

DESIGN, SYNTHESIS AND APPLICATIONS OF COMPLEMENTARY QUADRUPLY HYDROGEN BONDING MODULES

- a. Redox responsive naphthyridine module and application in polymers
- b. Probing the polymeric environmental effect on the complexation of strong hydrogen bonding species

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Final Seminar

12 August 2009

DNA duplex formation has been explored extensively and been found useful for the construction of nanoscale structures with near-angstrom precision.¹ DNA duplexes make useful building materials for nanotechnology. Because single-stranded DNA and duplexes can be made by automated methods, a broad range of discrete nanoscale objects have been built entirely of DNA via programmed self-assembly. However, DNA is relatively expensive and thus not readily available in multi-gram scales. In addition, DNA molecules are significantly large in size and are only soluble in water.

An alternate approach involves the design of simpler DNA inspired molecules capable of forming multiple hydrogen bonds. Molecules can be made from inexpensive starting materials and are thus readily prepared in large quantities. By design, they can have high affinities for homo- or hetero-complexation, enabling high fidelity assembly. Indeed, a wide variety of hydrogen bonded molecules exist today (Chart 1). A major step forward in this area was reported by the Meijer group on the 2-ureido-4[1H]-pyrimidinone (UPy) unit.² In addition, the Zimmerman group has developed the deazapterin (DeAP) unit, numerous 2,7-diamido-1,8-naphthyridine (DAN) analogues, ureido guanosine (UG) units, 7-deaza-ureido guanine (DeUG) modules and others.³ Other labs have developed different hydrogen bonding motifs and an assortment of hydrogen bonded supramolecules, including polymers and polymer blends, solution aggregates, engineered crystals, and liquid crystals.⁴

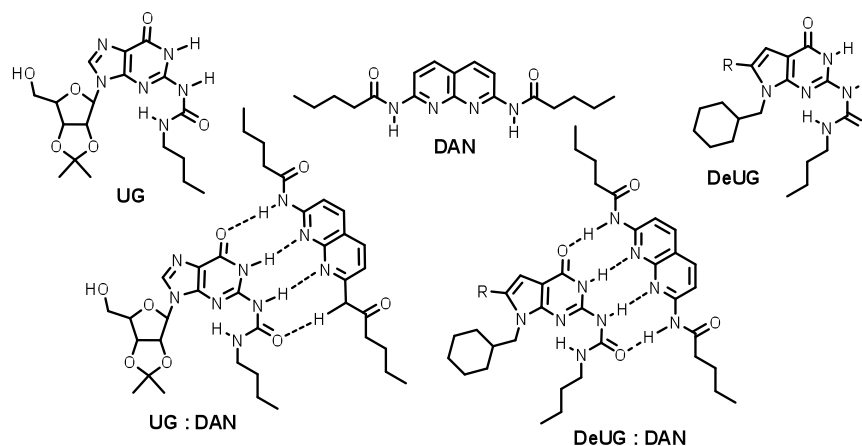


Chart 1 : Quadruply hydrogen bonding modules

Synthetic procedures for the UG and DAN modules have been reported but improvements were possible.^{2b,3} Here, we report on the optimization of reproducible reaction

conditions for the synthesis of DAN and UG, and their analogues. To illustrate the utility of DAN and UG in supramolecular chemistry, DAN and DeUG functionalized monomers were synthesized and copolymerized with styrene and butyl methacrylate.^{3b} The ability of these functionalized polymers to exhibit enhanced properties that are unavailable to traditional unfunctionalized polymers is demonstrated. Blends of these hydrogen bonded molecules with polystyrene (PS) and poly(butyl methacrylate) (PBMA) can be formed, where miscibility is driven by the high affinity exhibited by the DAN and UG recognition units (Figure 1). In addition, these units are utilized in the surface functionalization of silica particles.

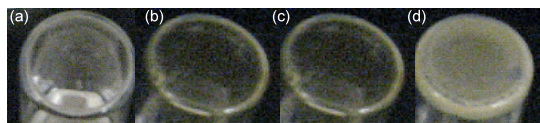
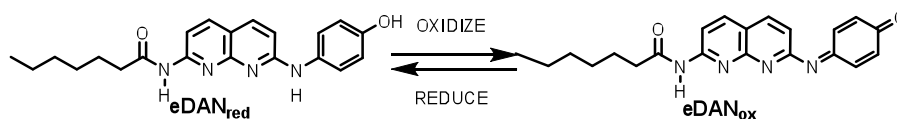


Figure 1: Films formed from polymers: (a) PS-DAN; (b) PBMA-UG; (c) 1:1 PS-DAN:PBMA-UG, the transparent film is evidence of complete mixing, no evidence of phase separation; (d) PS:PBMA, the opaque film indicates immiscibility of the polymers without hydrogen bonding groups to mediate intermolecular interaction.

There is a growing interest in “smart” materials that display specific responses to stimuli.⁵ The design, synthesis and application of an oxygen and redox responsive hydrogen bonding module, *N*-(2-(4-hydroxyphenylamino)-1,8-naphthyridin-7-yl)heptanamide (eDAN), is reported here. The reduction-oxidation of eDAN is reversible over multiple cycles without evidence of decomposition. By taking advantage of the changes in binding affinity of the eDAN:UG complex upon oxidation-reduction ($K_a(\text{eDAN}_{\text{red}}:\text{UG}) = \sim 10^7 \text{ M}^{-1}$ and $K_a(\text{eDAN}_{\text{ox}}:\text{UG}) = \sim 100 \text{ M}^{-1}$), eDAN is incorporated into polymers that gel and liquefy upon redox stimulation.



Scheme 1: Redox of eDAN

In general, it is well understood that the binding affinity of hydrogen bonding complexes are affected by external parameters, as well as substituents and electronics.⁶ What is not well understood, however, is the effect of larger macromolecules and polymeric environment on hydrogen bonding. Polymers were synthesized with the quadruply hydrogen bonding module, DAN, situated at the middle of a linear backbone. Using polymers with different backbone polarities (i.e., PS and PBMA) and various molecular weights, a guanosine analogue, G, was used as a sensitive probe of the nature of the polymeric environment created around the host situated at the core of the polymer. We wanted to determine how changes in polarity and molecular weight of the polymer backbone affect the final properties of the supramolecular material. The binding affinity (K_a) of the hydrogen bonding modules at the core of the polymeric system is influenced by the molecular weight of the polymer. Binding is enhanced with increasing molecular weight, up to an optimal molecular weight. At molecular weights above

this optimum, access to the core and host hydrogen module is restricted. However, the binding affinity is not affected significantly by the polarity of the polymeric backbone.

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