs at the same fraction of "sergeant". However, the transition from the type I CD spectrum to the type II CD spectrum, which was probed at 250 nm, occurs at different fractions of "sergeant" (Figure 1E,F). For the (*R*)-**3**:**2** system, this transition occurs at ~0.45 fraction of "sergeant", while for (*R*)-**5**:**2** this happens at a fraction of ~0.65. This would indicate that stacks of (*R*)-**3** are more stable than stacks of (*R*)-**5**, which is in line with the higher isotropization temperature of (*R*)-**3** in the bulk and a higher temperature of elongation in dilute solution.[42]

Along with sergeants-and-soldiers experiments, we also performed majority-rules experiments. Mixtures of the enantiomers of **3**, **4**, or **5** were mixed in different ratios at room temperature at 3.0 × 10^{-5} M in MCH (Figure 2A−C).[50] For all three systems we observed a strong nonlinear increase in the Cotton effect upon increasing the ee, indicative of a majority-rules effect. Normalizing these data yielded the net helicity as a function of ee (Figure 2D).[49] Similarly as observed for the sergeants-and-soldiers experiments, for the enantiomers of **3** and **5** the majority-rules results were virtually identical. Comparing the majority-rules results for the enantiomers of **4** with those of **3** and **5**, it was found that a stronger amplification of chirality is observed for the former; i.e., a net helicity of 1 is reached at lower ee for **4**. This is opposite to the sergeants-and-soldiers experiments where for (*R*)-**4**:**2** a weaker amplification of chirality

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(50) The ee values of the (*S*)-**4** and (*R*)-**4** disk were only 60%.

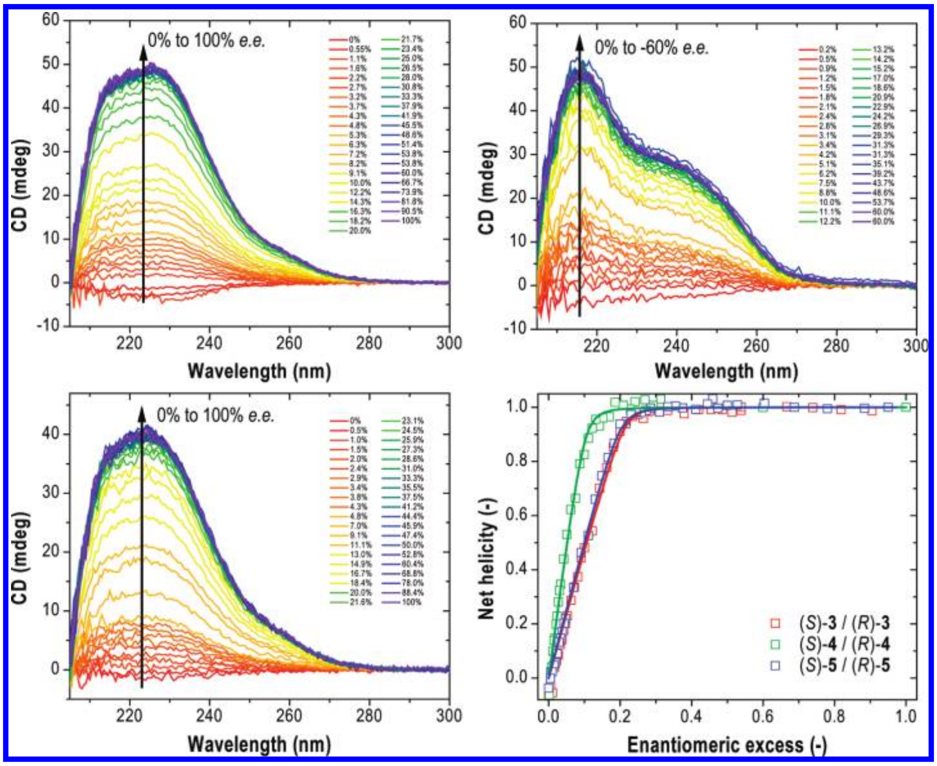

Figure 2. CD spectra of mixtures of (*R*)-**3**:(*S*)-**3** (A), (*R*)-**4**:(*S*)-**4**[51] (B), and (*R*)-**5**:(*S*)-**5** (C). Net helicity versus ee[52] for mixtures of (*R*)-**3**:(*S*)-**3**, (*R*)-**4**:(*S*)-**4**, and (*R*)-**5**:(*S*)-**5** with corresponding fit (D). Concentration, 3.0×10^{-5} M in MCH; temperature, 20 °C.

was observed, as more of the "sergeant" (*R*)-**4** had to be added to reach a net helicity of 1.

We fitted the majority-rules data for the three systems and found for **3** and **5** results in agreement with results for the sergeants-and-soldiers data (Table 1), i.e., a HRP of 15 (±4) kJ mol^{-1} and a MMP of 1.0 (±0.2) kJ mol^{-1}. This MMP is smaller than the value of 1.9 kJ mol^{-1} found for the (*R*)-**1**:**2** system at room temperature. This suggests that the position of the stereogenic center with respect to the amide moiety does not have an effect on the MMP, but that the number of stereogenic centers does affect the degree of chiral amplification. The effect of the number of stereogenic centers will be discussed below.

For the enantiomers of **4** HRP = 16(±4) kJ mol^{-1} and MMP = 0.5 (±0.2) kJ mol^{-1} were determined. Again the HRP is high for all systems, which can be related to the strong intermolecular hydrogen bonds, as discussed above. The stronger majority-rules effect for **4**, compared to **3** and **5**, is reflected in the lower MMP determined for **4**. A lower MMP means it is more favorable to incorporate the enantiomer in minority in stacks with the helicity corresponding to the enantiomer in majority. As a result, at lower ee a fully homochiral system can be obtained.

When considering the effect on chiral amplification of changing the position of the stereogenic center, the only difference observed is between the α- and γ-substituted derivatives **3** and **5** on the one hand and the β-substituted derivative **4** on the other hand. That is, there is an odd−even effect in the degree of chiral amplification. However, shifting the methyl closer to the benzene core does not result in a change in the chiral amplification behavior of the asymmetrical BTAs, other than the odd−even effect described above.

Effect of the Number of Stereogenic Centers on the Chiral Amplification in Benzene-1,3,5-tricarboxamide Derivatives. To study the influence of the number of stereogenic centers per molecule, the results obtained for the asymmetrically substituted monomer **5** equipped with one 3,7-dimethyloctyl side chain can be compared with those of the symmetrically substituted derivative **1** with three 3,7-dimethyloctyl side chains. Modeling the sergeants-and-soldiers and majority-rules data for **1** and **5** resulted in a HRP of about 12 kJ mol^{-1} for both systems. More interestingly, for **1** we found a MMP of 1.9 kJ mol^{-1}, whereas for **5** this energy penalty was only 1.0 kJ mol^{-1}. These results suggest that the MMP increases with the number of stereogenic centers present in the molecule, while the HRP remains constant. To investigate this hypothesis we also synthesized the asymmetrical derivative **6**, comprising two chiral 3,7-dimethyloctyl side chains and one achiral *n*-octyl side chain, and studied its majority-rules behavior (Figure 3A).

When considering the majority-rules results for the three derivatives, with one (**5**), two (**6**), or three (**1**) stereogenic centers, we observed a decrease in the degree of chiral amplification with increasing number of stereocenters. Modeling of the data for **6** resulted in HRP = 15(±4) kJ mol^{-1} and MMP = 1.6(±0.3) kJ mol^{-1}. This latter value is nicely between the values determined for the derivative with one stereogenic center (1.0 kJ mol^{-1}) and the molecule with three stereogenic centers (1.9 kJ mol^{-1}). Consequently, it can be concluded that the MMP can be directly related to the number of stereogenic centers present in the molecule.

Inspired by this conclusion, we performed so-called "mixed" majority-rules experiments in which two monomers with opposite chirality and different numbers of stereogenic centers were mixed (Figure 3B−D). Similar experiments have been

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(51) It should be noted that the majority-rules experiments for **4** were performed with two enantiomers with an ee of 60%. Recently, (*R*)-**4** was synthesized with high ee (>97%), which was used for the sergeants-and-soldiers experiments, as well as for the self-assembly studies.

(52) A positive ee value corresponds to an excess of the (*R*)-enantiomer.

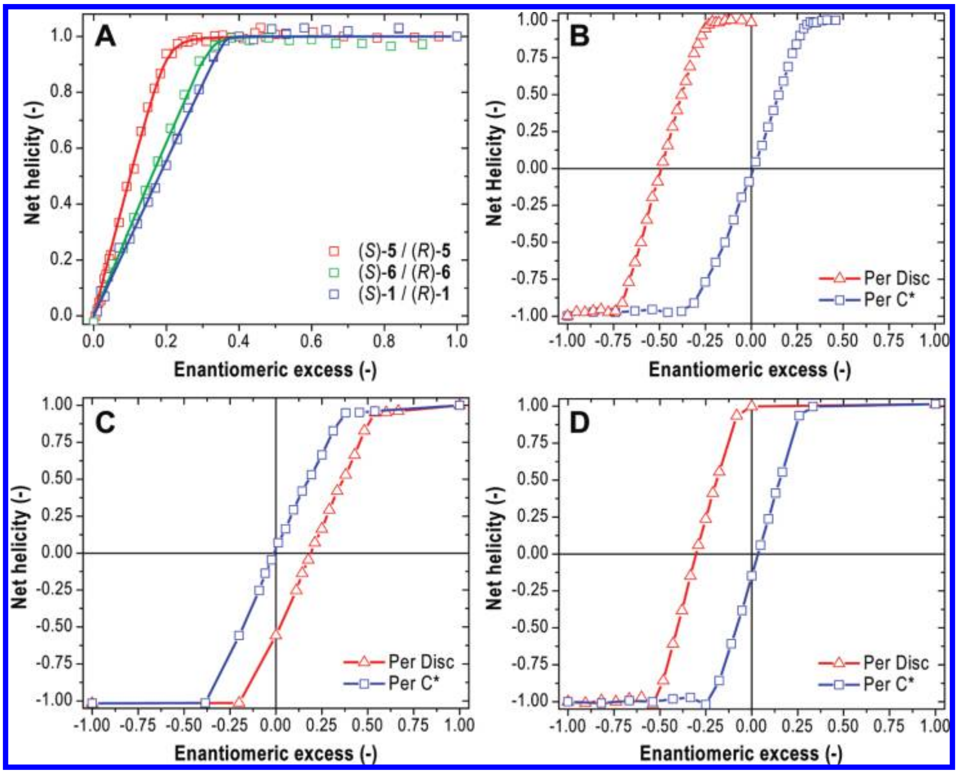

Figure 3. Majority-rules results for mixtures of (*R*)-**1**:(*S*)-**1**, (*R*)-**5**:(*S*)-**5**, and (*R*)-**6**:(*S*)-**6** with corresponding fit (A). Mixed majority-rules results for (*R*)-**1**:(*S*)-**5** (B), (*S*)-**1**:(*R*)-**6** (C), and (*R*)-**5**:(*S*)-**6** (D). The ee was calculated on a per-molecule basis and a per-stereocenter basis. Concentration, 3.0×10^{-5} M in MCH; temperature, 20 °C.

reported by Green and co-workers, who investigated the "chiral conflict" that arises when helical polymers are prepared from structurally different enantiomeric monomers.[53] When performing the mixed majority-rules experiments, care is needed to calculate the ee. First of all, the ee can be calculated on the basis of the number of molecules with a given stereochemistry. However, as the number of stereocenters per molecule is different, we can also determine the ee on the basis of the number of stereocenters with a given stereochemistry.

For each of the three possible mixed majority-rules experiments, we find that only when we determine the ee on the basis of the number of stereocenters do we arrive at a proper majority-rules plot in which no net helicity is found at ee = 0 and in which the origin is a point of symmetry. Therefore, these majority-rules results strongly support the hypothesis that the MMP is determined by the number of stereogenic centers. Finally, it is good to note that although the MMP is dependent on the number of stereocenters, no effect on the HRP was observed.

Limits of the Majority-Rules Principle. The chiral amplification behavior observed in the BTA-based supramolecular polymer can be characterized by a high and more or less constant HRP and a MMP that can change depending on concentration, temperature, or chemical structure. Consequently, if we want to enhance the degree of chiral amplification in this system, we can only influence the MMP. In case of the majority-rules principle, this would mean that we have to reduce the MMP to arrive at a stronger majority-rules effect, as was also observed experimentally (*vide supra*). Lowering the MMP can be achieved either by increasing the temperature, as was discussed in the preceding contribution, or by reducing the number of stereogenic centers. However, there is a limit to the extent to which the MMP can be lowered and still result in an enhancement of the majority-rules effect. Ultimately, at MMP = 0, the enantiomers will become effectively achiral at the supramolecular level, as they no longer have a preference to be in a right- or left-handed helical stack. Indeed, if we simulate, for a constant HRP, the net helicity versus ee for decreasing values of the MMP, an optimum in chiral amplification is observed (Figure 4A).

When the MMP is high, no chiral amplification can occur as the two enantiomers cannot be incorporated in stacks of their unpreferred helicity. As a result, the system is reminiscent of a phase-separated system and the net helicity increases linearly with the ee. Upon lowering the MMP, chiral amplification becomes possible. This is evident in Figure 4A from the nonlinearity of the curves, which show a higher net helicity at a given ee compared to the linear curve for an infinitely high MMP. As the MMP is further reduced, however, the curves decrease to values below the linear curve, and ultimately the net helicity becomes 0 for every ee. This happens as the MMP has become 0, meaning that chirality is no longer expressed at the supramolecular level. To illustrate the effect of lowering the MMP, the ee required to reach a net helicity of 0.95 can be plotted as a function of the MMP (Figure 4B). Figure 4B clearly shows that there is an optimal MMP at which homochirality becomes 1 at the lowest ee. Also indicated in Figure 4B are the determined mismatch penalties for the C_3-derivatives with one, two, or three stereocenters, i.e., for **5**, **6**, and **1**, respectively. As can be seen, the reduction in MMP observed when lowering the number of stereocenters leads to an enhancement of the degree of chiral amplification, in agreement with the results in Figure 3A. This shows that the limit of the majority-rules

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[53] Tang, K.; Green, M. M.; Cheon, K. S.; Selinger, J. V.; Garetz, B. A. *J. Am. Chem. Soc.* **2003**, *125*, 7313–7323.

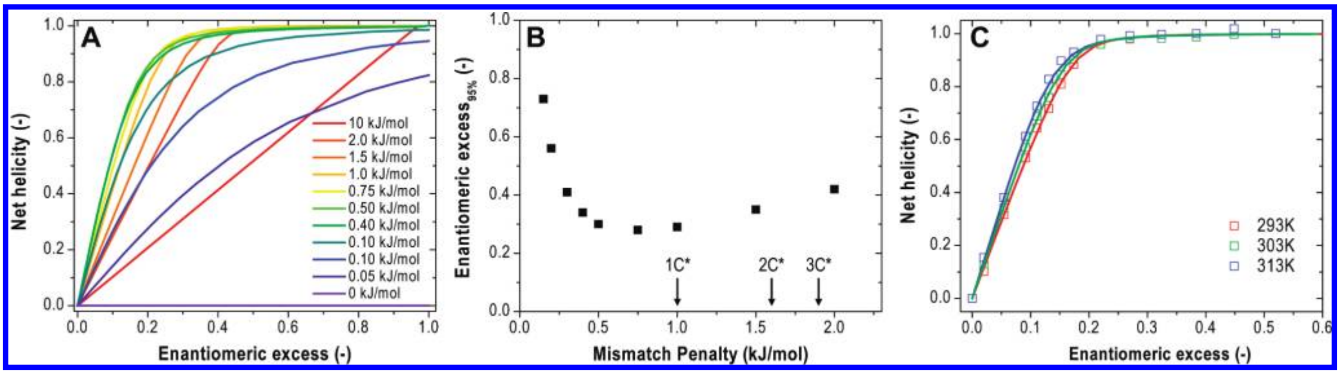

Figure 4. (A) Simulated majority-rules curves for different values of the MMP at a constant helix reversal penalty of 12.6 kJ mol^{-1}. (B) Enantiomeric excess required to obtain a net helicity of 0.95, assuming a constant HRP of 12.6 kJ mol^{-1}. The determined mismatch penalties for the enantiomers with one (**5**), two (**6**), and three (**1**) stereocenters are also indicated. (C) Majority-rules experiment for (*S*)-**5**:(*R*)-**5** at different temperatures. Concentration, 2.4 × 10^{-5} M in MCH.

principle is not yet reached by reducing the number of stereocenters to one.

To confirm the above simulations, we studied the majority-rules principle for the (*S*)-**5**:(*R*)-**5** system as a function of temperature. At room temperature already a rather low MMP of 1.0 kJ mol^{-1} was determined for this mixture of enantiomers. Raising the temperature in this system should further decrease the MMP but not necessarily enhance the majority-rules effect. Indeed, performing these majority-rules experiments at elevated temperatures (303 and 313 K) hardly improved the majority-rules effect (Figure 4C), suggesting that the optimum of the majority-rules principle was reached. Modeling did reveal that the MMP decreased from 0.8 kJ mol^{-1} at 303 K to 0.7 kJ mol^{-1} at 313 K.

These results show that, in order to amplify a small ee (e.g., as small as 5% excess) to a homochiral state, simply reducing the MMP is not sufficient. Such amplification is only possible if also the HRP is raised. The reason is that the optimal MMP depends on the HRP: a higher HRP will lead to a lower optimal MMP and a lower ee, for which a homochiral system can still be reached. For example, if the HRP is raised to 22 kJ mol^{-1}, a net helicity of 1 can be reached already at ~4% ee, which requires a MMP of 0.10 kJ mol^{-1}.[49]

Since the HRP is related to the strength of the intermolecular hydrogen bonds present in the stack, we are currently investigating how we could vary the strength of these hydrogen bonds, thereby also changing the HRP. For example, we are currently investigating chiral amplification phenomena in amide-functionalized porphyrin derivatives, which will form four intermolecular hydrogen bonds per supramolecular bond. Another approach we have investigated is to reverse the amide group with respect to the benzene core, i.e., synthesis of *N*-centered BTAs.[54]

However, a high HRP implies a high amplification length, which is the distance between two helix reversals, of ~10^4 molecules.[43] Reaching such lengths in a one-dimensional supramolecular polymer is not trivial and would require a high degree of cooperativity in the supramolecular polymerization mechanism. Alternatively, to attain such amplification lengths, two (or three)-dimensional structures would be necessary, so that the chirality can be transferred into more than one dimension.

Conclusion

By systematic variation of the chemical structure of benzene-1,3,5-tricarboxamide derivatives, the effect of chemical structure on the amplification of chirality was studied and quantified. For all benzene-1,3,5-tricarboxamide derivatives a high, constant helix reversal penalty was determined, which is related to the intermolecular hydrogen bonds that are present in all studied derivatives. For asymmetrically substituted benzene-1,3,5-tricarboxamide derivatives an odd−even effect was found in the degree of chiral amplification when changing the position of the stereogenic center with respect to the amide functionality. More interestingly, it was found that the mismatch penalty is directly related to the number of stereocenters present in the molecules. Increasing this number from one to three resulted in an increase in this energy penalty while leaving the HRP unaffected. Further evidence that the MMP is directly related to the number of stereocenters was obtained from mixed majority-rules experiments where two benzene-1,3,5-tricarboxamide derivatives with different numbers of stereocenters with opposite stereoconfiguration were used in a majority-rules experiment.

Finally, the ultimate limits of chiral amplification were investigated, revealing that, given a certain HRP, there is an optimum to which the MMP can be reduced while also enhancing the degree of chiral amplification. Majority-rules experiments could indeed verify these simulations. These findings show the relevance of both energy penalties when trying to enhance the degree of chiral amplification for the majority-rules principle in a one-dimensional helical supramolecular polymer.

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Supporting Information Available: Experimental conditions, synthetic procedures, details about the amplification model, modeling procedures, and supporting figures and tables. This material is available free of charge via the Internet at http://pubs.acs.org.

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