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The ability of DNA to store information through duplex formation has been widely exploited in nanotechnology for preparation of programmable building materials.¹ Modified versions of DNA have been prepared, where the phosphate linker² or the sugar ring³ or the base paring⁴ system have been replaced, and these systems all form stable duplexes. This suggests that it might be possible to make completely different information oligomers, which will be able to manipulate chemical information through sequence selective duplex formation.

Design

Basic requirements for duplex formation and template directed synthesis are a recognition-based pairing system and a polymeric backbone that allows complementary recognition sites on the two chains to reach each other. We propose a fully synthetic information system where H-bond acceptor (A) or H-bond donor (D) moieties are linked together through reductive amination to form oligomers. The presence on the backbone of long alkyl chains makes these molecules soluble in organic solvents. Sequence complementary oligomers will form a stable duplex.^{5,6}



Figure 1 a) Schematic representation of how, by stripping down the DNA molecule to its basic constituents, a synthetic information oligomer able to form a stable duplex has been designed; b) The equilibrium between free oligomers and fully bound duplex. The equilibrium constant K_N depends on the association constant for the formation of one H-bond K₁ the effective molarity (EM).

Synthesis of oligomers

Oligomers were prepared stepwise via iterative reductive amination and acetal deprotection steps starting from monomer 1. The pyridine N-oxide 4-mer proved difficult to obtain by this route and was therefore prepared by direct oligomerisation of compound 1. Reverse phase chromatography was used to separate the mixture of oligomers obtained.



Duplex formation

- Association constants of all the complementary complexes, An•Dn, were measured in toluene via ¹H and ³¹P NMR titrations. A uniform increase of an order of magnitude for each additional H-bond formed is observed, indicating cooperative duplex formation (Figure 2a).
- Cooperativity for the duplex formation is quantified by the product K₁EM, where K₁ is the association constant for the 1-mer interaction and EM is the effective molarity. Pyridine N-oxide oligomers are the most cooperative ones as the single point phenol-pyridine N-oxide H-bond is rigid (high EM) and strong (logK₁ = 2.5).
- Denaturation experiments data for phosphine oxide oligomers are shown in Figure 2b. Higher values of number of H-bonds that can be formed (N) are associated with an increase in the transition melting temperature. These features are characteristic of cooperative interactions between the H-bonding sites along the duplex.
- Single crystal X-ray structure of phenol-pyridine N-oxide 2-mer duplex is shown in Figure 3. Each molecule is arranged in an antiparallel conformation relative to another molecule and adopts an H-bonded duplex structure, where two H-bonds are formed with the same connectivity.





Figure 2 a) Association constants for duplex formation K_N plotted as a function of the number of H-bonding sites N; b) ³¹P NMR chemical shift plotted as d function of temperature for 1 : 1 mixtures (from left to right) of A+D, AA+DD, AA+DDD in toluene. The horizontal bars show the transition melling temperatures: m_{MN}.

Conclusions

We present here a general strategy for the design of synthetic information molecules. In all duplexes H-bond formation along the oligomers is cooperative and it should be possible to propagate the assembly of longer structures using these architectures. Although all oligomers have relatively flexible backbones, this lack of preorganisation does not impede assembly of the duplex. However, for single point H-bonds of similar strength, the most rigid one would lead to a more cooperative duplex formation.

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References

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Figure 3 Single crystal X-ray structure of phenol-pyridine N-oxide 2-mer duplex. Three adjacent unit cells (joined along the c-axis edge of the unit cell) with a total of six molecules are shown. Hydrogen atoms have been omitted for clarity. Oxygen, nitrogen and carbon atoms are shown in red, blue and grey respectively. The intermolecular H-bond between the phenol and pyridine-N-oxide is shown in yellow.