Self-Assembly

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Aggregation-Driven Reversible Formation of Conjugated Polymers in Water**

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Herein we show how the formation of dynamic covalent conjugated polymers in water can be achieved by stabilizing reversible covalent bonds through molecular self-assembly. Conventional conjugated macromolecules offer rich optical properties and charge mobility along the polymer backbone through extensive covalent π conjugation, but their behavior is typically rather static and they often require tedious synthetic methodologies.[1] In contrast, supramolecular polymers can be highly dynamic and responsive, and can be made by self-assembly of small building blocks.[2] However, these noncovalently linked polymers lack an efficient π-conjugated backbone and the associated control over optical properties.[3] Merging features of both polymer classes, dynamic covalent conjugated polymers potentially offer the covalent, fully conjugated backbone of a conventional polymer, combined with the ease of formation and dynamics of supramolecular polymers.[4] Besides their typical applications in optoelectronic devices, conjugated polymers in aqueous environments could find use in biomedical imaging and sensors,[5] as well as chemical[6] and pH[7] detectors. In these fields, aqueous supramolecular conjugated polymers have already attracted great attention over the past decades[3] for their potential application in light-emitting devices,[8] organic transistors, and photovoltaics.[9] Dynamic covalent chemistry is shown to be a powerful concept for the construction of adaptive and responsive molecular systems,[10] and has occasionally been used for the synthesis of reversible conjugated macromolecules, albeit mostly in organic solvents and not in water.[11]

Herein we report the reversible formation of a fully π-conjugated dynamic covalent polymeric system in aqueous media. Imine bonds, obtained through the well-known reversible condensation reaction of amines with aldehydes, offer a reversible molecular connection which potentially allows a fully conjugated path between aromatic building blocks. For this reason, we explored the formation of imine-based dynamic covalent conjugated polymers. In general, the degree of polymerization in reversible polymerizations depends on the equilibrium constant of the reversible reaction and the monomer concentration.[2,12] The equilibrium constant for the formation of imines from aromatic aldehydes and aromatic amines in water, in contrast to organic solvents,[13] is very small.[14] Therefore such polymerization in water will generally result in the formation of very short oligomers with subordinate properties. However, we and others have recently shown that these reversible bonds gain stability through self-assembly in supramolecular aggregates.[15] Accordingly, self-assembly of the formed polyimine oligomers should lead to stabilization of the imine bonds, thereby enabling the formation of longer conjugated polymers in water. For this purpose, we designed the following system for construction of potentially self-assembling π-conjugated imine polymers.

The present study requires two types of monomers: water-soluble bis(aldehyde)s and bis(amine)s, both with a conjugated pathway between the termini (Figure 1a).

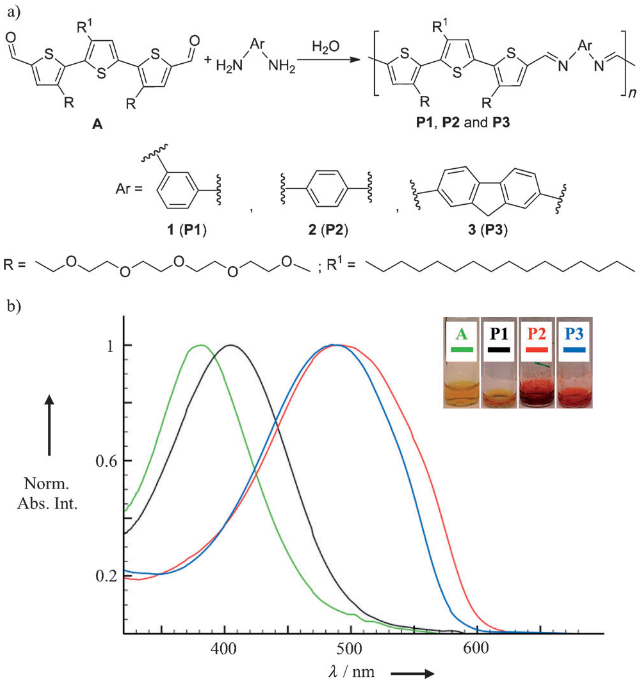

Figure 1. a) Formation of polymers **P1**, **P2**, and **P3** from the terthiophene bis(aldehyde) **A** and aromatic bis(amine)s **1**, **2**, and **3**. b) UV/Vis absorption of 1 mm aqueous solutions of **A** (green line), **P1** (black), **P2** (red), and **P3** (blue). Inset: photographs of typical aqueous samples of **A**, **P1**, **P2**, and **P3**.

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The bis(aldehyde) **A** was obtained in one step from the parent terthiophene,[16] which was previously reported as forming micellar aggregates in water.[17] As amine monomers we chose the soluble phenyl- and fluorene-based aromatic bis(amine)s **1**, **2**, and **3**. Self-assembly of the terthiophene building block should stabilize any formed imine bonds in aqueous media and potentially lead to the formation of the polymers **P1**, **P2**, and **P3**, respectively.

A was found to self-assemble in water into micellar aggregates (Figure 2a), above a critical aggregation concentration (CAC) of 0.3 mM. Equilibration of 1 mM aqueous solutions containing stoichiometric amounts of the bis(aldehyde) **A** and either of the bis(amine)s **2** or **3** resulted in bright-red solutions showing absorption maxima around $\lambda = 490$ nm (Figure 1b). This pronounced bathochromic shift of around 110 nm with respect to the yellow parent bis(aldehyde) **A** is likely caused by the formation of polymeric structures with an increased conjugation length along the polymer backbone. In contrast, the equilibrated mixture of **P1** (made from **A** and **1**) has a very modest bathochromic absorption shift of around 20 nm compared to **A**, and is likely caused by the cross-conjugated nature of the amine used.[18]

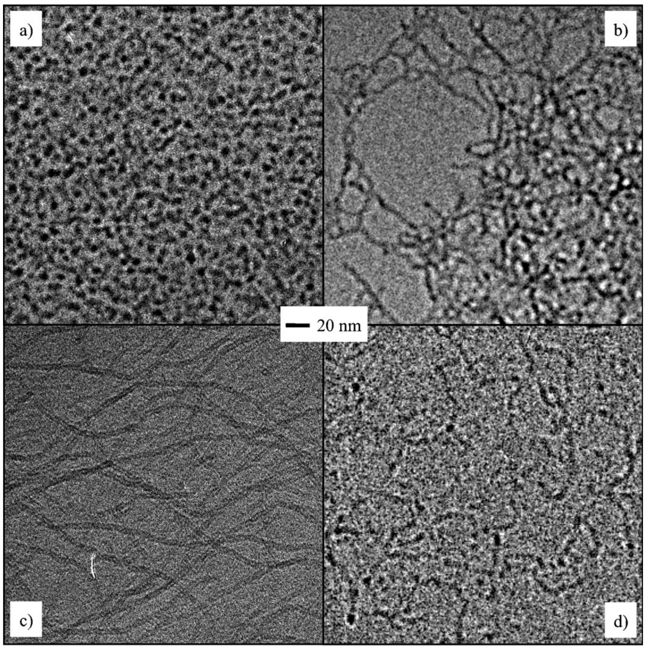

Figure 2. Cryo-TEM images of 1 mM aqueous solutions of a) **A** as spherical and elongated objects of (6.0 ± 1.3) nm; b) **P1** as 100 nm long entangled wormlike objects with a width of (4.1 ± 1.2) nm; c) **P2** as twisted, rigid rods with a (4.0 ± 0.3) nm diameter and length of more than 500 nm; d) **P3** as wormlike structures with a (5.2 ± 1.0) nm diameter and length of more than 200 nm.

The formation and structure of the imine polymers **P1**, **P2**, and **P3** were analyzed by ^{1}H NMR spectroscopy,[16] FT/IR, cryo-transmission electron microscopy (cryo-TEM), MALDI-TOF mass spectrometry, and GPC. FT/IR spectra of **P1**, **P2**, and **P3** showed the disappearance of the signals corresponding to the aldehyde and amine, and the appearance of signals corresponding to the formation of imine bonds, thus indicating the formation of polymers. The near absence of signals for the aldehyde or amine end groups in the FT/IR spectra indicates the formation of high-molecular-weight polymers.[16,19] Apart from color changes, an increase in viscosity could be observed upon reaction, and is indicative of changes in the aggregate morphology. Using cryo-TEM, **A** was found to assemble into spherical and slightly elongated micelles, with diameters of (6.0 ± 1.3) nm (Figure 2a). In contrast to **A**, **P1** and **P3**, at a 1 mM concentration, exist as wormlike micelles with widths of (4.1 ± 1.2) and (5.2 ± 1.0) nm, respectively (Figure 2b and d). In contrast, **P2** mainly consisted of relatively monodisperse, rigid fibers with a diameter of (4.0 ± 0.3) nm, and typical lengths of over 500 nm (Figure 2c). Overall, significant changes in morphology of the obtained structures were observed upon addition of the bis(amine) to the parent bis(aldehyde), thus suggesting that the formation of oligomers or polymers is accompanied by a drastic change in packing mode.

The molecular weight of the formed polymers was investigated using multiple techniques. Gel permeation chromatography (GPC) in water revealed the exclusive formation of entities larger than 100 kDa, which is the upper detection limit of the GPC. Although hinting at the formation of high-molecular-weight polymers, it is also possible that the polymer structures elute as noncovalently bound supramolecular assemblies. To rule out self-assembly, GPC analysis in organic solvent (THF) was performed. For quantification in THF, it was necessary to render the imine formation irreversible by quenching the equilibrated aqueous mixtures using $NaBH_4$, thus reducing the imines and remaining aldehydes in **A**, **P1**, **P2**, and **P3** to their corresponding nondynamic amines and alcohols.[15c] After dissolution of the resulting mixtures by addition of THF, GPC showed molecular weights (M_n) for polymers **P2** and **P3** of around 6 kDa (PDI ≈ 1.9) and 10.1 kDa (PDI ≈ 2), respectively. **P1** appeared to have a very low molecular weight of only 1.3 kDa (M_n, PDI = 1.7). In this particular case, however, there was a significant fraction which would not dissolve in THF and could therefore not be analyzed, thus distorting the observed molecular weight.[16] Furthermore, it must be also taken into account that prior to each injection any remaining unquenched imine bonds will be hydrolyzed by water upon addition of THF (which removes the amphiphilic imine stabilization), thus leading to the formation of shorter polymer chains and the subsequent observation of reduced molecular weights by GPC. MALDI-TOF mass spectrometry was also used to investigate the formation of the macromolecular structures, and showed the formation of polymers with degrees of polymerization (DP) up to 18 (**P1**, $M \approx 9$ kDa), 21 (**P2**, $M \approx 10.5$ kDa), and 22 (**P3**, $M \approx 11$ kDa). The repetitive units were found to correspond to the monomeric fragments bearing amine or aldehyde functional groups.[16] However, MALDI-TOF may again underestimate the average molecular weight of long polymer chains. Overall, this means that the observed molecular weights should probably be regarded as lower-limit values, especially when taking the FT/IR data into account. The polydispersity indexes of all three polymers are near the theoretically ideal value for step-growth polymerization.

Imine formation between aromatic amines and aromatic (including thienyl) aldehydes in water under nonstabilizing conditions is characterized by small equilibrium constants ($K < 50\,\mathrm{M}^{-1}$; $K = 34\,\mathrm{M}^{-1}$ for thienylaldehyde and aniline),[14] which generally impede the formation of long imine polymers. For the present system, it is possible to determine the imine equilibrium constant (K) values from the degree of polymerization (DP) for each polymer using Equation (1).[12]

$$K = \frac{\mathrm{DP}(\mathrm{DP}-1)}{4\,[\mathrm{monomer}]} \qquad (1)$$

Using the DP as obtained from GPC (M_n), the apparent imine equilibrium constants of **P2** and **P3** were determined to be at least 3×10^4 and $7.5\times10^4\,\mathrm{M}^{-1}$, respectively. From these equilibrium constants the Gibbs free energies for imine formation in the polymers were calculated at $-25\,\mathrm{kJ\,mol^{-1}}$ (**P2**) and $-27\,\mathrm{kJ\,mol^{-1}}$ (**P3**).[16] The Gibbs free energy for micellization, based on the CMC of **A**, is $-20\,\mathrm{kJ\,mol^{-1}}$, and can account for the large change in the Gibbs free energy when going from the unstabilized imines ($\Delta G_{\mathrm{im}} = -8.7\,\mathrm{kJ\,mol^{-1}}$ for imine formation between thienylaldehyde and aniline, calculated from $K = 34\,\mathrm{M}^{-1}$[14]) to the stabilized imines found in polymers **P2** and **P3**.[16] The evident importance of surfactant assembly indicates that a higher local monomer concentration, a decreased local water concentration, and additional stabilization by hydrophobic interactions could all contribute to achieving higher degrees of polymerization. The observation that the Gibbs free energies of micellization and of imine formation are not entirely additive may stem from two aspects. The first one is the experimental uncertainty in the determination of the degree of polymerization. The second is the change in packing (visible in the cryo-TEM image; Figure 2) and therefore aggregation energy of the imine oligomers or polymers with respect to **A**. Nevertheless, these results clearly indicate that aggregation leads to stabilization of the imine bonds and thereby drives polymerization.

Dynamic π-conjugated polymers should show large visual responses to changes in their composition, length, or environment, and can be used in sensors or in tuning their optical properties.[11c] The addition of hydrochloric acid (5 mM) to either **P1** or **P2** caused abrupt hypsochromic shifts to the $\lambda_{\max}$ of the parent bis(aldehyde) **A**, thus indicating a shift towards a monomeric state. Neutralization of acid with triethanolamine leads to nearly complete recovery of the $\lambda_{\max}$ values and colors for the original polymer,[16] thus showing that dynamic imine bonds are restored, and the π-conjugated polyimines **P1** and **P2** were again obtained. Likewise, heating red aqueous samples of **P2** to 50 °C resulted in a 31 nm hypsochromic shift and an associated color change to yellow (Figure 3), which is indicative of the formation of shorter π-conjugated chains (GPC) through depolymerization.[16,20]

Cooling the samples back to 20 °C and incubating for 3 minutes resulted in the full restoration of the original red color and indicated the reversibility of this process. As a result of the reversibility of the dynamic covalent bonds, this process could be repeated many times, during which a slight evolution of $\lambda_{\max}$ at 20 °C and 50 °C to longer wavelengths was observed, thus indicating a slow progression of the system towards equilibrium.

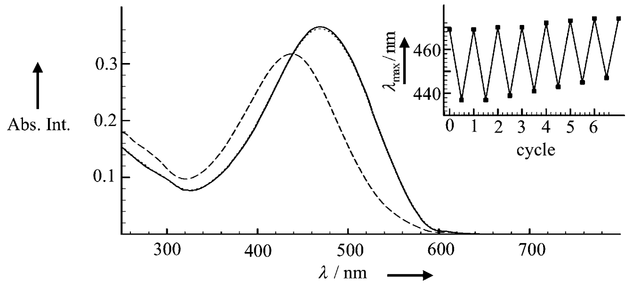

Figure 3. UV/Vis absorption of 1 mM aqueous solutions of **P2** at 20 °C (dotted line), which is then heated to 50 °C (dashed line), and then back to 20 °C (solid line). Inset: $\lambda_{\max}$ changes during the heating (20→50 °C) and cooling (50→20 °C) cycles.

In summary, we showed that despite unfavorable equilibrium constants for imine formation, water-soluble π-conjugated polymers can easily be formed by imine formation between amphiphilic conjugated bis(aldehyde)s and various aromatic bis(amine)s. The imine bonds in the structures are stabilized by self-assembly of the polymer, and is driven by the amphiphilic nature of terthiophene fragment. Aggregation-induced stabilization of the imine bonds resulted in imine equilibrium constants which were three orders of magnitude higher than that for analogous non-aggregating systems, thus leading to a significant increase in the degree of polymerization. Small changes in the structure of the aromatic bis(amine) are shown to have a profound effect on both the morphology and the optical properties of the obtained materials. As a result of the reversible nature of the dynamic covalent bond, the obtained polymers were found to respond to changes in pH and temperature by reversible depolymerization. These findings represent a new entry into fully π-conjugated, water-soluble, readily tunable, responsive polymers, which are easy to obtain by simple mixing of monomers in water.

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