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A Facile Strategy for the Synthesis of Block Copolymers Bearing an Acid-Cleavable Junction

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Post-cleavable block copolymers is crucially important for nanoporous structures fabrications from self-assembly of block copolymers by selective etching of one block. Here, we present a facile and inexpensive approach to get block copolymers bearing an acid-cleavable junction. Disfunctional inifer containing an acetal group is synthesized for sequential reversible addition-fragmentation transfer (RAFT) polymerization of tert-butyl methacrylate and sequentially atom transfer radical polymerization (ATRP) of styrene. Moreover, the polymerization sequence of the monomers can be altered. The acetal juncture in the resultant block copolymers can be readily cleaved by acid at ambient conditions. Aldehyde or monoglyceride end groups are left at the end of PS residue, which can be used as binding site for future application.

1. Introduction

Block copolymers can self-assemble into various ordered nanostructures (spherical, cylindrical, gyroidal, lamellar) as the function of volume fraction, Flory-Huggings interaction of the blocks. 1-2 This offers promising applications in fields of nanoscience and nanotechnology, such as capacitors, 3-4 surface patterning, 5-7 separation membrane, 8,11 and so on. If one phase in the microphase separated structure is selectively removed, nanoporous structures with periodic styles are formed, which is particularly useful for templating for nanodots, 12-15 nanowires, 16-18 etc.

In the past years, many efforts have been focused on the synthesis of cleavable block copolymers and creation of nanoporous structures. UV etching techniques have been widely used. UV degradation of polymethyl methacrylate (PMMA) in the PMMA based block copolymers leads to ordered nanoporous thin film. 19,20 Also, photochemically sensitive groups, such as ortho-nitrobenzyl group, 21-24 photodimer of anthracene, 25 triphenylmethyl ether, 26,27 etc. are installed as a linker. Although the UV-etching technique has advantages of easy operation and free of contamination, the target samples are always limited in submicrometer thickness. Further, deep UV exposure may cause unexpected side reaction with the other constituent blocks.

There are also treatments confined to specific polymers, such as ozonolysis of polydienes, 28 hydrys of polyesters, 29 HF etching of PDMS, 30 hydroiodic acid degrading of PEO, 31 removing fillers in the supramolecular assembling. 32-35 These methods have limited application scope. Some treatments are carried on under the harsh reaction conditions. We are interested in developing a versatile and facile synthetic methodology that provides access to a broad class of block copolymers, meanwhile, the block copolymers are cleaved under mild conditions.

In this contribution, we put a kind of acid-cleavable juncture, an acetal linkage, into block copolymers. It is known that the acetal groups have been widely used in the protection/deprotection strategies of aldehydes and ketones. The acetal groups are stable under neutral and basic conditions, while instable under acidic condition. 36-43 We synthesized heterofunctional inifer containing an acetal group (see Scheme 1). The agents we used here are all cheap and of easy preparation. Meanwhile, two different initiation sites are introduced, which are able to work via different polymerization mechanisms selectively and independently. The choice of monomers and the polymerization sequences are arbitrary. Moreover, the potential end groups of the residue are controllable. The atom transfer radical polymerization (ATRP) method is one of the most efficient controlled radical polymerization (CRP) techniques, with very good architectural and molecular weight control. Extensive monomers have been successfully polymerized by ATRP, including styrenics, (meth)acrylates, (meth)acrylamides, and acrylonitrile. 44,45 The reversible addition-fragmentation chain transfer (RAFT) method is another powerful and versatile CRP technique for the preparation of well-defined architectures, and also tolerance of wide scope of monomers. 46,47

\[
\begin{align*}
\text{Br}\text{O} & \text{O} \text{O} \\
\text{Br}\text{O} & \text{O} \text{O} \\
\end{align*}
\]

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2. Experimental

Materials

Chlorobenzene (Analytical purity, Beijing Chemical Reagents Co.) was treated with powdered CaH₂ and distilled before use. Tolueno, THF (Analytical purity, Beijing Chemical Reagents Co.) were distilled from Na/benzophene under N₂. CuBr was synthesized from CuBr₂, 7-Hydroxyl-4-methylcoumarin (CA, Analytical purity, Beijing Chemical Reagents Co.), N, N', N', N'-pentamethyldiethylenetriamine (PMDETA, 99.5%, TCI), 1-(chloromethyl)-4-vinylbenzene (97%, Aldrich), were used as received. Styrene (Analytical purity, Beijing Chemical Reagents Co.) was distilled prior to use. 4-formylphenyl 2-bromo-2-methylpropanoate was prepared according to the literature. The organic solution was dried with MgSO₄, sodium carbonate to remove the acid catalyst and the remaining water. The mixture was refluxed for 12 h, then, the mixture was washed with solution of toluene, 8.0 mg of CuBr (0.0556 mmol), 20.0 mg of PMDETA (0.116 mmol), 1.0 g of styrene (9.62 mmol) were added. The mixture was degassed by three freeze-pump-thaw cycles, and sealed under vacuum. The reaction tube was placed in an oil bath at 90 °C. After 20 h, the reaction was quenched by dipping the tube in ice/water and the tube was broken. The mixture was diluted with CH₂Cl₂, passed through a basic alumina column, precipitated into methanol. The block copolymer was filtered and dried under vacuum. The product was a canary yellow solid.

General Procedure for PrBA-b-PS with PrBA-Br Macroinitiator

In a typical procedure, 0.70 g of PrBA macroinitiator (Mr=39.9 kg/mol, PDI=1.17, 0.0175 mmol) was dissolved in 3 mL of chlorobenzene, 8.0 mg of CuBr (0.0556 mmol), 20.0 mg of PMDETA (0.116 mmol), 1.0 g of styrene (9.62 mmol) were added. The mixture was degassed by three freeze-pump-thaw cycles, and sealed under vacuum. The reaction tube was placed in an oil bath at 90 °C. After 20 h, the reaction was quenched by dipping the tube in ice/water and the tube was broken. The mixture was diluted with CH₂Cl₂, passed through a basic alumina column, precipitated into methanol. The block copolymer was filtered and dried under vacuum. The product was a canary yellow solid.

Acid-cleavage of PrBA-b-PS

50 mg PrBA-b-PS-1 was dissolved in 2 mL CH₂Cl₂, 0.5 mL TFA was added, stirring for 8 h. Precipitating into methanol, the product was filtered and dried under vacuum. (Mr=10100, PDI=1.13).

RAFT Polymerization of PrBA

In a typical procedure, 10.0 g of tert-butyl acrylate (0.078 mol) was dissolved in 12.0 g of chlorobenzene. Then 0.270 g of CTA (0.39 mmol), 12.7 mg of AIBN (0.078 mmol) were added. The mixture was degassed by three freeze-pump-thaw cycles, and sealed under vacuum. The reaction tube was placed in an oil bath at 60 °C. After 20 h, the reaction was quenched by dipping the tube in ice/water and the tube was broken. After concentrating the mixture, 2 mL of THF added, precipitated in methanol/water (6:4) solution, the polymer was filtered and dried under vacuum. The product (7.8 g, yielding 78.0%) was a yellow solid. The molecular weight by GPC was 39900, PDI=1.17.

RAFT Polymerization of PS

In a typical procedure, 8.0 g of styrene (76.9 mmol) and 1.3 g of coumarin derived styrene (4.4 mmol) were dissolved in 1.0 g of chlorobenzene. Then 66.5 mg of CTA (0.0962 mmol), 1.05 mg of AIBN (0.0064 mmol) were added. The mixture was degassed by three freeze-pump-thaw cycles, and sealed under vacuum. The reaction tube was placed in an oil bath at 65 °C. After 48 h, the reaction was quenched by dipping the tube in ice/water and the tube was broken. After concentrating the mixture, 2 mL of CH₂Cl₂ added, precipitated into methanol, the polymer was filtered and dried under vacuum. The product was a canary yellow solid (3.5 g, yielding 43.8%).
Scheme 2. Synthetic procedure of block copolymers containing PrBA and PS with an acid-cleavable junction between the blocks by ATRP and RAFT processes, and acid degradation of the block copolymer.

3. Results and discussion

Firstly, 2-bromoisobutyrate group derived benzaldehyde is condensed with glycerol to form acetals. The application of glycerol is crucial, because the resultant product has hydroxyl end group for further modification. It is worth to note that the product acetals are approximately equimolar amounts of five- and six-number rings. The content of six-number-ring acetals is about 53.5% calculated from $^1$H NMR. The isolation of the isomer mixture was carried out by gas chromatography on a small scale, or separation of the converted derivatives, resulting in expensive purification cost and product lost. Considering that the acetal linkage is ready to cleaved, both the five- and six-number-ring acetals are exclusively degraded by acid without selectivity. We are not going to isolate the isomers (For clarity, only five-number-ring acetals are shown in the molecular formula). The remaining hydroxyl group in the acetals is cleaved, both the five-number-ring acetals are exclusively degraded by acid without selectivity. We are not going to isolate the isomers (For clarity, only five-number-ring acetals are shown in the molecular formula). The remaining hydroxyl group in the acetals is esterified with RAFT agent containing carboxylic acid group. Heterofunctional inifer is obtained. All the synthetic procedures are easy prepared, and the yields are high.

<table>
<thead>
<tr>
<th>Samples</th>
<th>$M_n^{PrBA}$</th>
<th>$M_n^{PS}$</th>
<th>$M_n^a$</th>
<th>$M_n^b$</th>
<th>$%$(PS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PrBA$<em>{300}$-b-PS$</em>{111}$</td>
<td>39900</td>
<td>51900</td>
<td>1.17</td>
<td>1.22</td>
<td>23.1</td>
</tr>
<tr>
<td>PrBA$<em>{300}$-b-PS$</em>{140}$</td>
<td>39900</td>
<td>61000</td>
<td>1.17</td>
<td>1.15</td>
<td>27.5</td>
</tr>
<tr>
<td>PrBA$<em>{300}$-b-PS$</em>{161}$</td>
<td>39900</td>
<td>67900</td>
<td>1.17</td>
<td>1.21</td>
<td>30.4</td>
</tr>
</tbody>
</table>

$^a$ determined by GPC.

$^b$ determined by $^1$H NMR.

To demonstrate the feasibility and controllability of our inifer, a series of diblock copolymers are synthesized. Firstly, the PrBA macroinitiators are synthesized by RAFT. The advantage of choosing PrBA is that PrBA can be easily removed under the same acidic condition as acetal groups degradation. Then ATRP of styrene is carried on by using the PrBA macroinitiator. From the GPC curves, we can see that obvious shifts to the higher molecular weight occur, retaining monomodal shapes. The characterizations of the block copolymers are summarized in Table 1. The advantage of our heterofunctional inifer is that the choice of monomers and polymerization sequence is arbitrary. Taken the polymerization sequence as an example, PS is firstly polymerized by RAFT and PrBA sequentially polymerized by ATRP. Figure 2 shows the PS macroinitiator, and the subsequent PS-b-PrBA. The slight shoulder on the left side of the GPC curve is ascribed to coupling reaction of the polymeric radicals.

Figure 2. GPC curves of PS macroinitiator and the successive PS$_{250}$-b-PrBA$_{66}$.
hydrogen, indicating the success of introduction of acid-cleavable group. The above results strongly demonstrate that precise block copolymer was prepared using the combination of RAFT and ATRP processes with acid cleavable acetal junction.

Figure 3. $^1$H NMR (A) and $^{13}$C NMR (B) of block copolymer PBA$_{111}$-b-PS$_{111}$, indicating the successful polymerization of block copolymer and introduction of acid-cleavable acetal junction.

The next step is to demonstrate the acid-cleavage of the obtained block copolymers by acid. Solutions of the block copolymer PBA$_{300}$-b-PS$_{111}$ and PS$_{250}$-b-PtBA$_{66}$ in dichloromethane were added with trifluoroacetic acid (TFA). The acetal group was degraded, as well as the tert-butyl groups. The remaining PS block was collected. Figure 4A shows the contrastive GPC curves of PBA macroinitiator, PBA$_{300}$-b-PS$_{111}$ before and after TFA cleavage. After TFA cleavage, the peak of the BCP is no longer observed. Instead, a new peak is visible with lower molecular weight ($M_n=10100$, PDI=1.13). Figure 4B shows the contrastive GPC curves of PS macroinitiator, PS$_{250}$-b-PtBA$_{66}$ before and after TFA cleavage. After TFA cleavage, the peak shifts to lower molecular weight, and the peak has the same elution time as that of PS macroinitiators. These results indicate that the acetal group junction holding the two blocks together can be efficiently cleaved under the mild condition.

Figure 4. (A) GPC curves of the PBA macroinitiator (I), block copolymers PBA$_{300}$-b-PS$_{111}$ (II), and PS residue after acid degradation (III), and (B) GPC curves of the PS macroinitiator (I), block copolymers PS$_{250}$-b-PtBA$_{66}$ (II), and PS residue after acid degradation (III), indicating successful degradation of block copolymers.

The acid cleaved process was also confirmed by SEM. We chose the PS dominated sample PBA$_{300}$-b-PS$_{250}$. The sample was spin coated onto silicon wafer, then the sample film was treated with TFA, and washed with methanol. The PS block was left on the silicon wafer. From the SEM image, we can see the ravine-like surface topologies of the sample after acid cleavage (Figure 5).

Figure 5. The SEM image of PBA$_{169}$-b-PS$_{339}$ after acid-cleavage, indicating the successful cleavage of PBA block.

Moreover, another advantage of our strategies is that the end groups of the residue can be controlled. The $^1$H NMR of degradation product from PBA$_{300}$-b-PS$_{111}$ shows that the typical peaks of PBA disappear, and the PS peaks remain. From the inset of Figure 6, we can see a peak appears at the chemical shift of 9.9, corresponding to the aldehyde group from the degradation of acetal linkage. If we choose the PS-b-PtBA block copolymers to degrade, the other part of acetal group is left on the residue end. From the inset in Figure 7, we can see that the monoglyceride group, with the chemical shift around δ~4 ppm, is left when PS$_{250}$-b-PtBA$_{66}$ block copolymers are acid-cleaved. Compared to other works, the advantage of our strategies is that the end groups of the residues after degradation is controllable, and can be chosen between aldehyde group and monoglyceride group. Both the remaining end groups are very useful in the future chemical modification.
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Figure 7. The 1H NMR of PS residue after acid-cleavage of PrBA$_{300}$-$b$-PS$_{111}$, indicating the successful acid etching of block copolymer. The inset shows the characteristic peak of aldehyde end group.

In conclusion, we have presented an inexpensive and facile strategy to prepare block copolymers bearing an acetal-cleavable acetal junction. PrBA-$b$-PS block copolymers are synthesized, as well as PS-$b$-PrBA. The acid-cleavage of acetal junction occurs under mild conditions, as well as the PrBA blocks. The PS blocks are fully conserved after acid etching. Moreover, the residual PS blocks bear a functional aldehyde group or monoglyceride group, and this gives opportunities to perform further chemistry.

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