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Supramolecular graft copolymers in moderately polar media based on hydrogen-bonded aromatic oligoamide units†

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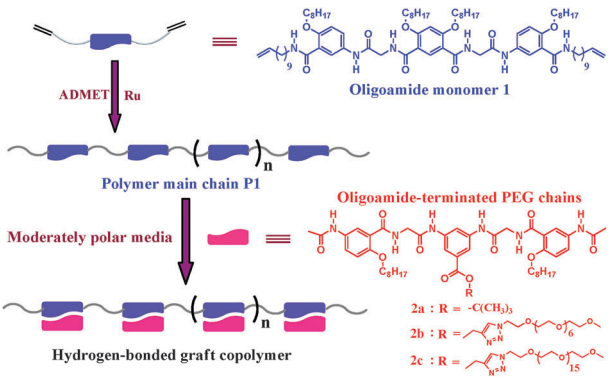
By exploiting hetero-complementary aromatic oligoamide units containing hextuple hydrogen bonds, supramolecular graft copolymers were successfully constructed in moderately polar media.

Multiple hydrogen bonding, along with other non-covalent forces such as solvophobic,[1] metal-coordination[2] and ionic interactions,[3] endows supramolecular architectures with high strength and order due to its directionality, complementarity and specificity. Supramolecular polymers constructed based on multiple (number of hydrogen bonds >3) hydrogen bonds hold the high potential for the advanced dynamic, reversible, and self-healing materials.[4,5] So far, few examples[6] of supramolecular graft copolymers based on main-chain insertion of multiple hydrogen bonding units that are able to pair specifically with complementary units have been reported. In the meanwhile, the sensitivity in polar surroundings encoded in hydrogen bonding also constitutes a hurdle for hydrogen bonding mediated association.[7] So far hydrogen bonds have been exploited alone,[8] or in association with other non-covalent[1,3] and covalent[9] interactions to increase the stability of molecular assemblies in a polar environment. Several examples were known to involve in forming hydrogen-bonded supramolecular polymers in polar solvent.[1b–d,8] However, construction of supramolecular graft copolymers using hydrogen bonding recognition units in polar media still represents a challenging task.

Among various recognition units based on hydrogen bonding interaction,[10] oligoamide strands are a class of association units with the preorganized backbones containing multiple amide oxygen and hydrogen atoms that could associate into duplexes *via* intermolecular hydrogen bonding.[11] Recently, the hierarchical self-assembly of the molecular duplex was demonstrated by gelation of solvents underlining the essential function of π–π stacking interactions in forming an extended network of fibers.[12] Multiple hydrogen-bonded oligoamides bearing terminal alkene groups when treated with Grubbs' catalyst provided covalently crosslinked zippers in almost quantitative yield, but failed to afford polymers under the reaction conditions.[13]

In this report we demonstrate the first construction of supramolecular graft copolymers based on main-chain insertion of hextuple hydrogen-bonded aromatic oligoamide units that are of high fidelity and strength in a moderately polar media (Scheme 1).

We initiated our investigation by polymerizing the olefin-terminated strand **1** (Scheme S4, ESI†) arrayed in the DADDAD sequence *via* acyclic diene metathesis (ADMET) polymerization[14] to obtain the polymer main-chain **P1**. Monomer **1** was treated with 1st or 2nd generation Grubbs' ruthenium catalyst (10 mol%) in dry toluene at 55 °C for 48 h (Table S1, ESI†). Under reduced pressure, **1** converted to **P1** in only *ca.* 80% using 1st generation Grubbs' ruthenium catalyst. However, the complete conversion of monomer was observed employing the 2nd generation catalyst, giving the degree of polymerization (DP) of 17. Further enhancement of DP up to 35 was achieved by using the supramolecular protecting strategy[15] (Scheme S5 and Table S1, ESI†) in 2 : 1 molar ratio of **1** and protecting agent **2a** in the ADAADA sequence that is specifically complementary to **1** ($\sim 10^9$ M^{-1} in $CHCl_3$). The large discrepancy in DP with and without **2a** is attributed mainly to completely preventing coordination of oxygens of monomer **1** to ruthenium,[6] leading to further chain propagation. In order to investigate the graft behaviour of **P1**, the oligoamide-terminated



Scheme 1 Schematic representation of supramolecular graft copolymers based on hydrogen-bonded aromatic oligoamide units.

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poly(ethylene glycol) **2b** and **2c** with different lengths of PEG chains were obtained *via* click coupling reaction between alkyne-containing oligoamide and azido-terminated PEG chains (Scheme S3, ESI†).

The formation of hydrogen-bonded graft copolymers was firstly examined by ^{1}H NMR technique in moderately polar media. In $CDCl_3$–DMF-d_7 (3 : 2, v/v), **P1** or **2a** exhibits distinct sharp signals over the region of aromatic and amide protons; however, the signals of **P1** turn broad upon gradual addition of **2a** to **P1** along with downfield shifts of amide protons H_d (0.27 ppm) and H_c (0.41 ppm) and upfield shifts of aromatic protons H_a (0.27 ppm) and H_f (0.17 ppm) (Fig. S2, ESI†). Two-dimensional NOESY provided direct evidence for the interaction between **P1** and **2a** in $CDCl_3$–DMF-d_7 (3 : 2, v/v). This is indicated by the presence of cross-strand NOEs between protons **P1**-H_d and **2a**-H_m, **P1**-H_d and **2a**-H_h, **P1**-H_i and **2a**-H_a, **P1**-H_b and **2a**-H_a, **P1**-H_h and **2a**-H_c (Fig. S1, ESI†). These results suggest the occurrence of binding of **2a** with recognition units of **P1** along the main chain.

To better demonstrate the formation of hydrogen-bonded graft copolymers, gel permeation chromatography (GPC) experiments were performed using a mixed solvent of $CHCl_3$–DMF (1 : 1, v/v) as eluent at 30 °C. For the polymer main chain **P1**, the number-average molecular weight (M_n) was determined to be 3.0×10^4. In contrast, M_n of **P1·2a** increased with increment of the content of **2a**, reaching 4.8×10^4 with two equivalents of **2a** to **P1** based on recognition units (Table S2, ESI†). Also, excess **2a** brought extra M_n increment highlighting the dynamic feature of the non-covalent bond in moderately polar media. Increasing the temperature from 30 to 50 °C led to the decline of M_n as shown in temperature-dependent GPC profiles, indicating decreased stability of the copolymer at higher temperature (Table S5, ESI†). Furthermore, under the same conditions, M_n of **P1·2b** and **P1·2c** exhibited a similar increment with respect to **P1**, indicating the successful formation of H-bonded graft copolymers (Table S3 and S4, ESI†). The above results contrast sharply with the fact that a mixture of **P1** and **1** arrayed in the same sequence fails to exhibit any association in GPC, indicating the binding specificity of these supramolecular graft copolymers (Fig. S7, ESI†).

Graft behaviour of main chain **P1** was further investigated by two-dimensional diffusion ordered ^{1}H NMR spectroscopy (2D-DOSY). As expected for small molecules, **2a**, **2b** and **2c** display high diffusion constants (6.45×10^{-10}, 5.41×10^{-10} and 5.04×10^{-10} m^2 s^{-1}, respectively), while **P1** offers a low diffusion coefficient of 1.27×10^{-10} m^2 s^{-1}, giving an experimental hydrodynamic radius (R_h) of 26.6 Å in $CDCl_3$–DMF-d_7 (3 : 2, v/v). Graft copolymer **P1·2a** has a smaller diffusion coefficient of 1.05×10^{-10} m^2 s^{-1}, corresponding to a larger R_h of 32.2 Å. Furthermore, when **2b** or **2c** bearing the PEG chain was mixed with **P1**, an even smaller diffusion coefficient (0.97×10^{-10} or 0.87×10^{-10} m^2 s^{-1}, respectively) and larger R_h (34.9 Å or 38.9 Å, respectively) were obtained. These results indicate efficient grafting of the polymer main chain with oligoamide-terminated PEG chains (Table S6, ESI†).

The enhanced binding strength of the side moieties grafted along the polymer main chain in moderately polar media (up to 40% DMF in chloroform) was demonstrated by comparing the association constants (K_a) of recognition units of **P1·2a**, **P1·2b**, **P1·2c** and **1·2a** based on the ^{1}H NMR titration experiments (Table 1). For example, the K_a value of **P1·2a** was found to be 1.5×10^5 M^{-1} in $CDCl_3$–DMF-d_7 (4 : 1, v/v), while that of **1·2a** was determined to be 2.5×10^4 M^{-1} in the same mixed solvent, a difference of around one order of magnitude. For **P1·2b** and **P1·2c** grafted by oligoamide-terminated PEG chains, the K_a values are also larger than that of **1·2a**. This enhancement of binding strength in the graft copolymers over the monomeric dimer holds true within the range of varying DMF percentage examined. We ascribe the added stability in moderately polar media to the solvophobic double-stranded oligoamide backbone that offers additional aggregation force and, at the same time, protects hydrogen bonds from polar solvent molecules that are strongly competitive for hydrogen bonding (Fig. 1b). The cooperative action of solvophobic interaction and hydrogen bonding is known to be responsible for stabilization of intermolecular and/or intramolecular aggregation in polar media.[1] Furthermore, the decrease of the binding strength from **P1·2a** to **P1·2c** is mainly attributed to an increase in steric crowding upon increasing the length of the PEG chain[16] and competitive hydrogen bonding between recognition units and PEG chains.[17]

Table 1 Association constants (M^{-1}) in chloroform–DMF mixtures[a]

Compounds	Solvent[b]	Association constants
1·2a	20%	2.5×10^4
	30%	3.1×10^3
	40%	1.5×10^2
P1·2a	20%	1.5×10^5
	30%	3.2×10^4
	40%	0.9×10^3
P1·2b	20%	1.1×10^5
	30%	2.0×10^4
	40%	0.6×10^3
P1·2c	20%	0.7×10^5
	30%	1.7×10^4
	40%	2.8×10^2

[a] Association constants were determined *via* ^{1}H NMR titration and an average value from three experiments was obtained at 298 K, with an error of less than 15%. [b] Percentage of DMF-d_7 in the mixed solvent of DMF-d_7–$CDCl_3$.

The enhanced stabilizing effect by both hydrogen bonding and solvophobic aggregation was also revealed by variable-polarity ^{1}H NMR experiments in $CDCl_3$–DMF-d_7 (Fig. 1a). In the first stage with DMF below 40%, signals of aromatic and amide protons **P1**-H_c and **2a**-H_b/**2a**-H_d become considerably broadened, which is in sharp contrast to the change of the corresponding proton signals of **1·2a** (Fig. S16, ESI†). This reflects that the solvophobic aggregation is strengthened with increasing polarity and hence intermolecular hydrogen bonding is shielded more efficiently than that in complex **1·2a** (Fig. 1b). In the second stage with DMF above 40%, signals of protons **P1**-H_d and **2a**-H_a/**2a**-H_c shift downfield and grow sharper along with all other signals, which is in the opposite direction compared to the change in the first stage. This could be explained by the predominance of polar solvent molecules in solution that start to disrupt intermolecular hydrogen bonding and result in the collapse of the regional large π–π stacking surface of

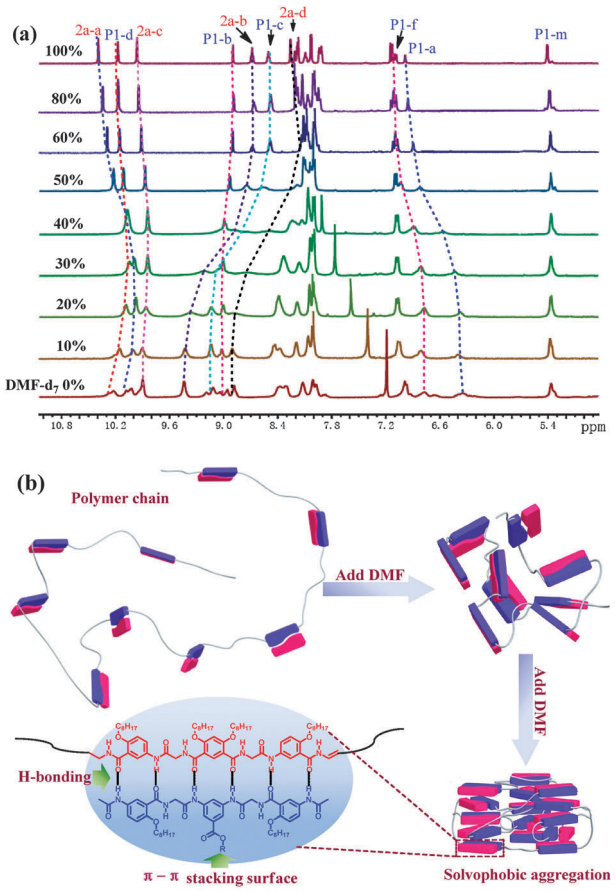

Fig. 1 (a) Stacked partial ^{1}H NMR spectra of the mixture of **P1** and **2a** (1 : 1 based on recognition units, 2.0 g L^{-1}) in $CDCl_3$–DMF-d_7 binary solvents containing different percentage of DMF-d_7 at 298 K; (b) possible mechanism of self-assembly of the polymer chain in a moderately polar solvent.

P1·2a responsible for the solvophobic aggregation, leading finally to loss of shielding capability for hydrogen bonding. Since **1·2a** is totally disassociated in DMF above 40% (Fig. S16, ESI†), whereas **P1·2a** is subjected to full disassociation only beyond *ca.* 60%, it is inferred that the intensified aggregation caused by solvophobic interaction should be accountable for the added stability of the hydrogen-bonded graft copolymers in moderately polar media. In addition, the UV-vis spectra of **P1** in $CHCl_3$–DMF (3 : 2, v/v) (10^{-5} M) contains a new broad peak around 310 nm at 30 °C with increasing intensity upon gradual addition of **2a** (Fig. S29, ESI†). This result provides additional evidence for solvophobic aggregation of **P1·2a** in moderately polar media.

In conclusion, we have demonstrated the successful construction of hydrogen-bonded graft copolymers and their enhanced stabilization by the cooperative action of both highly sequence-specific hydrogen bonding which offers a larger π–π stacking surface, and solvophobic aggregation in a moderately polar environment. As far as we know, no examples of hydrogen-bonded graft copolymers in organic polar media have been reported. Further derivatization of these polymers may provide opportunities for constructing a variety of polymeric architectures with enhanced stability in polar or even in aqueous media.

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