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Self-Assembly of Chiral Propeller-like Supermolecules with Unusual "Sergeants-and-Soldiers" and "Majority-Rules" Effects

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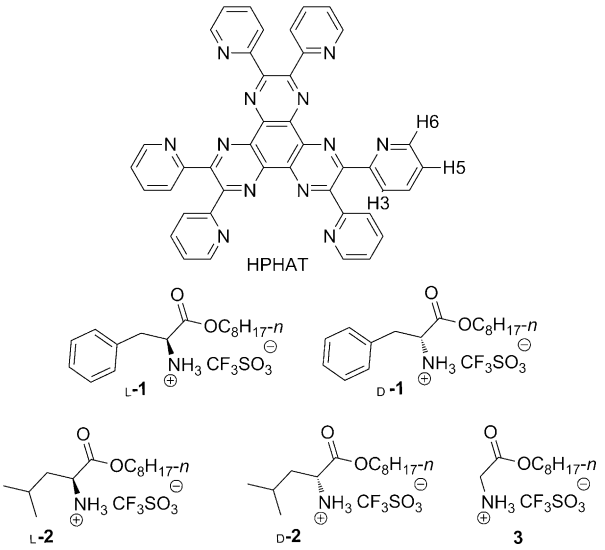
Abstract: Chiral amplification is an interesting phenomenon in supramolecular chemistry mainly observed in complicated systems in which cooperative effect dominate. Herein, chiral, supramolecular, propeller-like architectures have been constructed through coassembly of an achiral disk-shaped molecule and chiral amino acid derivatives driven by intermolecular hydrogen bonding. Both the "sergeants-and-soldiers" principle and "majority-rules" effect are applicable in these discrete four-component supermolecules, which are the simplest supramolecular system ever reported that exhibit chiral amplification.

The construction of chiral supramolecular architectures is one of the central themes of self-assembly because it is not only crucial to the understanding of chiral phenomena in biological systems, but is also important for the rational design of catalysts for asymmetric catalysis.[1] Direct incorporation of stereogenic centers into supramolecular tectons is undoubtedly the most direct approach for the construction of chiral supramolecular systems.[2] However, this method sometimes suffers from tedious and time-consuming organic synthesis. In this context, induction of supramolecular chirality, that is, the construction of chiral supramolecular architectures by coassembly of achiral tectons with chiral inducers, has been widely exploited.[3] In the process of chiral transfer from chiral inducers to achiral tectons, amplification of chirality might occur. Amplification of chirality includes two aspects: the sergeants-and-soldiers principle and the majority-rules effect. In the former, the chirality of a system is controlled by a few chiral units, the "sergeants", whereas the major analogues (the "soldiers") are achiral. In the latter, the chirality of a system is determined by which isomer is present in a slight excess in a pair of enantiomers. These two principles were initially observed in the construction of chiral macromolecules[4] and have lately been extended to supramolecular polymers.[5] It was suggested that such phenomena arose from the helix reversal penalty and mismatch penalty,[6] which could be magnified in systems consisting of a large number of building blocks, such as polymeric systems and extended macro/nanoscale aggregates.[7] However, in simple discrete systems, the total energy penalty might be too small to achieve chiral amplification due to the lack of a cooperative effect. For this type of self-assembled architecture, effective chiral amplification was only observed in a few nine- and fifteen-component hydrogen-bonded capsules developed by Reinhoudt et al.[8] We report herein an unusual chiral amplification phenomenon in an even simpler four-component supramolecular system constructed by the coassembly of achiral hexa-2-pyridyl-hexaazatriphenylene (HPHAT), which is a hexaazatriphenylene (HAT) derivative developed previously by us,[9] with amino acid derivatives **1**–**3** (Scheme 1). Both sergeants-and-soldiers and majority-rules effects are applicable to this simple system. To the best of our knowledge, this is the simplest



Scheme 1. Chemical structures of HPHAT and amino acid derivatives **1**–**3**.

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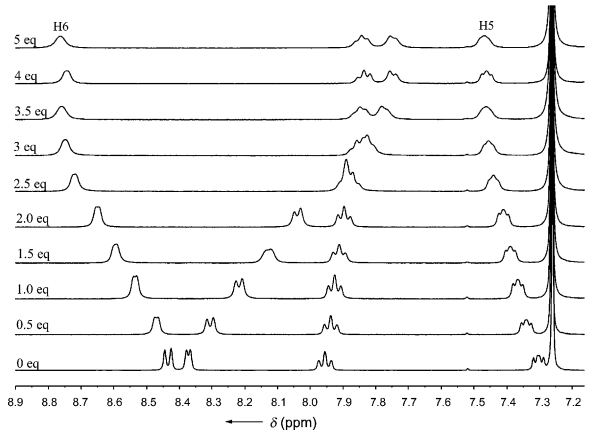

Figure 1. ^{1}H NMR titration spectra of HPHAT with D-**1** in $CDCl_3$ at 25 °C. The concentration of HPHAT was 5×10^{-3} M.

supramolecular system ever reported in which these two effects are operational.

The coassembly behavior of HPHAT and amino acid ester triflate salts **1**–**3** was first investigated through ^{1}H NMR titration experiments (Figure 1 and Figures S1 and S2 in the Supporting Information). Upon the incremental addition of D-**1**, the signals of H-5 and H-6 of the pyridyl unit of HPHAT exhibited considerable downfield shifts; this suggested the formation of intermolecular hydrogen bonds between the pyridine nitrogen atom of HPHAT and the three hydrogen atoms of the ammonium salt. Only a very small shift was exhibited after approximately three equivalents of the salts were added; this suggested that the bonding was saturated by the formation of a complex with 1:3 stoichiometry. The formation of intermolecular hydrogen bonds was also evidenced by IR spectroscopy, which showed a dramatic attenuation of the C=N stretching vibration of pyridyls and sharpening of the vibration of an ammonium group after HPHAT was mixed with D-**1** (1:3; Figure S3 in the Supporting Information). The coassembly behavior was also studied by UV/Vis titration experiments. Upon increasing the amount of amino acid ester salts, the UV/Vis absorption of HPHAT decreased and exhibited a redshift (Figure S4 in the Supporting Information). The UV/Vis titration experiments also showed saturation of complexation after the addition of three equivalents of the salts, which again suggested a 1:3 binding model for HPHAT and the amino acid ester salts. On the basis of the UV/Vis titration data, the apparent association constants between HPHAT and compounds **1**–**3** were estimated to be 1.3 $(\pm0.31)\times10^4$, 3.3 $(\pm0.54)\times10^4$, and 1.7 $(\pm0.20)\times10^4$ M^{-1} (Figure S5 in the Supporting Information),[10] respectively, and suggested remarkably high stability of the complexes.

We previously found that the complex formed by the coassembly of HPHAT and *n*-dodecyl ammonium triflate at high concentration (10 mM) could further aggregate into fine microbelts.[9a] However, in this system, spectroscopic results suggested that no higher-order aggregates except discrete 1:3 complexes existed in dilute solutions (see Figure 3 below for the structures of the complexes). This might be attributed to steric hindrance generated by the secondary ammonium of the amino acid derivatives. The first evidence was obtained from a UV/Vis dilution experiment. It revealed that no red- or blueshift of the absorption peaks of the HPHAT–(D-**1**) complex occurred and the absorbance of the complex obeyed the Beer–Lambert law if its concentration was diluted from 0.1 to 0.01 mM (Figure S6 in the Supporting Information); this suggested that no aggregation occurred in solution over this range of concentration. Furthermore, almost the same change in the UV/Vis spectrum of HPHAT was observed when it bound to chiral salts **1** and **2**, which contained different side chains. If the resulting HPHAT–ammonium salt complexes further aggregated, aggregates with dissimilar structures should form as a result of different steric hindrance of the side chains of the two chiral amino acid derivatives, which should lead to different changes in the UV/Vis absorption of HPHAT. This result further confirmed the existence of discrete complexes in dilute solution. The formation of discrete supermolecules without further aggregation in solution was also confirmed by dynamic light scattering (DLS) experiments, which gave a hydrodynamic diameter (D_h) of 2.2 nm for a solution of the 1:3 mixture of HPHAT–(D-**1**) at 0.1 mM (Figure S7 in the Supporting Information); this corresponded to the size of the expected single complex estimated from the crystal structure of HPHAT (the diameter of HPHAT is 1.7 nm).[9a] ESI-MS results for a solution of HPHAT and L-**1** (1:3) in dichloromethane displayed strong peaks at *m*/*z* 1979.8 and 1829.7, which corresponded to the exact masses of complexes $[HPHAT+3(L\text{-}\mathbf{1})+H^+]^+$ and $[HPHAT+3(L\text{-}\mathbf{1})-CF_3SO_3^-]^+$, respectively; this again corroborated the existence of a discrete 1:3 HPHAT–(L-**1**) complex (Figure S8 in the Supporting Information).

The crystal structure of HPHAT revealed that the six pyridyl units were not coplanar, but twisted out of the plane of the HAT core as a result of steric hindrance between the hydrogen atoms at the 3-position; this gave HPHAT a propeller-like conformation.[9a] The whole HPHAT molecule is achiral as a result of rotation of the single C–C bond that connects the pyridyl units and the HAT core. However, once bound to a chiral ammonium salt, a spatially asymmetric environment might be created by fixing the twisted orientation of the pyridyl units in a certain direction, which therefore induces the formation of chiral complexes. Circular dichroism (CD) spectroscopy was employed to investigate this possibility. The CD spectrum of HPHAT was recorded in dichloromethane and was found to be CD silent, which was consistent with its achiral character. However, upon mixing HPHAT with L-**1**, the mixture displayed a positive Cotton effect in the range of $\lambda=280$–400 nm (Figure 2). A mirror-symmetry CD signal was observed when D-**1** was used (Figure 2). Adding compounds L-**2**/D-**2** to a solution of HPHAT in dichloromethane led to a similar result (Figure S9 in the Supporting Information). Because compounds **1** and **2** did not exhibit UV/Vis absorption in this range, the origin of the CD signals could be attributed to the induced

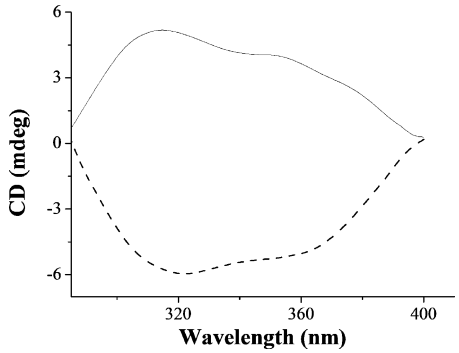

Figure 2. CD spectra of the mixtures of HPHAT and L-**1**/D-**1** (1:3) in CH_2Cl_2 at 25 °C. The concentration of HPHAT was 4×10^{-5} M. The spectra did not exhibit full mirror symmetry, which could be attributed to the excursion of the signals and instrumental errors. —— HPHAT and L-**1**. – – – HPHAT and D-**1**.

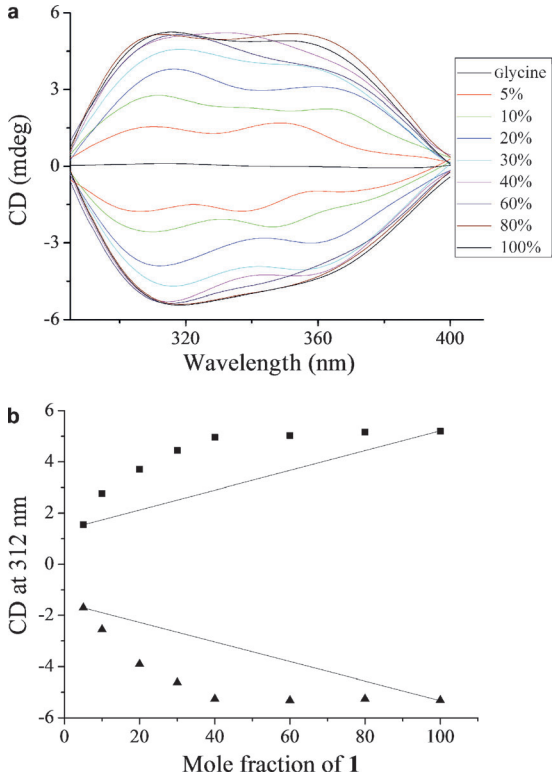

Figure 4. a) CD spectra of mixtures of HPHAT and (**1**+**3**) with variation of the molar fraction of L-**1** (positive region) and D-**1** (negative region) in CH_2Cl_2 at 25 °C. The molar ratio for HPHAT and the total amino acid ester salts was 1:3 and the concentration of HPHAT was 4×10^{-5} M. b) Plot of CD intensity at $\lambda = 315$ nm versus different molar fractions of **1** in the mixtures of **1** and **3**. ■ L-**1**. ▲ D-**1**.

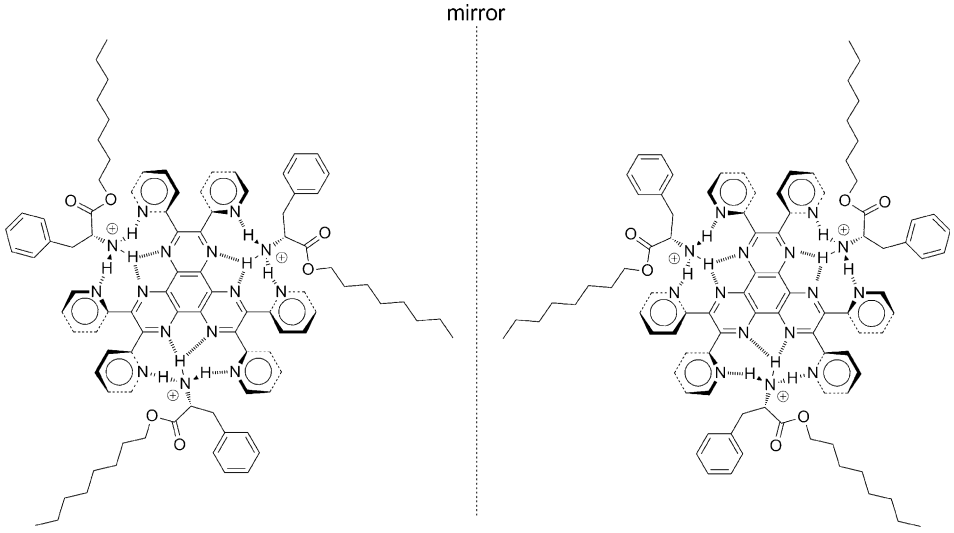

Figure 3. Schematic illustration of the enantiomeric complexes of HPHAT–(L-**1**) and HPHAT–(D-**1**).

circular dichroism (ICD) of HPHAT, which should result from the adoption of a certain asymmetric conformation of the pyridyl units of HPHAT. As shown in Figure 3, achiral HPHAT was induced to form one pair of enantiomeric complexes after binding with L- and D-amino acid derivatives. DFT calculations were performed to understand the origin of the chiral structures. The results clearly revealed that the six pyridyl units adopted M-helicity in the optimized geometry of the complex HPHAT–L-amino acid derivative (Figure S10 in the Supporting Information). Any other conformations will result in steric hindrance between the substituent group on the chiral center of the amino acid derivative and the pyridyls of HPHAT, which will destabilize the complexes. As a result, asymmetric preference arises.

The sergeants-and-soldiers principle was then examined for these propeller-like supermolecules. Glycine ester triflate salt **3** was used as an achiral component (soldiers) and L-**1** as sergeants. As shown in Figure 4, no Cotton effect was detected for a mixture of HPHAT and **3**. However, a solution of HPHAT and mixture of L-**1** (5%) and **3** (95%) exhibit a CD signal that is similar in shape to that of a mixture of HPHAT and pure L-**1** and its intensity reached about one fifth of that of the latter. Furthermore, upon increasing the content of L-**1** in the mixture of L-**1** and **3**, the intensity of the CD signals first increased and then became saturated when the molar fraction of L-**1** reached 40%, which indicated that the sergeants-and-soldiers principle was operational in this system. A sergeants-and-soldiers principle experiment was also performed by using D-**1** as the sergeant and a similar phenomenon was observed (Figure 4a, negative region). The operation of the sergeants-and-soldiers principle in this system was clearly demonstrated by plotting the CD intensity against the molar fraction of

chiral **1** (Figure 4b), which displayed a strong nonlinear dependence.

The majority-rules effect was also examined to see if it was applicable to this system. Mixtures of L-**1** and D-**1** with different enantiomeric excess (*ee*) were used for this purpose. As expected, no Cotton effect was observed at an *ee* of 0%. However, a positive Cotton effect, which was similar in shape to that of a mixture of HPHAT and pure L-**1**, was observed when an *ee* of only 5% was reached for L-**1**, although its intensity was just one fifth of the saturated one (that of HPHAT and pure L-**1**; Figure 5a, positive region).

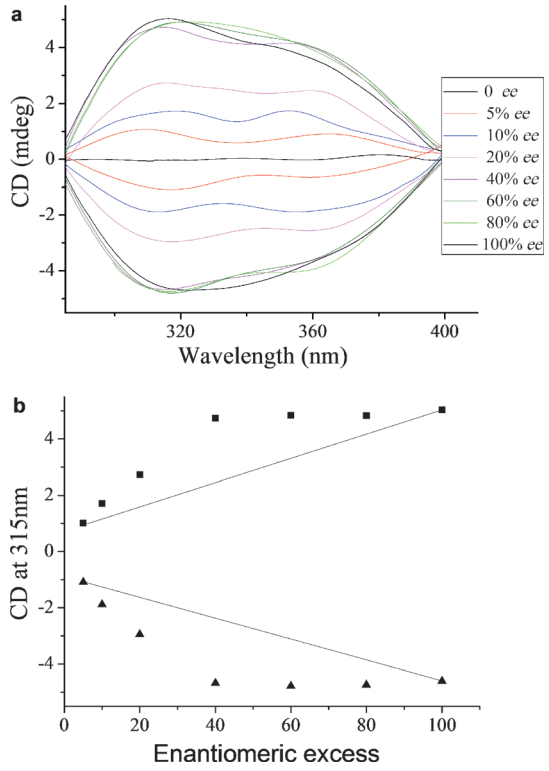

Figure 5. a) CD spectra of mixtures of HPHAT and (L-**1**+D-**1**) at different *ee* values for L-**1** (positive region) and D-**1** (negative region) in CH_2Cl_2 at 25°C. The molar ratio of HPHAT and the total amino acid ester salts was 1:3 and the concentration of HPHAT was 4×10^{-5} M. b) Plot of CD intensity at $\lambda=315$ nm versus *ee*. ■ *ee* of L-**1**. ▲ *ee* of D-**1**.

The intensity of the CD signal increased with increasing *ee* of L-**1** and remained almost constant after an *ee* of 40% was reached. The use of excess D-**1** resulted in mirror-symmetric changes to the CD signals (Figure 5a, negative region). Plotting the intensity of the CD signals at $\lambda=315$ nm against the *ee* revealed a significant nonlinear dependence (Figure 5b), which strongly indicated the presence of the majority-rules effect in this simple supramolecular system.

The origin of the sergeants-and-soldiers principle in these supermolecules could be explained as follows: communication among all pyridyl units is accessible through the steric repulsion of the adjacent pyridyl units. The bonding of one pyridyl unit will certainly affect the bonding environment of its neighboring pyridyl group. This information could be further relayed to the next pyridyl unit through the complexation of the ammonium salt. As a result, once one chiral species bound to the two pyridyl units of one hydrogen-bonding pocket, the chiral information was transferred from the two pyridyl units to all other pyridyl units, although they were hydrogen bonded to an achiral glycine derivative. In this way, chiral transfer and amplification arose. This mechanism, as illustrated in Figure 6, could explain the experimen-

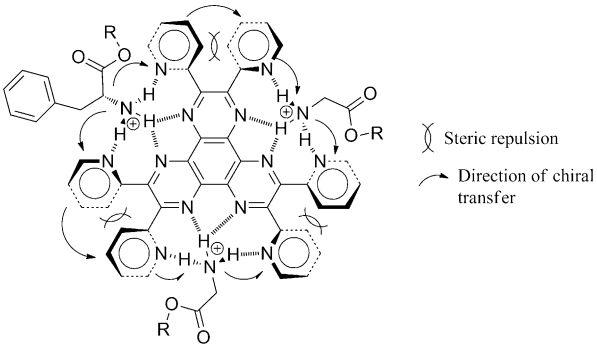

Figure 6. Schematic illustration of the origin of the sergeants-and-soldiers principle on the basis of the transfer of chirality from the D-phenylalanine derivative to the other part of the complex.

tal results that the intensity of the CD signal becomes saturated when the molar fraction of the sergeant reached 40%: statistically 33.3% of sergeant is required to ensure that at least one complex has one sergeant. For the origin of the majority-rules effect, if L-**1** is in excess in the mixture of L-**1** and D-**1**, the complex that has at least two molecules of L-**1** in the three hydrogen-bonding pockets of HPHAT will dominate in solution. The chirality of the whole complex should be dictated by the two molecules of L-**1** that are hydrogen bonded to four pyridyl units, not by D-**1** bound to the other two pyridyl units. The chiral information will also be transferred from the four pyridyl units to the other two through the steric repulsion of the adjacent pyridyl units.

In summary, discrete chiral propeller-like supermolecules have been constructed through the coassembly of achiral disc-like molecules and chiral amino acid derivatives. Thanks to intramolecular steric hindrance between the hydrogen-bonding segments, the operation of both the sergeants-and-soldiers principle and majority-rules effect could be realized in these simple four-component supermolecules through chiral transfer, which was mediated by steric repulsion. Although these two effects have already been observed in supramolecular polymerization of small molecules, the phenomena reported herein are unique because in supramolecular polymers the cooperativities of a large amount of building blocks contribute greatly to the magnification of the original chirality, but in our case the cooperative effect is very low or there may not be any cooperativity in these simple four-component supermolecules at all. This work demonstrated that chiral amplification could also be applicable in very simple supramolecular systems if a suitable chan-

nel for chiral transfer could be provided, which should be helpful to better understand the principles in asymmetric catalytic processes in which asymmetric induction plays a key role.[11] Moreover, extending the amplification of chirality from complicated architectures to discrete, simple, self-assembled objects might open up a way to the construction of novel chiral supramolecular systems with various structures.

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Keywords: chirality · cooperative effects · hydrogen bonding · steric hindrance · supramolecular chemistry

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