Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron
Tetrahedron 61 (2005) 9600–9610

Self-assembly of a new series of quadruply hydrogen bonded heterotrimers driven by the donor–acceptor interaction

Xiao-Qiang Li,[a] Mu-Xin Jia,[b] Xiao-Zhong Wang,[a] Xi-Kui Jiang,[a] Zhan-Ting Li,[a,*] Guang-Ju Chen[b,*] and Yi-Hua Yu[c,*]

[a]*State Key Laboratory of Bio-Organic & Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China*
[b]*Department of Chemistry, Beijing Normal University, Beijing 100875, China*
[c]*School of Science and Engineering, East China Normal University, Shanghai 200062, China*

Received 16 May 2005; revised 22 July 2005; accepted 22 July 2005

Available online 10 August 2005

Abstract—This paper describes the self-assembly of a new series of heterotrimers in chloroform-*d* by utilizing the cooperative interaction of hydrogen bonding and donor–acceptor interaction. Compounds **1** and **11**, in which an 2-ureido-4[1*H*]-pyrimidinone unit is connected to 34-crown-10 or 36-crown-10, were used as donor monomer, and **2** and **19**, in which an 2-ureido-4[1*H*]-pyrimidinone unit is connected to NDI, were used as acceptor monomer, while linear compound **4**, which contains two diamido-1,8-naphthyridines, was used as template. A large tri-*p*-(*t*-butyl)phenylmethoxyl group was introduced to **19** in order to compare its assembling behavior with that of **2**. Mixing **4** with dimer **1**·**2** caused **1**·**2** to fully decompose and to afford 55% of 'in–in'-oriented heterotrimer **1**·**4**·**2**. Adding **4** to the solution of **2**·**11** or **11**·**19** in chloroform-*d* also led to full dissociation of the dimers. However, in these systems the 'in–in'-arranged heterotrimer **2**·**4**·**11** or **11**·**4**·**19** could be produced exclusively.
© 2005 Elsevier Ltd. All rights reserved.

1. Introduction

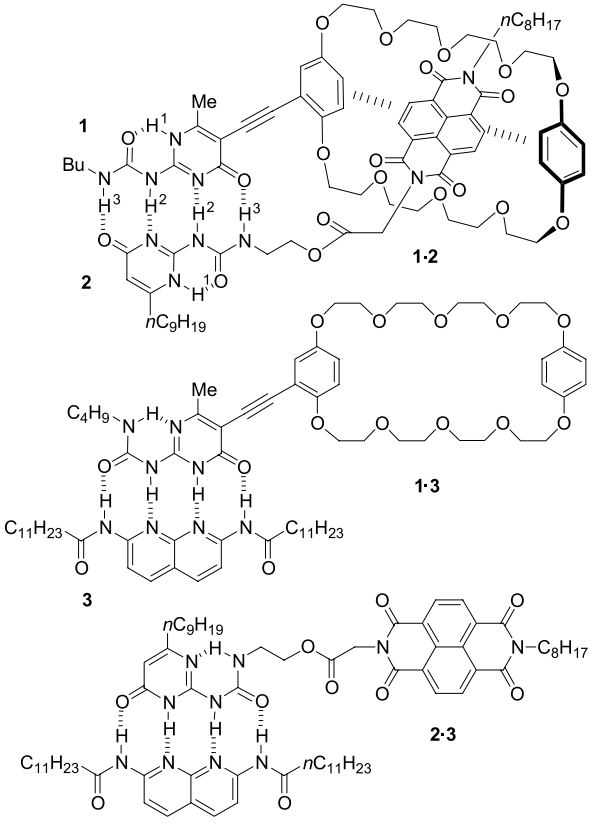
Cooperative interaction of different non-covalent forces play a critical role in the formation of biological structures and functions.[1] For example, the DNA double helixes are stabilized mainly by intermolecular hydrogen bonds between the complementary bases and stacking interactions between adjacent base pairs, whereas the secondary and tertiary structures of proteins are generated as a result of the cooperative behavior of specifically located hydrogen bonds, hydrophobic interaction, and Van der Waals force. One of the challenges in supramoleulcar chemistry is the construction of new molecular assemblies with defined structures or functions in a strong, selective, and directional way.[2] In the past decade, a large number of artificial supramolecular architecture have been constructed based on single non-covalent force including transition metal–ligand interaction,[3] hydrophobic interaction,[4] hydrogen bonding,[5] and electrostatic interaction.[6] In principle, the combination of two or more different non-covalent interactions may also function well or even more efficiently in constructing new supramolecular species. Nevertheless, only recently have examples of supramolecular assemblies of this kind been reported.[7]

Due to their remarkable stability and directionality, the self-complimentary 2-ureido-4[1*H*]-pyrimidinone-based quadruply hydrogen bonded AADD (A, hydrogen bonding acceptor; D, hydrogen bonding donor) homodimers have recently found extensive applications in self-assembly of discrete supramolecular systems.[8–10] Previously, we had reported that AADD-featured homodimers of **1** and **2** could dissociate to generate more stable quadruply hydrogen bonded heterodimer **1**·**2**,[11,12] as a result of the additional intermolecular donor–acceptor interaction between the electron-rich bis(*p*-phenylene)-34-crown-10 moiety of **1** and the electron-deficient naphthalene diimide (NDI) of **2**.[13] Moreover, the addition of **3** to the solution of **1**·**2** in chloroform-*d* led to the formation of heterodimers **1**·**3** and **2**·**3**, both of which possess a new ADDA–DAAD binding motif.[11a] The formation of the hydrogen bonded heterodimers from hydrogen bonded homodimers driven by additional donor–acceptor interaction represents a new and useful assembling strategy. In this paper we report that linear compounds incorporating two diamido-1,8-naphthyridine moieties have been successfully utilized to

Keywords: Hydrogen bonding; Donor–acceptor interaction; Self-assembly; Heterocycle; Supramolecular chemistry.
* Corresponding authors. Tel.: +86 21 5492 5122; fax: +86 21 6416 6128; e-mail addresses: ztli@mail.sioc.ac.cn; gjchen@bnu.educ.cn; yhyu@phy.ecnu.edu.cn

0040–4020/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2005.07.075

template the selective self-assembly of a new series of hydrogen bonded heterotrimers whose structures are regulated by additional donor–acceptor interaction.[14]



2. Results and discussion

Previous investigation has revealed that ADDA–DAAD-typed heterodimers such as **1**·**3** and **2**·**3** are remarkably more stable than the corresponding AADD–DDAA homodimers.[11a] In principle, linear molecules (A, Fig. 1) incorporating two 2,7-diamido-1,8-naphthyridine moieties connected by a flexible linker of proper length might also induce the dissociation of heterodimers of monomers B and C to generate a new generation of heterotrimers (Fig. 1). To explore this possibility, compound **4** was prepared. The four *n*-octyl groups were expected to provide solubility in common organic solvents. Molecular modeling for a system of **1**, **2**, and **4** revealed that the length of the linker between the two binding moieties of **4** is suitable for the formation of a potential heterotrimer **1**·**4**·**2**.

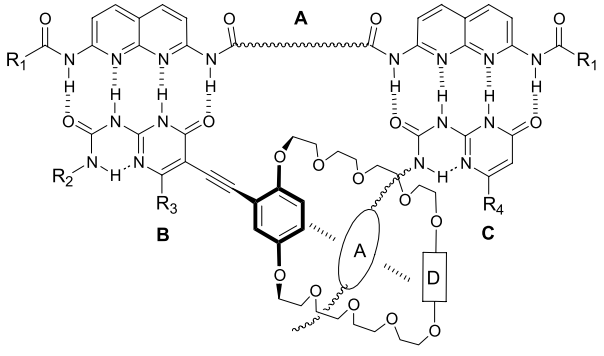
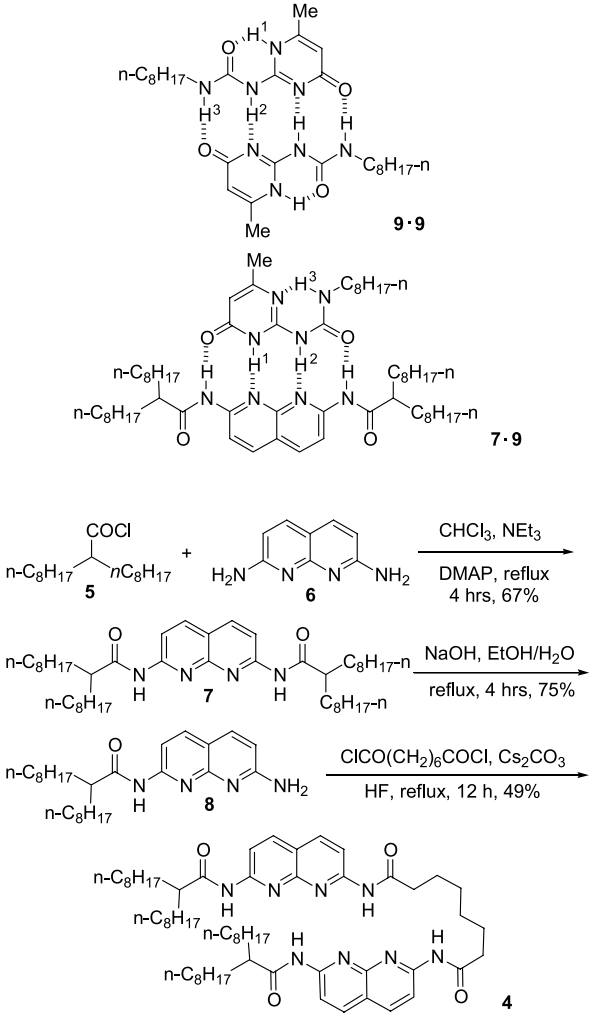


Figure 1. The underlying assembling strategy for the new generation of heterotrimers driven by cooperative hydrogen bonding and donor–acceptor interactions.

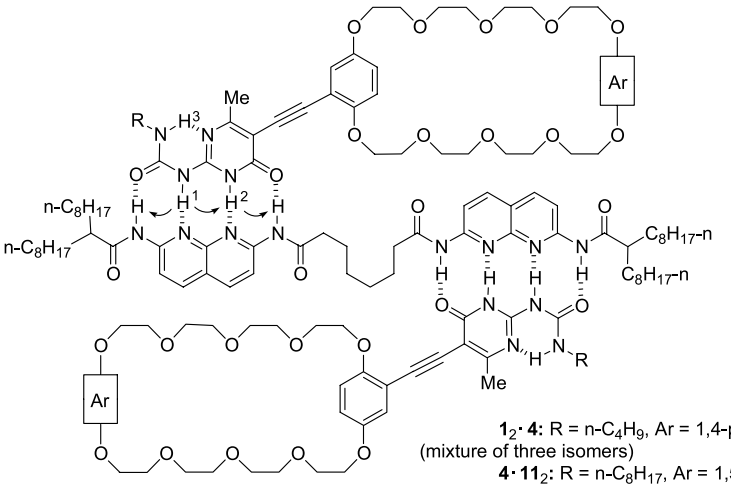
The synthetic route for **4** is shown in Scheme 1. Thus, diamide **7** was first produced from the reaction of **5** and **6** and then hydrolyzed with sodium hydroxide to yield **8**.[15] Subsequent treatment of **8** with suberoyl chloride in refluxed THF produced **4**, which is of good solubility in organic solvents such as chloroform and dichloromethane.



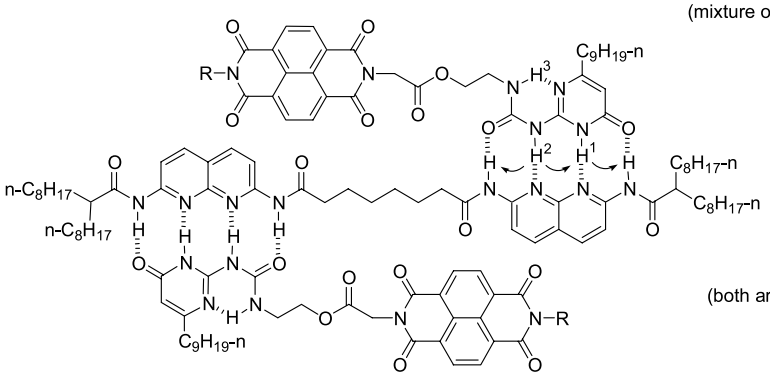
Scheme 1.

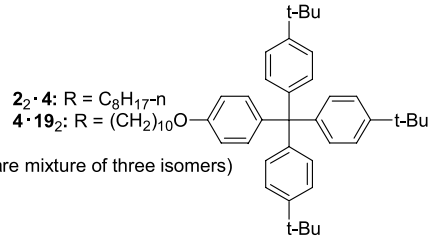
Prior to binding studies with **4**, the ability of **7** to induce the dissociation of homodimer **9**·**9** in chloroform-*d* were investigated by ^{1}H NMR spectroscopy.[16,17] Adding 1 equiv of **7** to the solution of **9** in chloroform-*d* induced the homodimer of the latter to fully dissociate and to afford heterodimer **7**·**9** exclusively (Fig. 2). The structure of **7**·**9** has been characterized by using the methods for the characterization of other similar heterodimers.[11a]

The binding behaviors of **4** with homodimers **1**·**1** and **2**·**2** were then investigated. As revealed by Figure 3b and d, adding 1 equiv of **4** to the solution of **1** or **2** in $CDCl_3$ also led to complete dissociation of the latter's homodimer due to the formation of new heterotrimers $\mathbf{1}_2$·**4** and $\mathbf{2}_2$·**4**, respectively. In principle, the two molecules of **1** or **2** in the

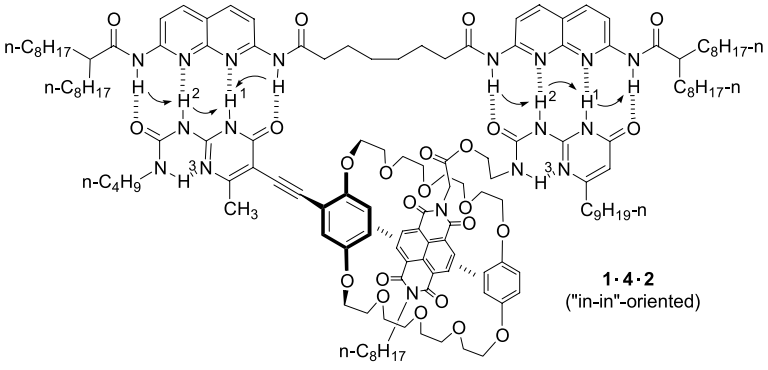


$1_2 \cdot 4$: R = n-C_4H_9, Ar = 1,4-phenylene
(mixture of three isomers)
$4 \cdot 11_2$: R = n-C_8H_{17}, Ar = 1,5-naphthylene
(mixture of three isomers)

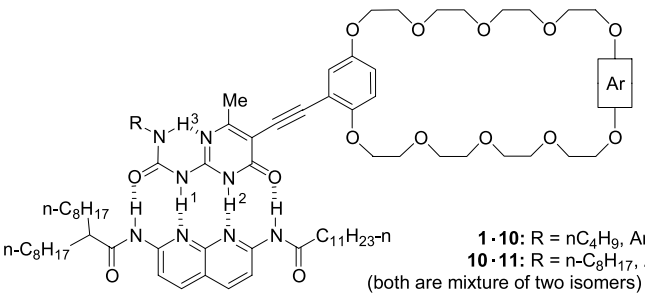




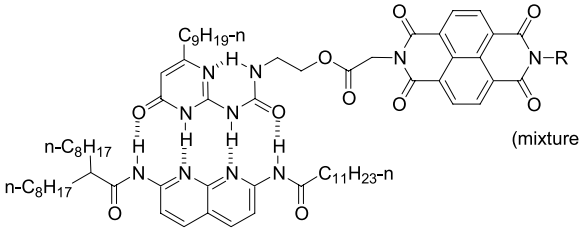
$2_2 \cdot 4$: R = C_8H_{17}-n
$4 \cdot 19_2$: R = $(CH_2)_{10}O$
(both are mixture of three isomers)



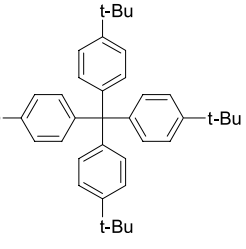
1·4·2
("in-in"-oriented)



1·10: R = nC_4H_9, Ar = 1,4-phenylene
10·11: R = n-C_8H_{17}, Ar = 1,5-naphthylene
(both are mixture of two isomers)



2·10: R = n-C_8H_{17}
10·19: R = $(CH_2)_{10}O$
(mixture of two isomers)



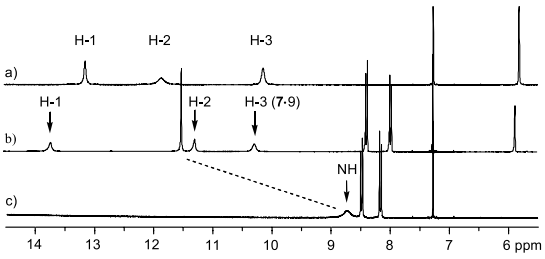


Figure 2. Partial ^{1}H NMR spectra (400 MHz, 5.0 mM) in $CDCl_3$ at 25 °C: (a) **9**; (b) **7**+**9** (1:1); (c) **7**. For signal numbering, see the structures in the text.

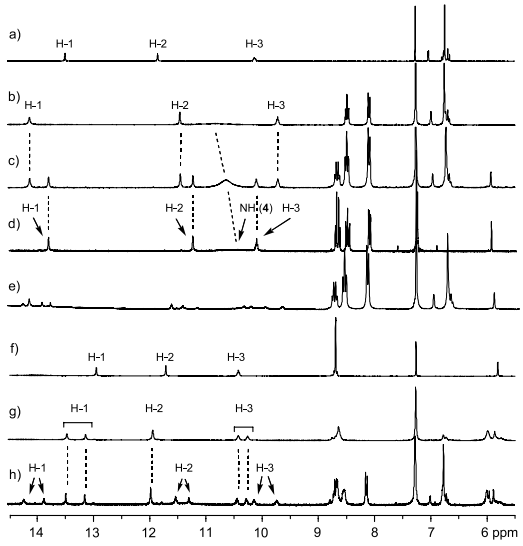
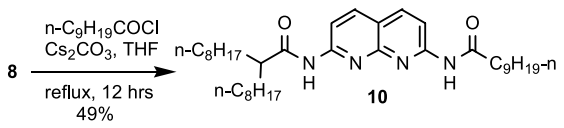


Figure 3. Partial ^{1}H NMR (400 MHz) spectra in $CDCl_3$ at 25 °C: (a) **1** (6.0 mM); (b) $\mathbf{1}_2\cdot\mathbf{4}$ ([**4**]=3.0 mM); (c) **1**·**2**·**4** ([**4**]=6.0 mM); (d) $\mathbf{2}_2\cdot\mathbf{4}$ ([**4**]=3.0 mM); (e) **1**·**2**·**4** ([**4**]=6.0 mM) at −20 °C; (f) **2**; (g) **1**·**2**; (h) **1**+**2**+**10** (12 mM) ([**1**]=[**2**]=6.0 mM).

trimers should have three possible arranging patterns, that is, the 'in–in', 'in–out', and 'out–out'-orientations for the cyclophane unit of **1** or the NDI unit of **2** relative to **4**. The fact that only one set of new signals were displayed in both systems implies that the exchange of the monomers among the possible trimeric isomers was fast on the NMR time scale. Intermolecular NOE effect was observed for both trimers. The facts that **1**·**1** and **2**·**2** were not formed in the mixture solution also implied that trimers $\mathbf{1}_2\cdot\mathbf{4}$ and $\mathbf{2}_2\cdot\mathbf{4}$ were formed quantitatively.

When 1 equiv of **4** was added to 1 equiv of the 1:1 solution of **1** and **2** in chloroform-*d*, the highly stable heterodimer **1**·**2** was also fully decomposed (Fig. 3c and g). The ^{1}H NMR spectrum revealed two sets of NH signals at 14.11, 11.44, 9.71 ppm and 13.78, 11.21, 10.09 ppm, respectively, which could be easily assigned to those of the binding moiety that exists in $\mathbf{1}_2\cdot\mathbf{4}$ or $\mathbf{2}_2\cdot\mathbf{4}$ by comparing Figure 3c with Figure 3b and d and also by adding $\mathbf{1}_2\cdot\mathbf{4}$ or $\mathbf{2}_2\cdot\mathbf{4}$ to the solution, which caused the corresponding signals to increase. NOESY experiment revealed intermolecular connections (see the structures of the trimers), which is also consistent with the DAAD–ADDA motif of the trimers. The identical result was obtained when 1 equiv of the 2:1 solution of **1** and **4** to 1 equiv of the 2:1 solution of **2** and **4** in chloroform-*d*. UV–vis experiment afforded an apparent ε value of 320 $cm^{-1}\,M^{-1}$ (λ_{max}=470 nm) for the charge-transfer absorbance band of the new mixture solution. Because the ^{1}H NMR spectrum had revealed that there was no important amount of **1**·**2** in the solution, this charge-transfer absorbance band was obviously produced by the 'in–in'-oriented heterotrimer **1**·**4**·**2**, which, together with other isomeric trimers, contributed to the two sets of signals in Figure 3c. Similar to the above structurally similar heterotrimers, trimer **1**·**4**·**2** should also be mixtures of four possible isomers, depending on the orientation of **1** and **2** relative to **4**. Reducing the solution temperature to −20 °C led to the NH signals to split (Fig. 3e). Although these signals could not be definitely assigned to either of the heterotrimers, this observation revealed that, besides the 'in–in'-oriented **1**·**4**·**2**, other isomeric heterotrimers might also exist in the solution and at the lowered temperature, the exchange of the monomers among the different trimers became slow on the ^{1}H NMR time scale.

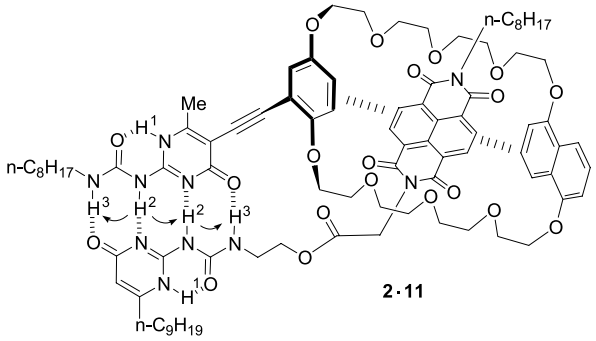
Because the above ^{1}H NMR and UV–vis results could not be utilized to determine the percentage of the 'in–in'-oriented heterotrimer **1**·**4**·**2**, compound **10** was prepared from **8** and docanoyl chloride in refluxed THF (Scheme 2). Adding 2 equiv of **10** to the solution of **1**·**2** in chloroform-*d* induced the heterodimer to partially dissociate as a result of the formation of heterodimers **1**·**10** and **2**·**10**, which gave rise to two sets of new signals at 14.21, 11.51, 9.72 and 13.85, 11.28, 10.12 ppm, respectively, in the ^{1}H NMR spectrum. Although only one set of signals was displayed for each of them, in principle both **1**·**10** and **2**·**10** should also be mixtures of two isomeric dimers. Figure 3h shows the partial ^{1}H NMR spectrum of the 1:1:2 solution of **1**, **2**, and **10** in chloroform-*d*. Based on the relative integrated intensity of the H-1 signals of **1**·**10** and **2**·**10**, we determined the yields of both **1**·**10** and **2**·**10** to be approximately 44%, which implied approximately 44% dissociation of **1**·**2** in the tri-component solution. Because the linker between the two heterocyclic moieties of **4** is not short, it should be acceptable to assume that the DAAD–ADDA motifs of dimers **1**·**10** and **2**·**10** and all possible trimers $\mathbf{1}_2\cdot\mathbf{4}$, $\mathbf{2}_2\cdot\mathbf{4}$, and **1**·**4**·**2** should possess comparable stability when the donor–acceptor interaction in the 'in–in'-oriented **1**·**4**·**2** was not considered. Quantitative dissociation of **1**·**2** in the 1:1:1 solution of **1**, **2**, and **4** in chloroform-*d* suggested that at least 56% of 'in–in'-oriented **1**·**4**·**2** was formed as a result of the additional donor–acceptor interaction between the electron-rich cyclophane unit of **1** and the electron-deficient NDI unit of **2**.[18]



Scheme 2.

It is well-established that 1,5-dialkoxynaphthalene (DAON) is a stronger electron donor than 1,4-dialkoxybenzene for supramolecular self-assembly.[13,19] Therefore, it was envisioned that replacement of the 1,4-dialkoxybenzene unit of **1** with the DAON unit would produce a compound

with a stronger electron-donating ability than **1**. Such a compound might lead to more selective formation of more stable heterotrimers similar to **1**·**4**·**2**. Therefore, compound **11** was synthesized as outline in Scheme 3. In brief, **12** was first reacted with **13** in refluxed acetonitrile to produce cyclophane **14**. The Heck reaction of **14** with **15** in hot pyrrolidine yielded **16**, which was then de-protected with sodium hydroxide to afford **17**. Finally, a palladium(II)-catalyzed reaction of **17** with **18** in THF yielded **11** in 31% yield.

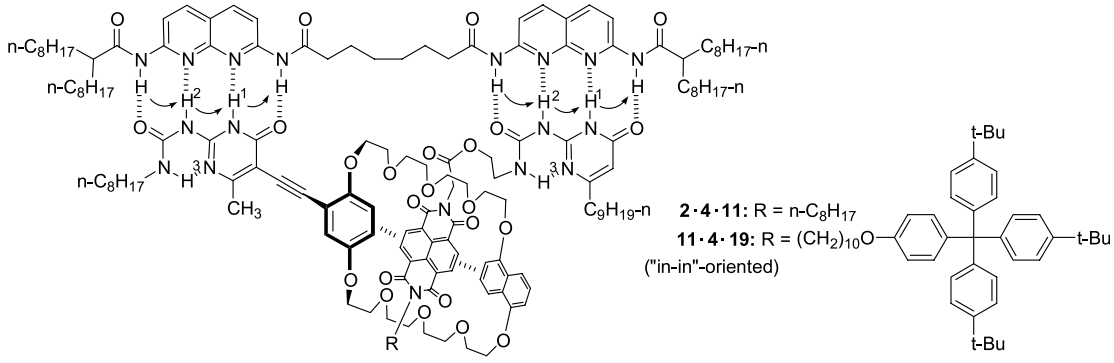


As expected, mixing 1 equiv of **11** with 1 equiv of **2** in chloroform-*d* caused complete dissociation of homodimers **11**·**11** and **2**·**2** and led to the formation of heterodimer **2**·**11** exclusively (Fig. 4d–f). The structure of heterodimer **2**·**11** had been determined by using the methods reported previously for dimer **1**·**2**.[11a] The solution turned to dark orange as a result of the strong intermolecular donor–acceptor interaction between the cyclophane unit of **11** and the NDI unit of **2**. UV–vis experiment afforded a ε value of 1020 M^{-1} cm^{-1} (λ_{max}=488 nm) for the charge-transfer absorbance band of dimer **2**·**11**. This value is substantially larger than that of dimer **1**·**2** (429 M^{-1} cm^{-1}, λ_{max}=475 nm),[11a] indicative of the higher stability of **2**·**11** compared to **1**·**2**. ^{1}H NMR dilution experiments in $CDCl_3$–DMSO-d_6 (4%) derived a binding constant of ca. 2.1×10^5 M^{-1} for dimer **2**·**11**.[11a] The value is significantly larger than that of dimer **1**·**2** (3.7×10^4 M^{-1}),[11a] which is consistent with the above UV–vis result.

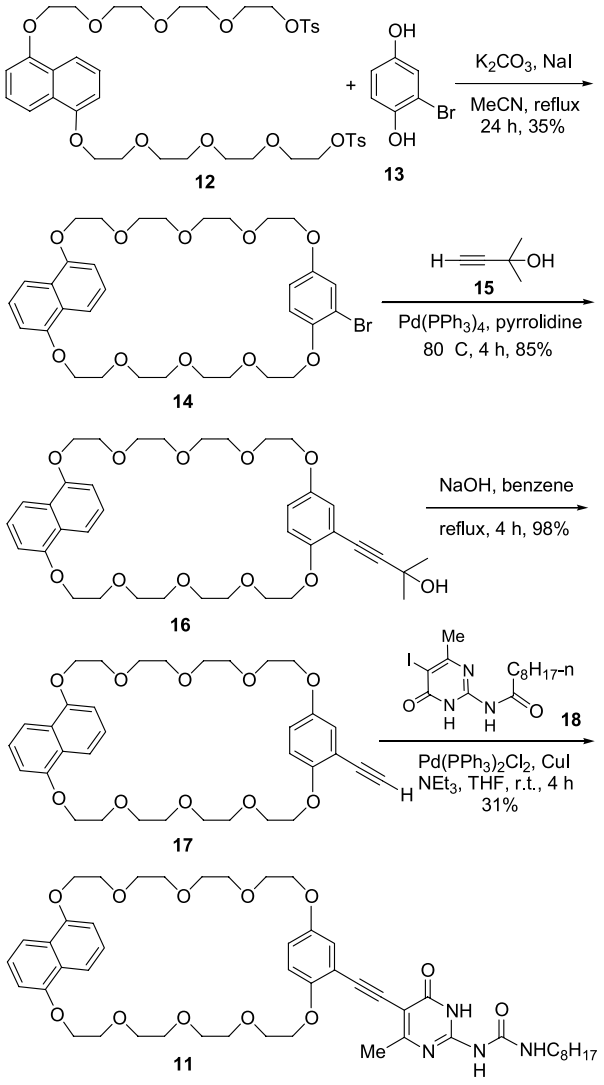
The addition of 1 equiv of **4** to the solution of heterodimer **2**·**11** in chloroform-*d* led to the signals of the heterodimer to disappear in the ^{1}H NMR spectrum (Fig. 4c). Similar to the system of **1**, **2**, and **4** (Fig. 3), two new sets of NH signals were also displayed at 14.13, 11.46, 9.70 ppm and 13.82, 11.26, 10.10 ppm, respectively. These signals were assigned to those of the two binding moieties in heterotrimers **2**·**4**·**11**, $\mathbf{2}_2$·**4**, and $\mathbf{11}_2$·**4** by using the methods described above for other tri-component systems. The orange color of the solution did not change substantially after **11** was added, and UV–vis experiment gave an apparent ε value of 850 M^{-1} cm^{-1} (λ_{max}=487 nm) for the charge-transfer absorbance band. Since the ^{1}H NMR study revealed that there was no detectable amount of dimer **2**·**11** in the tri-component solution, this absorbance band should be produced exclusively by the 'in–in'-arranged heterotrimer **2**·**4**·**11**.

Adding 2 equiv of **10** to 1 equiv of the solution of heterodimer **2**·**11** in chloroform-*d* induced the dimer to partially decompose as a result of the formation of heterodimers **2**·**10** and **10**·**11** (vide supra) (Fig. 4a and d). Based on the integrated intensity of the H-1 signals of the dimers, we determined the yields of dimers **2**·**10** and **10**·**11** to be approximately 12%. If the additional donor–acceptor interaction in the 'in–in'-arranged trimer **2**·**4**·**11** were not considered, it should be reasonable to assume that the ADDA–DAAD binding motif in dimers **2**·**10** and **10**·**11** and all possible trimers **2**·**4**·**11**, $\mathbf{2}_2$·**4**, and $\mathbf{11}_2$·**4** should be comparable. The above ^{1}H NMR result suggested that at least 88% of 'in–in'-oriented trimer **2**·**4**·**11** was formed in the 1:1:1 solution of **2**, **4**, and **11** in $CDCl_3$ due to the additional intermolecular donor–acceptor interaction between **2** and **11**.

Different from the observation that the NH protons split at lowered temperature (−20 °C) (Fig. 3e), reducing the temperature to −25 °C did not lead to the ^{1}H NMR signals of the 1:1:1 mixture solution of compounds **2**, **4**, and **11** to split in chloroform-*d*. Because compounds **1** and **11** possess the same binding unit, heterotrimers of the same skeleton generated from them with **2** and **4** should have very close stability except the 'in–in'-oriented heterotrimers **1**·**4**·**2** and **2**·**4**·**11**, in which the additional donor–acceptor interaction existed. Therefore, the above observation suggested that the 'in–in'-oriented heterotrimer **2**·**4**·**11** was actually formed exclusively at least at the low temperature of −20 °C (≥97% considering the sensitivity of the ^{1}H NMR method).



Further evidence to support the selective formation of the 'in–in'-oriented heterotrimer **2**·**4**·**11** came from the ^{1}H NMR and UV–vis studies of the system of **4**, **11**, and **19**. A large tri-*p*-(*t*-butyl)phenylmethoxyl group was introduced in **19** in order to reduce the exchanging rate between the threaded pseudorotaxane-styled trimeric isomer and all other possible isomers, because such a large group could not



Scheme 3.

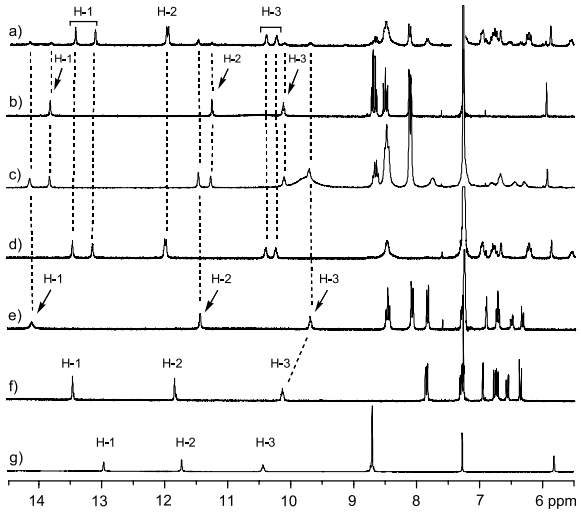
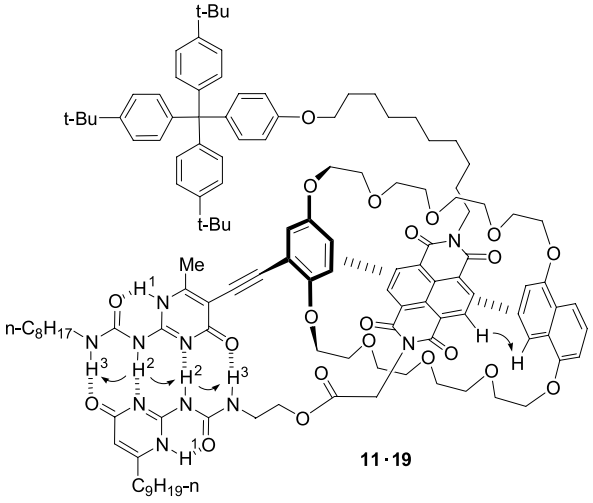


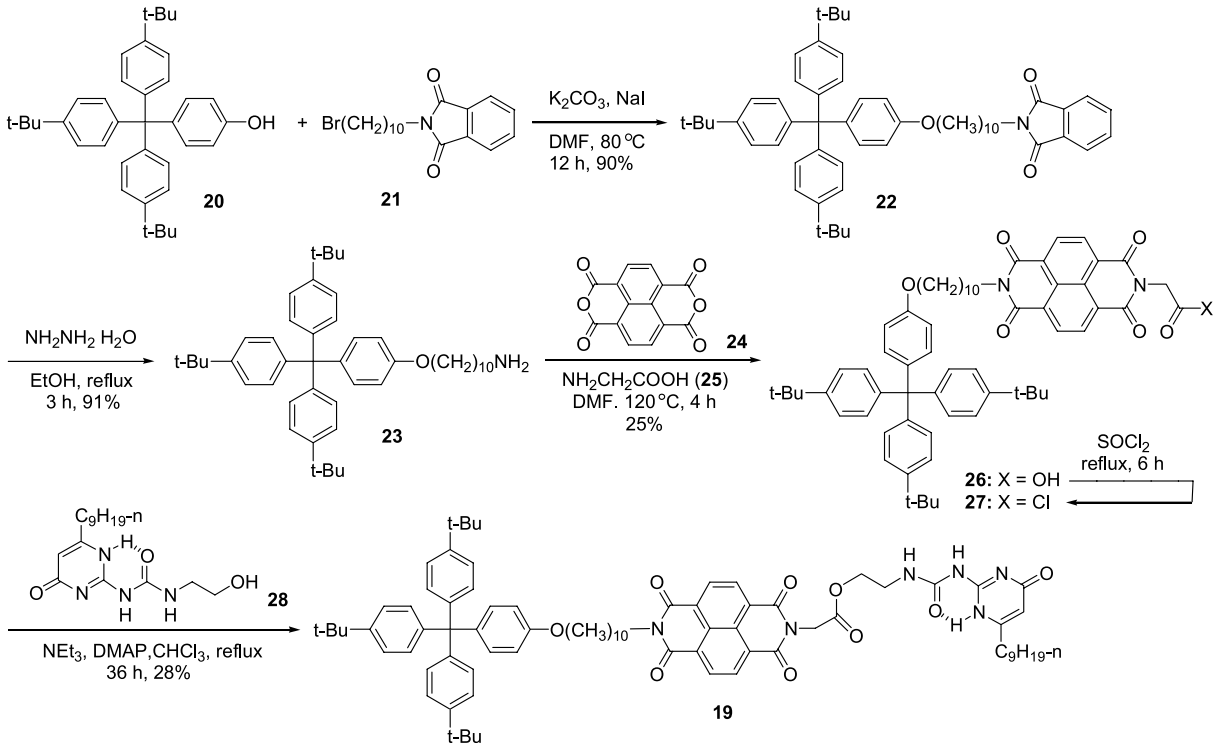
Figure 4. Partial ^{1}H NMR (400 MHz, 4.0 mM) spectra in $CDCl_3$ at 25 °C: (a) **2**+**11**+**10** (1:1:2); (b) **2**+**4** (2:1, [**4**]=2.0 mM); (c) **2**+**4**+**11** (1:1:1); (d) **2**+**11** (1:1); (e) **4**+**11** (1:2, [**4**]=2.0 mM); (f) **11**; (g) **2**.

be de-threaded from the cavity of the cyclophane of **11**.[20] The synthesis of **19** is shown in Scheme 4. In brief, **22** was first prepared from the reaction of **20** and **21** in hot DMF and then hydrolyzed with hydrazine to produce **23**. Treatment of **23** with **24** and **25** in hot DMF yielded **26**, which was then converted into **27** in refluxed thionyl chloride. Finally, compound **27** was reacted with **28** in hot chloroform to afford **19** in 28% yield.

As expected, heterotrimer $\mathbf{4}\cdot\mathbf{19}_2$ (vide supra) was generated exclusively when adding 1 equiv of **14** to 2 equiv of **19** in chloroform-*d* (Fig. 5a and b), and heterodimer **11**·**19** was also formed quantitatively in the 1:1 mixture solution of **11** and **19** in chloroform-*d*. The structure of dimmer **11**·**19** was supported by the NOESY spectrum, which revealed intermolecular NOEs between the NH signals as shown in the structure. Different from that of dimer **2**·**11**, which revealed a single signals at 8.40 ppm for the four protons of the NDI unit (Fig. 4d), the ^{1}H NMR spectrum of **11**·**19** revealed two sets of doublets (8.56, 8.50, 8.43, and 8.34 ppm) for the NDI protons as a result of the increased shielding effect of the cyclophane unit of **11** (Fig. 5d). Moreover, lowering the solution temperature to −35 °C did not cause the NH signals of the dimer to split. By using the ^{1}H NMR dilution method, we determined the K_a of **11**·**19** in chloroform-*d* and DMSO-d_6 (4%) to be ca. 2.2×10^5 M^{-1}, which is very close to that of dimer **2**·**11** in the same solvent. The solution of dimer **11**·**19** in chloroform-*d* displayed a dark orange color as a result of the strong intermolecular donor–acceptor interaction and UV–vis study afforded an apparent ε value of 880 M^{-1} cm^{-1}. This value was independent of concentration (0.5–50 mM) and also comparable to that of dimer **2**·**11**. All these observations indicated that the NDI moiety of **19** was completely threaded through the cavity of the cyclophane of **11** and **11**·**19** existed as a stable pseudo[2]rotaxane.



Adding 2 equiv of **10** to the solution of dimer **11**·**19** in chloroform-*d* caused approximately 15% of the dimer to dissociate and to afford new heterodimers **10**·**11** and **10**·**19** (vide supra) as indicated by the ^{1}H NMR spectrum (Fig. 5f). In contrast, addition of a small excess of **4** to a solution of dimer **11**·**19** in chloroform-*d* caused the NH signals of the dimer to disappear, and two sets of NH signals at 14.15, 11.46, 9.70 ppm and 13.82, 11.25, 10.11 ppm, respectively,



Scheme 4.

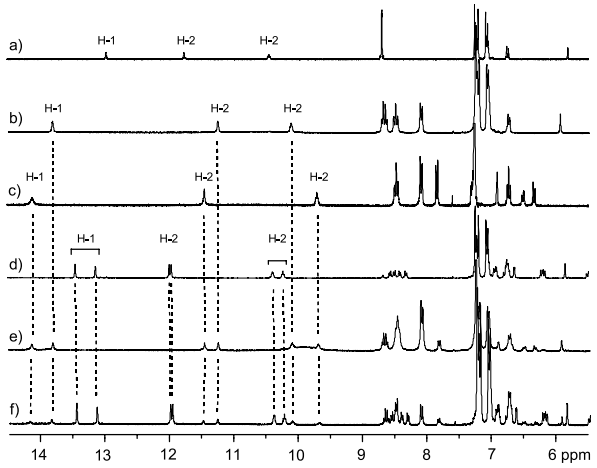


Figure 5. Partial ^{1}H NMR (400 MHz) spectra in $CDCl_3$ at 25 °C: (a) **19** (4.0 mM); (b) **4**+**19** (1:2, [**4**]=2.0 mM); (c) **4**+**11** (1:2 [**11**]=4.0 mM); (d) **11**+**19** (1:1, 4.0 mM); (e) **4**+**11**+**19** (1:1:1, 4.0 mM); (f) **10**+**11**+**19** (1:1:2, [**10**]=4.0 mM).

were displayed. The result is very similar to that observed for the system of **2**, **4**, and **11**, indicating the formation of new heterotrimers **11**·**4**·**19** (vide supra). The ^{1}H NMR spectrum did not exhibit new signals at the low temperature of −25 °C. In principle, the existence of the large tri-*p*-(*t*-butyl)phenylmethoxyl group in **19** would greatly slow down the exchanging processes between the 'in–in'-oriented heterotrimer **11**·**4**·**19** and any other possible trimers.[20] The above results clearly showed that there were no important amount of other kinds of heterotrimers in the tri-component solution, because such possible exchange processes, if existing, would be revealed by the NH signal splitting at the temperature of ≥ −20 °C, as observed above for the solution of compounds **1**, **2**, and **4** in chloroform-*d*.

Different from those of dimers **2**·**11** and **11**·**19**, the NOESY spectrum of the 1:1:1 solution of **2**, **4**, and **11** or **4**, **11**, and **19** in chloroform-*d* did not reveal any intermolecular NOEs between the NH signals of the 2-ureido-4-pyrimidinone units. This observation is also consistent with the formation of heterotrimers **2**·**4**·**11** and **11**·**4**·**19** in the solution. In addition, vapor pressure osmometry (VPO) in chloroform–toluene (85:15 v:v) at 30 °C gave average molecular masses of 2400 (±300 u) and 2800 (±400 u) for the two systems, which was also in agreement with the formation of the two heterotrimers, whose calculated masses are 2620 and 3150, respectively. A energy-minimized structure of heterotrimer **2**·**4**·**11** has been obtained and is shown in Figure 6, which reveals a triangle skeleton for the trimer due to the intermolecular hydrogen bonding and donor–acceptor interactions.

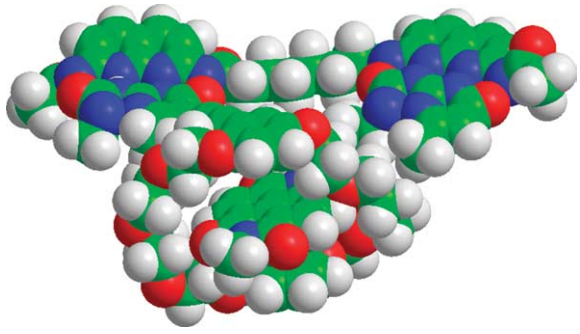


Figure 6. Energy-minimized structures of dimers **2**·**4**·**11**. All the side chains of the monomers are replaced with methyl groups for clarity.

3. Conclusion

We have reported the self-assembly of a new class of heterotrimers in chloroform by making use of both the quadruply hydrogen bonding and the donor–acceptor interaction as the driving forces. The effect of the structure of the monomers on the self-assembling selectivity of the new series of heterotrimers has been investigated. Strong ADDA–DAAD quadruply hydrogen bonding has been used to 'glue' three discrete components together, whereas additional intermolecular donor–acceptor interaction makes the components arrange in order. As a result, among other nine possible heterotrimers, one special heterotrimer has been selectively assembled from elaborately designed monomer molecules. The results demonstrate the great potential of the cooperative interaction between different co-valent forces for assembling new kind of supramolecular architectures.

4. Experimental

4.1. General procedure. See Ref. 11a

4.1.1. Compound 7. To a suspension of **6** (0.72 g, 4.50 mmol), NEt_3 (2.00 mL) and DMAP (50 mg) in chloroform (300 mL) was added a solution of **5**[21] (2.95 g, 9.90 mmol) in chloroform (25 mL). The mixture was stirred under reflux for 4 h and then cooled. The insoluble materials were filtered off and the filtrate was washed with dilute hydrochloric acid, saturated $NaHCO_3$ solution, water, brine, and dried over sodium sulfate. After the solvent was removed, the crude product was purified by column chromatography (hexane/dichloromethane 5:1–1:2) to afford compound **7** as a yellowish oil (2.10 g, 67%). ^{1}H NMR ($CDCl_3$): δ 0.82–0.86 (m, 12H), 1.23–1.28 (m, 48H), 1.46–1.55 (m, 4H), 1.64–1.74 (m, 4H), 2.29–2.35 (m, 2H), 8.13 (d, J=9.0 Hz, 2H), 8.48 (d, J=8.7 Hz, 2H), 8.70 (s, 4H). MALDI-HRMS: m/z: 693.6020 [M^++H]. Calcd for $C_{44}H_{76}N_4O_2$: 693.6041.

4.1.2. Compound 8. A solution of **7** (1.25 g, 1.80 mmol) and NaOH (0.30 g) in ethanol (20 mL) and water (4 mL) was heated under reflux for 4 h and then concentrated in vacuo. The residue was triturated with dichloromethane (250 mL). The organic phase was washed with water, brine, and dried over magnesium sulfate. After the solvent was removed, the crude product was purified by column chromatography (CH_2Cl_2/MeOH 20:1) to obtain **8** as a white solid (0.57 g, 75%). Mp 197–198 °C. ^{1}H NMR ($CDCl_3$): δ 0.82–0.89 (m, 6H), 1.28–1.39 (m, 24H), 1.43–1.56 (m, 2H), 1.64–1.73 (m, 2H), 2.26–2.32 (m, 1H), 5.45 (s, 2H), 6.66 (d, J=8.4 Hz, 1H), 7.81 (d, J=8.7 Hz, 1H), 7.94 (d, J=9.0 Hz, 1H), 8.27 (d, J=9.0 Hz, 1H), 8.57 (s, 1H). MALDI-MS: m/z: 427 [M+H]$^+$. Elemental Anal. Calcd (%) for $C_{26}H_{42}N_4O$ (426.64): C, 73.20; H, 9.92; N, 13.13. Found: C, 73.30; H, 9.97; N, 13.04.

4.1.3. Compound 4. To a stirred suspension of **8** (0.43 g, 1.00 mmol) and Cs_2CO_3 (0.50 g, 1.56 mmol) in THF (40 mL) was added a solution of suberoyl chloride (91 mg, 0.45 mmol) in THF (5 mL). The mixture was refluxed for 12 h and then concentrated. Chloroform (300 mL) was added and the insoluble solid was filtered off. The filtrate was washed with water, brine, and dried. After the solvent was removed in vacuo, the crude product was chromatographed (CH_2Cl_2/MeOH 50:1) to give **4** as a yellow solid (0.22 g, 49%). Mp 156–158 °C. ^{1}H NMR ($CDCl_3$): δ 0.84 (t, J=6.9 Hz, 12H), 1.22–1.54 (m, 52H), 1.63–1.75 (m, 12H), 2.27–2.30 (m, 2H), 2.46 (t, J=7.2 Hz, 4H), 8.11 (d, J=9.0 Hz, 4H), 8.44 (t, J=8.4 Hz, 4H), 8.65 (s, 4H). ^{13}C NMR ($CDCl_3$): δ 14.1, 22.7, 24.7, 27.6, 28.6, 29.3, 29.5, 29.7, 31.8, 33.0, 37.6, 49.3, 113.7, 118.3, 139.0, 139.1, 154.0, 154.0, 172.8, 175.8. IR (cm^{-1}): ν 3421, 3307, 2926, 2855, 1708, 1689, 1610, 1388, 1286, 1136, 855, 803. MALDI-HRMS: m/z: 991.7435, [M+H]$^+$. Calcd for $C_{60}H_{94}N_8O_4$: 991.7471.

4.1.4. Compound 9. This compound was prepared from 2-amino-4-hydroxy-6-methylpyrimidine and *n*-octyl isocyanate (97%) as a white solid following the reported procedure for preparation of a similar compound.[8] Mp 171–173 °C. ^{1}H NMR: δ 0.86 (t, J=6.6 Hz, 3H), 1.25–1.30 (m, 10H), 1.54–1.61 (m, 2H), 2.22 (s, 3H), 3.20–3.26 (m, 2H), 5.81 (s, 1H), 10.13 (s, 1H, NH), 11.85 (s, 1H, NH), 13.14 (s, 1H, NH). MS (EI): m/z: 280 [M^+]. Elemental Anal. Calcd (%) for $C_{14}H_{24}N_4O_2$ (280.37): C, 59.98; H, 8.63; N, 19.98. Found: C, 59.84; H, 8.60; N, 19.97.

4.1.5. Compound 10. To a stirred solution of **8** (0.30 g, 0.70 mmol), NEt_3 (1 mL), and DMAP (50 mg) in $CHCl_3$ (20 mL) was added a solution of docanoyl chloride (0.22 g, 1.0 mmol) in $CHCl_3$ (5 mL). The solution was then stirred under reflux for 14 h. After work-up, the crude product was subjected to flash chromatography (CH_2Cl_2) to give **10** as a white solid (0.30 g, 73.5%). Mp 133–134 °C. ^{1}H NMR ($CDCl_3$): δ 0.83–0.89 (m, 9H), 1.23–1.26 (m, 36H), 1.47–1.56 (m, 2H), 1.64–1.80 (m, 4H), 2.25–2.29 (m, 1H), 2.46 (t, J=7.5 Hz, 2H), 8.12–8.15 (m, 4H), 8.45 (t, J=6.3 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 14.1, 22.7, 25.3, 27.6, 29.2, 29.3, 29.3, 29.4, 29.7, 31.9, 31.8, 33.1, 38.0, 49.4, 113.5, 113.6, 118.4, 139.0, 153.9, 154.0, 172.5, 175.6. IR (cm^{-1}): ν 3310, 2925, 2854, 1689, 1610, 1506, 1288, 1136, 854, 802. MALDI-MS: m/z: 581 [M+H]$^+$. Elemental Anal. Calcd (%) for $C_{36}H_{60}N_4O_2$ (580.89): C, 74.44; H, 10.41; N, 9.64. Found: C, 74.66; H, 10.51; N, 9.62.

4.1.6. Compound 14. To a stirred suspension of **12**[13a] (7.30 g, 11.4 mmol), K_2CO_3 (13.0 g, 94.2 mmol) and NaI (2.00 g, 13.3 mmol) in MeCN (200 mL) was added a solution of **13**[22] (2.15 g, 11.4 mmol) in MeCN (20 mL). The reaction mixture was then heated at 80 °C for 24 h and cooled. The solid was filtered off and washed with AcOEt. The combined filtrate was concentrated in vacuo and the resulting residue triturated with AcOEt (200 mL). The organic phase was washed with water, brine, and dried. Upon removal of the solvent, the oily residue was purified by column chromatography (EtOAc/CH_3OH 50:1) to afford **14** as a yellow solid (2.66 g, 35%). Mp 98–100 °C. ^{1}H NMR ($CDCl_3$): δ 3.65–3.86 (m, 24H), 3.98–4.01 (m, 4H), 4.20–4.24 (m, 4H), 6.48 (d, J=1.5 Hz, 2H), 6.74 (d, d, J_1=3.0 Hz, J_2=7.2 Hz, 2H), 6.94 (d, J=0.9 Hz, 1H), 7.26–7.29 (m, 2H), 7.85 (d, d, J_1=2.7 Hz, J_2=8.4 Hz, 2H). EI-MS: m/z: 664 [M^+]. Elemental Anal. Calcd (%) for $C_{32}H_{41}BrO_{10}$ (665.57): C, 57.75; H, 6.21. Found: C, 57.77; H, 6.27.

4.1.7. Compound 16. To a solution of **14** (0.33 g, 0.50 mmol) in pyrrolidine (4 mL) were added $Pd(PPh_3)_4$ (30.0 mg, 0.040 mmol, 8%) and **15** (65.0 mg, 0.75 mmol). The mixture was stirred at 80 °C for 4 h and then concentrated in vacuo. The resulting residue was triturated with CH_2Cl_2 (50 mL). The organic phase was washed with hydrochloric acid, water, brine, and dried. After the solvent was removed, the crude product was purified by column chromatography (EtOAc/CH_3OH 50:1) to obtain **16** as a yellow solid (0.29 g, 85%). Mp 95–96 °C. ^1H NMR ($CDCl_3$): δ 1.57 (s, 6H), 3.69–3.89 (m, 24H), 3.98–4.01 (m, 4H), 4.17–4.25 (m, 4H), 4.48 (d, $J=9.0$ Hz, 1H), 6.61 (d, d, $J_1=3.0$ Hz, $J_2=9.0$ Hz, 1H), 6.67 (d, $J=8.1$ Hz, 1H), 6.73–6.75 (m, 2H), 724–7.28 (m, 2H), 7.83 (d, d, $J_1=3.0$ Hz, $J_2=8.1$ Hz, 2H). EI-MS: *m/z*: 668 $[M]^+$. Elemental Anal. Calcd (%) for $C_{37}H_{48}O_{11}$ (668.77): C, 66.45; H, 7.23. Found: C, 66.59; H, 7.08.

4.1.8. Compound 17. To a solution of **16** (0.29 g, 0.43 mmol) in benzene (10 mL) was added NaOH (52.0 mg, 1.30 mmol). The mixture was refluxed for 4 h, cooled and washed with water, brine, and dried. After the solvent was removed in vacuo, the residue was chromatographed (EtOAc/CH_3OH 50:1) to afford **17** as a white solid (0.26 g, 98%). Mp 92–93 °C. ^1H NMR ($CDCl_3$): δ 3.21 (s, 1H), 3.67–3.92 (m, 24H), 3.97–4.01 (m, 4H), 4.21–4.25 (m, 4H), 4.48 (d, $J=9.0$ Hz, 1H), 6.56 (d, d, $J_1=3.0$ Hz, $J_2=9.0$ Hz, 1H), 6.75 (d, d, $J_1=3.3$ Hz, $J_2=7.8$ Hz, 2H), 6.82 (d, $J=2.7$ Hz, 1H), 728–7.29 (m, 2H), 7.85 (d, d, $J_1=2.4$ Hz, $J_2=8.1$ Hz, 2H). EI-MS: *m/z*: 610 $[M]^+$. Elemental Anal. Calcd (%) for $C_{34}H_{42}O_{10}$ (610.69): C, 66.87; H, 6.93. Found: C, 66.90; H, 6.89.

4.1.9. Compound 18. A solution of 2-amino-5-iodo-6-methyl-3*H*-pyrimidin-4-one[23] (3.00 g, 12.0 mmol) and *n*-*n*-octyl isocyanate (2 mL) in THF (200 mL) was heated under reflux for 24 h. After work-up,[11a] the crude product was purified by column chromatography (CH_2Cl_2/MeOH 30:1) to afford **18** (3.50 g, 73%) as a white solid. Mp 150–152 °C. ^1H NMR ($CDCl_3$): δ 0.85–0.88 (m, 3H), 1.27–1.32 (m, 10H), 1.58–1.62 (m, 2H), 2.45 (s, 3H), 3.26 (m, 2H), 9.83 (s, 1H), 11.66 (s, 1H), 13.44 (s, 1H). EI-MS: *m/z*: 406 $[M^+]$. Elemental Anal. Calcd (%) for $C_{14}H_{23}IN_4O_2$ (406.27): C, 41.39; H, 5.71; N, 13.79. Found: C, 41.30; H, 5.71; N, 13.52.

4.1.10. Compound 11. A suspension of **17** (0.31 g, 0.50 mmol), **18** (0.31 g, 0.77 mmol), $Pd(PPh_3)_2Cl_2$ (30 mg, 6%), and CuI (10 mg, 10%) in THF (10 mL) and NEt_3 (1.5 mL) was stirred at rt for 5 h and then concentrated under reduced pressure. The residue was triturated with CH_2Cl_2 (50 mL). After work-up, the resulting residue was purified by column chromatography (CH_2Cl_2/CH_3OH 20:1) to produce **11** (0.14 g, 31%) as a yellow solid. Mp 150–152 °C. ^1H NMR $CDCl_3$): δ 0.84 (t, $J=6.6$ Hz, 3H), 1.23–1.28 (m, 12H), 2.49 (s, 3H), 3.22–3.29 (m, 2H), 3.65–3.84 (m, 24H), 3.96–4.02 (m, 4H), 4.21–4.23 (m, 4H), 6.35 (d, $J=9.0$ Hz, 1H), 6.56 (d, d, $J_1=3.3$ Hz, $J_2=9.0$ Hz, 1H), 6.71–6.78 (m, 2H), 6.95 (d, $J=3.3$ Hz, 1H), 7.26–7.29 (m, 2H), 7.84 (d, d, $J_1=2.1$ Hz, $J_2=8.7$ Hz, 2H), 10.13 (t, $J=5.1$ Hz, 1H), 11.83 (s, 1H), 13.45 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 14.2, 18.7, 22.7, 27.0, 29.3, 29.4, 29.6, 29.7, 31.9, 40.2, 53.2, 68.0, 68.5, 69.7, 69.7, 69.8, 70.6, 70.8, 70.9, 71.0, 71.1, 93.7, 104.3, 105.6, 105.7, 113.1, 113.4, 114.6, 116.7, 118.2, 125.2, 125.2, 126.7, 151.5, 152.4, 152.8, 153.8, 154.3, 156.5, 170.4. IR (cm^{-1}): ν 3211, 2926, 2855, 1697, 1594, 1264, 1080, 768. MALDI-HRMS: *m/z*: 911.4406 $[M+Na]^+$. Calcd for $C_{48}H_{64}N_4O_{12}$: 911.4413.

4.1.11. Compound 22. A solution of **20**[24] (1.04 g, 2.00 mmol), **21**[25] (0.74 g, 2.00 mmol), K_2CO_3 (1.10 g, 8.00 mmol), and KI (0.10 g) in DMF (20 mL) was stirred at 80 °C for 12 h and then cooled. The insoluble materials were filtered off and the solvent was removed under reduced pressure. The residue was triturated with AcOEt (150 mL). The organic phase was washed with aqueous HCl solution, $NaHCO_3$ solution, water, brine, and dried (Na_2SO_4). After the solvent was removed in vacuo, the crude product was recrystallized from AcOEt to obtain **22** (1.44 g, 90%) as a white solid. Mp 154–156 °C. ^1H NMR ($CDCl_3$): δ 1.26–1.36 (m, 39H), 1.65–1.77 (m, 4H), 3.67 (t, $J=7.2$ Hz, 2H), 3.91 (t, $J=6.9$ Hz, 2H), 6.75 (d, $J=7.8$ Hz, 2H), 7.05–7.09 (m, 8H), 7.21–7.26 (m, 6H), 7.70–7.71 (m, 2H), 7.82–7.84 (m, 2H). MALDI-MS: *m/z*: 812 $[M+Na]^+$. Elemental Anal. Calcd (%) for $C_{55}H_{67}NO_3\cdot 0.25H_2O$ (794.64): C, 83.13; H, 8.58; N, 1.76. Found: C, 83.31; H, 8.54; N, 1.33.

4.1.12. Compound 23. Hydrazine hydrate (2.0 mL, 85%) was added to a solution of **22** (1.10 g, 1.40 mmol) in ethanol (30 mL). The solution was refluxed for 3 h and then concentrated in vacuo to give a residue, which was triturated with chloroform (100 mL). The organic phase was washed with water, brine, and dried ($NaSO_4$). After removal of the solvent under reduced pressure, the crude product was recrystallized from AcOEt to afford compound **23** as a white solid (0.90 g, 91%). Mp 94–96 °C. ^1H NMR ($CDCl_3$): δ 1.26–1.43 (m, 39H), 1.73–1.78 (m, 4H), 2.68 (t, $J=7.2$ Hz, 2H), 3.92 (t, $J=6.6$ Hz, 2H), 6.75 (d, $J=9.0$ Hz, 2H), 7.06–7.10 (m, 8H), 7.21–7.26 (m, 6H). ESI-MS: *m/z*: 610 $[M+H]^+$. Elemental Anal. Calcd (%) for $C_{47}H_{65}NO\cdot 0.25H_2O$ (664.54): C, 84.94; H, 9.96; N, 2.11. Found: C, 84.99; H, 9.98; N, 1.55.

4.1.13. Compound 26. A solution of compounds **23** (0.45 g, 0.68 mmol), **24** (0.18 g, 0.68 mmol), and **25** (0.05 g, 0.68 mmol) in DMF (10 mL) was stirred at 120 °C for 4 h. Upon cooling, the insoluble materials were filtered off and the solvent was removed in vacuo. The resulting residue was triturated in chloroform (50 mL) and the solution was washed with water, brine, and dried ($MgSO_4$). The solvent was then removed and the crude product purified by column chromatography (CH_2Cl_2/MeOH 50:1) to give **26** as a pink solid (0.17 g, 25%). Mp 242–243 °C. ^1H NMR ($CDCl_3$): δ 1.25–1.39 (m, 39H), 1.71–1.75 (m, 4H), 3.91 (t, $J=6.6$ Hz, 2H), 4.19 (t, $J=7.2$ Hz, 2H), 5.00 (s, 2H), 6.75 (d, $J=8.4$ Hz, 2H), 7.05–7.09 (m, 8H), 7.22 (d, $J=8.7$ Hz, 6H), 8.78 (s, 4H). MALDI-MS: *m/z*: 989 $[M+Na]^+$. Elemental Anal. Calcd (%) for $C_{63}H_{70}N_2O_7$ (967.24): C, 78.23; H, 7.29; N, 2.90. Found: C, 78.45; H, 7.01; N, 2.76.

4.1.14. Compound 19. A suspension of **26** (0.28 g, 0.29 mmol) in thionyl chloride (5 mL) was refluxed for 6 h and then concentrated in vacuo to afford compound **27** as an oil, which was used directly for next step. To a stirred solution of **28**[11a] (94 mg, 0.29 mmol), triethylamine (0.8 mL) and DMAP (10 mg) in $CHCl_3$ (15 mL) was added a solution of the above **27** in chlroform (5 mL). The

mixture was heated under reflux for 36 h, cooled, washed with water, brine, and dried ($MgSO_4$). The solvent was removed and the residue was subjected to flash chromatography (CH_2Cl_2/MeOH 50:1) to afford **19** as a pink solid (104 mg, 28%). Mp 212–214 °C. ^{1}H NMR ($CDCl_3$): δ 0.84 (t, J=6.9 Hz, 3H), 1.24–1.67 (m, 57H), 2.49 (t, J=8.1 Hz, 2H), 3.57–3.59 (m, 2H), 3.98 (t, J=7.2 Hz, 2H), 4.16 (t, J=8.4 Hz, 2H), 4.40 (t, J=5.4 Hz, 2H), 5.02 (s, 2H), 5.82 (s, 1H), 6.73–6.76 (m, 2H), 7.04–7.09 (m, 8H), 7.20–7.25 (m, 6H), 8.70 (s, 4H), 10.44 (t, J=3.6 Hz, 1H), 11.76 (s, 1H), 12.97 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 14.1, 22.7, 26.2, 27.0, 27.1, 28.1, 29.0, 29.2, 29.3, 29.4 (d), 29.5 (d), 29.6, 31.4, 31.8, 32.7, 34.3, 34.3, 38.7, 41.1, 41.8, 63.0, 63.9, 67.8, 106.0, 112.9, 124.0, 124.2, 126.1, 126.7, 126.8, 126.9, 130.6, 130.7, 130.8, 131.2, 132.2, 139.3, 143.6, 144.2, 148.3, 148.5, 152.5, 154.3, 156.8, 156.9, 162.4, 162.6, 167.6, 172.9. IR (cm^{-1}): ν 3040, 2959, 2928, 2856, 1757, 1709, 1672, 1584, 1246, 823, 771. MALDI-MS: *m/z*: 1273 [M^++H]. Elemental Anal. Calcd (%) for $C_{79}H_{96}N_6O_9\cdot 0.25H_2O$ (1278.15): C, 74.23; H, 7.63; N, 6.58. Found: C, 74.09; H, 7.70; N, 6.34.

4.2. Vapor pressure osmometry (VPO)

The VPO experiments were performed in chloroform–toluene (85:15 v:v) at 30 °C with a Knauer-K-700 osmometer, with a synthetic amide (M_W: 1772) used for calibration. Reported results represent single experimental runs.

4.3. Binding constants

Measurement of binding constants has been described in the previous paper.[11a]

4.4. Computational method

The binding pattern was constructed by using the Builder program within the package HyperChem. Then they were optimized by the conjugate gradient with the AMBER force field and the RMS derivative criteria of 0.00001 kcal mol^{-1}. In order to explore lower-energy conformation on the potential energy surface, molecular dynamics calculations were performed with constraint of hydrogen bonds at ca. 2.15 Å. After 100 ps molecular dynamics simulation, an additional round of energy minimization was again completed.

Acknowledgements

This work was supported by the Ministry of Science and Technology (No. G2000078101) and the National Natural Science Foundation of China.

References and notes

1. (a) Voet, D.; Voet, J. G. *Biochemistry*, 2nd ed.; Wiley: New York, 1995. (b) Dugas, H. *Bioorganic Chemistry*, 3rd ed.; Springer: Berlin, 1996.
2. (a) Vögtle, F. *Supramolecular Chemistry: An Introduction*; Wiley: Chichester, UK, 1991. (b) Lehn, J.-M. *Supramolecular Chemistry: Concepts and Perspectives*; VCH: Meinheim, 1995. (c) Schneider, H.-J.; Yatsimirsky, A. *Principles and Methods in Supramolecular Chemistry*; Wiley: New York, 2001. (d) Steed, J. W.; Atwood, J. L. *Supramolecular Chemistry*; Wiley: New York, 2001.
3. (a) Sauvage, J.-P. *Transition Metals in Suparamolecular Chemistry*; Wiley: New York, 1999. (b) Lehn, J.-M. *Chem. Eur. J.* **1999**, *5*, 2455–2463. (c) Sanders, J. K. M. *Pure Appl. Chem.* **2000**, *72*, 2265–2274. (d) Leininger, S.; Olenyuk, B.; Stang, P. J. *Chem. Rev.* **2000**, *100*, 853–908. (e) Sun, W.-Y.; Yoshizawa, M.; Kusukawa, T.; Fujita, M. *Curr. Opin. Chem. Biol.* **2002**, *6*, 757–764.
4. (a) Hill, D. J.; Mio, M. J.; Prince, R. B.; Hughes, T. S.; Moore, J. S. *Chem. Rev.* **2001**, *101*, 3893–4012. (b) Bowden, N. B.; Weck, M.; Choi, I. S.; Whitesides, G. M. *Acc. Chem. Res.* **2001**, *34*, 231–238. (c) Zhao, D.; Moore, J. S. *Chem. Commun.* **2003**, 807–818.
5. (a) Conn, M. M.; Rebek, J., Jr. *Chem. Rev.* **1997**, *97*, 1647–1668. (b) Zimmerman, S. C.; Corbin, P. S. *Struct. Bond. (Berlin)* **2000**, *96*, 63–94. (c) Brunsveld, L.; Folmer, B. J. B.; Meijer, E. W.; Sijbesma, R. P. *Chem. Rev.* **2001**, *101*, 4071–4098. (d) Sherrington, D. C.; Taskinen, K. A. *Chem. Soc. Rev.* **2001**, *30*, 83–93. (e) Schmuck, C.; Wienand, W. *Angew. Chem., Int. Ed.* **2001**, *40*, 4363–4369. (f) Prins, L. J.; Reinhoudt, D. N.; Timmerman, P. *Angew. Chem., Int. Ed.* **2001**, *40*, 2383–2426. (g) Archer, E. A.; Gong, H.; Krische, M. J. *Tetrahedron* **2001**, *57*, 1139–1159. (h) Sijbesma, R. P.; Meijer, E. W. *Chem. Commun.* **2003**, 5–16.
6. (a) Raymo, F. M.; Stoddart, J. F. *Chem. Rev.* **1999**, *99*, 1643–1664. (b) Cubberley, M. S.; Iverson, B. L. *Curr. Opin. Chem. Biol.* **2001**, *5*, 650–653. (c) Pease, A. R.; Jeppesen, J. O.; Stoddart, J. F.; Luo, Y.; Collier, C. P.; Heath, J. R. *Acc. Chem. Res.* **2001**, *34*, 433–444.
7. (a) Amabilino, D. B.; Dietrich-Buchecher, C. O.; Livoreil, A.; Pérez-García, L.; Sauvage, J.-P.; Stoddart, J. F. *J. Am. Chem. Soc.* **1996**, *118*, 3905–3913. (b) Hirschberg, J. H. K. K.; Brunsveld, L.; Ramzi, A.; Vekemans, J. A. J. M.; Sijbesma, R. P.; Meijer, E. W. *Nature* **2000**, *407*, 167–170. (c) Zhao, X.; Jiang, X.-K.; Shi, M.; Yu, Y.-H.; Xia, W.; Li, Z.-T. *J. Org. Chem.* **2001**, *66*, 7035–7043. (d) Brunsveld, L.; Vekemans, J. A. J. M.; Hirschberg, J. H. K. K.; Sijbesma, R. P.; Meijer, E. W. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4977–4982. (e) Cary, J. M.; Moore, J. S. *Org. Lett.* **2002**, *4*, 4663–4666. (f) Yang, X.; Brown, A. L.; Furukawa, M.; Li, S.; Gardinier, W. E.; Bukowski, E. J.; Bright, F. V.; Zheng, C.; Zeng, X. C.; Gong, B. *Chem. Commun.* **2003**, 56–57.
8. Beijer, F. H.; Sijbesma, R. P.; Kooijman, H.; Spek, A. L.; Meijer, E. W. *J. Am. Chem. Soc.* **1998**, *120*, 6761–6769.
9. (a) González, J. J.; González, S.; Priego, E. M.; Luo, C.; Guldi, D. M.; de Mendoza, J.; Martin, N. *Chem. Commun.* **2001**, 163–164. (b) Rieth, L. R.; Eaton, R. F.; Coates, G. W. *Angew. Chem., Int. Ed.* **2001**, *40*, 2153–2156. (c) Rispens, M. T.; Sánchez, L.; Knol, J.; Hummelen, J. C. *Chem. Commun.* **2001**, 161–162. (d) Ikegami, M.; Arai, T. *Chem. Lett.* **2001**, 694–695. (e) Sánchez, L.; Rispens, M. T.; Hummelen, J. C. *Angew. Chem., Int. Ed.* **2002**, *40*, 838–840. (f) Cate, A. T.; Dankers, P. Y. W.; Kooijman, H.; Spek, A. L.; Sijbesma, R. P.; Meijer, E. W. *J. Am. Chem. Soc.* **2003**, *125*, 6860–6861. (g) Ligthart, G. B. W. L.; Ohkawa, H.; Sijbesma, R. P.; Meijer, E. W. *J. Am. Chem. Soc.* **2005**, *127*, 810–811.
10. For examples of other kinds of quadruply hydrogen bonded

homodimers, see: (a) Lüning, U.; Kühl, C. *Tetrahedron Lett.* **1998**, *39*, 5735–5738. (b) Sessler, J. L.; Wang, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 1726–1729. (c) Corbin, P. S.; Zimmerman, S. C. *J. Am. Chem. Soc.* **1998**, *120*, 9710–9711. (d) Gong, B.; Yan, Y.; Zeng, H.; Skrzypczak-Jankunn, E.; Kim, Y. W.; Zhu, J.; Ickes, H. *J. Am. Chem. Soc.* **1999**, *121*, 5607–5608. (e) Corbin, P. S.; Lawless, L. J.; Li, Z.-T.; Ma, Y.; Witmer, M. J.; Zimmerman, S. C. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 5099–5104.

11. (a) Wang, X.-Z.; Li, X.-Q.; Shao, X.-B.; Zhao, X.; Deng, P.; Jiang, X.-K.; Li, Z.-T.; Chen, Y.-Q. *Chem. Eur. J.* **2003**, *9*, 2904–2913. (b) Li, X.-Q.; Jiang, X.-K.; Wang, X.-Z.; Li, Z.-T. *Tetrahedron* **2004**, *60*, 2063–2069. (c) Li, X.-Q.; Feng, D.-J.; Jiang, X.-K.; Li, Z.-T. *Tetrahedron* **2004**, *60*, 8275–8284.
12. For recent examples of other kinds of quadruply hydrogen bonded heterodimers, see: (a) Corbin, P. S.; Zimmerman, S. C.; Thiessen, P. A.; Hawryluk, N. A.; Murray, T. J. *J. Am. Chem. Soc.* **2001**, *123*, 10475–10488. (b) Brammer, S.; Lüning, U.; Kühl, C. *Eur. J. Org. Chem.* **2002**, 4054–4062. (c) Zeng, H.; Yang, X.; Flowers, R. A., II; Gong, B. *J. Am. Chem. Soc.* **2002**, *124*, 2903–2910. (d) Zhao, X.; Wang, X.-Z.; Jiang, X.-K.; Chen, Y.-Q.; Chen, G.-J.; Li, Z.-T. *J. Am. Chem. Soc.* **2003**, *125*, 15128–15139.
13. The interaction have been utilized for the self-assembly of a number of interlocked supramolecules and artificial duplexes, see: (a) Hamilton, D. G.; Davies, J. E.; Prodi, L.; Sanders, J. K. M. *Chem. Eur. J.* **1998**, *4*, 608–620. (b) Hansen, J. G.; Feeder, N.; Hamilton, D. G.; Gunter, M. J.; Becher, J.; Sanders, J. K. M. *Org. Lett.* **2000**, *2*, 449–452. (c) Raehm, L.; Hamilton, D. G.; Sanders, J. K. M. *Synlett* **2002**, 1743–1761. (d) Gabriel, G. J.; Iverson, B. L. *J. Am. Chem. Soc.* **2002**, *124*, 15174–15175. (e) Zhou, Q.-Z.; Jiang, X.-K.; Shao, X.-B.; Chen, G.-J.; Jia, M.-X.; Li, Z.-T. *Org. Lett.* **2003**, *5*, 1955–1958. (f) Feng, D.-J.; Li, X.-Q.; Wang, X.-Z.; Jiang, X.-K.; Li, Z.-T. *Tetrahedron* **2004**, *60*, 6137–6144.
14. For a recent example of the hydrogen bonded trimeric supramolecule, see: Sessler, J. L.; Jayawickramarakah, J.; Sathiosatham, M.; Sherman, C. L.; Brodbelt, J. S. *Org. Lett.* **2003**, *5*, 2627–2630.
15. Compound **8** could not be obtained from the reaction of **5** and **6**, possibly due to its increased solubility in chloroform and higher reactivity than **6**.
16. The K_{dim} values for the self-association of **7** were determined to be approximately $<11\ M^{-1}$ by ^1H NMR dilution studies (60–0.1 mM) in $CDCl_3$. Therefore, its self-association could be reasonably ignored.
17. (a) Conners, K. A. *Binding Constants: The Measurement of Molecular Complex Stability*; Wiley: New York, 1987. (b) Wilcox, C. S. In *Frontiers in Supramolecular Organic Chemistry and Photochemistry*; Schneider, H. J., Dürr, H., Eds.; VCH: New York, 1991; Chapter 5, p 123.
18. Because all the possible heterotrimers exchange to each other in the solution, the 'in–in' arranged heterotrimer **1**·**4**·**2** should be of higher yield, since only in this trimer that the additional donor–acceptor interaction could occur.
19. (a) Amabilino, D. B.; Ashton, P. R.; Balzani, V.; Boyd, S. E.; Credi, A.; Lee, J. Y.; Menzer, S.; Stoddart, J. F.; Venturi, M.; Williams, D. J. *J. Am. Chem. Soc.* **1998**, *120*, 4295–4307. (b) Shao, X.-B.; Jiang, X.-K.; Wang, X.-Z.; Li, Z.-T.; Zhu, S.-Z. *Tetrahedron* **2003**, *59*, 4881–4889.
20. For examples of using this group for rotaxane assembly, see: (a) Gibson, H. W.; Lee, S. H.; Engen, P. T.; Lecavalier, P.; Sze, J.; Shen, Y. X.; Bheda, M. *J. Org. Chem.* **1993**, *58*, 3748–3756. (b) Balzani, V.; Becher, J.; Credi, A.; Nielsen, M. B.; Raymo, F. M.; Stoddart, J. F.; Talarico, A. M.; Venturi, M. *J. Org. Chem.* **2000**, *65*, 1947–1956. (c) Hübner, G. M.; Nachtsheim, G.; Li, Q. Y.; Seel, C.; Vögtle, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 1269–1272. (d) Jimenez-Molero, M. C.; Dietrich-Buchecker, C. O.; Sauvage, J. P. *Chem. Eur. J.* **2002**, *8*, 1456–1466. (e) Li, X.-Y.; Illigen, J.; Nieger, M.; Michel, S.; Schalley, C. A. *Chem. Eur. J.* **2003**, *9*, 1332–1347.
21. Buehlmann, P.; Badertscher, M.; Simon, W. *Tetrahedron* **1993**, *49*, 595–602.
22. Hu, C.-M.; Hong, F.; Xu, Y.-Y. *J. Fluorine Chem.* **1993**, *64*, 1–4.
23. Wierenga, W.; Skulnick, H. I.; Stringfellow, D. A.; Weed, S. D.; Renis, H. E.; Eidson, E. E. *J. Med. Chem.* **1980**, *23*, 237–239.
24. Ashton, P. R.; Philp, D.; Spencer, N.; Stoddart, J. F. *J. Chem. Soc., Chem. Commun.* **1992**, 1124–1127.
25. Mary, A.; Renko, D. Z.; Guillou, C.; Thal, C. *Bioorg. Med. Chem.* **1998**, *6*, 1835–1850.