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Nucleobase-Templated Polymerization: Copying the Chain Length and Polydispersity of Living Polymers into Conjugated Polymers

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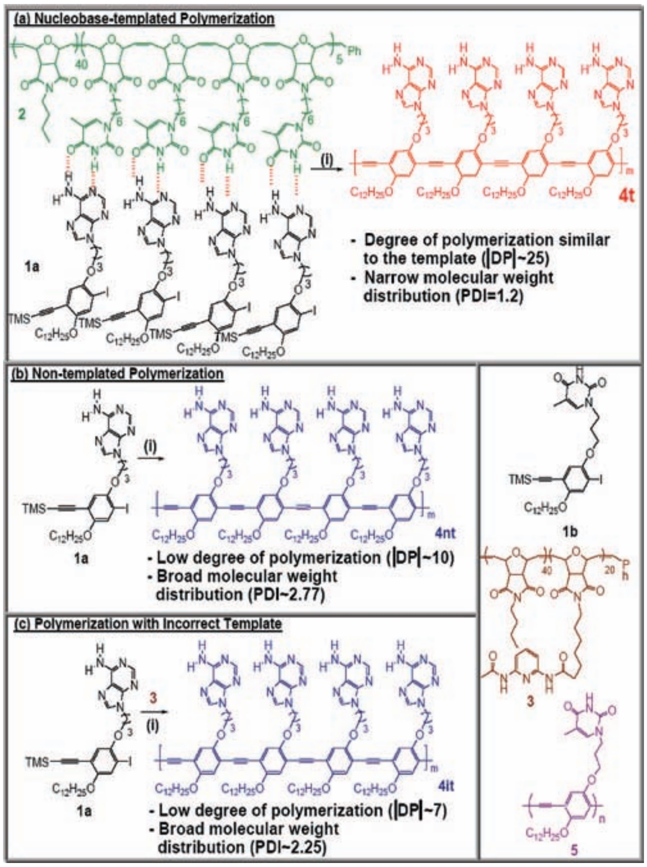
Nucleic acid templated polymerization is a fundamental biological process that enables the precise copying of the sequence and length of a DNA or RNA strand into a daughter polymer.[1] Over the past few years, nonenzymatic nucleobase-templated polymerization has been examined, notably to construct DNA analogues and peptide nucleic acids that reproduce the information of their templates.[2−9] A particularly attractive goal would be to use nucleobase-templated polymerization to address problems in synthetic polymer chemistry. For instance, polymers synthesized by step polymerization mechanisms, and in particular conjugated polymers, suffer from poor molecular weight control and broad molecular weight distributions.[10] By using a polymer generated by living methods as the template strand, nucleobase-templated polymerization can possibly result in copying the controlled molecular weight and narrow polydispersity of this parent strand into a daughter conjugated polymer. However, to our knowledge, this approach, which would significantly enhance the properties of conjugated polymers, has not been previously reported.

We here report the construction of a thymine-containing block copolymer **2** using living ring-opening metathesis polymerization (ROMP),[17] resulting in a polymer with a narrow molecular weight distribution. Aligning complementary adenine-containing monomers **1a** on this parent template using hydrogen-bonding interactions, and subsequently carrying out a Sonogashira polymerization, leads to the templated synthesis of a conjugated polymer. Remarkably, this daughter strand is found to possess a narrow molecular weight distribution and a chain length nearly equivalent to that of the parent template. This is in contrast to nontemplated polymerization, or polymerization with an incorrect template, which gives a short polymer with a broad molecular weight distribution. Thus, nucleobase-templated polymerization is a useful tool in polymer synthesis, in this case allowing the faithful transfer of chain length and polydispersity from parent template to a daughter conjugated polymer strand.

Initial work focused on the synthesis of monomers **1a** and **1b**, containing adenine and thymine units, and solubilizing alkyl chains (Scheme 1).[18,20] Nontemplated Sonogashira coupling polymerization of **1a** or **1b** was carried out in THF (Scheme 1b). Polymers **4nt** and **5nt** were characterized by ^{1}H NMR, UV−vis, fluorescence spectroscopy, and gel permeation chromatography (GPC, Table 1).[20] The degree of polymerization in these polymers was low ($|DP|_{\mathbf{4nt}} = 9.8$ and $|DP|_{\mathbf{5nt}} = 12.1$), and their molecular weight (MW) distributions were broad (polydispersity index (PDI) = M_w/M_n = 2.77 for **4nt** and 2.89 for **5nt**), consistent with their generation via a step polymerization mechanism.

Scheme 1. (a) Templated, (b) Nontemplated Polymerization and (c) Polymerization Using Noncomplementary Template of **1a**[a]



[a] Conditions: (i) (a) $CH_3(CH_2)_3N^+F^-$, THF; (b) $Pd(PPh_3)_2Cl_2$, CuI, PPh_3, Et_3N.

The templated creation of adenine-conjugated polymer **4t** was then examined. For this, thymine diblock copolymer template **2** was synthesized by living ROMP, to give a polymer with a narrow MW distribution (PDI = 1.07) and an average |DP| of 20 for the thymine block.[17] Sonogashira polymerization of **1a** was carried out in the presence of complementary template **2** (Scheme 1a).[11] Interestingly, the resulting polymer **4t** now exhibits a significantly narrower MW distribution (PDI = 1.2), a higher MW (Mn = 14800), and degree of polymerization (|DP| = 30.7) (Table 1).[20] When templated polymerization was repeated using a slight excess (1.5 equiv) of monomer **1a** as compared to the template, a polymer with low PDI (1.22) and an even closer chain length to the template were observed (|DP| = 25).[12] The standard used for GPC analysis is a relatively flexible poly(methyl methacrylate),[13] which can overestimate the MW of rigid conjugated polymers by GPC. Thus, the |DP| ≈ 25 obtained is, within error, comparable to the |DP| of the thymine block of template **2** of 20 units. MALDI MS confirmed the |DP| of this polymer.[20] Polymer **4t** shows red-shifted emission and absorption maxima, corresponding to $\pi-\pi^*$ transitions along the conjugated backbone, as compared to nontemplated polymer **4nt**. **4t** and **4nt** have equally short fluorescence lifetimes. Thus, this red shift is likely the result of an increase in the length

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Table 1. GPC and Photophysical Data of Conjugated Polymers and Templates in $CHCl_3$

	M_n	M_w	PDI	$\lvert DP \rvert$	λ^{abs}_{max}	λ^{em}_{max}[a]
2	18 000	18 700	1.04	40(C4), 20(THY)	265	0
3	18 600	19 900	1.07	40 (C4), 20(DAP)	293	0
4nt	4700	13 000	2.77	9.8	408	449
4t	14 800	17 700	1.2	30.7	427	458
4t[b]	12 500	15 300	1.22	25.3	427	458
4it	3200	7200	2.25	6.6	295	450

[a] Excitation at 400 nm. [b] 1.5 equiv of **1a**.[20]

of polymer **4t** by the template effect, rather than aggregation and excimer formation. To the best of our knowledge, this is the first example of transfer of the controlled molecular weight and narrow molecular weight distribution from a polymer generated by living methods to a conjugated polymer and is one of very few examples of the generation of conjugated polymers with controlled molecular weight distribution.[14−16]

In a control experiment, monomer **1a** was polymerized with the noncomplementary, incorrect template **3** (Scheme 1c). The resulting polymer **4it** showed no improvement in properties, as compared to nontemplated **4nt**, with low molecular weight, high PDI, and similar absorption/emission spectra (Table 1). Thus, the templated synthesis of **4t** occurs by selective molecular recognition of complementary nucleobases.[19] Similar improvement in chain length, PDI, and red shifts in absorption/emission maxima were observed for the templated polymerization of thymine monomer **1b** on diamidopyrimidine (DAP) template **3** to generate **5t** (Scheme 1).[20,21]

Hydrogen-bonding of monomers to templates was confirmed by ^1H NMR, with downfield shifts of the NH resonances of adenine or thymine units of **1a** and **1b** upon binding to complementary polymers (e.g., 8.33 to 8.46 ppm for thymine).[20] As well, we previously showed that copolymer **3** forms spherical aggregates in $CHCl_3$, held together by weak DAP−DAP interactions (Figure 1a).[17] Addition of monomer **1b** resulted in the complete disappearance of these aggregates, consistent with disruption of the DAP−DAP interchain interactions, and replacement by the far stronger DAP−thymine interactions of **1b** to polymer **3** (Figure 1b).[17] On the other hand, noncomplementary adenine monomer **1a** does not deaggregate the micelles from **3** (Figure 1c). This is consistent with hydrogen-bonding of template **2** and **3** with complementary monomers, correctly aligning them on these strands for efficient template polymerization.

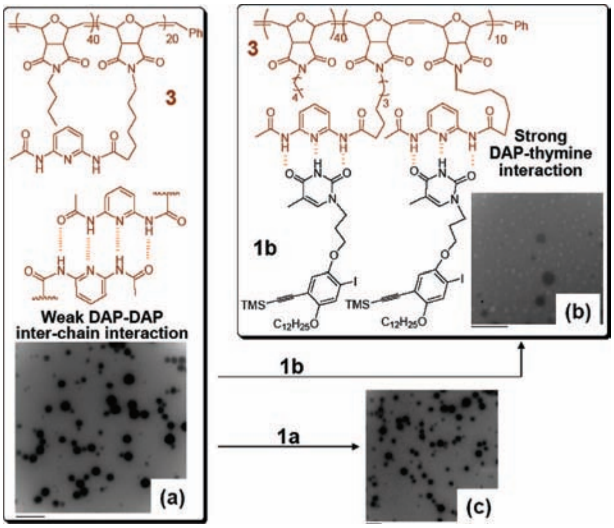

Figure 1. Transmission electron microscopy (TEM) images of (a) template **3**, (b) **3** with **1b**, and (c) **3** with noncomplementary **1a** in $CHCl_3$. Average size of aggregates is ~240 nm (bar is 500 nm).

In summary, we presented a new method that uses nucleobase recognition to read out and efficiently copy the controlled chain length and narrow molecular weight distribution of a polymer template generated by living polymerization, into a daughter conjugated polymer. Nontemplated polymerization or polymerization with the incorrect template generates a short conjugated oligomer with a significantly broader molecular weight distribution. This opens the door to the use of a large number of polymers generated by living methods, such as anionic polymerization, controlled radical polymerizations, and other mechanisms to program the structure, length, and molecular weight distribution of polymers normally generated by step polymerization methods and significantly enhance their properties. Efforts to explore the transfer of a nucleobase sequence from template to daughter strands, to ultimately mimic DNA-templated polymerization with fully synthetic polymers, are ongoing in our laboratory.

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Supporting Information Available: Synthetic procedures, photophysical, NMR, GPC, MALDI MS, and molecular modeling. This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) Polymerization of **1a** (1.5 equiv) was carried out in the presence of a template with 10 thymine units, also resulting in a polymer with narrower MW distribution, and |DP| close to the template.[20]
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(19) Molecular models for the H-bond alignment of template **2** with daughter strand **4t** are described in the Supporting Information.
(20) See Supporting Information.
(21) We chose a DAP- rather than an adenine-polymer template because adenine-polymers self-associate, rendering their adenine units inaccessible for H-bonding.[9] DAP units self-associate only weakly.

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