Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron
Tetrahedron 62 (2006) 11933–11941

Hydrogen bonding-mediated self-assembly of anthranilamide-based homodimers through preorganization of the amido and ureido binding sites

Jiang Zhu,[a,b] Jian-Bin Lin,[a] Yun-Xiang Xu,[a] Xi-Kui Jiang[a] and Zhan-Ting Li[a,*]

[a]*State Key Laboratory of Bio-Organic and Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China*
[b]*Division of Chemistry, North Sichuan Medical College, 234 Fujiang Lu, Nanchong 637007, China*

Received 11 August 2006; revised 20 September 2006; accepted 21 September 2006
Available online 18 October 2006

Abstract—The self-assembly of a novel series of hydrogen bonding-mediated homodimers in chloroform-*d* has been described. Six anthranilamide-based monomers have been prepared, in which two self-binding formamido, trifluoroacetamido, acetamido, butyl or methyl ureido units are introduced at the two ends of the backbones. Quantitative ^{1}H NMR investigations in chloroform-*d* revealed that the formamido and ureido units are more efficient than acetamido to induce the formation of stable homodimers. The association constants of all the new homodimers have been determined by ^{1}H NMR dilution method. Multiply hydrogen bonding-driven binding patterns have been proposed for the homodimers. It is also found that ureido-derived homodimers do not adopt common linear binding pattern observed for simple urea derivatives.
© 2006 Elsevier Ltd. All rights reserved.

1. Introduction

Self-assembly of linear molecules into duplexes is a common phenomenon in biological systems.[1,2] In recent years, there has been intensive interest in constructing artificial duplexes or dimers of defined structures through the self-assembly of synthetic monomers.[3–5] Particularly, hydrogen bonding has been proved to be ideal non-covalent force for this purpose due to its great directionality and strength.[6] Two general strategies have been developed for the design of hydrogen bonding-mediated molecular building blocks. The first one is based on heterocyclic derivatives, in which hydrogen bonding donors or acceptors are compactly arranged in a designed direction, as demonstrated by the recent self-assembly of quadruply hydrogen bonded binding modes.[7] The second one is to iteratively incorporate simple binding residues into linear backbones. Examples of this family of dimeric aggregates include sheet-like aromatic and aliphatic amide duplexes,[8,9] 3,6-diaminopyridazine-based homodimers[10] and hydrazide-derived heterodimers.[11] To achieve high binding stability and selectivity, both strategies require preorganization and rigidity of the backbones and binding sites of monomers, which is usually realized by making use of intramolecular hydrogen bonding.[12]

In the past decade, the construction of foldamers, linear molecules that are induced by non-covalent forces to adopt well-established secondary structures, has received increasing attention.[13] Also due to its directionality and strength, hydrogen bonding has been widely utilized to construct aromatic oligoamide-based foldamers.[14–23] In addition, some of the synthetic folded structures represent new generation of acyclic receptors for saccharides,[22b,c] alkyl ammoniums[22d] or encapsulation of water.[23b] As part of a program in hydrogen bonding-mediated self-assembly, we had reported the construction of a new series of planar zigzag secondary structures.[24] Recently we also succeeded in utilizing the rigidified structural motif as preorganized backbones to assemble a new family of homoduplex **1**·**1** (Chart 1).[25] In order to explore the assembling diversity and also to screen ideal binding sites for more efficient assembling patterns, we have designed several new monomers. In this paper, we report the synthesis of these new monomers and their self-assembling features in chloroform.

2. Results and discussion

Six monomers **2**–**5** have been designed (Chart 2), which contain two formamido, trifluoroacetamido, acetamido or ureido units, respectively. All these units have been established to be able to self-associate in solvents of low polarity. It was expected that a comparison of their self-associating features would reveal the ideal binding modes for this class

Keywords: Self-assembly; Hydrogen bonding; Aromatic amide; Dimer.
* Corresponding author. Tel.: +86 21 5492 5122; fax: +86 21 6416 6128; e-mail: ztli@mail.sioc.ac.cn

0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.09.073

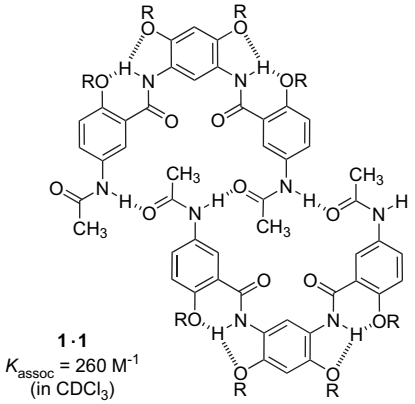


Chart 1.

of homodimers, which should be useful for future design of more elaborate supramolecular architectures.

The synthetic route for **2** is shown in Scheme 1. Thus, ester **6**[25] was first hydrolyzed with lithium hydroxide to give acid **7** in 80% yield. The latter was then treated with formic acetic anhydride in THF to afford **8** in 65% yield. Finally, **8** reacted with diamine **9**[25] in DMF in the presence of HATU and THF produced **2** in 84% yield.

For the synthesis of **3** (Scheme 2), aniline **7** was first treated with trifluoroacetic anhydride in THF to produce **10** in 95% yield. The acid was then coupled with **11**[22b] in DMF and THF in the presence of HATU to afford **3** in 65% yield. For the preparation of **4** (Scheme 3), compound **9** was first coupled with **12**[24a] in THF in the presence of DCC to give intermediate **13** in 65% yield. Then, another intermediate **15** was

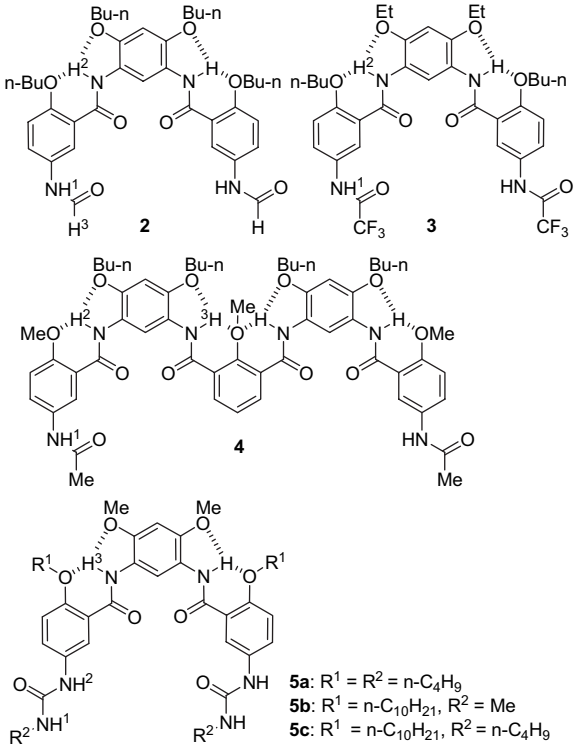
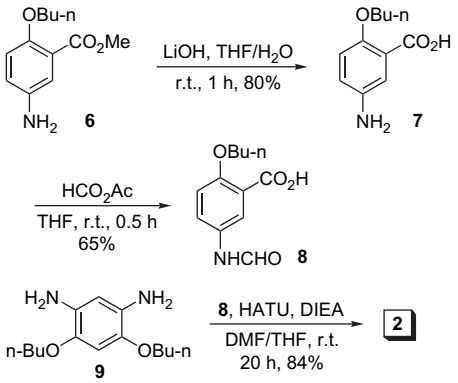
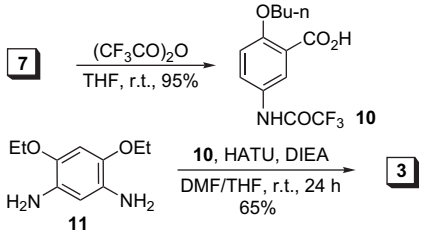


Chart 2.

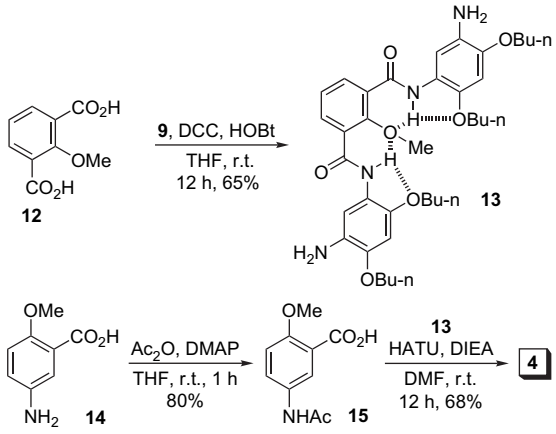


Scheme 1.

obtained in 80% yield from the reaction of **14**[26] with acetic anhydride in THF. Finally, HATU-mediated coupling reaction of **13** with **15** in DMF generated **4** in 68% yield.



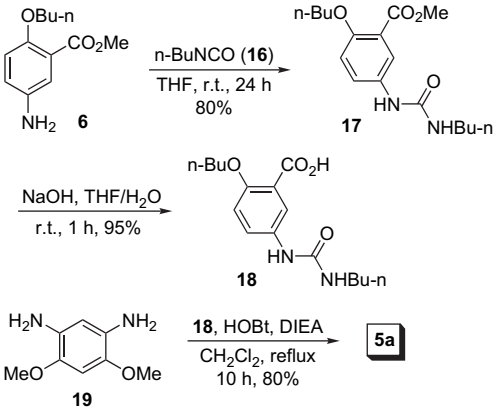
Scheme 2.



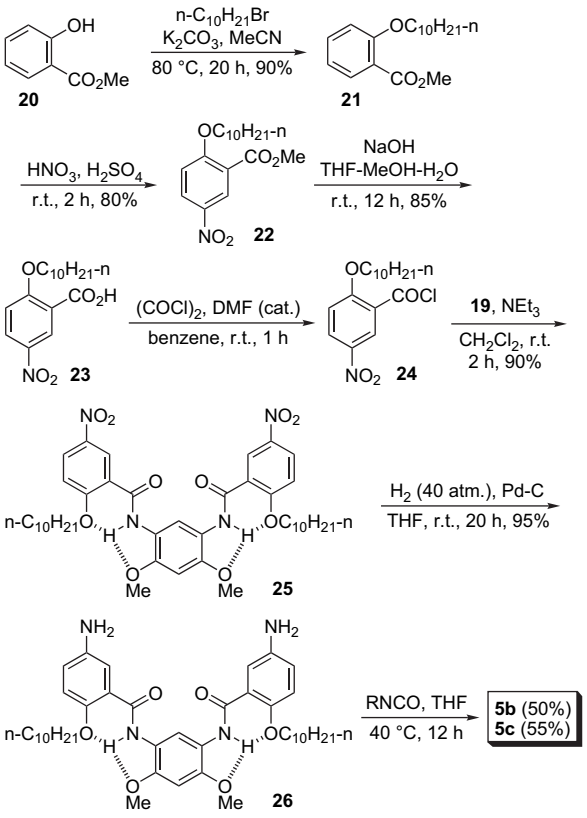
Scheme 3.

To prepare **5a** (Scheme 4), **6** was first treated with butyl isocyanide **16** in THF to give urea **17** in 80% yield. The latter was then hydrolyzed with sodium hydroxide to afford **18** in 95% yield. Compound **18** was again coupled with **19** in dichloromethane in the presence of HOBt to generate **5a** in 80% yield. The synthetic routes for **5b** and **5c** are shown in Scheme 5. Thus, compound **20** was first alkylated in hot acetonitrile with potassium carbonate as base to give **21** in 90% yield. The latter was nitrated in concd sulfuric acid to produce **22** in 80% yield. The intermediate was then hydrolyzed with sodium hydroxide to acid **23** in 85% yield. Treatment of **23** with oxalyl chloride yielded acyl chloride **24**, which was then reacted with compound **19** in dichloromethane in the presence of triethylamine to produce compound **25** in 90% yield. Palladium-catalyzed hydrogenation of **25**

in THF gave diamine **26** in 95% yield. Finally, the reaction of **26** with methyl and butyl isocyanide in THF yielded **5b** and **5c**, respectively.



Scheme 4.



Scheme 5.

Previously, the rigidified preorganized conformation of the anthranilamide backbones of compounds **2**–**5** has been established by the X-ray analysis and ^{1}H NMR techniques.[24a] The ^{1}H NMR spectra of **2**–**5** in $CDCl_3$ are shown in Figure 1. All the linking amide protons display signals at the downfield area, which is consistent with the result observed for their corresponding backbone molecules and suggests the formation of the similar rigidified conformation for **2**–**5**.[24a]

The ^{1}H NMR spectrum of compound **2** in $CDCl_3$ displays one set of sharp signals and the HCON*H* signal appears at

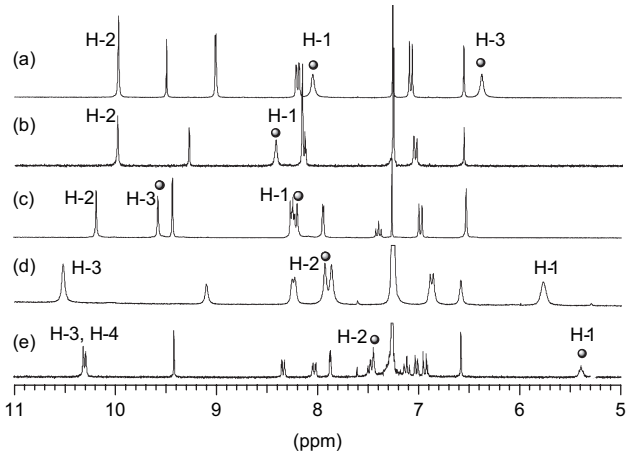


Figure 1. Partial ^{1}H NMR spectrum (400 MHz) of (a) **2**, (b) **3**, (c) **4**, (d) **5c** and (e) **30** in $CDCl_3$ at 25 °C (6.0 mM) (for numbering, see Chart 2).

8.01 ppm. Nevertheless, it has been reported that *N*-phenyl formamide and related derivatives exist as cis and trans isomers as a result of the restricted rotation of the N–C═O bond.[27] The discrepancy suggests that the NH protons were involved in important intermolecular hydrogen bonding, as observed for **1**.[25] ^{1}H NMR dilution experiments were then carried out, which revealed important upfield shifting of both the HCON*H* and HNC*H*O signals (Fig. 2). By fitting the data of the amide proton to a 1:1 binding mode, a K_{assoc} of 2.6 ($\pm$0.3)$\times 10^3$ M^{-1} was obtained for homodimer **2**·**2**.[28] This value is substantially higher than that of **1**·**1** in the same solvent, reflecting the increased efficiency of the self-binding formamide unit obviously as a result of the decreased steric hindrance. Because it has been established that in solution homodimer **1**·**1** mainly adopts a linear binding mode[25] and the X-ray analysis has also revealed a linear assembling pattern for *p*-chlorophenyl-formamide,[29] it is reasonable to propose that dimer **2**·**2** should also adopt a linear self-associating mode (Chart 3), which is stabilized by three intermolecular hydrogen bonds. The upfield shifting of the HCON*H* signal with dilution may be ascribed to the weakening of the intermolecular shielding at reduced concentration. Also based on the ^{1}H NMR dilution experiments, a K_{assoc} of 80 ($\pm$7) M^{-1} was estimated for homodimer **3**·**3** in $CDCl_3$ (Chart 3). The values of **1**·**1** and **3**·**3**

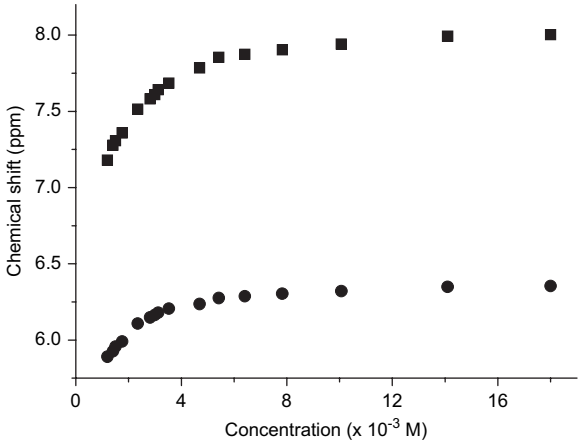


Figure 2. Plot of the chemical shift of the N*H* (■) and O═C*H* (●) protons of **2** (18.2 mM to 1.2 mM) in $CDCl_3$ at 25 °C.

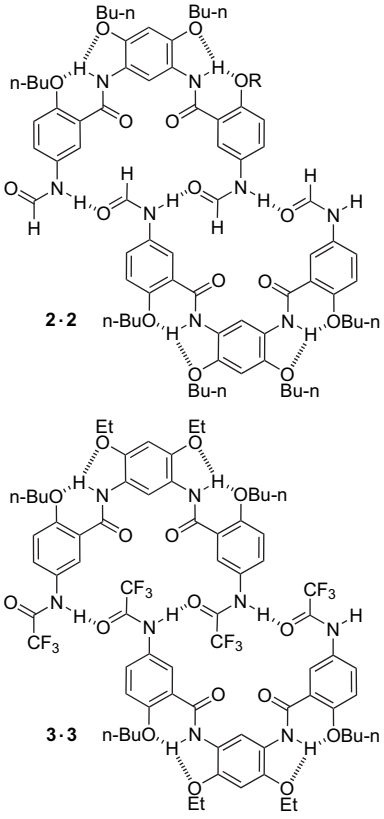


Chart 3.

are pronouncedly smaller than that of **2·2**, which reflect the increased steric hindrance of the CH_3 and CF_3 groups compared to that of the hydrogen atom.

The self-associating property of longer **4** was also investigated by the ^{1}H NMR spectroscopy. 2D-NOESY experiment in $CDCl_3$ revealed modest intermolecular NOE connections between the appended methyl protons and the centrally located benzene protons, which are shown in Chart 4. This observation suggests dimer **4·4** also forms in the solution. The ^{1}H NMR dilution experiments in $CDCl_3$ were then performed, which revealed that the signal of the appended NH protons moved upfield substantially with the decrease of the concentration (Fig. 3). By fitting the data to a 1:1 binding mode, a K_{assoc} of 230 ($\pm$20) M^{-1} could be derived for

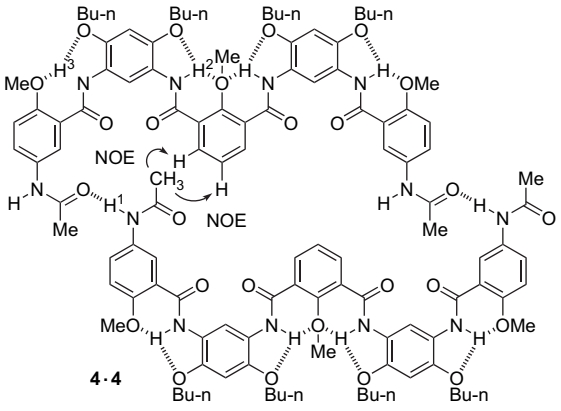


Chart 4.

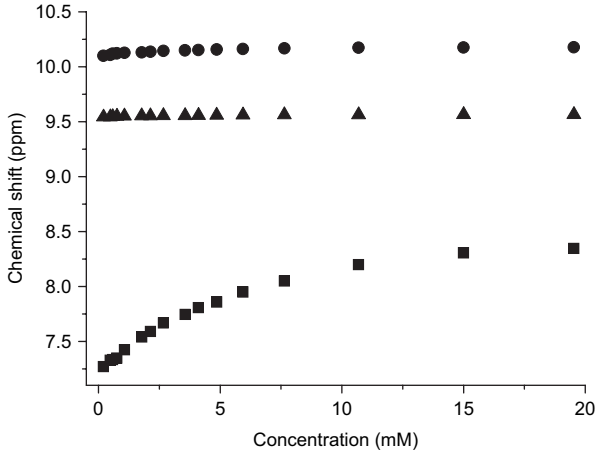


Figure 3. Plot of the chemical shift of the NH-1 (■), NH-2 (▲) and NH-3 (●) protons of **4** (19.5 mM to 0.2 mM) in $CDCl_3$ at 25 °C.

homodimer **4·4**. The value is close to that of homodimer **1·1**, probably as a result of decreased steric hindrance in this dimeric structure, which increases the strength of the single intermolecular hydrogen bond.

Alkyl ureido unit is an efficient self-binding site, which has been widely used for the formation of numerous dimeric capsules.[30] It was envisioned that replacement of the acetamide unit in **1** with the alkyl ureido unit might lead to the formation of more stable homodimers. Therefore, compounds **5a**–**5c** were prepared. Unfortunately, **5a** and **5b** were only slightly soluble in chloroform, which made it impossible to investigate their self-associating property in chloroform. However, a single crystal of **5a** suitable for the X-ray analysis was grown from evaporation of its solution in chloroform. Surprisingly, the solid-state structure revealed a dimeric structure (Fig. 4), in which one of the ureido unit of the monomer was hydrogen bonded to the centrally located C=O oxygen. In addition, the aromatic backbone of the molecule is also twisted considerably. We attribute these results to the large size of the butyl group connected to the ureido unit, which retards the linear self-associating mode (Chart 5). ^{1}H NMR dilution experiments in $CDCl_3$ were carried out for the soluble analogue **5c**, which revealed important upfield shifting of the protons of the two ureido NH groups. Because the signal of the benzene-connected NH protons was

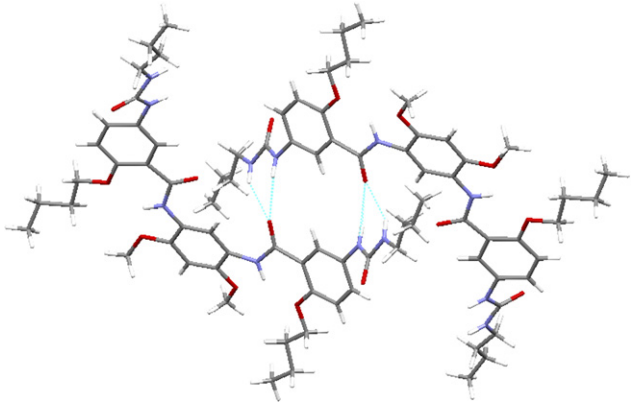


Figure 4. The solid-state structure of **5a**, highlighting the dimeric binding pattern.

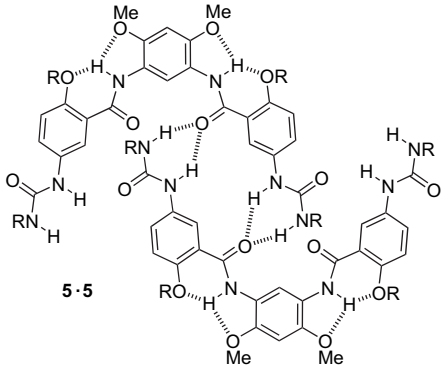


Chart 5.

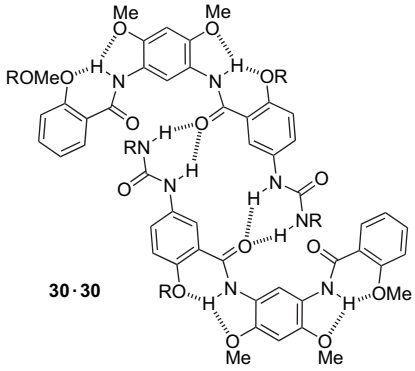
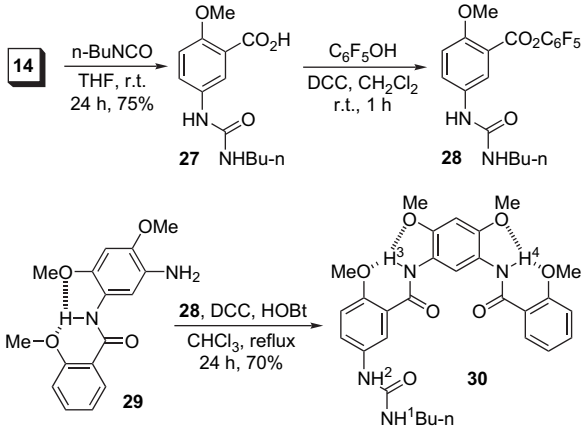


Chart 6.

overlapped with other aromatic signals upon dilution, the signal of the BuNH unit was used as probe for quantitative self-associating study, which gave rise to a K_{assoc} of 1.1 ($\pm$0.1)$\times 10^3$ M^{-1} for homodimer **5c·5c**. This value is also remarkably larger than that of **1·1** probably as a result of the increased number of the intermolecular hydrogen bonds.

It has been reported that simple *N*-alkylated urea derivatives form extended linear stacking structures in the solid state, which are stabilized by intermolecular hydrogen bonding between the ureido units.[31] In order to explore the influence of the rigidified backbone on the self-assembly of the urea derivatives, compound **30** was also prepared according to the route shown in Scheme 6. The ^{1}H NMR spectrum of **30** in $CDCl_3$ is provided in Figure 1. The intramolecular hydrogen bonding is evidenced by the fact that the signals of both amide protons appear in the downfield area. Based on the ^{1}H NMR dilution experiments, we determined the K_{assoc} of the homodimer **30·30** of this molecule in $CDCl_3$ to be approximately 820 M^{-1}. This value is lower than that of homodimer **5c·5c** but notably larger than that of *N*,*N*′-dimethylurea (ca. 400 M^{-1}) in benzene of less polarity.[32] This result indicates that homodimer **30·30** should also mainly adopt the quadruply hydrogen bonded binding pattern, as shown in Chart 6. In principle, if monomers have good solubility, replacement of the ending butyl groups with smaller methyl groups would remarkably reduce the steric hindrance and increase the stability of the corresponding homodimers.



Scheme 6.

3. Conclusion

In summary, we have reported the hydrogen bonding-mediated self-assembly of a new series of homodimers. The key feature of the new supramolecular architectures is the preorganization of their anthranilamide backbones, which is realized by introduction of consecutive three-centered intramolecular hydrogen bonding. The formamido and ureido units display greater binding affinity and may be ideal binding sites for the self-assembly of more stable dimeric structures. Future work will point to the development of longer oligomeric or polymeric monomers, which might lead to the construction of new generation of duplexes of well-ordered structures or self-duplication.

4. Experimental

4.1. General methods

Melting points are uncorrected. All solvents were dried before use following standard procedures. All reactions were performed under an atmosphere of dry nitrogen. The ^{1}H NMR spectra were recorded on 400 or 300 MHz spectrometers in the indicated solvents. Chemical shifts are expressed in parts per million (δ) using residual solvent protons as internal standards. Chloroform (δ 7.26 ppm) was used as an internal standard for chloroform-*d*. Elemental analysis was carried out at the SIOC analytical center. Unless otherwise indicated, all starting materials were obtained from commercial suppliers and were used without further purification.

4.1.1. Compound 7. A solution of **6**[25] (2.23 g, 10.0 mmol) and lithium hydroxide monohydrate (0.13 g, 30.0 mmol) in THF (50 mL) and water (25 mL) was stirred at room temperature for 1 h and then neutralized with dilute hydrochloric acid (1 N) to pH=7. The solvent was removed under reduced pressure and the resulting residue washed with cold water and ether. The crude product was dried in vacuo and purified by recrystallization from methanol to give **7** as a white solid (1.68 g, 80%). ^{1}H NMR ($CDCl_3$) δ: 7.49–7.48 (m, 1H), 6.89–6.87 (m, 2H), 4.17 (t, *J*=6.8 Hz, 2H), 1.88–1.83 (m, 2H), 1.54–1.47 (m, 2H), 1.00 (t, *J*=6.4 Hz, 3H). MS (EI): *m/z* 209 $[M]^+$. Anal. Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.05l; H, 7.28; N, 6.54.

4.1.2. Compound 8. To a stirred solution of compound **7** (0.51 g, 2.42 mmol) in THF (10 mL) was added a solution

of formic acetic anhydride (0.26 g, 3.00 mmol) in THF (2 mL). The solution was stirred at room temperature for 0.5 h and then concentrated under reduced pressure. The resulting residue was dissolved in chloroform (20 mL). The solution was then washed with saturated sodium bicarbonate solution (10 mL), water (10 mL×2), brine (10 mL) and dried over sodium sulfate. After the solvent was removed under reduced pressure, the crude product was purified by recrystallization from THF and petroleum ether to give **8** as pale yellow solid (0.37 g, 65%). ^{1}H NMR ($CDCl_3$) δ: 11.07 (br, 1H), 8.40 (d, J=1.7 Hz, 1H), 8.30 (dd, J_1=2.9 Hz, J_2=9.0 Hz, 1H), 7.94 (d, J=2.8 Hz, 1H), 7.61 (s, 1H), 7.05 (d, J=9.0 Hz, 1H), 4.29–4.25 (m, 2H), 1.95–1.86 (m, 2H), 1.57–1.47 (m, 2H), 1.04–0.99 (m, 3H). ^{1}H NMR (DMSO-d_6) δ: 8.63 (s, 1H), 8.22 (s, 1H), 7.87 (d, J=2.7 Hz, 1H), 7.66 (dd, J_1=2.8 Hz, J_2=8.9 Hz, 1H), 7.08 (d, J=9.0 Hz, 1H), 4.01–3.97 (m, 2H), 1.72–1.62 (m, 2H), 1.50–1.37 (m, 2H), 0.93–0.88 (m, 3H). MS (ESI): m/z 238 $[M+H]^+$, 260 $[M+Na]^+$. Anal. Calcd for $C_{12}H_{15}NO_4$: C, 60.75; H, 6.37; N, 5.90. Found: C, 60.70; H, 6.28; N, 5.79.

4.1.3. Compound 2. To a stirred solution of compounds **8** (0.24 g, 1.00 mmol) and **9** (0.13 g, 050 mmol) in DMF (10 mL) and THF (10 mL) were added HATU (0.40 g, 1.05 mmol) and DIEA (0.2 mL). The mixture was stirred at room temperature for 20 h and then concentrated in vacuo. The resulting residue was triturated with methanol (10 mL). The mixture was stirred for 0.5 h. The precipitate formed was filtered, washed with ether and recrystallized from methanol and chloroform to give **2** as a yellow solid (0.29 g, 84%). ^{1}H NMR ($CDCl_3$) δ: 10.14 (s, 2H), 9.31 (s, 2H), 9.15 (s, 2H), 8.31 (dd, J_1=2.7 Hz, J_2=8.9 Hz, 2H), 8.25 (d, J=2.7 Hz, 1H), 8.01 (s, 2H), 6.95 (d, J=9.0 Hz, 2H), 6.59 (s, 2H), 4.22–4.18 (m, 4H), 4.19–4.14 (m, 4H), 1.91–1.77 (m, 8H), 1.52–1.43 (m, 8H), 0.99–0.93 (m, 12H). ^{1}H NMR (DMSO-d_6) δ: 10.03 (s, 2H), 9.24 (s, 1H), 8.24 (s, 2H), 8.17 (d, J=2.8 Hz, 2H), 7.83 (dd, J_1=2.8 Hz, J_2=8.9 Hz, 2H), 7.23 (d, J=9.0 Hz, 2H), 6.87 (s, 1H), 4.27–4.23 (m, 4H), 4.17–4.13 (m, 4H), 1.85–1.69 (m, 8H), 1.49–1.35 (m, 8H), 0.94–0.88 (m, 12H). ^{13}C NMR ($CDCl_3$) δ: 162.4, 161.6, 161.5, 159.3, 152.8, 152.3, 145.0, 131.8, 124.0, 122.6, 122.5, 122.0, 120.9, 120.0, 115.0, 114.8, 114.3, 98.6, 69.2, 68.6, 30.7, 30.4, 18.5, 13.6. MS (MALDI-TOF): m/z 691 $[M+1]^+$, 713 $[M+Na]^+$, 729 $[M+K]^+$. HRMS (MALDI-TOF) Calcd for $C_{38}H_{51}N_4O_8$ $[M+H]^+$: 691.3687. Found: 691.3701.

4.1.4. Compound 10. Compound **10** was prepared as a white solid (95%) from the reaction of compound **7** and trifluoroacetic anhydride in THF according to the procedure described above for the preparation of **8**. ^{1}H NMR ($CDCl_3$) δ: 9.07 (s, 1H), 8.29 (dd, J_1=2.8 Hz, J_2=9.0 Hz, 1H), 8.22 (d, J=2.8 Hz, 1H), 7.04 (d, J=9.1 Hz, 1H), 4.23 (t, J=6.8 Hz, 2H), 1.95–1.90 (m, 2H), 1.48–1.43 (m, 2H), 0.96 (t, J=6.5 Hz, 3H). ^{19}F NMR ($CDCl_3$) δ: −76.03. MS (ESI): m/z 305 $[M]^+$. Anal. Calcd for $C_{13}H_{14}F_3NO_4$: C, 51.15; H, 4.62; N, 4.59. Found: C, 51.02; H, 4.70; N, 4.51.

4.1.5. Compound 3. Compound **3** was prepared as a white solid (65%) from the reaction of **10** and **11**[22b] according to the procedure described above for the preparation of **2**. ^{1}H NMR ($CDCl_3$) δ: 10.00 (s, 2H), 9.24 (s, 1H), 9.15 (s, 2H), 8.12–8.16 (m, 4H), 7.02 (d, J=9.8 Hz, 2H), 6.55 (s, 1H), 4.23–4.10 (m, 8H), 1.94–1.86 (m, 4H), 1.51–1.42 (m, 10H), 0.99–0.94 (m, 6H). ^{19}F NMR ($CDCl_3$) δ: −76.01. MS (MALDI-TOF): m/z 771 $[M+1]^+$, 793 $[M+Na]^+$, 809 $[M+K]^+$. HRMS (MALDI-TOF) Calcd for $C_{36}H_{41}N_4O_8F_6$: 771.2802. Found: 771.2823.

4.1.6. Compound 13. A solution of compounds **9** (0.51 g, 2.00 mmol), **12**[24a] (0.20 g, 1.00 mmol), DCC (0.45 g, 2.20 mmol) and HOBt (0.30 g, 2.20 mmol) in THF (25 mL) was stirred at room temperature for 12 h and then concentrated in vacuo. The resulting residue was triturated with chloroform (50 mL). The organic phase was then washed with saturated sodium bicarbonate solution (25 mL), water (25 mL×2), brine (25 mL) and dried over sodium sulfate. After the solvent was removed under reduced pressure, the crude product was purified by column chromatography (dichloromethane/acetone 100:1 to 50:1) to give **13** as a pale yellow solid (0.40 g, 65%). ^{1}H NMR ($CDCl_3$) δ: 9.65 (s, 1H), 8.21 (d, J=7.8 Hz, 2H), 8.04 (s, 2H), 7.39 (t, J=7.8 Hz, 1H), 6.52 (s, 2H), 4.01–3.96 (m, 11H), 3.65 (s, 4H), 1.85–1.72 (m, 8H), 1.59–1.38 (m, 8H), 1.02–0.97 (m, 6H), 0.90–0.85 (m, 6H). ^{13}C NMR ($CDCl_3$) δ: 162.4, 155.9, 143.1, 141.2, 134.7, 130.1, 128.6, 125.2, 121.7, 108.7, 99.4, 69.9, 68.8, 64.2, 31.5, 19.4, 19.2, 13.9, 13.8. MS (MALDI-TOF): m/z 687 $[M+Na]^+$. HRMS (MALDI-TOF) Calcd for $C_{37}H_{52}N_4O_7Na^+$ $[M+Na]^+$: 687.3733. Found: 687.3728.

4.1.7. Compound 15. A solution of compound **14** (0.84 g, 5.00 mmol), acetic anhydride (1.02 g, 10.0 mmol) and DMAP (10 mg) in THF (25 mL) was stirred at room temperature for 1 h. After workup, the crude product was subjected to column chromatography (AcOEt/petroleum ether 1:5) to give **15** as a white solid (0.84 g, 80%). ^{1}H NMR ($CDCl_3$) δ: 8.26 (dd, J_1=3.0 Hz, J_2=9.0 Hz, 1H), 7.85 (d, J=3.0 Hz, 1H), 7.06 (d, J=9.0 Hz, 1H), 4.08 (s, 3H), 2.20 (s, 3H). MS (EI): m/z 209 $[M]^+$. Anal. Calcd for $C_{10}H_{11}NO_4$: C, 57.41; H, 5.30; N, 6.70. Found: C, 57.29; H, 5.25; N, 6.60.

4.1.8. Compound 4. To a stirred solution of compounds **13** (0.14 g, 0.21 mmol) and **15** (0.094 g, 0.45 mmol) in DMF (10 mL) were added HATU (0.17 g, 0.45 mmol) and DIEA (0.1 mL). The mixture was stirred at room temperature for 12 h and then the solvent was removed under reduced pressure. The resulting residue was triturated with methanol (3 mL). The yellow precipitate formed was filtered, dried in vacuo and then subjected to column chromatography (CH_2Cl_2/AcOEt 10:1) to give **4** as a light-yellow solid (0.15 g, 68%). ^{1}H NMR ($CDCl_3$) δ: 10.18 (s, 2H), 9.57 (s, 2H), 9.43 (s, 2H), 8.27–8.20 (m, 6H), 7.94 (d, J=2.6 Hz, 2H), 7.40 (t, J=7.7 Hz, 1H), 6.98 (d, J=9.1 Hz, 2H), 6.53 (s, 2H), 4.06–3.99 (m, 17H), 2.16 (s, 6H), 1.86–1.72 (m, 8H), 1.60–1.39 (m, 8H), 1.02–0.97 (m, 6H), 0.90–0.85 (m, 6H). ^{13}C NMR ($CDCl_3$) δ: 169.1, 162.9, 162.3, 155.9, 153.6, 145.9, 134.8, 132.6, 128.5, 125.3, 125.2, 123.6, 122.2, 121.1, 120.3, 116.2, 112.1, 97.3, 69.0, 68.9, 64.3, 56.4, 31.5, 31.4, 24.3, 19.2, 13.8, 13.8. MS (MALDI-TOF): m/z 1047 $[M+H]^+$, 1069 $[M+Na]^+$. HRMS (MALDI-TOF) Calcd for $C_{57}H_{71}N_6O_{13}$ $[M+H]^+$: 1047.5072. Found: 1047.5074.

4.1.9. Compound 17. To a solution of aniline **6** (0.93 g, 4.20 mmol) in THF (20 mL) was added *n*-butyl isocyanide **16** (0.60 mL). The solution was stirred at room temperature

for 24 h and then concentrated in vacuo. The resulting residue was washed with ether thoroughly and the resulting solid subjected to column chromatography (petroleum ether/AcOEt 2:1) to give **17** as a white solid (1.00 g, 75%). ^{1}H NMR ($CDCl_3$) δ: 7.61 (d, J=2.8 Hz, 1H), 7.49 (dd, J_1=8.9 Hz, J_2=2.77 Hz, 1H), 7.27 (s, 1H), 6.92 (d, J=8.9 Hz, 1H), 6.44 (s, 1H), 4.77 (s, 1H), 4.00 (s, 2H), 3.87 (s, 3H), 3.24–3.20 (m, 2H), 1.94–1.75 (m, 2H), 1.57–1.46 (m, 4H), 1.39–1.26 (m, 2H), 0.99–0.88 (m, 6H). MS (EI): m/z 323 $[M+H]^+$. Anal. Calcd for $C_{17}H_{26}N_2O_4$: C, 63.33; H, 8.13; N, 8.69. Found: C, 63.20; H, 8.20; N, 8.52.

4.1.10. Compound 18. A solution of compound **17** (0.65 g, 2.00 mmol) and sodium hydroxide (0.24 g, 4.00 mmol) in THF (20 mL) and water (5 mL) was stirred at room temperature for 1 h and then hydrochloric acid (1 N) added to pH=6. The solvent was removed under reduced pressure and the resulting residue washed with cold water and dried in vacuo. The crude product was purified by flash chromatography (CH_2Cl_2/MeOH 20:1) to give **18** as a white solid (0.59 g, 95%). ^{1}H NMR ($CDCl_3$) δ: 11.40 (s, 1H), 8.31 (dd, J_1=9.0 Hz, J_2=2.9 Hz, 1H), 7.71 (d, J=2.9 Hz, 1H), 7.60 (s, 1H), 7.02 (d, J=9.0 Hz, 1H), 5.55 (t, J=5.4 Hz, 1H), 4.27–5.22 (m, 2H), 3.30–3.25 (m, 2H), 1.92–1.84 (m, 2H), 1.59–1.36 (m, 6H), 1.06–0.92 (m, 6H). MS (MALDI-TOF): m/z 309 $[M+H]^+$. Anal. Calcd for $C_{16}H_{24}N_2O_4$: C, 62.32; H, 7.84; N, 9.08. Found: C, 62.20; H, 7.94; N, 9.01.

4.1.11. Compound 5a. A solution of compound **18** (0.31 g, 1.00 mmol) and pentafluorophenol (0.18 g, 1.00 mmol), DCC (0.23 g, 1.10 mmol) and DMAP (20 mg) in dichloromethane (20 mL) was stirred at room temperature for 1 h. The solid formed was filtered off and the filtrate added to a stirred solution of diamine **19** (84 mg, 0.50 mmol) and HOBt (0.14 g, 1.00 mmol) in dichloromethane (20 mL). The solution was heated under reflux for 10 h and then cooled to room temperature. After workup, the crude product was purified by column chromatography ($CHCl_3$/MeOH 100:1–20:1) to give **5a** as a white solid (0.24 g, 80%). ^{1}H NMR (DMSO-d_6) δ: 10.52 (s, 2H), 9.45 (s, 1H), 8.47 (s, 2H), 7.93 (d, J=2.8 Hz, 2H), 7.74 (dd, J_1=8.8 Hz, J_2=3.0 Hz, 2H), 7.17 (d, J=9.0 Hz, 1H), 6.92 (s, 1H), 6.07 (t, J=5.9 Hz, 1H), 4.02 (s, 6H), 3.98 (s, 6H), 3.12–3.06 (m, 4H), 1.46–1.27 (m, 8H), 0.92–0.87 (m, 6H). MS (ESI): m/z 665 $[M+H]^+$, 687 $[M+Na]^+$.

4.1.12. Compound 21. To a solution of compound **20** (6.30 g, 41.0 mmol) and *n*-decyl bromide (11.0 g, 49.0 mmol) in acetonitrile (100 mL) was added potassium carbonate (14.0 g, 0.10 mol). The suspension was heated under reflux for 20 h and then concentrated under reduced pressure. The resulting residue was triturated with ethyl acetate (200 mL). The organic phase was washed with saturated sodium bicarbonate solution (100 mL), water (100 mL×2), brine (100 mL) and dried over sodium sulfate. Upon removal of the solvent under reduced pressure, the crude product was purified by column chromatography (petroleum ether/AcOEt 10:1) to afford **21** as colorless oil (11.8 g, 90%). ^{1}H NMR ($CDCl_3$) δ: 7.78 (dd, J=7.8 Hz, 1.6 Hz, 1H), 7.48–7.38 (m, 1H), 6.97 (dd, J_1=7.6 Hz, J_2=3.7 Hz, 1H), 4.05–4.01 (m, 2H), 3.89 (s, 3H), 1.88–1.78 (m, 2H), 1.51–1.28 (m, 14H), 0.89 (t, J=6.5 Hz, 3H). MS (EI): m/z 293 $[M+H]^+$. Anal. Calcd for $C_{18}H_{28}O_3$: C, 73.93; H, 9.65. Found: C, 73.81; H, 9.80.

4.1.13. Compound 22. To a stirred solution of compound **21** (12.9 g, 44.0 mmol) in concd sulfuric acid (98%, 30 mL), cooled in ice bath, was added dropwise a mixture of concd nitric acid (4 mL) and concd sulfuric acid (15 mL). The mixture was stirred at room temperature for 2 h and then poured into ice water (400 mL). The precipitate formed was filtered, washed with water and dissolved with ether (200 mL). The organic phase was washed with aqueous sodium hydroxide solution (0.5 N, 50 mL), water (100 mL× 2), brine (100 mL) and dried over sodium sulfate. Upon removal of the solvent under reduced pressure, the resulting residue was purified by flash chromatography (petroleum ether/AcOEt 10:1) to give **22** as a yellow solid (10.1 g, 80%). ^{1}H NMR ($CDCl_3$) δ: 8.70 (d, J=2.9 Hz, 1H), 8.34 (dd, J=9.2 Hz, 2.9 Hz, 1H), 7.04 (d, J=9.2 Hz, 1H), 4.15 (t, 2H), 3.93 (s, 3H), 2.14–1.68 (m, 2H), 1.59–1.17 (m, 14H), 0.89 (t, J=6.4 Hz, 3H). MS (EI): m/z 338 $[M+H]^+$. Anal. Calcd for $C_{18}H_{27}NO_5$: C, 64.07; H, 8.07; N, 4.15. Found: C, 63.92; H, 8.21; N, 4.09.

4.1.14. Compound 23. To a solution of compound **22** (6.76 g, 20.0 mmol) in THF (10 mL) and methanol (100 mL) was added a solution of sodium hydroxide (1.80 g, 40.0 mmol) in water (40 mL). The mixture was added at room temperature for 12 h and then neutralized with hydrochloric acid to pH=5. The solvent was distilled under reduced pressure and the resulting residue triturated with ethyl acetate (100 mL). After workup, the crude product was purified by recrystallization from ethyl acetate to afford **23** as a pale yellow solid (5.49 g, 85%). ^{1}H NMR ($CDCl_3$) δ: 9.05 (d, J=3.0 Hz, 1H), 8.44 (dd, J_1=9.3 Hz, J_2=3.0 Hz, 1H), 7.17 (d, J=9.3 Hz, 1H), 4.38–4.33 (m, 2H), 2.00–1.95 (m, 2H), 1.54–1.30 (m, 14H), 0.90–0.86 (t, J=6.8 Hz, 3H). MS (EI): m/z 323 $[M]^+$. Anal. Calcd for $C_{17}H_{25}NO_5$: C, 63.14; H, 7.79; N, 4.33. Found: C, 62.95; H, 7.87; N, 4.26.

4.1.15. Compound 24. A solution of compound **23** (3.23 g, 10.0 mmol), oxalyl chloride (6 mL, 24 mmol) and DMF (0.05 mL) in benzene (60 mL) was stirred at room temperature for 1 h and then concentrated under reduced pressure. The resulting residue **24** was dissolved in dichloromethane (40 mL). The solution was used for the next step.

4.1.16. Compound 25. To a stirred solution of **19** (0.84 g, 5.00 mmol) and triethylamine (1.10 mL, 10.0 mmol) in dichloromethane (20 mL) was added the above solution of **24** in dichloromethane. The mixture was stirred at room temperature for 2 h and then another part of dichloromethane was (50 mL) added. The solution was washed with dilute hydrochloric acid (1 N, 20 mL), saturated sodium bicarbonate solution (20 mL), water (25 mL×2), brine (25 mL) and then dried over sodium sulfate. After the solvent was removed under reduced pressure, the resulting residue was subjected to column chromatography (CH_2Cl_2/EtOAc 15:1) to give **25** as a yellow solid (3.50 g, 90%). ^{1}H NMR ($CDCl_3$) δ: 9.93 (s, 2H), 9.66 (s, 1H), 9.30 (d, J=2.7 Hz, 2H), 8.31 (dd, J_1=9.2 Hz, J_2=2.6 Hz, 2H), 7.10 (d, J=9.1 Hz, 2H), 6.57 (s, 1H), 4.33–4.29 (m, 4H), 3.93 (s, 6H), 2.72–1.59 (m, 4H), 1.65–1.14 (m, 32H), 0.86 (t, J=6.4 Hz, 6H). MS (ESI): m/z 779 $[M+H]^+$. Anal. Calcd For $C_{42}H_{58}N_4O_{10}$: C, 64.76; H, 7.51; N, 7.19. Found: C, 64.65; H, 7.62; N, 7.14.

4.1.17. Compound 26. A suspension of compound **25** (2.33 g, 3.00 mmol) and Pd–C (0.2 g, 10%) in THF (100 mL) was stirred under the atmosphere of hydrogen gas (40 atm) in an autoclave for 20 h. The solid was then filtered and the filtrate concentrated under reduced pressure. The resulting residue was subjected to column chromatography (chloroform/methanol 20:1) to give **26** as a pale yellow solid (2.05 g, 95%). ^{1}H NMR ($CDCl_3$) δ: 10.23 (s, 2H), 9.52 (s, 1H), 7.70 (d, J=2.7 Hz, 2H), 6.83–6.79 (m, 4H), 6.55 (s, 1H), 4.12–4.07 (m, 4H), 3.90 (s, 6H), 3.56 (br, 4H), 1.94–1.86 (m, 4H), 1.46–1.25 (m, 28H), 0.89–0.85 (m, 6H). MS (ESI): *m/z* 719 $[M+H]^+$, 741 $[M+Na]^+$, 757 $[M+K]^+$. Anal. Calcd for $C_{42}H_{62}N_4O_6$: C, 70.16; H, 8.69; N, 7.79. Found: C, 69.73; H, 8.68; N, 7.67.

4.1.18. Compound 5c. To a solution of compound **26** (0.19 g, 0.27 mmol) in THF (5 mL) was added *n*-butyl isocyanide **16** (60 mg, 0.60 mmol). The solution was stirred at 40 °C for 12 h and then concentrated under reduced pressure. The resulting residue was washed with ether thoroughly and then purified by recrystallization from methanol and chloroform to afford **5c** as a white solid (0.11 g, 55%). ^{1}H NMR ($CDCl_3$) δ: 10.48 (s, 2H), 9.18 (s, 1H), 8.23 (d, J=8.1 Hz, 2H), 7.96 (s, 2H), 7.86 (s, 2H), 6.88 (d, J=9.0 Hz, 2H), 6.58 (s, 1H), 5.79 (s, 2H), 4.12–4.06 (m, 4H), 3.92 (s, 6H), 2.75 (s, 4H), 1.95–1.90 (m, 4H), 1.60–0.97 (m, 32H), 0.88 (t, J=6.4 Hz, 6H), 0.79 (t, J=6.3 Hz, 6H). MS (ESI): *m/z* 916 $[M]^+$. HRMS (ESI) Calcd for $C_{52}H_{80}N_6O_8$: 916.6038. Found: 916.6054.

4.1.19. Compound 5b. Compound **5b** was prepared as a white solid (50%) from the reaction of compound **26** and methyl isocyanide in THF under similar conditions. ^{1}H NMR ($CDCl_3$) δ: 10.49 (s, 2H), 9.08 (s, 1H), 8.25 (d, J=9.10 Hz, 2H), 8.00 (s, 2H), 7.87 (s, 2H), 6.91 (d, J=9.7 Hz, 2H), 6.63 (s, 1H), 5.53 (s, 2H), 4.15–4.10 (m, 4H), 3.93 (s, 6H), 2.30 (s, 4H), 1.96–1.90 (m, 4H), 1.48–1.26 (m, 30H), 0.89–0.85 (m, 6H). MS (ESI): *m/z* 833 $[M+H]^+$, 855 $[M+Na]^+$, 871 $[M+K]^+$. Anal. Calcd for $C_{46}H_{68}N_6O_8$: C, 66.32; H, 8.23; N, 10.09. Found: C, 66.12; H, 8.25; N, 9.92.

4.1.20. Compound 27. A solution of compound **14** (1.67 g, 10.0 mmol) and *n*-butyl isocyanide **16** (1.22 mL, 10.0 mmol) in THF was stirred at room temperature for 24 h. The solvent was removed under reduced pressure and the resulting residue washed with ether thoroughly. The crude product was purified by recrystallization from THF to give **27** as a white solid (1.55 g, 70%). ^{1}H NMR ($CDCl_3$) δ: 8.30 (dd, J_1=9.0 Hz, J_2=3.0 Hz, 1H), 7.72 (d, J=3.0 Hz, 1H), 7.35 (s, 1H), 7.03 (d, J=9.0 Hz, 1H), 5.36–5.32 (m, 1H), 4.08 (s, 3H), 3.31–3.24 (m, 2H), 1.58–1.50 (m, 2H), 1.46–1.36 (m, 2H), 0.97–0.92 (t, J=6.4 Hz, 3H). MS (EI): *m/z* 266 $[M]^+$. Anal. Calcd for $C_{13}H_{18}N_2O_4$: C, 58.63; H, 6.81; N, 10.52. Found: C, 58.49; H, 6.85; N, 10.46.

4.1.21. Compound 30. A solution of compound **27** (0.13 g, 1.00 mmol), pentafluorophenol (0.10 g, 1.00 mmol), DCC (0.27 g, 1.00 mmol) and DMAP (10 mg) in chloroform (20 mL) was stirred at room temperature for 1 h. The solid formed was filtered off. The filtrate, the solution of compound **28**, was added to a solution of compound **29**[24a] (0.15 g, 0.50 mmol) and HOBt (0.14 g, 1.00 mmol) in chloroform (20 mL). The solution was heated under reflux for 24 h and then washed with hydrochloric acid (0.5 N, 10 mL), saturated sodium bicarbonate solution (15 mL), water (15 mL), brine (15 mL) and dried over sodium sulfate. After the solvent was removed under reduced pressure, the resulting residue was purified by column chromatography to give **30** as a white solid (0.39 g, 70%). ^{1}H NMR ($CDCl_3$) δ: 10.32 (s, 1H), 10.30 (s, 1H), 9.42 (s, 1H), 8.34 (d, J=8.3 Hz, 1H), 8.04 (dd, J_1=9.1 Hz, J_2=2.9 Hz, 1H), 7.87 (d, J=2.7 Hz, 1H), 7.48 (t, J=7.5 Hz, 2H), 7.12 (t, J=7.6 Hz, 1H), 7.03 (d, J=8.3 Hz, 1H), 6.94 (d, J=8.8 Hz, 1H), 6.58 (s, 1H), 5.41–5.38 (m, 1H), 4.06 (s, 3H), 4.00 (s, 3H), 3.96 (s, 3H), 3.93 (s, 3H), 3.01–2.94 (m, 2H), 1.29–1.14 (m, 4H), 0.82–0.77 (m, 3H). MS (MALDI-TOF): *m/z* 551 $[M+H]^+$. Anal. Calcd for $C_{29}H_{34}N_4O_7$: C, 63.26; H, 6.22; N, 10.18. Found: C, 63.08; H, 6.31; N, 10.14.

4.2. The determination of binding constants

The methods have been reported in a previous paper.[11]

Acknowledgements

We thank the National Natural Science Foundation of China (20321202, 20372080, 20332040, 20425208, 20572126) and Chinese Academy of Sciences for financial support.

References and notes

1. Horton, R. H.; Moran, L. A.; Ochs, R. S.; Rawn, D. J.; Scrimgeour, G. K. *Principles of Biochemistry*; Prentice Hall International: London, 1992; 826 pp.
2. Venkatraman, J.; Shankaramma, S. C.; Balaram, P. *Chem. Rev.* **2001**, *101*, 3131–3152.
3. (a) Zimmerman, S. C.; Corbin, P. S. *Struct. Bonding* **2000**, *96*, 63–94; (b) Archer, E. A.; Gong, H.; Krische, M. J. *Tetrahedron* **2000**, *57*, 1139–1159; (c) Gong, B. *Synlett* **2001**, 582–589; (d) Lehn, J.-M. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4763–4768; (e) Raehm, L.; Hamilton, D. G.; Sanders, J. K. M. *Synlett* **2002**, 1743–1761; (f) Würthner, F. *Chem. Commun.* **2004**, 1564–1579; (g) Zhan, C.; Léger, J.-M.; Huc, I. *Angew. Chem., Int. Ed.* **2006**, *45*, 4625–4628.
4. (a) Guelev, V.; Sorey, S.; Hoffman, D.; Iverson, B. L. *J. Am. Chem. Soc.* **2002**, *124*, 2864–2865; (b) Gabriel, G. J.; Iverson, B. L. *J. Am. Chem. Soc.* **2002**, *124*, 15174–15175.
5. Zhou, Q.-Z.; Jiang, X.-K.; Shao, X.-B.; Chen, G.-J.; Jia, M.-X.; Li, Z.-T. *Org. Lett.* **2003**, *5*, 1955–1958.
6. (a) Lawrence, D. S.; Jiang, T.; Levitt, M. *Chem. Rev.* **1995**, *95*, 2229–2260; (b) Conn, M. M.; Rebek, J., Jr. *Chem. Rev.* **1997**, *97*, 1647–1668; (c) Brunsveld, L.; Folmer, B. J. B.; Meijer, E. W.; Sijbesma, R. P. *Chem. Rev.* **2001**, *101*, 4071–4098; (d) Schmuck, C.; Wienand, W. *Angew. Chem., Int. Ed.* **2001**, *40*, 4363–4369; (e) Sijbesma, R. P.; Meijer, E. W. *Chem. Commun.* **2003**, 5–17; (f) Shenhar, S.; Rotello, V. M. *Acc. Chem. Res.* **2003**, *36*, 549–561; (g) Lukin, O.; Vögtle, F. *Angew. Chem., Int. Ed.* **2005**, *44*, 1456–1477.
7. (a) Lüning, U.; Kühl, C. *Tetrahedron Lett.* **1998**, *39*, 5735–5738; (b) Beijer, F. H.; Kooijman, H.; Spek, A. L.; Sijbesma, R. P.; Meijer, E. W. *Angew. Chem., Int. Ed.* **1998**, *37*, 75–78; (c) Sessler, J. L.; Wang, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 1726–1729; (d) Beijer, F. H.; Sijbesma, R. P.; Kooijman, H.; Spek, A. L.; Meijer, E. W. *J. Am. Chem. Soc.* **1998**, *120*,

6761–6769; (e) Corbin, P. S.; Zimmerman, S. C. *J. Am. Chem. Soc.* **1998**, *120*, 9710–9711; (f) Gong, B.; Yan, Y.; Zeng, H.; Skrzypczak-Jankunn, E.; Kim, Y. W.; Zhu, J.; Ickes, H. *J. Am. Chem. Soc.* **1999**, *121*, 5607–5608; (g) Park, T.; Zimmerman, S. C.; Nakashima, S. *J. Am. Chem. Soc.* **2005**, *127*, 6520–6521; (h) Park, T.; Todd, E. M.; Nakashima, S.; Zimmerman, S. C. *J. Am. Chem. Soc.* **2005**, *127*, 18133–18142; (i) Ong, H. C.; Zimmerman, S. C. *Org. Lett.* **2006**, *8*, 1589–1592.

8. (a) Zeng, H.; Yang, X.; Flowers, R. A.; Gong, B. *J. Am. Chem. Soc.* **2002**, *124*, 2903–2910; (b) Yang, X. W.; Gong, B. *Angew. Chem., Int. Ed.* **2005**, *44*, 1352–1356.
9. Nowick, J. S.; Chung, D. M. *Angew. Chem., Int. Ed.* **2003**, *42*, 1765–1768.
10. (a) Archer, E. A.; Sochia, A. E.; Krische, M. J. *Chem.—Eur. J.* **2001**, *7*, 2059–2066; (b) Archer, E. A.; Cauble, D. F., Jr.; Lynch, V.; Krische, M. J. *Tetrahedron* **2002**, *58*, 721–725; (c) Archer, E. A.; Krische, M. J. *J. Am. Chem. Soc.* **2002**, *124*, 5074–5083; (d) Gong, H.; Krische, M. J. *J. Am. Chem. Soc.* **2005**, *127*, 1719–1725.
11. Zhao, X.; Wang, X.-Z.; Jiang, X.-K.; Chen, Y.-Q.; Li, Z.-T.; Chen, G.-J. *J. Am. Chem. Soc.* **2003**, *125*, 15128–15139.
12. Hydrogen bonded duplexes from unpreorganized monomers have been reported, see: (a) Bisson, A. P.; Carver, F. J.; Eggleston, D. S.; Haltiwanger, R. C.; Hunter, C. A.; Livingstone, D. L.; McCabe, J. F.; Rotger, C.; Rowan, A. E. *J. Am. Chem. Soc.* **2000**, *122*, 8856–8868.
13. For reviews, see: (a) Gellman, S. H. *Acc. Chem. Res.* **1998**, *31*, 173–180; (b) Stigers, K. D.; Soth, M. J.; Nowick, J. S. *Curr. Opin. Chem. Biol.* **1999**, *3*, 714–721; (c) Hill, D. J.; Mio, M. J.; Prince, R. B.; Hughes, T. S.; Moore, J. S. *Chem. Rev.* **2001**, *101*, 3893–4012; (d) Cubberley, M. S.; Iverson, B. L. *Curr. Opin. Chem. Biol.* **2001**, *5*, 650–654; (e) Schmuck, C. *Angew. Chem., Int. Ed.* **2003**, *42*, 2448–2452; (f) Huc, I. *Eur. J. Org. Chem.* **2004**, 17–29; (g) Cheng, R. P. *Curr. Opin. Struct. Biol.* **2004**, *14*, 512–520; (h) Sanford, A.; Yamato, K.; Yang, X. W.; Yuan, L. H.; Han, Y. H.; Gong, B. *Eur. J. Biochem.* **2004**, *271*, 1416–1425; (i) Licini, G.; Prins, L. J.; Scrimin, P. *Eur. J. Org. Chem.* **2005**, 969–977; (j) Stone, M. T.; Heemstra, J. M.; Moore, J. S. *Acc. Chem. Res.* **2006**, *39*, 11–20.
14. Hamuro, Y.; Geib, S. J.; Hamilton, A. D. *J. Am. Chem. Soc.* **1996**, *118*, 7529–7541.
15. (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) Mayer, M. F.; Nakashima, S.; Zimmerman, S. C. *Org. Lett.* **2005**, *7*, 3005–3008; (c) Violette, A.; Averlant-Petit, M. C.; Semetey, V.; Hemmerlin, C.; Casimir, R.; Graff, R.; Marraud, M.; Rognan, D.; Guichard, G. *J. Am. Chem. Soc.* **2005**, *127*, 2156–2164; (d) Sinkeldam, R. W.; van Houtem, M. H. C. J.; Koeckelberghs, G.; Vekemans, J. A. J. M.; Meijer, E. W. *Org. Lett.* **2006**, *8*, 383–386.
16. (a) Yang, X. W.; Martinovic, S.; Smith, R. D.; Gong, B. *J. Am. Chem. Soc.* **2003**, *125*, 9932–9933; (b) Yang, X. W.; Yuan, L. H.; Yamato, K.; Brown, A. L.; Feng, W.; Furukawa, M.; Zeng, X. C.; Gong, B. *J. Am. Chem. Soc.* **2004**, *126*, 3148–3162.
17. Kolomiets, E.; Berl, V.; Odriozola, I.; Stadler, A.-M.; Kyritsakas, N.; Lehn, J.-M. *Chem. Commun.* **2003**, 2868–2869.
18. Recker, J.; Tomcik, D.; Parquette, J. R. *J. Am. Chem. Soc.* **2000**, *122*, 10298–10307.
19. (a) Hunter, C. A.; Spitaleri, A.; Tomas, S. *Chem. Commun.* **2005**, 3691–3693; (b) Hu, Z.-Q.; Hu, H.-Y.; Chen, C.-F. *J. Org. Chem.* **2006**, *71*, 1131–1138.
20. Kanamori, D.; Okamura, T.; Yamamoto, H.; Ueyama, N. *Angew. Chem., Int. Ed.* **2005**, *44*, 969–972.
21. Masu, H.; Sakai, M.; Kishikawa, K.; Yamamoto, M.; Yamaguchi, K.; Kohmoto, S. *J. Org. Chem.* **2005**, *70*, 1423–1431.
22. (a) Wu, Z.-Q.; Jiang, X.-K.; Zhu, S.-Z.; Li, Z.-T. *Org. Lett.* **2004**, *6*, 229–232; (b) Hou, J.-L.; Shao, X.-B.; Chen, G.-J.; Zhou, Y.-X.; Jiang, X.-K.; Li, Z.-T. *J. Am. Chem. Soc.* **2004**, *126*, 12386–12394; (c) Yi, H.-P.; Shao, X.-B.; Hou, J.-L.; Li, C.; Jiang, X.-K.; Li, Z.-T. *New J. Chem.* **2005**, *29*, 1213–1218; (d) Li, C.; Ren, S.-F.; Hou, J.-L.; Yi, H.-P.; Zhu, S.-Z.; Jiang, X.-K.; Li, Z.-T. *Angew. Chem., Int. Ed.* **2005**, *44*, 5725–5729; (e) Hou, J.-L.; Yi, H.-P.; Shao, X.-B.; Li, C.; Wu, Z.-Q.; Jiang, X.-K.; Wu, L.-Z.; Tung, C.-H.; Li, Z.-T. *Angew. Chem., Int. Ed.* **2006**, *45*, 796–800.
23. (a) Jiang, H.; Léger, J.-M.; Huc, I. *J. Am. Chem. Soc.* **2003**, *125*, 3448–3449; (b) Dolain, C.; Zhan, C.; Léger, J.-M.; Daniels, L.; Huc, I. *J. Am. Chem. Soc.* **2005**, *127*, 2400–2401.
24. (a) Zhu, J.; Wang, X.-Z.; Chen, Y.-Q.; Jiang, X.-K.; Chen, X.-Z.; Li, Z.-T. *J. Org. Chem.* **2004**, *69*, 6221–6227; (b) Wu, Z.-Q.; Shao, X.-B.; Li, C.; Hou, J.-L.; Wang, K.; Jiang, X.-K.; Li, Z.-T. *J. Am. Chem. Soc.* **2005**, *127*, 17460–17468.
25. Zhu, J.; Lin, J.-B.; Xu, Y.-X.; Shao, X.-B.; Jiang, X.-K.; Li, Z.-T. *J. Am. Chem. Soc.* **2006**, *128*, 12307–12313.
26. Ogata, M.; Matsumoto, H.; Kida, S.; Shiomi, T.; Eigyo, M.; Hirose, K. *J. Med. Chem.* **1984**, *27*, 1137–1141.
27. Moriyasu, M.; Kawanishi, K.; Kato, A.; Hashimoto, Y. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 1766–1770.
28. (a) Conners, K. A. *Binding Constants: The Measurement of Molecular Complex Stability*; Wiley: New York, NY, 1987; 432 pp; (b) Wilcox, C. S. *Frontiers in Supramolecular Organic Chemistry and Photochemistry*; Schneider, H.-J., Dürr, H., Eds.; VCH: New York, NY, 1991; p 123.
29. Tam, C. N.; Cowan, J. A.; Schultz, A. J.; Young, V. G., Jr.; Trouw, F. R.; Sykes, A. G. *J. Phys. Chem. B* **2003**, *107*, 7601–7606.
30. (a) Hof, F.; Craig, S. L.; Nuckolls, C.; Rebek, J., Jr. *Angew. Chem., Int. Ed.* **2002**, *41*, 1488–1508; (b) Rebek, J., Jr. *Acc. Chem. Res.* **1999**, *32*, 278–286.
31. Nguyen, T. L.; Fowler, F. W.; Lauher, J. W. *J. Am. Chem. Soc.* **2001**, *123*, 11057–11064.
32. Jadzyn, J.; Stockhausen, M.; Zywucki, B. *J. Phys. Chem.* **1987**, *91*, 754–757.