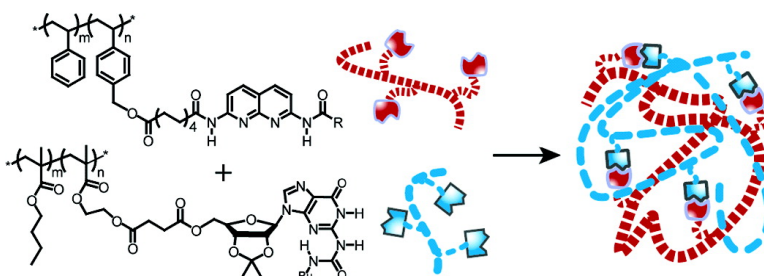


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## A Highly Stable Quadruply Hydrogen-Bonded Heterocomplex Useful for Supramolecular Polymer Blends

Taiho Park, Steven C. Zimmerman,\* and Shoji Nakashima

Department of Chemistry, University of Illinois at Urbana-Champaign, 600 S. Matthews Avenue, Urbana, Illinois 61801

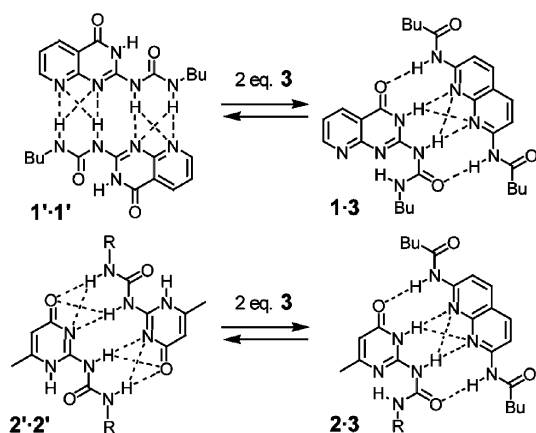
Received February 16, 2005; E-mail: sczimmer@uiuc.edu

Despite many advances in supramolecular polymer chemistry, there remains a need for recognition units that form complexes with high stability and selectivity.<sup>1</sup> There is a particular lack of easily prepared units that form hetero-complexes but weakly self-associate.<sup>2</sup> Our deazapterin (**1**, DeAP)<sup>3</sup> and Meijer's widely used UPy unit (**2**)<sup>4</sup> were shown to form, via their ADDA forms, very stable hydrogen-bonded complexes with 2,7-diamido-1,8-naphthyridine (**3**, DAN).<sup>3,5</sup> However, **1** and **2** were designed as AADD units **1'** and **2'** and strongly dimerize via these forms. In fact, other tautomeric and conformational isomers are available to both **1/1'** and **2/2'**. For many applications self-recognition and competing equilibria can have deleterious effects. Recognizing the structural similarity between **1** and **2** and the spectator role of the fused pyridine ring in **1·3**, we wondered whether other substituents or pyrimidinone ring fusions might favor the ADDA form. Given that alternative tautomers of DNA bases are rare, attention focused on guanosine, with an imidazole in place of the pyridine ring of **1**. Herein we report that urea **4** (UG) weakly self-associates and forms a highly stable complex with **3**. The utility of the UG·DAN complex is illustrated by the formation of blends from polystyrene (PS) and poly(butyl methacrylate) (PBMA) containing units of **3** and **4**.

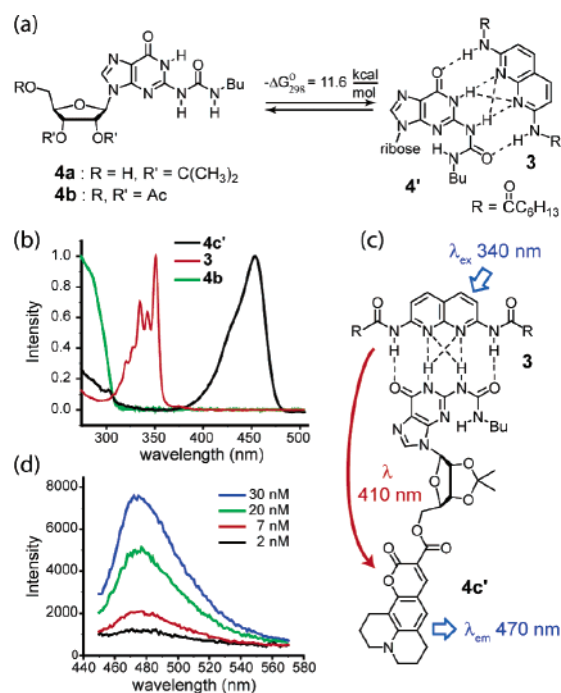
Compound **4a** was synthesized in three steps from guanosine tri-*O*-acetate in overall yields of ca. 70–95%.<sup>6</sup> The preparation of **4a** did not require chromatographic purification, so it was readily made on a >10 g scale. The ribose unit affords multiple points for functionalization, but we expect that the base alone will function similarly. The structure and self-association of **4b** was studied by <sup>1</sup>H NMR and vapor pressure osmometry (VPO). The data indicate **4** to be the dominant conformer and tautomer in chloroform-*d*. The VPO data fit best to an oligomeric model with aggregates bound through two hydrogen bonds from the urea group to the Hoogsteen site of the guanosine nucleus. The average  $K_{\text{assoc}}$  is ca. 200 M<sup>-1</sup>. No tight dimers analogous to **1'·1'** and **2'·2'** were observed under any conditions, suggesting that the desired *tautomeric fixation* had been achieved.

A 1:1 mixture of **3** and **4'** gave a sharp <sup>1</sup>H NMR spectrum in CDCl<sub>3</sub> with the NH protons shifting downfield by >1–2 ppm relative to the free components. The chemical shifts and NOEs observed between NH groups were consistent with complex **3·4'** (Figure 2a), indicating that **4'** is energetically accessible. No new peaks appeared nor did any shift occur upon dilution to 10 μM, indicating a very strong ( $K_{\text{assoc}} > 10^7$  M<sup>-1</sup>) complex. To quantify the complex stability **4** was covalently linked to coumarin 343 to give **4c'**.<sup>7</sup> Excitation of the naphthyridine unit at  $\lambda_{\text{max}} = 340$  nm produced an emission at  $\lambda_{\text{max}} = 410$  nm that was absorbed by the coumarin unit, leading to a fluorescence resonance energy transfer (FRET) effect whose emission at  $\lambda_{\text{max}} = 470$  nm was used to detect the complex at high dilution (Figure 2b–d). An association constant,  $K_{\text{assoc}} = 3 \times 10^8$  M<sup>-1</sup>, was determined.

To illustrate the utility of the **3·4'** complex in supramolecular polymer chemistry, monomers **5** and **6** were synthesized and



**Figure 1.** Strong DDAA dimers formed from **1'** and **2'.**<sup>3,4</sup> DAN **3** shifts equilibrium entirely toward **1·3** and **2·3.**<sup>3,5</sup> Unit **1** also dimerizes via the N1(H) form and may complex **3** similarly.



**Figure 2.** (a) Lowest energy form of **4**. Form **4'** with ADDA array that complexes **3**. (b) UV-visible spectra of **3**, **4b**, and **4c'**. (c) Schematic showing FRET mechanism in the **3·4c'** complex. (d) Fluorescence emission spectra of the **3·4c'** complex with dilution (background from 1:1 mixture of **3** and coumarin dye alone were subtracted). All spectra in CHCl<sub>3</sub>.

copolymerized with styrene and butyl methacrylate to produce, respectively, polymers **7** and **8** (Scheme 1, Table 1). PS and PBMA were chosen as immiscible polymers that do not form blends under normal circumstances.<sup>8</sup> Solutions of **7** and **8** in chloroform dried

Scheme 1

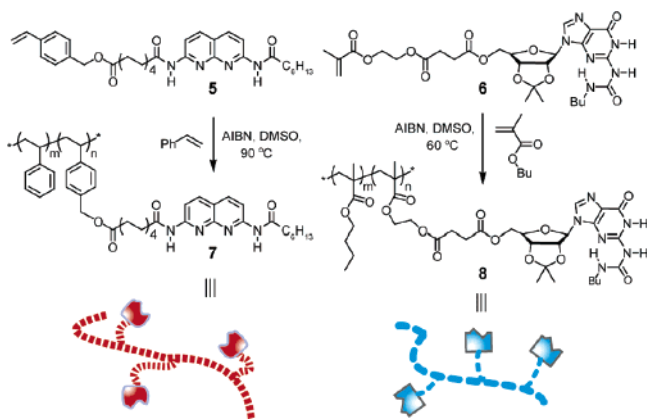


Table 1. Properties of Representative Polymers

polymer	recogn unit (F)	mol % unit F <sup>a</sup>	M <sub>n</sub> (kD)	M <sub>w</sub> (kD)	PDI	av no. F per chain
7a	3	1	15	29	1.9	1.4
7b	3	4	13	23	1.8	4.2
7c	3	7	16	33	2.1	8.2
8a	4	4	17	28	1.7	4.2
8b	4	10	11	16	1.5	5.7
9a	2	4	25	32	1.3	6.8
9b	2	10	33	43	1.3	21

<sup>a</sup> Calculated from feed ratios. Ratios determined by <sup>1</sup>H NMR integration were shown to be within experimental error of feed ratio.

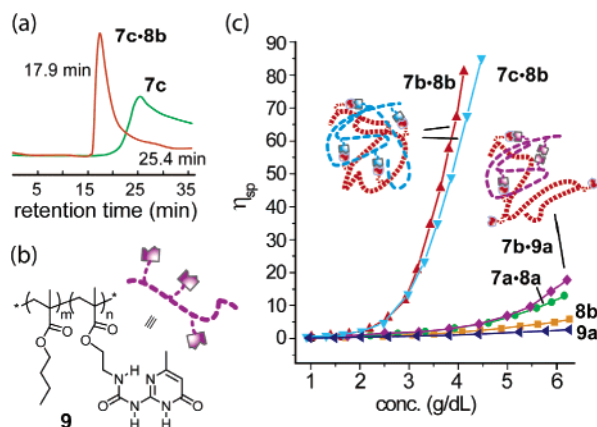


Figure 3. (a) SEC in toluene on double column (HR4E, HR5E). Tailing in 7c is due to interaction with matrix. (b) PBMA containing UPy (2) units. (c) Specific viscosity in CHCl<sub>3</sub> at 26 °C (Ubbelohde).

to give colorless, transparent films on glass. Differential scanning calorimetry (DSC) was performed on a 50% w/w mixture of 7c and 8b.<sup>6</sup> The single  $T_g = 73$  °C measured was between that of 7c (104 °C) and 8b (43 °C) consistent with a blend.<sup>9</sup>

We propose that 7 and 8 form a self-assembled, network polymer. Evidence for such a superstructure was the significantly reduced retention time observed by SEC for a 1:1 mixture of 7c and 8b at a concentration of ca. 2.5 g dL<sup>-1</sup> (Figure 3a). An  $M_n \approx 170$  kD was estimated. Larger assemblies could not be observed by SEC because of the high viscosity of higher concentration solutions. Viscosity measurements of blends and control compounds were performed in chloroform solution (Figure 3c).<sup>6</sup> Consistent with the

formation of a large network, mixtures of 7b and 7c with 8b containing a ca. 1:1 ratio of recognition groups exhibited large increases in  $\eta_{sp}$  with concentration. Polymer 7a with an average of 1.4 recognition units 3 per polymer chain showed only a modest increase in viscosity with concentration, as did 7b and 8b alone (data not shown for 7b).

PBMA 9a,b were synthesized<sup>10</sup> as analogues of 8a and 8b, but containing unit 2 (Figure 3b, Table 1). It was not possible to match perfectly the MWs and recognition units per chain. Nonetheless, the viscosity increases with concentration were significantly larger for 7b-8b and 7c-8b in comparison to both 7b-9a and 7c-9b, even though both 9a and 9b have higher MWs and the latter has many more recognition units per polymer (Figure 3). Although some of the diminished effect in 9 may originate in its shorter linking chain, self-recognition of the UPy units, especially intramolecularly (see schematic in Figure 3c), will reduce their availability for hydrogen bonding. Current efforts are focused on determining the role played by self-recognition.

Described herein is UG 4, a useful new unit for recognition. By virtue of its greater tendency toward *tautomeric fixation* (vs 1 and 2), 4 forms an exceptionally stable heterocomplex with DAN 3, while only weakly self-associating. The energy of 3-4 interaction can drive the formation of blends of PS and PBMA, with minimal competition from self-associative processes. It is anticipated that the ready availability of analogues of 3 and 4 and their strong and selective complexation will make them broadly useful in supramolecular construction.

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