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Dynamic Decomposition/Recombination of Hydrogen Bonds in Molecular Duplex Strands

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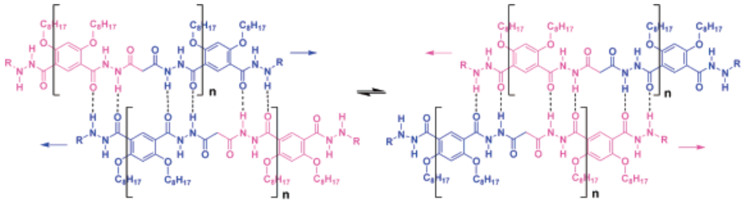
ABSTRACT



R = COOBu-*t*; n = 1, 2, 3

Dynamic decomposition/recombination of hydrogen bonds in the hydrazide based molecular duplex strands was explored by variable-temperature ^{1}H NMR experiments. A shuttle-like dynamic process of the two constituent molecules of the duplex strands between two degenerate states was observed.

The formation of duplex DNA via hydrophobic effects, hydrogen bonds, and $\pi-\pi$ stacking interactions represents one of the most elegant and best-known examples of self-assembly of biomolecules.[1] Other double- and multiple-stranded complexes self-assembled from linear oligomers with encoded recognition sites are ubiquitous in nature, which are the foundation of other higher structures and functions of biomolecules.[2] Inspired by their intriguing structures and functions, there is currently an intensive focus of chemical research on the construction of stable molecular duplex strands from hydrogen-bonding mediated assembly of unnatural backbones for structure mimicking and potential applications.[3−13] Investigations along this line will provide mimics of biomolecules and shed some light on the understanding of the complicated structures and functions as demonstrated by them. Eventually, new materials with functional properties can also be expected from these unnatural counterparts.

Dynamic decomposition/recombination of two complementary strands constituting double helical DNA is a prerequisite for accomplishment of its function as a genetic information carrier.[1] However, this important aspect is relatively untouched in artificial molecular duplex systems

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due to the lack of appropriate model systems. Recently, we reported a new family of helical molecular duplex strands[14] constructed from self-assembly of self-complementary oligomeric hydrazide derivatives **A1**−**A4** and **B1**−**B4**. Extensive studies revealed different molecular dynamics and association constants for the methyl-terminated oligomers **A1**−**A4** and Boc-terminated oligomers **B1**−**B4** (Figure 1).

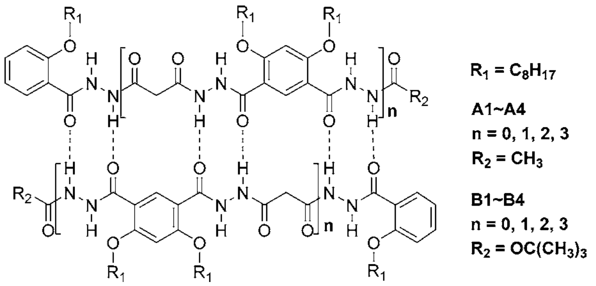

Figure 1. Representation of helical molecular duplex strands from self-complementary hydrazide based oligomers **A1**−**A4** and **B1**−**B4**.

In this Letter, we report a new kind of di-Boc-terminated oligomers **C1**−**C4** (Figure 2), which have abundant hydrogen-bonding sites in addition to forming duplex strands. Consequently, variable-temperature ^{1}H NMR experiments reveal a shuttle-like dynamic process of the two constituent molecules of the duplex strands based on dynamic decomposition and recombination of hydrogen bonds between two degenerate states.

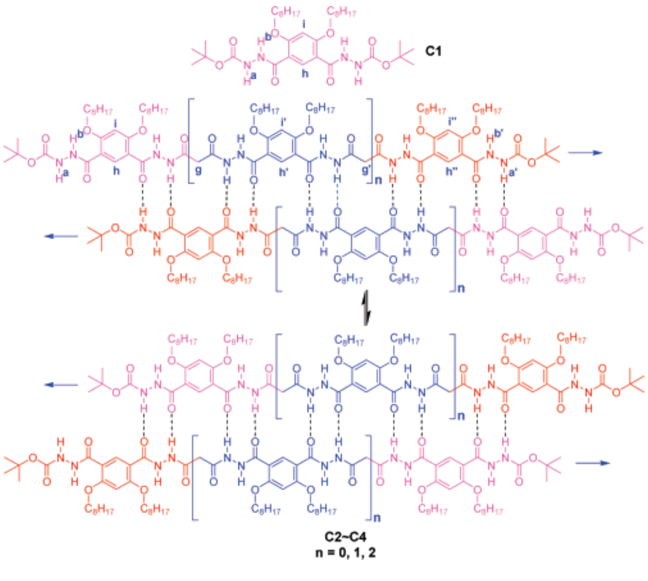

Figure 2. Representation of shuttle-like dynamic processes of **C2**−**C4**, with the proton-labeling scheme and the chemical structure of **C1** indicated.

No obvious association was observed for the di-Boc-terminated monomer **C1**, in which NHs exhibited two signals at 9.37 (H^b) and 6.99 ppm (H^a) (Figure 3a). For the di-Boc-terminated longer oligomers **C2**−**C4**, a multiple hydrogen bond mediated dimerization mode was undoubtedly established by 2D NOESY experiments.[15] Extensive cross contacts were observed between intercarbonyl aromatic protons (designated as the *h* zone) and methylene protons of malonyl groups (designated as the *g* zone).

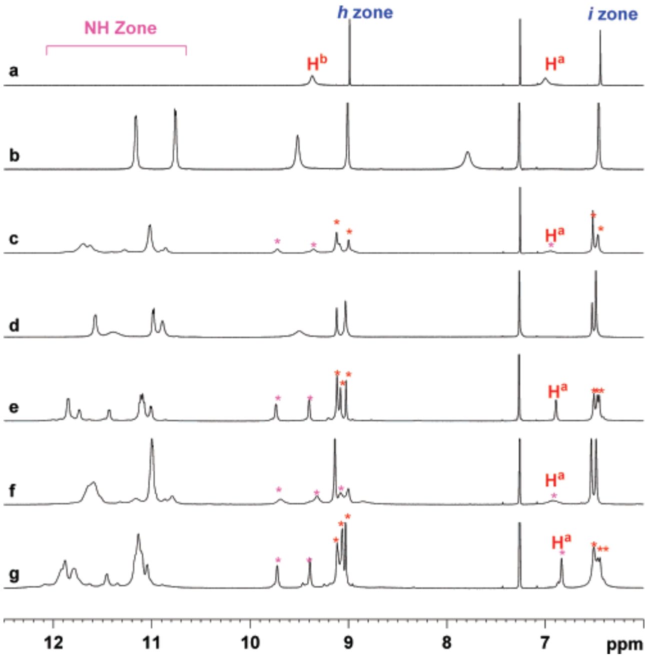

Figure 3. Stacked partial ^{1}H NMR spectra of (a) **C1** (298 K), (b) **C2** (293 K), (c) **C2** (223 K), (d) **C3** (298 K), (e) **C3** (223 K), (f) **C4** (318 K), and (g) **C4** (223 K), each 10 mM in CDCl$_3$, 600 MHz.

Variable-temperature ^{1}H NMR studies on **C2**−**C4** exhibited unique molecular dynamics in CDCl$_3$ solution. Unlike structure-similar mono-Boc-terminated oligomers **B1**−**B4**, shuttle-like dynamic processes were observed for **C2**−**C4** (Figure 3). At room temperature (298 K), **C2** exhibits the spectrum of a compound of C_2 symmetry (Figure 3b). With lowering of the temperature, signals corresponding to NHs broadened. At 223 K, a new broad signal at about 6.95 ppm appeared, a position typical of NHs adjacent to the Boc group not involved in hydrogen bonding; three new broad signals also appeared in the area between 9 and 10 ppm; signals for the inter-carbonyl aromatic protons (designated as the *h* zone) and the inter-octyloxy aromatic protons (designated as the *i* zone) each exhibited two peaks (Figure 3c). The whole spectrum corresponded to the centrodimeric structure with *i* symmetry. This molecular dynamics is accounted for by a

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[15] See the Supporting Information for more details.

shuttle-like dynamic process based on the decomposition and recombination of hydrogen bonds between two degenerate states as shown in Figure 2. At lower temperatures, the shuttle-like dynamic process was prohibited or slowed on the NMR time scale. With the strand extension to trimer **C3**, different results were obtained. At 298 K, the whole spectrum corresponded to a compound of C_2 symmetry (Figure 3d). The aromatic protons displayed two sets of signals, one at about 9 ppm (*h* zone) and one at about 6.5 ppm (*i* zone), each two peaks with an intensity ratio of 1:2. The NHs exhibited broad signals. With lowering of the temperature, contrary to that observed for dimer **C2**, signals corresponding to NHs sharpened. From 283 K on a new signal at about 6.91 ppm began to appear and from 243 K on signals corresponding to aromatic protons began to exhibit three peaks with an intensity ratio of 1:1:1 for each set (Figure 3e).

These findings can also be attributed to prohibition or slowing of the shuttle-like dynamic process. At room temperature, H^a and $H^{a'}$ are partly involved in intermolecular hydrogen bonding due to the shuttle-like dynamic process. But at lower temperature, one is fully involved while the other is not involved in intermolecular hydrogen bonding and the exchange processes are slow on the NMR time scale. The differences between **C2** and **C3** might come from different hydrogen-bonding strengths: six hydrogen bonds vs ten hydrogen bonds. Even at elevated temperature (318 K), tetramer **C4** exhibited a spectrum corresponding to the centrodimeric structure with *i* symmetry (Figure 3g), which might mean that with 14 interstrand hydrogen bonds, disruption and recombination of the duplex strands is difficult or slow on the NMR time scale even at this relatively high temperature. While ^{1}H NMR spectra[15] of **C2**−**C4** in DMSO-d_6 all corresponded to compounds of C_2 symmetry, which might mean that they existed as monomers in this hydrogen-bonding competitive solvent. Coalesced temperatures for **C2**, **C3**, and **C4** were determined to be 223, 283, and >318 K, respectively. ^{1}H NMR dilution experiments[16] gave a dimerization constant of $(1.6 \pm 0.7) \times 10^3$ M^{-1} for **C2·C2** at 298 K. Due to signal overlapping and broadening at room temperature, association constants for longer oligomers were not determined by the NMR method. Molecular mechanical calculations revealed double-helical conformations for the duplex strands.[17] The result for **C4·C4** was provided in Figure 4.

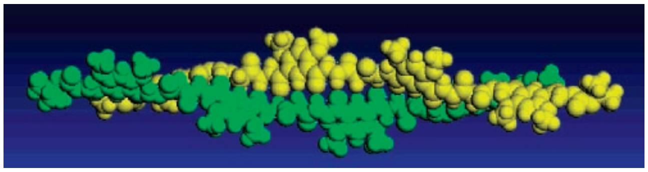

Figure 4. Energy-minimized conformation of **C4·C4**. For convenience, the long octyl groups were replaced by methyl groups.

In conclusion, we have presented here a new class of molecular duplex strands from hydrogen-bonding-mediated self-assembly of di-Boc terminated hydrazide oligomers, and for the first time systematically explored dynamic decomposition/recombination of hydrogen bonds in the artificial supramolecular duplex strands by variable-temperature ^{1}H NMR experiments. We believe that the results we provided here will give some hint on how to understand dynamic behavior of natural DNA and other hydrogen bonded double/multiple-stranded complexes found in biological systems.

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Supporting Information Available: Experimental preparations, NOESY spectra, stacked variable-temperature ^{1}H NMR spectra, energy-minimized conformations, and determination of dimerization constant for **C2·C2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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