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Noncovalent Synthesis of Shape-Persistent Cyclic Hexamers from Ditopic Hydrazide-Based Supramolecular Synthons and Asymmetric Induction of Supramolecular Chirality

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Abstract: With properly encoded recognition sites and a well-defined algorithm for intermolecular and intramolecular interactions, the 120° spacer linked ditopic hydrazide-based supramolecular synthons were found to self-assemble into shape-persistent cyclic hexamers in apolar solvents. The two hydrazide motifs displayed separate sets of signals in the NMR spectra because of the interlocked conformation. While in hydrogen bonding competitive solvent such as DMSO-d_6 the spectra were in agreement with the structures with C_2 axes. Moreover, the terminative groups were found to affect the stability of the assemblies substantially. Consequently, the monomer with ureido-hydrazide terminative groups could form the most stable cyclic hexamer in solution for the attractive spectator secondary electrostatic interactions. Owing to the dynamically and kinetically stable nature of these kinds of assemblies, the assembly from the monomer with chiral auxiliary terminative groups also displayed supramolecular chirality in solution, which was confirmed by concentration-dependent CD spectra.

Introduction

Self-assembly,[1] the process by which a target species forms spontaneously from its components without human intervention, has proven to be a powerful and efficient tool for the bottom-up construction of nanostructures in supramolecular chemistry.[2] Though self-assembly is a widespread phenomenon in biological systems,[3] the principles governing the process have not been completely mastered or understood by human beings. Thanks to lessons from biological systems, this pivotal and powerful tool has been widely used by chemists. Intensive attention has been paid to the construction of designed and well-defined structures with nanoscale dimensions from single fragments by self-assembly. Particularly, great interest goes into the H-bonding mediated cyclic rosettelike structures.[4] Nucleotide mimics have dominated in this field, thanks to the inspiration from the complementarity of nucleotides found in biological systems.[5] Successful examples include G-quartets[6] and Janus GC hybrids independently developed by Lehn et al.,[7] Mascal et al.,[8] Zimmerman et al.,[9] Fenniri et al.,[10] and Perrin et al.[11] Other examples include pyridone-based cyclic trimers,[12] carboxylic acid-based hexamers,[13] ureidodeazapterin (DeAP)-based hexamers,[14] and ureidopyrimidinone (UPy)-based pentamers,

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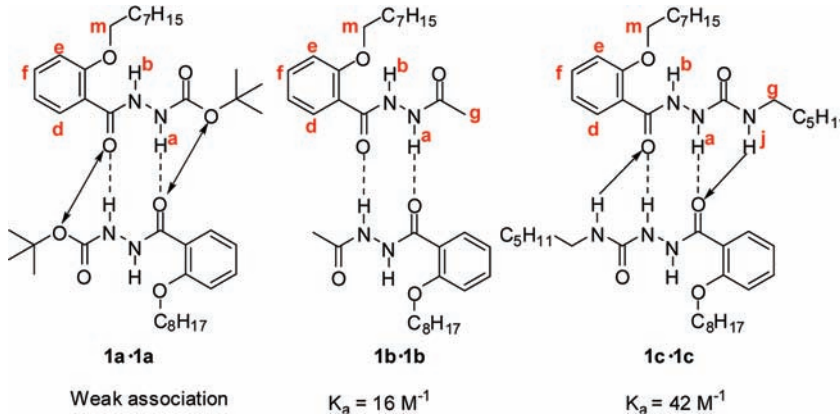

Figure 1. Spectator secondary electrostatic interaction analysis of the hydrazide-based supramolecular synthons with different terminative groups. Double-headed arrow: repulsive interaction; mono-headed arrow: attractive interaction.

hexamers,[15] and tetramers.[16] Whitesides and Reinhoudt's cyanuric acid-melamine rosettes are excellent examples of two component assemblies.[17,18] As we can see, all these examples are based on heterocyclic building blocks. As a consequence, long synthetic and purification procedures, difficulties of derivation, and isomerization often accompany self-assembly, which deeply limits their applications. Moreover, the formation of cyclic rosettes of most of the aforementioned examples relies on additional factors such as metal ion binding, periphery crowding, or covalent preorganization.

Shape-persistent macrocycles are structures with rigid, noncollapsible backbones and lumens of various sizes. Intensive focus of chemical research has been paid to this unique kind of structure because of its wide applications in material science.[19] However, the synthesis of shape-persistent macrocycles presents a great challenge even with the present-day synthetic technology. Rare examples of a one-step method have thus been reported, whereas multistep chemical reactions and purification procedures were also typically required in most cases. Alternatively, noncovalent synthesis could provide a convenient and economic way to construct such structures.[17c]

It is well-known that when the atoms of a molecule are arranged in one unique manner in space, it displays chirality.[20] Similarly, when the components (molecules) of a self-assembled noncovalent architecture are arranged asymmetrically, the assembly also displays chirality. This phenomenon is called supramolecular chirality.[18] Nature is the expert in the control of supramolecular chirality. It is this precise control that ensures complex biological processes such as protein folding, and the expression and transfer of genetic information to be fulfilled accurately. While it has dramatic consequences in chemical systems and is very important for applications in molecular recognition and mimicking of catalytic activity of enzymes, the control of supramolecular chirality in synthetic self-assembled systems is still in its infancy and presents a great challenge for chemists.

In this article, we report the noncovalent synthesis and characterization of the first examples of shape-persistent, rosettelike cyclic hexamers from the self-assembly of a 120° spacer linked nonheterocyclic ditopic hydrazide-based supramolecular synthons.[21−23] Moreover, by using a monomer with chiral auxiliary terminative groups, an asymmetric arrangement of the components for the assembly could also be achieved, and this supramolecular chirality in solution was confirmed by the concentration-dependent CD spectra.

Results and Discussion

Spectator Secondary Electrostatic Interaction Analysis. According to the results we previously reported,[22a,b] the acetyl-terminated hydrazide-based supramolecular synthon **1b** (Figure 1) is a dimer in both solution and solid states, with a dimerization constant of 16 M^{-1}. Weak association was observed for **1a**[22d] because of repulsive secondary electrostatic interaction[22h,24] inherent with the Boc group. For the purpose of this study, we need a stronger associating module. We envisioned that substitution of the Boc group with a urea group (i.e., the repulsive interaction was replaced by an attractive interaction)

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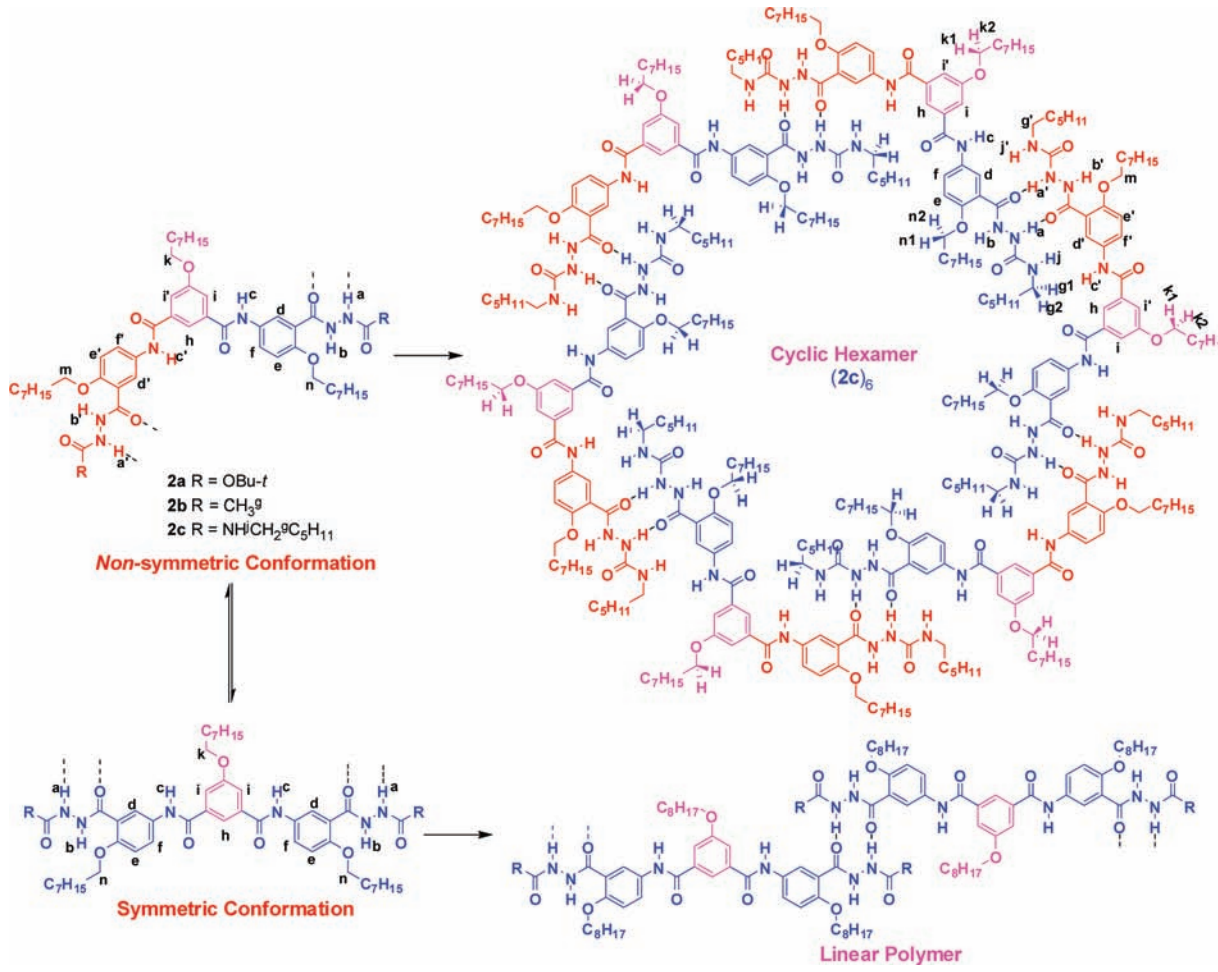

Figure 2. Conformation and aggregation analysis of 120° spacer linked hydrazide-based ditopic monomers: nonsymmetric conformation vs symmetric conformation; cyclic hexamer vs linear polymer, with hydrogen labeling scheme indicated.

would give rise to a stronger association module. Indeed, nonlinear regression analysis[25,26] of the dilution ^{1}H NMR data yielded a dimerization constant of 42 M^{-1} for ureido-hydrazide-based **1c·1c**.

Design and Synthesis. If the hydrazide-based supramolecular synthons were linked through a 120° spacer, with properly encoded recognition sites, the simple fragments could assemble spontaneously into well-defined rosettelike hexameric structures as shown in Figure 2. However, conformational flexibility could allow for many other isomers to be present in solution. For example, if the monomers adopt a conformation with a C_2 axis (Figure 2), there is the possibility of many linear polymers in solution. With this idea in mind, monomers **2a**−**2c** were designed and synthesized. The synthesis of the monomers was straightforward and based on standard amide/peptide coupling chemistry.[26]

Self-Assembly in Solution. The ^{1}H NMR spectrum of **2b** in $CDCl_3$ (10 mM) (Figure 3d) displayed a complicated picture: numerous minor peaks were present and each hydrazide motif displayed separate sets of signals. In DMSO-d_6, the spectrum is in agreement with its structure with the C_2 axis (Figure S5d in the Supporting Information). The ^{1}H NMR spectrum of **2a** in $CDCl_3$ (10 mM) (Figure 3b) displayed low resolvability, even though we can discern that the signals corresponding to H^e and $H^{e'}$ clearly displayed two double peaks. However, the ^{1}H NMR spectrum of **2c** contained well-defined peaks at the same concentration in $CDCl_3$, in which each hydrazide motif also displayed separate sets of signals (Figure 3f), whereas both compounds **2a** and **2c** displayed ^{1}H NMR spectra in DMSO-d_6 (Figures S5b,f in the Supporting Information) consistent with their structures with C_2 axes as indicated in Figure 2. These findings might indicate the different aggregation modes for compounds **2a**−**c** in $CDCl_3$ and DMSO-d_6.

The ^{13}C NMR experiments also provided results similar to those of the ^{1}H NMR experiments. Consequently, compound **2c** displayed a ^{13}C NMR spectrum in DMSO-d_6 (Figure 4b) corresponding to its structure with C_2 axis, whereas in $CDCl_3$ (Figure 4a) the spectrum displayed a complicated picture: the symmetric nature disappeared and each part displayed separate sets of signals. Especially in the range of 70−60 ppm where OCH_2 signals appeared, there were three signals (67.8, 66.8, 66.6 ppm) in the spectrum in $CDCl_3$ and two signals (69.7, 68.7 ppm) in DMSO-d_6. The ^{1}H−^{15}N correlation HMQC spectrum

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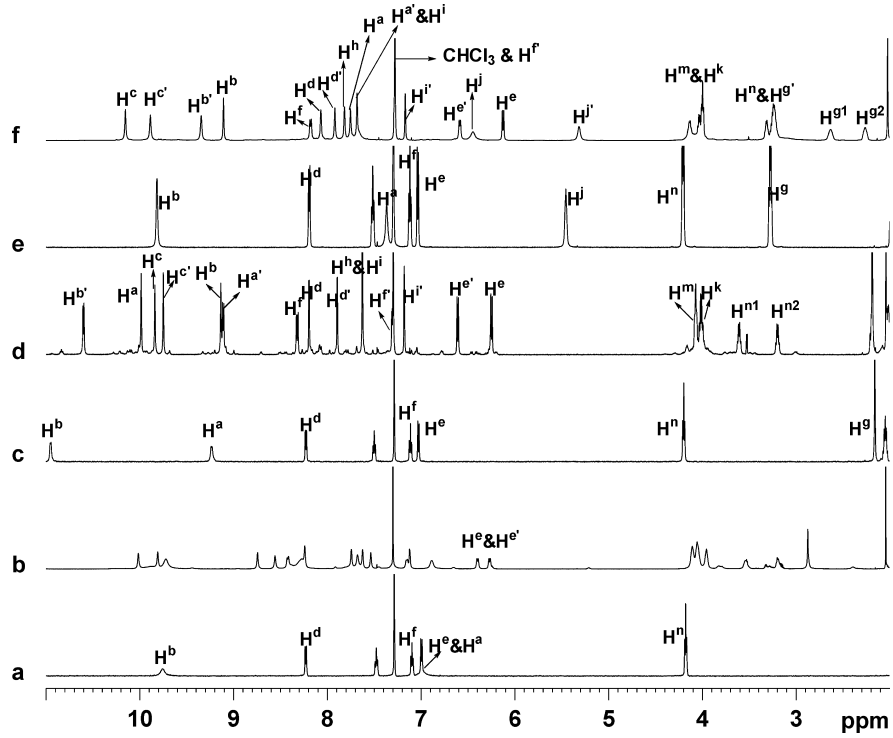

Figure 3. Stacked partial ^{1}H NMR spectra of (a) **1a**, (b) **2a**, (c) **1b**, (d) **2b**, (e) **1c**, and (f) **2c** in $CDCl_3$, 10 mM, 298 K, 600 MHz.

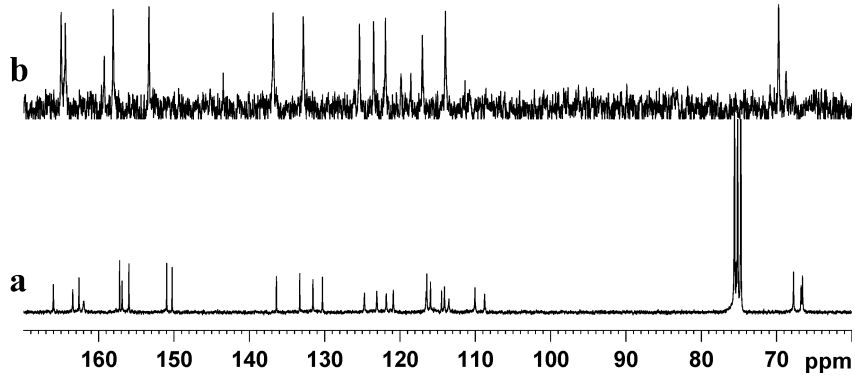

Figure 4. Stacked partial ^{13}C NMR spectra of **2c** in (a) in $CDCl_3$, 75 MHz, and (b) DMSO-d_6, 150 MHz, 298 K.

of **2c** in $CDCl_3$ (Figure 5) also displayed eight different kinds of NH groups, which might result from the nonsymmetrical nature of the two hydrazide motifs.

Vapor pressure osmometry (VPO) was used to determine the aggregation mode of the ditopic hydrazide monomers in apolar solvents. Consequently, VPO studies on **2c** were conducted at 37 °C in alcohol-free $CHCl_3$ over the concentration range of 10−64 g/kg (sample/solvent) using sucrose octaacetate as molecular weight standard, which consistently gave an apparent molecular weight of 6.3×10^3, corresponding to the hexamer (calculated for $(\mathbf{2c})_6$: 6428).[26] Because of the poor solubility of **2b**, VPO experiments failed to give satisfactory results. No satisfactory VPO result for **2a** was also obtained, maybe because of the low stability from the repulsive secondary electrostatic interactions inherent with the Boc groups in **2a**.

Formation of the hexamer of **2c** was further confirmed by its MALDI-TOF mass spectrum. As a result, a peak at *m*/*z* 6428 for $(\mathbf{2c})_6$ was clearly observed (Figure S38 in the Supporting Information). These observations suggested that the cyclic hexameric structures (Figure 2) could be formed for **2a**−**2c** in

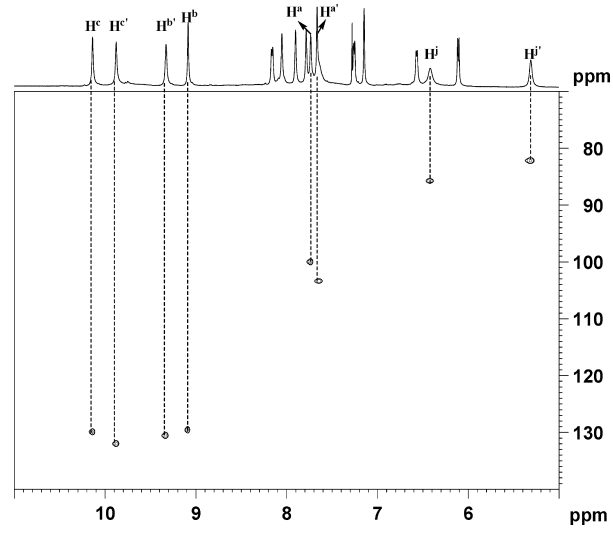

Figure 5. Partial ^{1}H−^{15}N correlation HMQC spectrum of **2c** in $CDCl_3$, 298 K, 600 MHz, showing eight kinds of NH groups in **2c**.

$CHCl_3$, in which successive hydrogen bonding interactions locked their conformation. Because of the difference in association strength derived from different spectator secondary electrostatic interactions associated with the terminative groups, for **2a** and **2b**, in addition to the main aggregation species, there were also other aggregates, whereas for **2c** with additional attractive interactions, cyclic hexamer architecture was exclusively formed in $CHCl_3$. Different chemical surroundings (Figure 2) for the inner and outer hydrazide motifs led to their different NMR (^{1}H NMR, ^{13}C NMR, ^{1}H−^{15}N correlation HMQC) signals, whereas in DMSO-d_6, which is a highly competitive solvent for hydrogen bonding, **2a**−**2c** existed as monomers, and they only displayed the NMR spectra corresponding to the structures with C_2 axes.

Combined with the results of COSY, TOCSY, and NOESY experiments, precise assignment of the ^{1}H NMR signals for 10 mM $(\mathbf{2b})_6$ and $(\mathbf{2c})_6$ in $CDCl_3$ was fulfilled (Figure 3).[26] The assignment process started with the assumption that the rotational freedom of the inner NCH_2 (H^{g1} and H^{g2}) and OCH_2 (H^{n1} and H^{n2}) groups was restricted because of stereo hindrance in a confined space, which displayed two separate peaks (Figure 3d,f).[27] Additionally, OCH_2 (H^{k1} and H^{k2}) groups from the central linkers also displayed two separate signals. This phenomenon was evidenced remarkably from **2e**[26] with a benzyl-substituted central spacer: two double peaks at 5.18 and 5.31 ppm were observed for the central OCH_2 group, with a relatively large coupling constant ($J = 11.3$ Hz) (Figure S39 in the Supporting Information). These observations suggested that there were two cycloenantiomers in solution. This hypothesis was further confirmed by **2d** with chiral auxiliary terminative groups (vide infra). Consequently, cross contacts between H^{g1} (H^{g2}) and $H^{c\prime}$, $H^{g\prime}$ and H^{c}, H^{j} and $H^{d\prime}$ were observed in the NOESY spectrum (Figures S27 and S28 in the Supporting Information), which provided diagnostic evidence for the hexameric structure.

To determine the stability of $(\mathbf{2c})_6$, dilution ^{1}H NMR experiments were performed. Within the concentration range of 100−1 mM (monomer concentration), no prominent changes were observed (Figure S30 in the Supporting Information), which might suggest high stability of the assembly. When 10 mM **2c** in $CDCl_3$ was titrated with DMSO-d_6, in addition to the signals corresponding to the hexamer, new signals corresponding to the monomer also appeared when DMSO-d_6/$CDCl_3$ ratio reached 3%.[26] No other signals were found during the whole titration process. This phenomenon suggested that the self-assembly/deassembly of hexamer $(\mathbf{2c})_6$ was a highly cooperative process and the process was slow on the NMR time scale. By precise integration of signal for $H^{e\prime}$ of $(\mathbf{2c})_6$ and signal for H^{e} of **2c**, the association constant at different solvent ratios could be determined. The results were provided in Table 1. Results based on titration experiments with a 20 mM solution were also provided. The similar results evidenced the legality of this method. Considering the dimerization constant (42 M^{-1}, vide supra) of ureido-hydrazide-based supramolecular synthon, the high association constants also indicated that the assembly/deassembly process was highly cooperative (i.e., the dimeriza-

Table 1. Association Constants K_a[a] (M^{-5}) for $(\mathbf{2c})_6$ Determined by DMSO-d_6 Titration ^{1}H NMR Experiments in $CDCl_3$ at Different Concentrations, 300 MHz, 298 K

DMSO-d_6/$CDCl_3$ (v/v) %	3	4	5	6	7	8	9	10	11	12	13	14	15
K_a[b]	3.67×10^{16}	6.67×10^{13}	2.61×10^{13}	3.21×10^{12}	7.23×10^{11}	9.04×10^{10}	1.40×10^{10}	3.893×10^{9}	9.59×10^{8}	2.90×10^{8}	[c]	[c]	[c]
K_a[d]	[e]	[e]	[e]	1.84×10^{12}	3.93×10^{11}	9.73×10^{10}	2.21×10^{10}	4.41×10^{9}	9.06×10^{8}	1.93×10^{8}	6.59×10^{7}	1.96×10^{7}	7.43×10^{6}

[a] The association constant is defined as $K_a = [(\mathbf{2c})_6]/[\mathbf{2c}]^6$ (M^{-5}). [b] Determined via a solution of 10 mM **2c** in $CDCl_3$. [c] Not determined because of complete deassembly. [d] Determined via a solution of 20 mM **2c** in $CDCl_3$. [e] Not determined because no signals corresponded to the monomer.

(27) Reinhoudt et al. also observed this phenomenon in their calyx[4]arene double rosettes: (a) Vreekamp, R. H.; van Duynhoven, J. P. M.; Hubert, M.; Verboom, W.; Reinhoudt, D. N. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1215–1218. Wang et al. also observed a similar phenomenon in their molecular baskets: (b) Wang, B.-Y.; Rieth, S.; Badjic, J. D. *J. Am. Chem. Soc.* **2009**, *131*, 7250–7252.

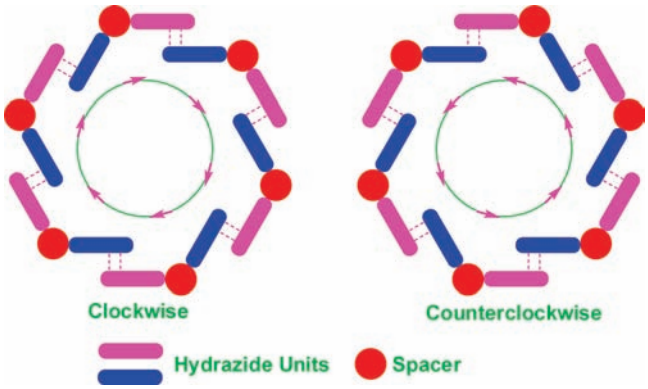

Figure 6. Representation of two forms of the cyclic hexamers: clockwise fashion vs counterclockwise fashion.

tion preference of ureido-hydrazide supramolecular synthon was largely amplified in this 120° spacer linked ditopic derivative).

Asymmetric Induction of Supramolecular Chirality. Because of their wide applications, preparation of enantiopure chiral molecules has been a widely explored and mature area in organic synthesis.[28] While in the field of noncovalent synthesis,[17c] the control of supramolecular chirality is still in its infancy for chemists. It was found that the above-discussed cyclic hexamers should exist as two forms: one with all monomers arranged in a clockwise fashion and the other with all monomers arranged in a counterclockwise fashion (Figure 6). We hypothesized that the dynamically and kinetically (at least on the NMR time scale) stable nature of the above cyclic hexamers would be an ideal model to explore supramolecular chirality of the cyclic rosette structures.[29,30] To bias the equilibrium between these two cycloenantiomers,[31,32] monomer **2d** (Figure 7a) with chiral auxiliary terminative groups was synthesized. For a comparison, monotopic monomer **1d** was also synthesized.[26]

Circular dichroism (CD) is an ideal tool for monitoring supramolecular chirality of self-assembled systems in solution because of its outstanding sensitivity to chiral perturbation of the systems under investigation.[33] As shown in Figure 7b, **2d** displayed concentration-dependent CD spectra in $CHCl_3$. Below a concentration of 2×10^{-4} M, no significant CD activities could be detected. By increasing the concentration, the CD spectra displayed stronger activities at about 350 nm, while the minimum showed red shift. At 9×10^{-4} M of **2d**, the strongest

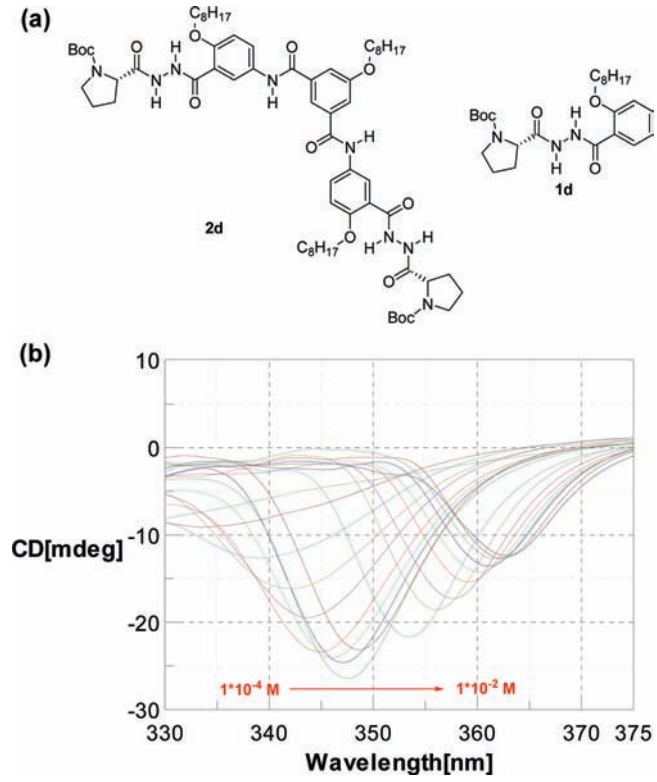

Figure 7. (a) Chemical structures of **2d** and **1d** with chiral auxiliary terminative groups. (b) CD spectra of **2d** at different concentrations in $CHCl_3$, concentration: $(1-9) \times 10^{-4}$ M (at 10^{-4} M intervals), $(1-10) \times 10^{-3}$ M (at 10^{-3} M intervals).

CD activity (−26.5 mdeg at 347.5 nm) was observed. Above this concentration, the CD activity became weaker, and the minimum still shifted toward red band. For the monotopic **1d**, the CD spectra did not show any significant CD activity within the range of concentrations investigated (1×10^{-6} to 1×10^{-2} M). The observed CD activity is thus clearly a direct result of assembly formation and not an intrinsic property of the individual components. The concentration-dependent behavior could be explained in three ways. First, the introduction of a chiral auxiliary group biases the equilibrium between the two cycloenantiomers, and one of the enantiomers predominates in solution. Second, when the concentration is too low, there are not enough cyclic hexamers in solution for a detectable CD spectrum. Third, the cyclic hexamer may further stack to form tubular structures, which might account for the red shift of the minimum of CD signals and weaker CD activity above 9×10^{-4} M. This unique phenomenon might be worthwhile for further investigation.

Conclusions

In conclusion, we have described the noncovalent synthesis and characterization of the shape-persistent cyclic hexamers from the self-assembly of 120° spacer linked ditopic hydrazide-based supramolecular synthons. We found that the self-assembly process was spontaneous and highly cooperative. The dimerization preference of the hydrazide-based supramolecular synthons was largely amplified. The self-assembly was just based on the instructions stored in the building blocks and the predefined algorithms of inter- and intramolecular interactions. Secondary electrostatic interactions led to varying stabilities for the assemblies. Because the flexible conformation of the monomers was interlocked, the different signals for the two

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(29) Reinhoudt et al. extensively studied supramolecular chirality in cyanuric acid-melamine hydrogen-bonded double-rosette assemblies: (a) Prins, L. J.; Huskens, J.; de Jong, F.; Timmerman, P.; Reinhoudt, D. N. *Nature* **1999**, *398*, 498–502. (b) Prins, L. J.; de Jong, F.; Timmerman, P.; Reinhoudt, D. N. *Nature* **2000**, *408*, 181–184. (c) Prins, L. J.; Verhage, J. J.; de Jong, F.; Timmerman, P.; Reinhoudt, D. N. *Chem.—Eur. J.* **2002**, *8*, 2302–2313.
(30) Supramolecular chirality was also studied by Fenniri et al. in their GC hybrid-based rosette structures; see refs 10b and 10e.
(31) Cycloenantiomerism was first discussed in the case of cyclopeptides where it depends on the ring direction and the distribution pattern of the stereogenic centers in the amino acid units: (a) Prelog, V.; Gerlach, H. *Helv. Chim. Acta* **1964**, *47*, 2288–2294. (b) Goodman, M.; Chorev, M. *Acc. Chem. Res.* **1979**, *12*, 1–7.
(32) For some examples of cycloenantiomers in supramolecular chemistry, see: (a) Yamamoto, C.; Okamoto, Y.; Schmidt, T.; Jäger, R.; Vögtle, F. *J. Am. Chem. Soc.* **1997**, *119*, 10547–10548. (b) Saito, S.; Nuckolls, C.; Rebek, J., Jr. *J. Am. Chem. Soc.* **2000**, *122*, 9628–9630. (c) Szumna, A. *Org. Biomol. Chem.* **2007**, *5*, 1358–1368. (d) Paletta, M.; Klaes, M.; Neumann, B.; Stammler, H.; Grimme, S.; Mattay, J. *Eur. J. Org. Chem.* **2008**, 555–562.
(33) Gottarelli, G.; Lena, S.; Masiero, S.; Pieraccini, S.; Spada, G. P. *Chirality* **2008**, *20*, 471–475.

hydrazide motifs in NMR spectra (^{1}H, ^{13}C, ^{1}H−^{15}N correlation HMQC) were observed. Moreover, precise determination of association constant in solution was also obtained because of the slow assembly/deassembly process at the NMR time scale. This is the first example of rosettelike structures from nonheterocycle-based building blocks, which are devoid of many problems intrinsic with heterocycle-based building blocks. Furthermore, the kinetically and dynamically stable nature of these kinds of assemblies led to an asymmetric induction of supramolecular chirality from a monomer with chiral auxiliary terminative groups, which subsequently exhibited concentration-dependent CD activities in apolar solvent because of excess of one of the cycloenantiomers. We believe that the synthetic accessibility, easy derivation, and fining tuned stability of the hydrazide-based supramolecular synthons can make them a good scaffold for the preorganization of functional groups with appealing properties. Further functionalization of the hexameric structures will be the aim of our future studies.

Experimental Section

Typical Procedure for the Preparation of 2c. Hydrogen was bubbled continually into a solution of *N*-hexyl-2-(5-nitro-2-(octyloxy)benzoyl)hydrazinecarboxamide (0.87 g, 2 mmol) in CH_2Cl_2/methanol (20 mL/20 mL) using Pd/C 10% (100 mg) as catalyst. The reduction was completed in about 2 h, and the catalyst was then removed via filtration. After evaporation of the solvent, the amine was used in the next step without further purification. The coupling of 5-(octyloxy)isophthalic acid (0.29 g, 1 mmol) and the above amine was realized using EDC·HCl (0.48 g, 2.2 mmol) as reagent in CH_2Cl_2. The purification was achieved via crystallization from hot acetonitrile. Compound **2c** (0.98 g) was obtained as a white solid in 92% yield via two steps. Mp: 140−141 °C. MALDI-TOF MS: *m*/*z* 1093.4 $[M + Na]^+$, 1109.4 $[M + K]^+$. Anal. Calcd for $C_{60}H_{94}N_8O_9 \cdot 2H_2O$: C, 65.07; H, 8.92; N, 10.12. Found: C, 65.21; H, 8.96; N, 10.29. ^{1}H NMR (600 MHz, DMSO-d_6, 10 mM, TMS, 298 K, ppm): δ 10.38 (s, 2H, H^c), 9.72 (s, 2H, H^b), 8.15 (s, 5H, H^d, H^a, H^h), 7.97 (dd, J = 2.2, 8.8 Hz, 2H, H^f), 7.68 (s, 2H, H^i), 7.18 (d, J = 9.1 Hz, 2H, H^e), 6.27 (t, J = 5.6 Hz, 2H, H^j), 4.12−4.09 (m, 6H, H^m, H^k), 3.02 (q, 4H, H^g), 1.81−1.74 (m, 6H, CH_2), 1.48−1.21 (m, 46H, CH_2), 0.86−0.82 (m, 15H, CH_3). ^{13}C NMR (150 MHz, DMSO-d_6, TMS, 298 K, ppm): δ 165.0, 164.4, 159.3, 158.1, 153.3, 136.9, 132.8, 125.4, 123.5, 121.9, 119.9, 118.6, 117.0, 114.0, 69.7, 68.7, 31.8, 31.6, 30.4, 29.2, 26.5, 26.1, 22.6, 14.5. ^{1}H NMR (600 MHz, $CDCl_3$, 10 mM, TMS, 298 K, ppm): δ 10.16 (s, 1H, H^c), 9.89 (s, 1H, $H^{c'}$), 9.35 (s, 1H, Hb′), 9.11 (s, 1H, Hb), 8.18 (d, J = 8.4 Hz, 1H, H^f), 8.07 (s, 1H, H^d), 7.92 (s, 1H, $H^{d'}$), 7.82 (s, 1H, H^h), 7.75 (s, 1H, H^a), 7.68 (s, 2H, $H^{a'}$, H^i), 7.26 (merged in the signal of $CHCl_3$, $H^{f'}$), 7.17 (s, 1H, $H^{i'}$), 6.59 (d, J = 8.3 Hz, 1H, $H^{e'}$), 6.50−6.40 (br, 1H, H^j), 6.13 (d, J = 9.2 Hz, 1H, $H^{e'}$), 5.35−5.27 (br, 1H, H^j), 4.20−3.95 (m, 4H, H^m, H^k), 3.35−3.18 (m, 4H, H^{n1}, H^{n2}, $H^{g'}$), 2.64−2.60 (m, 1H, H^{g1}), 2.30−2.22 (m, 1H, H^{g2}), 1.95−1.80 (m, 4H, CH_2), 1.52−1.00 (m, 48H, CH_2), 0.97−0.91 (m, 9H, CH_3), 0.89 (t, J = 7.2 Hz, 3H, CH_3), 0.82 (t, J = 7.3 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, TMS, 298 K, ppm): δ 166.0, 163.4, 162.6, 162.0, 157.2, 156.9, 156.0, 151.0, 150.3, 136.4, 133.3, 131.6, 130.3, 124.7, 123.1, 121.8, 120.9, 116.6, 116.4, 115.9, 114.5, 114.1, 113.5, 110.0, 108.8, 67.8, 66.8, 66.6, 38.3, 38.2, 30.00, 29.98, 29.94, 29.7, 29.6, 28.4, 27.7, 27.61, 27.56, 27.44, 27.39, 27.35, 27.26, 26.8, 24.8, 24.4, 24.3, 24.1, 20.8, 12.22, 12.16, 12.14.

See Supporting Information for detailed procedures and characterization data for other compounds.

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Supporting Information Available: Experimental procedures and characterization data for new compounds, determination of dimerization constant for **1c·1c**, NOESY, COSY, and TOCSY spectra for **2b** and **2c**, data analysis of VPO experiments, and determination of association constants for $(\mathbf{2c})_6$. This material is available free of charge via the Internet at http://pubs.acs.org.

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