

# Synthetic Strategies for a Range of pH-Responsive Polymer Structures involving ATRP and “Click” Chemistry

Filip E. Du Prez, Bart Dervaux and Wim Van Camp

Ghent University, Department of Organic Chemistry, Polymer Chemistry Research Group, Krijgslaan 281/S4bis, B-9000 Ghent, Belgium. E-mail: Filip.DuPrez@UGent.be, Web: www.filipduprez.com

## INTRODUCTION

In this research contribution, atom transfer radical polymerization (ATRP) of 1-ethoxyethyl acrylate (EEA), a precursor monomer for acrylic acid, was used as a method to synthesize diverse pH-responsive amphiphilic copolymer structures. Poly(acrylic acid) (PAA) is an important polymer for a variety of applications because of its pH-responsive nature, its hydrophilic characteristics, and its interaction with metal ions. PAA containing amphiphilic copolymers are used for example as emulsifiers, stabilizers, surfactants and dispersants. Using the 1-ethoxyethyl protecting group strategy, well-defined polymer structures containing poly(acrylic acid) (PAA) segments have been prepared. PEEA can be converted to PAA by a heating step without the need for further modification. This protecting strategy is indispensable since acrylic acid can not be prepared in a direct way via ATRP.<sup>1</sup>

For the hydrophobic parts of these amphiphilic polymer structures, we have carried out ATRP of isobornyl acrylate to create poly(isobornyl acrylate) (PiBA) segments with good control of the molecular weight and a narrow molecular weight distribution. PiBA has as glass transition temperature ( $T_g$ ) of 94 °C, comparable to the one of poly(methyl methacrylate) (PMMA) or polystyrene (PS). Nevertheless, the ATRP of PiBA proceeds in the most controlled way.<sup>2,3</sup> pH-responsive polymers with various topologies were prepared, including block copolymers, “block-like” copolymers and graft copolymers. In addition, similar structures were also prepared by combination of “click” chemistry and ATRP. Therefore, polymers with alkyne as well as azide functionalities have been synthesized. These polymers were subsequently “clicked” together to yield block and graft copolymers.<sup>4</sup>

In a next part of the research, we have compared the properties of PAA-containing block and “block-like” copolymers in terms of pigment stabilization abilities.

## EXPERIMENTAL

**Materials.** 1-ethoxyethyl acrylate (EEA)<sup>1</sup>, PiBA macroinitiator<sup>2</sup>, PEEA- $\equiv$ <sup>3</sup> and PiBA-N<sub>3</sub><sup>3</sup> were synthesized as described before. 3-Azidopropyl methacrylate (AzMA) was prepared as described by Sumerlin *et al.*<sup>5</sup> The copolymerization procedure of methyl methacrylate (MMA) and AzMA to yield poly(MMA<sub>39</sub>-co-AzMA<sub>9</sub>) was also reported before.<sup>3</sup> Isobornyl acrylate (iBA, Aldrich, tech.) was purified by vacuum distillation (121 °C/18 mmHg). *N,N,N',N',N'*-pentamethyldiethylenetriamine (PMDETA, Acros, 99 +%) was distilled (85–86 °C/12 mmHg). Methyl-2-bromopropionate (MBP, Acros, 99 %),  $\beta$ -copper phthalocyanine ( $\beta$ -CuPc, BASF AG, Ludwigshafen) with primary particle size 0.1  $\mu$ m and breadth of particle size distribution of 15 nm, and titanium dioxide rutile pigment Kronos 2310 with particle size 0.3  $\mu$ m and breadth of particle size distribution of 60 nm were used as received.

**Instrumentation.** Thermal AFM imaging was performed on a Solver-PRO system (NT-MDT, Moscow, Russia) equipped with a heatable sample stage (up to 300 °C). Samples were probed using NGS11s tips using varying resonant amplitudes and setpoint conditions. Samples were prepared by spincoating 8 mg/mL solutions of the block copolymer in chloroform onto 1 cm<sup>2</sup> pieces of silicon. Pigment dispersions were prepared as described elsewhere.<sup>6</sup> Details of all other instrumentation can be found elsewhere.<sup>2</sup>

**Synthesis of PiBA-*b*-PEEA Block Copolymers.** A typical procedure is as follows (entry 1, Table 1). The PiBA<sub>55</sub> macroinitiator

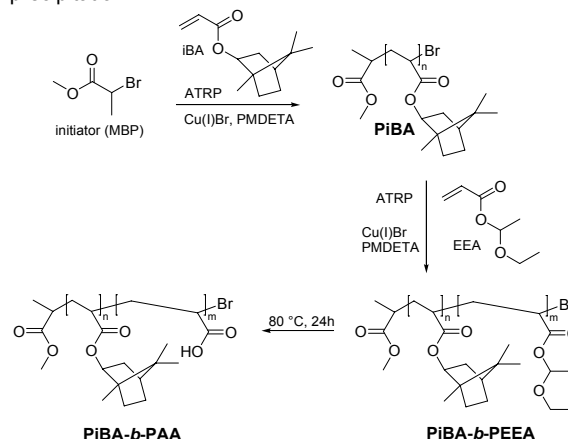
(1.0 g; 0.087 mmol) was dissolved in the monomer EEA (2.44 ml; 0.017 mol). The mixture was degassed by bubbling with N<sub>2</sub> for 1h. Cu(I)Br (0.036 g; 0.255 mmol) was added under nitrogen atmosphere and the reaction flask was immersed in a water bath thermostated at 60 °C. The polymerization was then started by adding PMDETA (0.079 ml; 0.382 mmol). After termination the resulting block copolymers were dissolved in THF, and purified (column with neutral alumina).

**Synthesis of PiBA-co-PEEA “Block-like” Copolymers.** A typical procedure is as follows (entry 4, Table 1). A mixture of iBA (4 ml; 0.0187 mol), ethyl acetate (1.3 ml) and PMDETA (0.079 ml, 0.378 mmol) was bubbled with N<sub>2</sub> for 1h. Cu(I)Br (0.054 g; 0.378 mmol) was added under nitrogen atmosphere and the reaction flask was immersed in a water bath thermostated at 75 °C. The polymerization was then started by adding MBP (0.028 ml; 0.252 mmol). After reaching a desired conversion, a degassed mixture of 7.27 ml (0.050 mol) EEA, 2.4 ml ethyl acetate, 0.158 ml (0.757 mmol) PMDETA and 0.090 g (0.063 mmol) Cu(I)Br was added to the solution. After termination in liquid nitrogen, the resulting copolymer was dissolved in THF, and purified by passing through a column with neutral alumina.

**“Click” Design of Block and Graft Copolymers.** The formation of a *block copolymer* by “click” reaction of PiBA-N<sub>3</sub> with PEEA- $\equiv$  (2 eq. to N<sub>3</sub>) was done using a Cu(I)Br/PMDETA catalyst system (3 eq. to alkyne) in a solution of tetrahydrofuran. Purification was done by passing through neutral Al<sub>2</sub>O<sub>3</sub> and the excess PEEA- $\equiv$  was removed by selective precipitation in methanol.<sup>3</sup> *Brush copolymers* were prepared by “clicking” poly(MMA<sub>39</sub>-co-AzMA<sub>9</sub>) with PEEA- $\equiv$  (1.5 eq. to N<sub>3</sub>) using a Cu(I)Br/PMDETA catalyst system (3 eq. to alkyne) in a solution of tetrahydrofuran.<sup>3</sup>

## RESULTS AND DISCUSSION

In this research, amphiphilic poly(acrylic acid) (PAA) containing polymer architectures are synthesized via ATRP. As the ATRP mechanism is not able to polymerize acrylic acid in a direct way, the 1-ethoxyethyl protecting group strategy was used to synthesize the PAA-containing polymer structures.<sup>1</sup> As a hydrophobic segment, PiBA was selected because of its high  $T_g$ , which facilitates purification by precipitation.



**Figure 1.** Synthesis of PiBA-*b*-PAA block copolymers using EEA as the protected acrylic acid monomer.

First a PiBA homopolymer with a narrow polydispersity index and high end-group functionality is prepared.<sup>2</sup> Next, this polymer is used as a macroinitiator for the polymerization of 1-ethoxyethyl acrylate (Figure 1), yielding PiBA-*b*-PEEA block copolymers. A variety of PiBA-*b*-PEEA block copolymers were prepared with different ratio of PiBA/PEEA content and lengths of both segments (entry 1 and 2, Table 1). In all cases, well-defined block copolymers with a controlled molecular weight and a narrow molar mass distribution were obtained.

Besides the synthesis of block copolymers via the macroinitiator strategy, iBA and AA copolymers were also prepared by a sequential monomer addition, leading to the formation of “block-like” copolymers. The molecular architecture of this type of copolymers is intermediate between those of block and random copolymers. Therefore, the

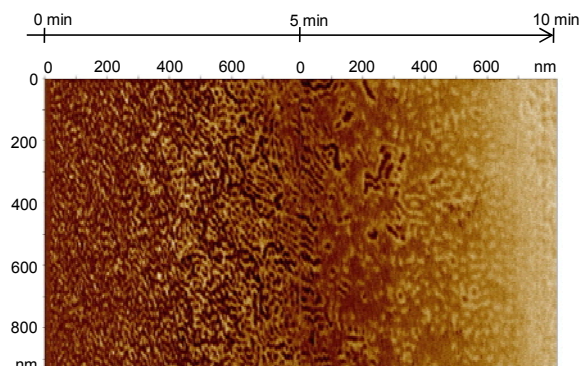
repulsive inter-chain interactions are less strongly changing along the chain in comparison with a conventional block copolymer. The major advantage of this synthetic strategy is that a time-consuming purification is avoided and replaced by a one-pot synthesis. Table 1 (entry 3 and 4) gives an overview of the result of some copolymerizations. Controlled kinetics were observed for all polymerizations. Moreover, polymers with a controlled molecular weight and low polydispersity index were obtained.

**Table 1. Summary of Results for the Synthesis of PiBA-co-PEEA Block and “Block-like” Copolymers by ATRP**

Entry	$M_{n,exp}^a$ ( $g \cdot mol^{-1}$ )	$M_w/M_n$	Composition <sup>b</sup>
1	17700	1.26	PiBA <sub>55</sub> - <i>b</i> -PEEA <sub>75</sub>
2	14100	1.22	PiBA <sub>17</sub> - <i>b</i> -PEEA <sub>72</sub>
3	12700	1.24	iBA <sub>54</sub> //iBA <sub>6</sub> /EEA <sub>46</sub> <sup>c</sup>
4	15100	1.30	iBA <sub>34</sub> //iBA <sub>19</sub> /EEA <sub>85</sub> <sup>c</sup>

<sup>a</sup> relative to polystyrene standards, <sup>b</sup> determined from <sup>1</sup>H-NMR, <sup>c</sup> notation “block-like” copolymers: before double line PiBA segment with average DP and after double line, composition second segment after adding second monomer.

After synthesis of the PiBA-co-PEEA copolymers, the conversion to the corresponding PiBA-co-PAA amphiphilic copolymers is done by a simple heating step (see Figure 1). The complete deprotection was confirmed by TGA analysis and also by in situ visualization of the morphological transition during the thermal deprotection process.<sup>7</sup> Figure 2 shows that complete deprotection is obtained at 120 °C after about 10 min.



**Figure 2.** Two consecutive AFM phase images (tapping mode) of a PiBA<sub>55</sub>-*b*-PEEA<sub>75</sub> block copolymer film (same scan area) at 120 °C.

By a combination of “click” chemistry and ATRP, similar structures as described before were synthesized.<sup>4</sup> First PiBA homopolymers with an azide functionality (PiBA-N<sub>3</sub>) and PEEA homopolymers with an alkyne functionality (PEEA-≡) were synthesized. These polymers were subsequently “clicked” to obtain the desired block copolymers. The reactions showed to be both quantitative and fast. After thermal deprotection, the desired amphiphilic block copolymers were obtained. The combination of PEEA-≡ and a poly(methyl methacrylate) backbone with multiple azide functions (poly(MMA-co-AzMA)), yielded amphiphilic graft copolymers after thermal deprotection (Table 2). As was revealed by GPC-analysis, an effective and fast coupling was obtained.

In a last part of this research, pigment stabilization tests were performed to get more insight on the effects of the different molecular architecture of block and “block-like” copolymers on the solid-liquid interface. Sedimentation measurements for titanium dioxide (TiO<sub>2</sub>; hydrophilic) and copper phthalocyanine (CuPc; hydrophobic) aqueous dispersions stabilized by a series of AB amphiphilic block copolymers containing PiBA and PAA segments have been carried out. The results are shown in Table 3.

**Table 2. Summary of the Results of the “Click” Coupling Reaction between Poly(MMA-co-AzMA) and PEEA-≡**

Entry	$M_n/M_p/PDI^a$ poly(MMA <sub>39</sub> -co-AzMA <sub>9</sub> ) <sup>b</sup>	$M_n/M_p/PDI^a$ PEEA-≡	$M_n/M_p/PDI^a$ coupled product
1	7000/9900/1.25	4600/5400/1.21 <sup>c</sup>	37100/46900/1.27
2	7000/9900/1.25	6100/7000/1.16 <sup>d</sup>	42200/56800/1.23

<sup>a</sup> relative to polystyrene standards.

**Table 3. Sedimentation Stability of TiO<sub>2</sub> and CuPc Aqueous Dispersions Stabilized by PiBA-PAA Copolymers**

Polymer	Suspension stability (half-time of the sedimentation, days)	
	TiO <sub>2</sub>	CuPc
PiBA <sub>51</sub> - <i>b</i> -PAA <sub>30</sub>	1	45
PiBA <sub>17</sub> - <i>b</i> -PAA <sub>72</sub>	30	5
PiBA <sub>21</sub> //PiBA <sub>19</sub> /PAA <sub>81</sub>	12	3
PiBA <sub>41</sub> //PiBA <sub>2</sub> /PAA <sub>12</sub>	5	10

Block copolymers exhibit a stronger interaction with TiO<sub>2</sub> and CuPc particles and show stronger stabilization compared to “block-like” copolymers. There is a distinct effect of the pigment surface nature on the copolymer structure acting as the best stabilizer: for hydrophilic TiO<sub>2</sub> dispersions, PiBA-PAA copolymers with a long PAA segment show good stabilization, while for hydrophobic CuPc, copolymers with the ratio PiBA/PAA ~ 2 revealed best results. Pigment stabilization tests showed that there is a significant difference between block and “block-like” copolymers in their solid-liquid interface behavior.

## CONCLUSION

In this research contribution, various amphiphilic copolymers structures were synthesized based on AA and iBA. Block and “block-like” copolymers with a controlled molecular weight and composition were prepared by ATRP. In addition, block and graft copolymer structures were successfully prepared by combination of “click” chemistry and ATRP, followed by thermal deprotection of the PEEA segments. Pigment stabilization tests on the block and block-like structures demonstrated several structure-property relations.

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