

Nanostructured Polymer Duplexes via the Covalent Casting of 1-Dimensional H-Bonding Motifs: A New Strategy for the Self-Assembly of Macromolecular Precursors

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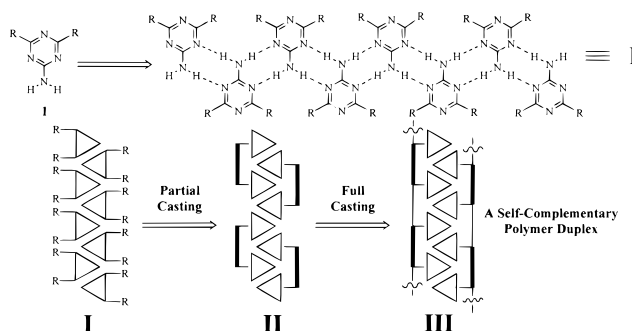
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A major theme in the development of the chemical sciences resides in improving the capability to negotiate issues of selectivity in the organization of matter on increasingly greater-length scales.¹ While molecular synthesis has advanced to an art through the precise control of chemo-, regio-, stereo-, and enantioselectivity, the identification and orchestration of persistent noncovalent binding motifs is extending synthetic technology to the nanoscopic regime by allowing the construction of supramolecular architectures through the self-assembly of instructed molecular components under equilibrium conditions.² Along these lines, the H-bond-mediated self-assembly of molecular precursors represents a powerful strategy for the logic-driven retrosynthesis and construction of nanoscopic materials in structurally homogeneous form.^{2e} Nevertheless, the nominal stability of most noncovalent aggregates detracts from their usefulness. To address this deficiency, template-directed syntheses involving the covalent capture of discrete noncovalent superstructures³ and the polymerization of organized assemblies^{4,5} have been described. Robust nanoscale assemblies may also be obtained through the stabilization of kinetically labile systems by the preorganization of binding sites and accumulation of multiple binding interactions.⁶ Macromolecular systems are well-suited to this latter strategy, and recently much attention has been given to the preparation of polymers incorporating H-bonding moieties⁷ and the self-assembly of dendritic macromolecules⁸ and block copolymers.^{5a,9,10} As part of a program involving the development of synthetic methodologies for the synthesis of nanostructured materials via self-assembly of macromolecular precursors, we herewith report preliminary

studies on the design and de novo synthesis of synthetic polymer strands capable of duplex formation through the “covalent casting” of 1-dimensional H-bonding motifs. Excluding systems that borrow from naturally occurring superstructural motifs (e.g., homo-DNA¹¹), to the best of our knowledge this report represents the first efforts toward unnatural polymer duplexes assembling through the action of inter-strand H-bonds.¹²

Cooperative binding via preorganization of multiple complementary binding sites enhances association through the reduction of entropic terms for the formation of discrete objects through receptor-substrate interactions.^{2e,13} For the application of this principle to 1-dimensional superstructures, such as the H-bonded tape **I**, it was hypothesized that preorganization of the molecules comprising the 1-dimensional superstructure could be achieved by introduction of a covalent linker as shown schematically for the partially cast H-bonded tape **II**. Introduction of a second linking group fully casts the H-bonded tape to afford a covalent-noncovalent ladder material, polymer duplex **III** (Scheme 1).

Scheme 1. Compound **1** and Anticipated 1-Dimensional H-bonding Motif **I** and Schematic Depiction of the Covalent Casting of **I** via Successive Introduction of Covalent Linkers to Provide Partially Cast 1-Dimensional Motif **II** and the Fully Cast Polymer Duplex **III**



In accord with this strategy, **I** should be comprised of molecules capable of functioning as a platform for subsequent elaboration to **III**. Trichloro-1,3,5-triazine, which undergoes stepwise substitution of the chloro-functionality without over-addition, proved suitable. However, the H-bonding motif of 2-amino-1,3,5-triazines is undescribed. For this reason, crystals of 2-amino-4,6-dichlorotriazine (**1**, R = Cl) were grown from carbon tetrachloride. The anticipated 1-dimensional H-bonding motif **I** was expressed, as

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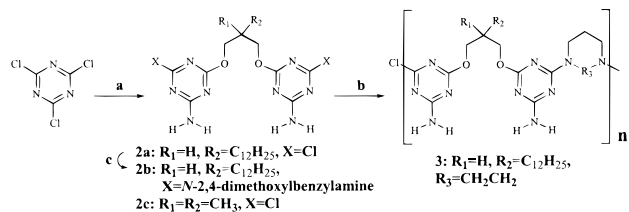
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Scheme 2. Synthesis of Molecular Components **2** for the Self-Assembly of Partially Cast 1-Dimensional Motif **II** and Polymerization of **2** to Yield Polymeric Strand **3**^a



^a Reagents: (a) 1,3-Diol, 2,6-lutidine, DCM, 25 °C, then Et₂O-dioxane, NH₃, 25 °C. **2a** = 82%, **2c** = 86% over two steps. (b) See Table 1. (c) 2,4-Dimethoxybenzylamine, *i*-Pr₂NEt, DMSO, 100 °C, 100%.

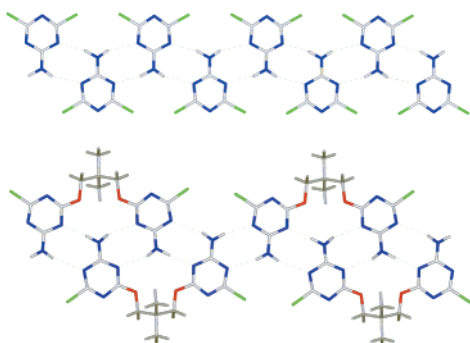


Figure 1. Top: X-ray crystal structure of **1**, R = Cl. Bottom: X-ray crystal structure of **2c** revealing the persistence of the encoded H-bonding motif upon introduction of a 1,3-diol linker.

revealed by X-ray crystallographic analysis (Figure 1, top). For the design of a linking moiety, it was recognized that a 1,3-diol, upon adoption of a *syn*-periplanar conformation, would impart a distance between heterocycles roughly commensurate with those distances defined by the H-bonding motif. Recognizing such conformational preorganization could be encoded in the form of geminal substitution via Thorpe–Ingold effect,¹⁴ neopentyl glycols were selected as linking moieties. Thus, bis-triazine **2c**, incorporating a geminal dimethyl residue, is readily obtained by the treatment of trichloro-1,3,5-triazine with 2,2-dimethyl-1,3-propanediol followed by exposure to ammonia (Scheme 2). That the 2-amino-1,3,5-triazine H-bonding motif persists upon introduction of the diol linker was demonstrated through X-ray crystallographic analysis of a single crystal of **2c** in which a superstructure identical to **II** is revealed (Figure 1, bottom).

Preparation of the fully cast H-bonded tape, duplex **III**, requires that the composite polymeric precursor **3** be obtained. Condensation polymerizations of diamines with simple dichlorotriazines have been described.^{7c} Polymerization of bis-triazine **2**, via substitution of the remaining chloro-functionality with a 1,3-diamine, should yield a covalent strand **3** possessing inter-triazine distances well-matched for duplex formation. The viability of amine nucleophiles was established in the quantitative conversion of **2a** to **2b**. Given the ease of chloro-substitution in this model system, the condensation polymerization of **2a** with 1,3-diamines was investigated. Homopiperazine, a conformationally constrained 1,3-diamine, was chosen as polymerizing agent. Initial polymerization experiments at 100 °C established a trend of increasing molecular weight with decreasing reaction time, suggesting thermal degradation is competitive with polymerization at this temperature (Table 1, entries 6–8). Successive increases in molecular weight were observed when the polymerizations were conducted at incrementally lower temperatures, e.g., 70 and 60 °C, respectively (Table 1, entries 3–5). Decomposition was not observed for prolonged reaction times at 60 °C (Table 1, entries 3–4). At 50 °C a dramatic increase in the degree of polymeri-

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Table 1. Polymerization of **2a**

entry ^a	temp (°C)	time (h)	mass balance, (%)	M_p^b	degree of polymerization
1	40	32.5	100	32500	62
2	50	43	100	38700	74
3	60	40	96	15700	30
4	60	26	91	13000	24
5	70	43	100	11300	21
6	100	4	83	7400	14
7	100	5	87	5500	10
8	100	20	82	1600	3

^a In a typical polymerization experiment, equimolar amounts of **2a** and homopiperazine were allowed to react in DMSO (0.2 M) in the presence of 5–7 equiv of Hunig's base. Addition of water to the reaction mixture gave a precipitate, which was collected, triturated, and dried in vacuo. ^b Determined by GPC at 25 °C using polystyrene standards and THF as eluent.

zation was observed (Table 1, entry 2). Further reduction of temperature occurs with a concomitant decrease in polymerization efficiency (Table 1, entry 1).

Under the dilute conditions employed for GPC analysis, intramolecular H-bonds mediate the folding of aminotriazine-functionalized polymers into compact globular structures.¹⁵ Accordingly, estimations of molecular size, as determined by GPC in conjunction with polystyrene standards, are best conducted in competitive media that serve to unfold the polymeric analyte and thereby ensure more accurate determinations. Nevertheless, strong H-bonding in competitive media such as DMSO, our polymerization solvent, has been noted.¹⁶ In this regard, the inverse temperature dependence on the degree of polymerization is noteworthy as it suggests an auto-templating effect. Indeed, polymer **3** may be viewed as a polymeric receptor for its monomer **2a**. Given the substantial negative entropy term associated with substrate-receptor binding, auto-templating effects would be expected to exhibit high temperature dependence. The ability of polymer **3** to form H-bonds in competitive media is supported by a large increase in apparent molecular weights at slightly elevated temperature (Table 2).

Table 2. Peak Molecular Weight of **3** Measured by GPC^a as a Function of Concentration and Temperature^b

entry	sample conc. (mg/mL) ^c	M_p (25 °C)	M_p (50 °C)
1	4.0	37100	46000
2	1.0	35500	42600

^a Gel permeation chromatography in THF, calibrated with polystyrene standards at both temperatures. ^b Column temperature maintained by heated enclosure. ^c Injection volume = 100 μ L.

The covalent casting of 1-dimensional H-bonding motifs represents a strategy for the design of synthetic polymer strands capable of duplex formation. The results herein allow this concept to take form by defining the structural and interactional features of the polymer strands required for duplex generation and, of equal importance, the determination of a practical synthetic route to such polymeric precursors. These studies lay the foundation for the design of self-replicating polymer duplexes with the potential for information storage akin to DNA and the self-assembly of functional nano-fibers.

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Supporting Information Available: X-ray crystallographic data for **1** and **2c** and spectral data for all new compounds (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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