

# IBM Research Report

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# Urea-Bearing Copolymers for Guest-Dependent Tunable Self-Assembly

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**RAFT polymerization was used to synthesize urea-bearing methacrylate copolymers for binding carboxylate isosteres.**

Supramolecular polymers are emerging as a promising class of materials for electronic applications<sup>1</sup> and as frameworks toward device fabrication.<sup>2</sup> The self-assembly of these materials is driven by noncovalent forces<sup>3</sup>—including electrostatic, hydrogen bonding, metal coordination, and van der Waals interactions—to afford noncovalent networks tunable in strength and reversibility.<sup>4</sup> Polymers bearing pendant molecular recognition elements are an important subset of these materials.<sup>5–10</sup> For example, Schubert and coworkers<sup>5</sup> synthesized methyl methacrylate copolymers bearing terpyridyl functionalities to create reversible supramolecular networks in the presence of Fe<sup>2+</sup> or Zn<sup>2+</sup> ions. Other researchers have utilized noncovalent interactions to alter the miscibility of polymer blends which are typically immiscible.<sup>6</sup>

Two approaches are possible in the formation of molecular recognition bearing polymers: (1) post-modification of a polymer backbone containing reactive side groups and (2) the polymerization of a molecular recognition-containing monomer. Rotello and coworkers<sup>7</sup> have derivatized polystyrene-based random and block copolymers with hydrogen bonding units for the formation of micelles and vesicles using the post-modification approach. Alternatively, there have been significant contributions by Weck and coworkers<sup>8</sup> who demonstrated the ring-opening metathesis polymerization (ROMP) of monomers bearing hydrogen bonding and metal coordination elements. While many of these polymers have been synthesized using radical polymerization schemes,<sup>9</sup> there has been less attention to employing controlled metal-free radical polymerization routes,<sup>10</sup> such as reversible

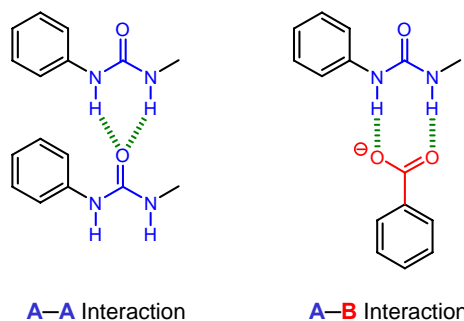
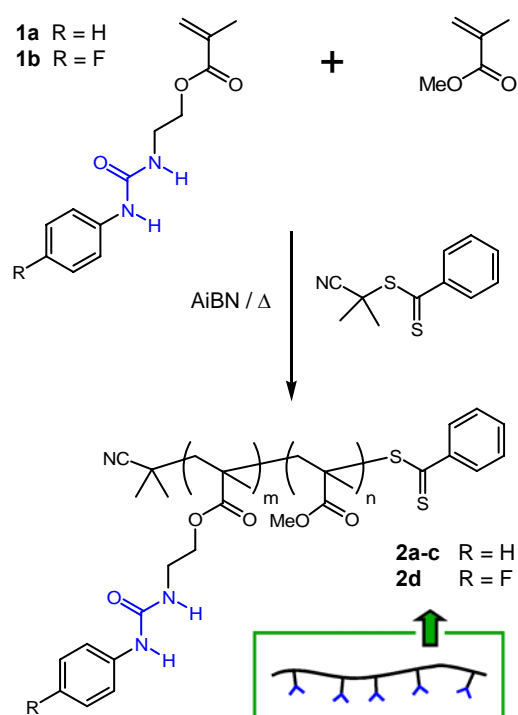


Fig. 1 A–A and A–B interactions with urea functionalities.

addition-fragmentation chain transfer (RAFT) polymerization<sup>11</sup> and nitroxide mediated polymerization (NMP).<sup>12</sup>

The choice of molecular recognition functionalities utilized is a key component of supramolecular polymers. Urea functionalities are one example that have been utilized to form supramolecular polymers and polymeric networks via self-recognition—i.e., urea



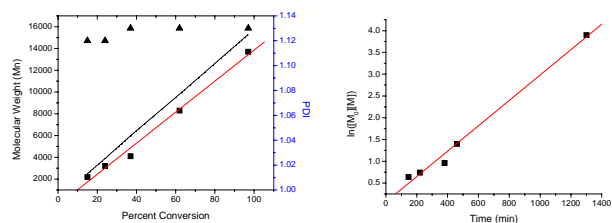
Scheme 1 Polymerization by RAFT.

functionalities interacting with other urea functionalities (A–A system)—particularly by Meijer and coworkers (Fig. 1).<sup>13</sup> To the best of our knowledge, urea derivatives have not been investigated, in polymeric regimes, with complementary recognition units to form A–B systems. Ureas are known<sup>14</sup> to bind carboxylate derivatives and their isosteres (such as sulfonates, phosphonates, and phosphates), and have been incorporated into host molecules for binding anion guests.<sup>15</sup> These noncovalent interactions employ ion-dipole forces in concert with hydrogen bonding—and are effective in a range of hydrogen bonding and non-hydrogen bonding solvents. Herein, we present the controlled radical copolymerization of methyl methacrylate and a urea-bearing methacrylate monomer—via RAFT polymerization—for binding a range of carboxylate isosteres.

The urea containing monomers **1a** and **1b** are easily synthesized from the commercially-available isocyanatoethylmethacrylate in

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† Electronic Supplementary Information (ESI) available: Experimental procedures and <sup>1</sup>H NMR spectra. See <http://dx.doi.org/10.1039/b000000x/>



**Fig. 2** RAFT copolymerization of **1b** and MMA in DMF (65 °C). (a)  $M_n$  and PDI (determined by GPC) versus percent conversion. The dotted line represents the theoretical molecular weight. (b) Semi-logarithmic plot versus reaction time.

the presence of aniline or 4-fluoroaniline, respectively. Both monomers are purified by recrystallization, and thus, does not require any chromatography (Supplementary Information). The fluorine in the para-position of **1b** was added both to increase the binding strength of the urea, and also as an  $^{19}\text{F}$  NMR probe to observe the binding of guest.

Copolymerization of methyl methacrylate (MMA) with the urea-containing monomer **1b** was investigated using a 122:12:1 ratio (methyl methacrylate to **1b** to cyanoisopropyl dithiobenzoate chain transfer agent) in DMF- $d_7$  at 65 °C. The relationship between the molecular weight ( $M_n$ ) and the percent conversion is linear, which suggests that the polymerization is a controlled living process. Moreover, the linearity of the semilogarithmic kinetic plot suggests a constant concentration of active radical species during the polymerization. The polydispersity index (PDI) was low, with the highest value being 1.14 at near full conversion. Several polymers, varying in composition and molecular weight, were synthesized by altering the monomer-to-initiator ratio and/or the methyl methacrylate to urea-bearing methacrylate ratio. The incorporation of the urea-bearing monomer **1a** or **1b** into the polymer backbone was verified by  $^1\text{H}$  NMR spectroscopy. The percent incorporation of **1a** into **2a** and **2b**, and **1b** into **2d**, was consistent with the initial

**Table 1** Characterization of polymers.

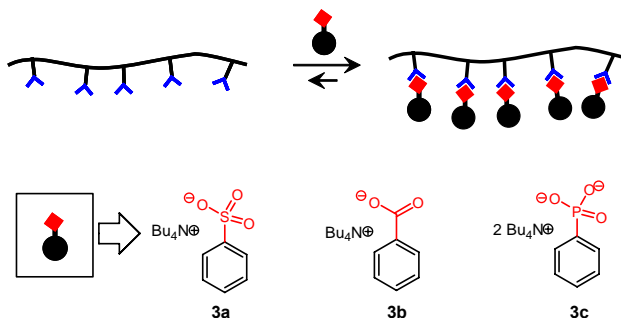
	$M_n$ ( $\times 10^{-3}$ ) g/mol <sup>a</sup>	PDI <sup>a</sup>	MMA monomer : Urea-MMA monomer	Urea Composition in Polymer (%) <sup>b</sup>
<b>2a</b>	22.1	1.09	20:1	4.5
<b>2b</b>	10.3	1.10	10:1	10.1
<b>2c</b>	4.6	1.16	8:1	23.5
<b>2d</b>	17.0	1.06	20:1	4.7

<sup>a</sup> Determined by GPC in THF.

<sup>b</sup> Determined by  $^1\text{H}$  NMR spectroscopy.

composition of **1a/b** and methyl methacrylate in the reaction mixture. However, in cases where the composition of **1a/b** in the reaction was greater than 10%, the polymerization rate was greatly diminished, resulting in a slightly higher PDI (1.16) and a lower yield of polymer **2c**. This data suggests that while both **1a** and **1b** have similar reactivities as methyl methacrylate, the intermolecular hydrogen bonding interactions by the urea moieties can hinder the polymerization.

The polymers were soluble in a range of polar and nonpolar solvents. In non-hydrogen bonding solvents such as  $\text{CDCl}_3$ , the urea N—H resonances in the  $^1\text{H}$  NMR spectrum (10 mM of the urea sidechain, 298 K) were significantly broad and flattened,



**Fig. 3** Sulfonate **3a**, carboxylate **3b**, and phosphonate **3c** guests for binding urea-bearing polymers.

suggesting their involvement in inter- and intramolecular hydrogen bonding interactions with other urea functionalities or methyl ester groups of the polymer backbone. While the polymer is initially soluble in  $\text{CDCl}_3$ , the large aggregates formed precipitate from the solution after a period of two days. However, in  $\text{DMSO-}d_6$ , the polymers are readily soluble and the N—H resonances were present as distinct broad singlets due to the solvation of the urea functionalities by solvent molecules.

The binding properties<sup>16</sup> of the copolymers were determined in  $\text{DMSO-}d_6$  by  $^1\text{H}$  NMR spectroscopy (and  $^{19}\text{F}$  NMR spectroscopy for the case of polymer **2d**). As representative examples for the binding studies, polymers **2a** and **2d** ( $M_n = 10\text{k}$  and  $15\text{k}$ , respectively) were investigated. Titration of a solution of guest **3a**, **3b**, or **3c** to the host copolymer **2a** resulted in a downfield shift of the N—H resonances (6.01 and 8.56 ppm) of the urea functionalities. The NMR-Tit curve-fitting program<sup>17</sup> was used to determine the association constants ( $K_a$ ) for the 1:1 interaction between guest and receptor.<sup>18</sup> The binding affinity was dependent upon the guest molecule, with the order of  $K_a$ 's from weakest to strongest being: sulfonate **3a** < carboxylate **3b** < phosphonate **3c**. Kelly<sup>14</sup> and coworkers, in the investigation of their urea-based anion receptors, noted the same trend for the binding of carboxylate

**Table 2** Association constants ( $K_a$ ) for polymers **2a** and **2d** (10 mM solutions in  $\text{DMSO-}d_6$  with respect to urea functionalities) for binding to guest molecules.

	$K_a$ for <b>1a</b> ( $\text{M}^{-1}$ ) <sup>a</sup>	$K_a$ for <b>2b</b> ( $\text{M}^{-1}$ ) <sup>a</sup>	$K_a$ for <b>2d</b> ( $\text{M}^{-1}$ ) <sup>a</sup>	$K_a$ for <b>2d</b> ( $\text{M}^{-1}$ ) <sup>b</sup>
<b>3a</b>	>10	>10	>10	>10
<b>3b</b>	149	117	145	146
<b>3c</b>	3010	2970	— <sup>c</sup>	— <sup>c</sup>

<sup>a</sup> The  $K_a$  values were determined by  $^1\text{H}$  NMR spectroscopy (400 MHz, 298 K) titration experiments and the data was analyzed using the NMR-Tit<sup>17</sup> curve fitting program.

<sup>b</sup> The  $K_a$  values were determined by  $^{19}\text{F}$  NMR spectroscopy (376 MHz, 298 K) and titration experiments and the data was analyzed using the NMR-Tit<sup>17</sup> curve fitting program.

<sup>c</sup> Decomposition of the urea functionalities was observed.

isosteres, which correlates to the  $\text{p}K_b$  of the guest ion—as the basicity increases, the strength of the interaction increases. Interestingly, the association constant observed for the binding of each guest to the polymer-bound urea is on the same order as the individual urea-guest interaction. And thus, the strength of the molecular recognition is only slightly mitigated by having the urea component attached to the polymer backbone.

Copolymer **2d**, which contains a fluorophenyl urea, was also investigated for its binding to the guest molecules. The fluorine atom was sensitive to the binding of guest and could be observed by  $^{19}\text{F}$  NMR spectroscopy. The shift of the fluorine signal with the titration of guest, was used to determine the  $K_a$ 's for binding of guests **3a** and **3b**. The association constants determined by  $^{19}\text{F}$  NMR spectroscopy for guests **3a** and **3b** were consistent with the values obtained by  $^1\text{H}$  NMR spectroscopy. In the presence of guest **3c**, the  $^{19}\text{F}$  NMR spectrum became increasingly complex—with the appearance of several new resonances, which is indicative of the decomposition of the urea functionalities. This phenomenon has been previously observed—Gale and Amendola have both previously noted<sup>19</sup> that electron withdrawing substituents increase the acidity of the urea protons, thus making them more susceptible to deprotonation by basic anions.

In conclusion, we have investigated the synthesis of methacrylate copolymers bearing pendant urea groups using RAFT polymerization. Copolymers containing up to 10 mol% of the urea functionality were synthesized in a controlled living process to afford polymers with defined molecular weight and a low PDI. The molecular recognition elements employed in this paper can all be synthesized relatively easily. The urea-containing methyl methacrylate monomers were synthesized and isolated with minimal purification required. Since urea functionalities interact with carboxylate anions and its isosteres with varying degrees of strength, a route for tuning the strength of these interactions has been developed.

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