A programmed hydrogen bonding array self-assembles into a polymeric zipper-like architecture†

Yong Yang,[ab] Ya-Zhou Zhang,[ab] Ya-Lin Tang[a] and Chuan-Feng Chen*[a]

Received (in Durham, UK) 2nd November 2005, Accepted 22nd December 2005
First published as an Advance Article on the web 6th January 2006
DOI: 10.1039/b515559b

With two hydrazide motifs installed at one edge, a novel supramolecular system self-assembled into a polymeric zipper-like structure *via* two hydrogen bonds at each knot, both in solution and in the solid state.

Recently, Keinan *et al.* proposed a new kind of molecular zipper system, based on the results of first principles DFT calculations.[1] While similar to the polymeric zipper structure of natural DNA[2] and other artificial molecular zipper systems,[3,4] hydrogen bonding components and information-bearing components in this kind of zipper system are located on different moieties. So that the physical properties derived from this kind of supramolecular structure can be modified by alternating the information-bearing components, with the supramolecular structure preserved. Following a similar strategy, the present contribution reports a molecular zipper system of such kind, based on a programmed hydrogen bonding motif, from an experimental perspective. The design employs a relatively simple monomeric building block, in which two hydrogen bonding motifs at one edge, linked by a rigid spacer, are responsible for assembling the infinite supramolecular zipper structure (Scheme 1). Interestingly, another two supramolecular zipper-like structures, having π–π stacking and van der Waals interactions as locking forces, are observed in the solid state. All of the constituent functional moieties in **2** are advantageously used to bring about three noncovalent interactions which together result in a multilayer architecture.

Hydrazide derivatives,[5] like the related amides, have proven to be good hydrogen bonding acceptors and donors. We envisaged that this functional group might be ideally suited for constructing new supramolecular systems, such as supramolecular zippers. As an initial test of this proposal, the monofunctional hydrazide **1** was synthesized by coupling acetohydrazide with the corresponding benzoic acid derivative. Variable-temperature (40 °C to −50 °C) ^{1}H NMR experiments with **1** showed that the H^2 resonance (Fig. 1) shifts downfield with a large temperature coefficient (-2.41×10^{-2} ppm K^{-1}). The observation suggests that **1** might exist as a dimer in solution. Unequivocal evidence for this suggestion comes from the result of a 2D NOESY experiment which shows that contact exists between CH_3 and H^3. Diluting the solution of **1** (in chloroform-*d* from 200 mM to 0.5 mM) results in a strong concentration-dependent change in the chemical shift of H^2. Nonlinear regression analysis[7] of the concentration dependent data yields a dimerization constant for **1** of 15.6 ± 0.9 M^{-1}.

X-Ray crystallographic analysis also showed that **1** exists as a dimer *via* two C(4)[8] type intermolecular hydrogen bonds in the solid state (Fig. 1a). Highly favorable, S(6) type[8] hydrogen bonding causes this molecule to be almost planar. Bond length and angle parameters indicate that both the intra- and intermolecular hydrogen bonds are moderate to strong in the solid state.[9]

We set out to determine if the hydrazide based structural unit could be used as a reliable synthon[10] for constructing supramolecular zippers. For this purpose, the difunctional hydrazide **2** was prepared by employing a procedure similar to the one used to construct **1**.[6] The contrastingly poor solubility[11] of **2** in $CDCl_3$ (<6 mM, 25 °C for **2** *vs.* >200 mM, 25 °C for **1**) gave the first indication that **2** self-assembles to form a polymeric, zipper-like structure.[12,13] The observation of contact between CH_3 and H^3 in the 2D NOESY spectrum of **2** provides unequivocal evidence for its solution polymeric structure. The results of variable-temperature ^{1}H NMR experiments with **2** are very similar to those of the monofunctional counterpart **1**. From 40 °C to −50 °C, the signal of H^2, which is involved in intermolecular hydrogen bonding, shifts downfield with a large temperature coefficient (-1.94×10^{-2} ppm K^{-1}). In contrast, the signal of H^1, which participates in S(6) type hydrogen bonding, has a much smaller temperature coefficient (-3.4×10^{-3} ppm K^{-1}) over the same temperature range. The observation that the signal for H^2 broadens and shifts upfield when a solution of **2** is diluted from 5 to 0.5 mM, supports the proposed role it plays in intermolecular hydrogen bonding. Nonlinear regression analysis[7] of the NMR data yields an association constant for chain extension of the aggregate of 179.6 ± 38.6 M^{-1}. In mixing ^{1}H NMR experiments, H^2 signals for both **1** and **2** shift downfield, which might indicate that stronger hydrogen bonds between **1** and **2** formed. As a result, corruption of the dimeric and polymeric structures in solution occurs (Fig. 2).

As expected, **2** forms an infinite, hydrogen bonding guided, supramolecular zipper structure in the solid state. The X-ray crystallographic structure of this substance‡ validates this

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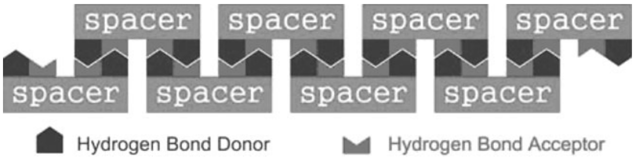
[a] *Laboratory of Chemical Biology, Center for Molecular Science, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100080, China. E-mail: cchen@iccas.ac.cn*
[b] *Graduate School, Chinese Academy of Sciences, Beijing 100039, China*

† Electronic supplementary information (ESI) available: Experimental preparations, NOESY spectra, diluting and variable-temperature ^{1}H NMR experimental data, packing diagrams and crystallographic data for **1** and **2** (CIF format). See DOI: 10.1039/b515559b



Scheme 1 Schematic representation of a supramolecular zipper structure locked by two hydrogen bonds at each knot.

conclusion (Fig. 1b and 3a). In a manner similar to **1**, the bond length and angle parameters (Fig. 1b) indicate that moderate to strong inter- and intramolecular hydrogen bonds exist in the solid state for **2**. Moreover, two strong S(6) type hydrogen bonds cause **2** to adopt a planar conformation. In addition, each molecule is fused to two adjacent molecules *via* two hydrogen bonds to form an infinite zipper. A dihedral angle of 37.0° exists between two adjacent molecules in **2**, whereas two neighboring molecules in the solid state dimer of **1** exist in a parallel orientation. Perhaps steric interactions caused by the methyl groups in **2** are responsible for the 37.0° tilted arrangement.

Careful examination of the crystal structures showed that the monofunctional molecule **1** adopts a 'simpler' packing pattern, forming a multilayer architecture that is devoid of any π–π stacking interactions.[6] However, the difunctional counterpart **2** employs a more sophisticated packing mode. Here, adjacent zippers have interdigitated aromatic rings oriented in an antiparallel fashion, forming a second supramolecular zipper (Fig. 3b). Strong face-to-face, center-to-edge (offset) π–π stacking[14] interactions are observed between two adjacent aromatic rings, with a vertical displacement of 3.516 Å and a horizontal displacement of 1.375 Å. Interestingly, only one face of the aromatic ring participates in π–π stacking. The planar conformation of the monomer facilitates this dense stacking. According to the results of a recent theoretical study,[15] this π–π stacking interaction should stabilize the first zipper structure locked by hydrogen bonding. Furthermore, the octyl side chains in **2** are also interdigitated[16] in the solid state, perhaps a consequence of van der Waals interactions. This results in a third supramolecular zipper (Fig. 3c). Hydrogen bonding and van der Waals interaction function alternatively, resulting in an infinite lamellar structure. Further π–π stacking of the lamellar structure results in a multilayer architecture. Thus, all the constituent parts of molecule **2** are utilized advantageously in creating a highly unique architecture.

In summary, we have developed a novel‡ supramolecular system, based on a bis(hydrazide) platform, that contains three types of infinite supramolecular zipper structures in the solid state. Formation of the supramolecular system is guided

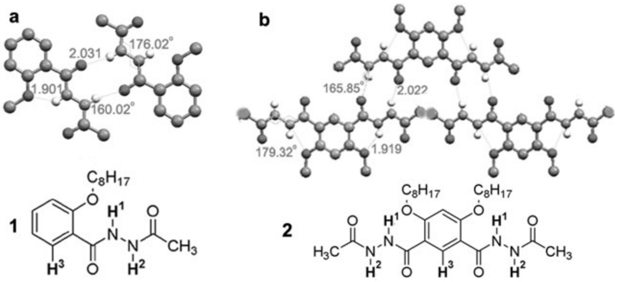


Fig. 1 Representation of intermolecular and intramolecular hydrogen bonds in the solid state. (a) Dimer structure of **1**, (b) supramolecular zipper structure of **2**. The octyl groups are replaced with methyl groups for clarity. Only hydrogen bonded hydrogen atoms are shown. Parameters of hydrogen bonds and torsion angles of C–N–N–C are also shown and the proton-labeling scheme is indicated.

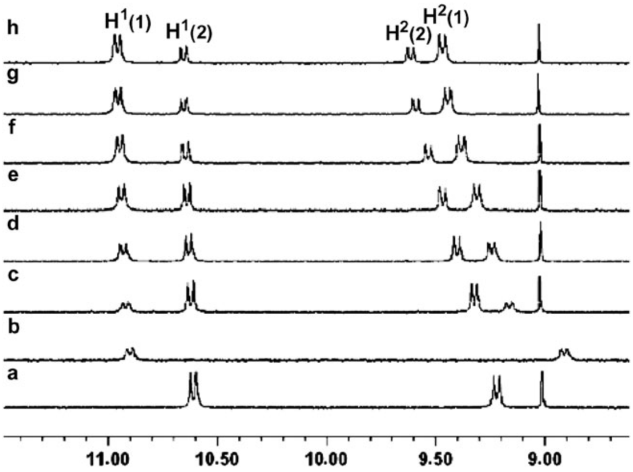


Fig. 2 Partial spectra of mixing ^{1}H NMR experiments. (a) **2** (2.5 mM), (b) **1** (2.5 mM), (c) **2** (2.5 mM) + **1** (2.5 mM), (d) **2** (2.5 mM) + **1** (5.0 mM), (e) **2** (2.5 mM) + **1** (7.5 mM), (f) **2** (2.5 mM) + **1** (10.0 mM), (g) **2** (2.5 mM) + **1** (12.5 mM), (h) **2** (2.5 mM) + **1** (15.0 mM).

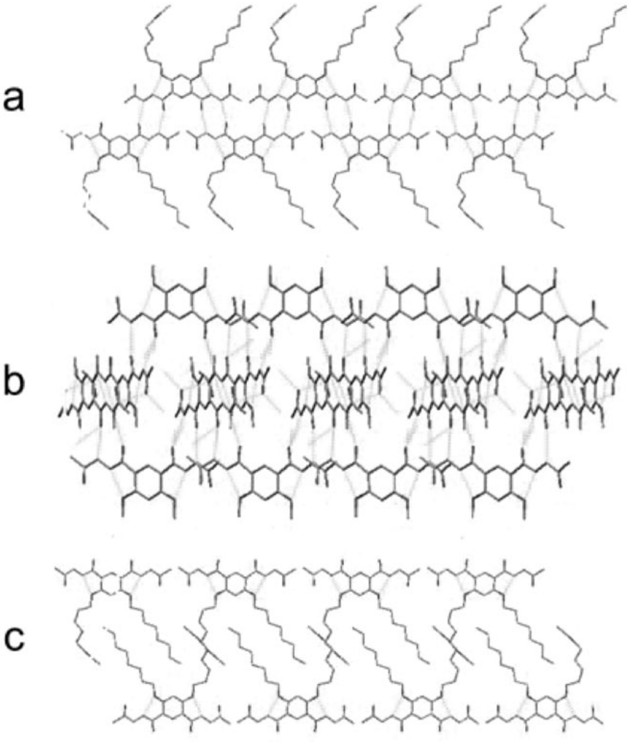


Fig. 3 Supramolecular zippers observed in the X-ray structure of **2**. (a) Zipper locked by hydrogen bonding. (b) Zipper locked by π–π stacking. For clarity, the octyl groups are replaced with methyl groups. (c) Zipper locked by van der Waals interaction.

by a combination of hydrogen bonding, π–π stacking and van der Waals interaction. We envision that this zipper system might serve as a good scaffold for the alignment and long-range ordering of functional entities as part of novel materials. Moreover, the abundant noncovalent interactions found in this supramolecular system could make it an ideal model for theoretical studies of cooperativity among multiple interactions that provide insight into understanding the polymeric zipper structure of DNA.

We thank the National Natural Science Foundation of China and the Chinese Academy of Sciences for financial support.

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‡ Crystal data for **1**: $C_{17}H_{26}N_2O_3$, $M_w = 306.40$, crystal size: $0.34 \times 0.30 \times 0.26$ mm^3, crystal system: monoclinic, space group: $P2_1/c$, $a = 8.329(2)$ Å, $b = 23.399(6)$ Å, $c = 9.458(3)$ Å, $\beta = 108.075(9)°$, $U = 1752.3(8)$ Å^3, $Z = 4$, $D_c = 1.161$ Mg m^{-3}, $T = 293(2)$ K, $\mu = 0.080$ mm^{-1}, 9000 reflections measured, 3090 unique ($R_{int} = 0.0270$), $R_1 = 0.0497$, w$R_2 = 0.1166$. Crystal data for **2**: $C_{28}H_{46}N_4O_6$, $M_w = 534.69$, crystal size: $0.20 \times 0.18 \times 0.14$ mm^3, crystal system: monoclinic, space group: $C2/c$, $a = 28.56(2)$ Å, $b = 14.706(10)$ Å, $c = 15.859(11)$ Å, $\beta = 113.10(2)°$, $U = 6127(8)$ Å^3, $Z = 8$, $D_c = 1.159$ Mg m^{-3}, $T = 293(2)$ K, $\mu = 0.081$ mm^{-1}, 15422 reflections measured, 5399 unique ($R_{int} = 0.1948$), $R_1 = 0.1250$, w$R_2 = 0.2706$. Numerous attempts to grow a better single crystal of **2** for X-ray analysis were unsuccessful. The disorder of the two octyl chains may account for the relatively high R factor. CCDC reference numbers 293557 and 293558. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b515559b

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