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One-Pot Preparation of Methacrylate/Styrene Alternating Copolymers via Radical Copolymerization and Alcoholysis Modification: Sequence Impacts on Glass Transition Temperature

Yuki Kametani and Makoto Ouchi*

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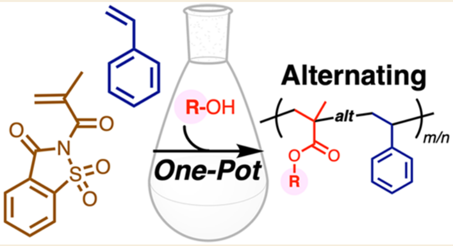
ABSTRACT: A series of methacrylate/styrene alternating copolymers were efficiently and systematically synthesized via alternating copolymerization of saccharin methacrylamide (**1**) with styrene and subsequent one-pot alcoholysis transformation with alcohols. The saccharin amide bond in **1** was stable enough that **1** was used as a bench-stable monomer, but the bond became reactive toward alcohols after the copolymerization. Thanks to the specific feature, the postpolymerization modification could be performed under mild conditions despite easy handling of the monomer. The quantitative transformation as well as the alternating sequence were certainly supported by ^{1}H NMR and MALDI-TOF-MS analyses. The alternating copolymers carrying relatively short alkyl pendants expressed lower glass transition temperatures than those of the statistical counterparts. Moreover, the alternating copolymerization was controlled via a RAFT polymerization system, affording a unique block copolymer composed of alternating copolymer segments.



KEYWORDS: *alternating copolymers, copolymerization, RAFT polymerization, sequence control, alcoholysis, glass transition temperature*

INTRODUCTION

Sequence control for artificial polymers has attracted huge interest, inspired by the excellent properties/functions of biopolymers.[1−5] In particular, sequence control for vinyl polymers is in high demand because many types of copolymers made of a variety of monomers have been used in practical materials applications. Some strategies have been reported for sequence control;[6−9] however, it is still challenging to comprehend general sequence impacts on their properties and to elucidate the sequence-oriented properties even for the simple AB alternating copolymers.[10−15] A versatile way for synthesizing sequence-controlled copolymers made of common monomer units in chain-growth polymerization is expected to solve the issue through comparisons with the corresponding sequence-uncontrolled or statistical copolymers (Figure 1A).

Postpolymerization modification (PPM)[16,17] for polymer side chains can be a powerful tool to evaluate sequence-oriented properties because it enables the construction of a series of sequence-controlled copolymers having different pendant groups (Figure 1B).[15,18] The modification must be quantitative for rigorous evaluation; however, it is not so straightforward to achieve reliable quantitativeness for macromolecular reactions. If one can design a special monomer to achieve both alternating copolymerization and quantitative pendant transformation under mild conditions during the PPM process, systematic syntheses of alternating copolymers carrying different pendant groups are expected. It is even better if the monomer is bench-stable despite having an efficient transformation ability. To the best of our knowledge, such advantageous monomers have been little developed in the history of polymer chemistry.

Quite recently, we have reported alternating sequence control with a saccharin-based methacrylamide (**1**, Figure 1C).[19] **1** showed no homopolymerization ability and unique radical copolymerization behaviors due to the bulky, highly conjugated, and electron-deficient features. Specifically, alternating copolymerization proceeded with styrene (St), and giving almost zero reactivity ratios ($r_1 = 0.040$, $r_2 = 0.045$ for $M_1 = \mathbf{1}$, $M_2 =$ St). The alternating copolymer was converted into methyl methacrylate and styrene (MMA/St) alternating copolymer via hydrolysis of the **1** unit and subsequent methylation with trimethylsilyl diazomethane. The double-step transformation is rather complicated, and more seriously, it is hard to convert into various methacrylate units other than the methyl counterparts.

In this work, our efforts were directed to a more facile and versatile approach for sequence control of methacrylates and styrene (Figure 1C). Eventually, we found that the saccharin amide bond of the monomer **1**, which was stable enough to be handled under air, turned very reactive to water and alcohol after polymerization. The unusual reactivity change of the pendant

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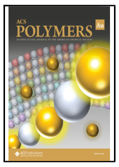

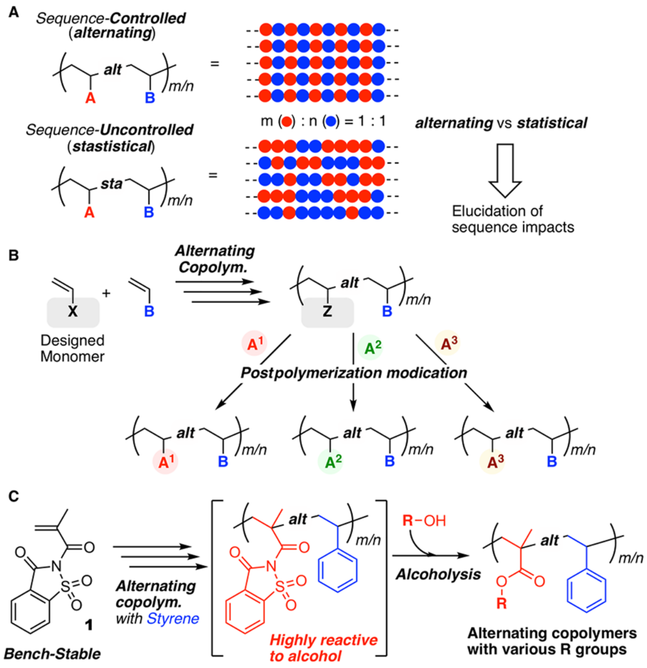

Figure 1. (A) AB alternating copolymer vs the corresponding 1:1 statistical copolymer. (B) Series of alternating copolymers via postpolymerization modification. (C) This work.

group allowed both the efficient postpolymerization modification and easy handling of the monomer. Thus, the one-pot copolymerization/alcoholysis process led to the syntheses of a series of alternating copolymers of alkyl methacrylate and styrene. Sequence effects on thermal properties were studied in comparison to the sequence-uncontrolled copolymers. Furthermore, the copolymerization could be controlled via the RAFT polymerization process, allowing the sequence analysis of the resultant alternating copolymer as well as the synthesis of a unique block copolymer consisting of different alternating copolymers.

RESULT AND DISCUSSION

The pivaloyl derivative (**2**) was prepared as a model compound for **1** unit in the alternating copolymer (Figure 2A), and the reactivity for the alcoholysis reaction of saccharin amide was compared with that of monomer **1**. Methanol (5 equiv) was added to the saccharin amide compounds in $CDCl_3$ at ambient temperature, and the reactions were monitored with ^1H NMR (see the Supporting Information). Monomer **1** hardly reacted with methanol, whereas **2** was quite smoothly converted into the methyl ester [i.e., methyl pivalate]. Also, the hydrolysis reactions were pursued using the saccharin amide solution in acetone-d_6/D_2O (9/1 v/v) at ambient temperature. Eventually, **2** smoothly underwent hydrolysis. In contrast, **1** did not react under the same conditions. From the model reactions, it was found that these model compounds show very different reactivity in the nucleophilic acyl transformation. The higher reactivity of **2** was also supported by ^{13}C NMR (Figure 2B) and density functional theory (DFT) calculations (Figure 2C). In ^{13}C NMR, the carbonyl carbon peak of **2** appears at a lower magnetic field, supporting the higher reactivity for nucleophilic substitution reactions. The higher Mulliken charge of the carbonyl carbon in DFT calculations also indicates that the carbonyl group is more polarized or reactive to nucleophiles. This trend was also seen for the acid chloride derivative (Figure S3). However, the reactivity difference between **1** and **2** was clearer, likely due to the highly conjugated nature of the saccharin methacrylamide[19] that strikingly decreases the orbital coefficient on the carbonyl carbon. These results revealed that the saccharin amide in the copolymer is highly reactive to alcohols and water, even though monomer **1** is stable to them. The less quantitative side-chain conversion in the previous report[19] was probably due to the partial hydrolysis of the **1** units in the copolymer during polymerization and/or purification.

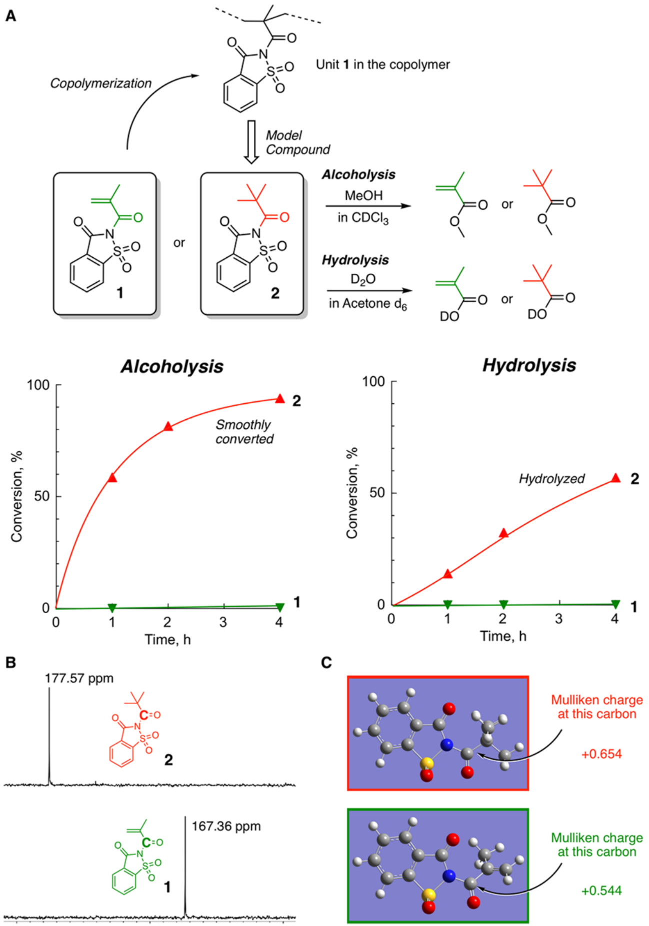

Figure 2. Comparison of the saccharin amide reactivity for alcoholysis and hydrolysis reaction between **1** and **2**. (A) Alcoholysis: $[\mathbf{1} \text{ or } \mathbf{2}]_0/[\mathrm{MeOH}]_0 = 100/500$ mM in $CDCl_3$. Hydrolysis: $[\mathbf{1} \text{ or } \mathbf{2}]_0 = 100$ mM in acetone-d_6/D_2O (9/1 v/v) at ambient temperature. (B) Comparison of the carbonyl carbon peak in ^{13}C NMR spectra. (C) Comparison of the optimized structure and the Mulliken charges of the carbonyl carbon determined by DFT calculation (B3LYP/6-31G* level).

Given by the results of the model reactions, the radical copolymerization of **1** and St was performed under anhydrous conditions using molecular sieves to avoid unfavorable hydrolysis (Figure 3A). Other conditions such as solvent, concentration, and temperature were set the same as in the previous study: $[\mathbf{1}]_0/[\mathrm{St}]_0/[\mathrm{AIBN}]_0 = 800/800/10$ mM in 1,4-dioxane/acetonitrile = 1:1 (v/v) at 60 °C. The dehydrated condition did not affect the copolymerization rate, and the two monomers were consumed at the same rate, similar to our previous study.[19] After a 24 h reaction (the conversion of **1** and St reached 58%), the copolymerization solution was directly added into the anhydrous methanol solution for the alcoholysis transformation. Herein, an inhibitor was also added together with the alcohol for inhibiting further copolymerization of the

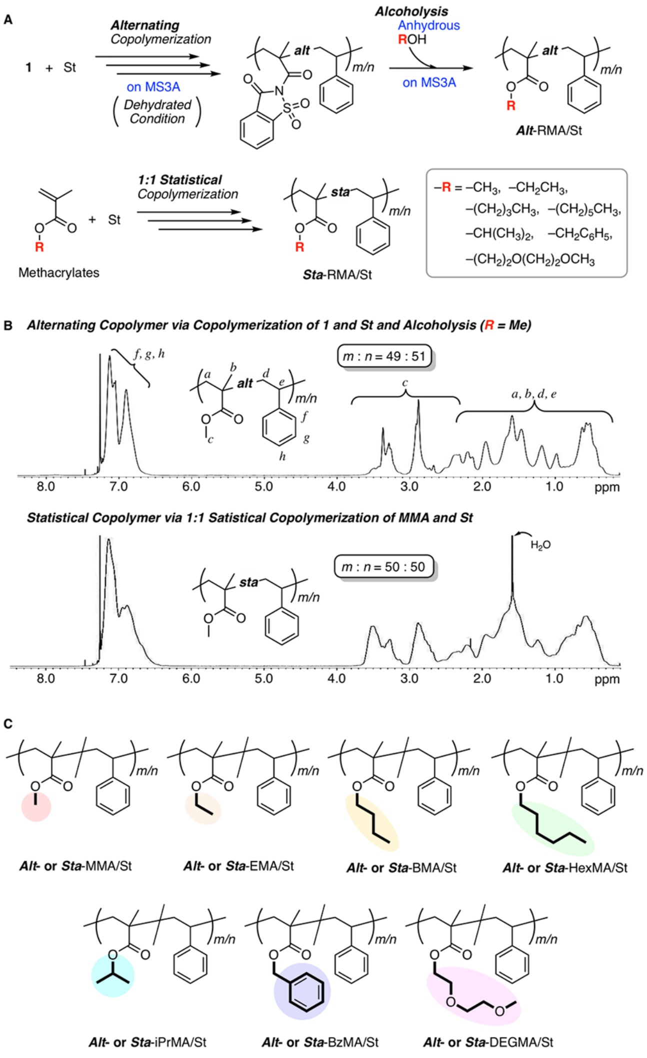

Figure 3. (A) Alternating copolymerization of **1** with St and subsequent alcoholysis reaction for syntheses of methacrylate/styrene alternating copolymers and radical copolymerizations of alkyl methacrylates with St. Polymerization condition: $[\mathbf{1}]_0/[\mathrm{St}]_0/[\mathrm{AIBN}]_0 = 800/800/10$ mM in dioxane/MeCN = 1:1 (v/v) at 60 °C. (B) ^{1}H NMR spectrum of the product via methanolysis in comparison with 1:1 MMA-St statistical copolymer. (C) List of alternating and statistical copolymers in this work.

remaining monomers. Phenothiazine was selected as the inhibitor because the common phenol-based inhibitor could react with the saccharin amides. The alcoholysis reaction was stirred for further 24 h at the higher temperature (60 °C) than the model reaction to ensure the quantitative transformation. The resultant copolymer was purified via reprecipitation in methanol and the number-averaged molecular weight of the resultant polymer was 24 800 (M_w/M_n = 1.71). The ^{1}H NMR spectrum of the purified polymer (Figure 3B) was very similar to that of the alternating copolymer of MMA and styrene obtained via the two-step transformation in the last study.[19] The peaks were sharper than those of the 1:1 statistical copolymer due to the alternating sequence.[19−21]

The advantage of this method is that various pendant groups can be introduced into the alternating copolymers through the selection of the alcohol for the postpolymerization reaction. We thus examined some types of alcohols, such as ethanol, butanol, hexanol, isopropanol, benzyl alcohol, and methoxy diethylene glycol for the alcoholysis transformation. The **1** units were successfully converted into the corresponding methacrylate units. The ^{1}H NMR spectra of resultant copolymers were basically the same as those of the corresponding 1:1 statistical copolymers of ethyl methacrylate (EMA), butyl methacrylate (BMA), hexyl methacrylate (HexMA), isopropyl methacrylate (iPrMA), benzyl methacrylate (BzMA), and methoxy diethylene glycol methacrylate (DEGMA) with St. The integration ratios supported 1:1 composition ratio, and the peaks were obviously sharper due to the uniform and periodic sequence (Figures S4−S10).

The difference of thermal properties between alternating and statistical copolymers was studied by differential scanning calorimetry (DSC, Figure 4A). The samples are listed in Table S1. The alternating copolymers having methacrylate units of shorter alkyl pendant groups corresponding to MMA, EMA, BMA, HexMA, and iPrMA showed lower T_g's by 3−6 °C than those of the statistical copolymers. On the other hand, T_g's of the alternating copolymers carrying larger substituents such as BzMA and DEGMA were almost the same as those of the statistical copolymers. Supposedly, in these alternating copolymers, the plasticizing effect was likely dominant for determining T_g over the main chain sequence. The lower T_g of the alternating copolymers might be caused by the lower molecular weights. However, the molecular weight differences between the two copolymers are small and the molecular weights of all the samples are not so low as to affect T_g (Table S1, M_n > 20 000). Furthermore, the results for BzMA and DEGMA likely dispel the concern.

The lower T_g of the alternating copolymers having smaller substituents might be related to the energy barrier of backbone rotation.[22,23] Hence, we conducted DFT calculations to investigate the energy transition by the C−C bond rotation of model dimer compounds for the MMA-St copolymer: St-MMA, St-St meso, St-St racemo, MMA-St, and MMA-MMA (Figure 4B; see the Supporting Information). Assuming that the energies of the optimized structures were zero, the relative energies to them were scanned by changing the dihedral angles defined by the four carbons forming the red-colored bonds in Figure 4B. The dimers having a styrene unit on the left (St-MMA, St-St meso, and St-St racemo) showed almost similar trends (see the left graph), but St-MMA, the model of an alternating sequence, showed lower total energies around the optimized structure (between 180 and 300°). This result indicates the St-MMAs are more accessible to the wide range of dihedral angles from the optimized structures with a lower energy gain than the two analogues. As for the dimers having an MMA unit on the left (MMA-St and MMA-MMA), the lower energy of the alternating model (MMA-St) was also observed (see the right graph). Thus, the calculation results indicate the alternating sequence is more flexible than the consecutive sequence, and this would be one of the reasons for the lower T_g of the alternating copolymers.

For further analysis and advanced synthesis of sequence-controlled copolymers, we studied the controlled copolymerization of **1** with styrene via RAFT polymerization under anhydrous condition. 2-Cyano-2-propylbenzodithioate (CPDB), which is known to be suitable for conjugated monomers, was used as the chain transfer agent (CTA)[24,25] Here, butanol was selected for the subsequent alcoholysis reaction (Figure 5A). Size exclusion chromatography (SEC) curves of the thus obtained copolymers shifted to a higher molecular weight as the copolymerization proceeded while keeping the unimodal shape (Figure 5B), indicating controlled

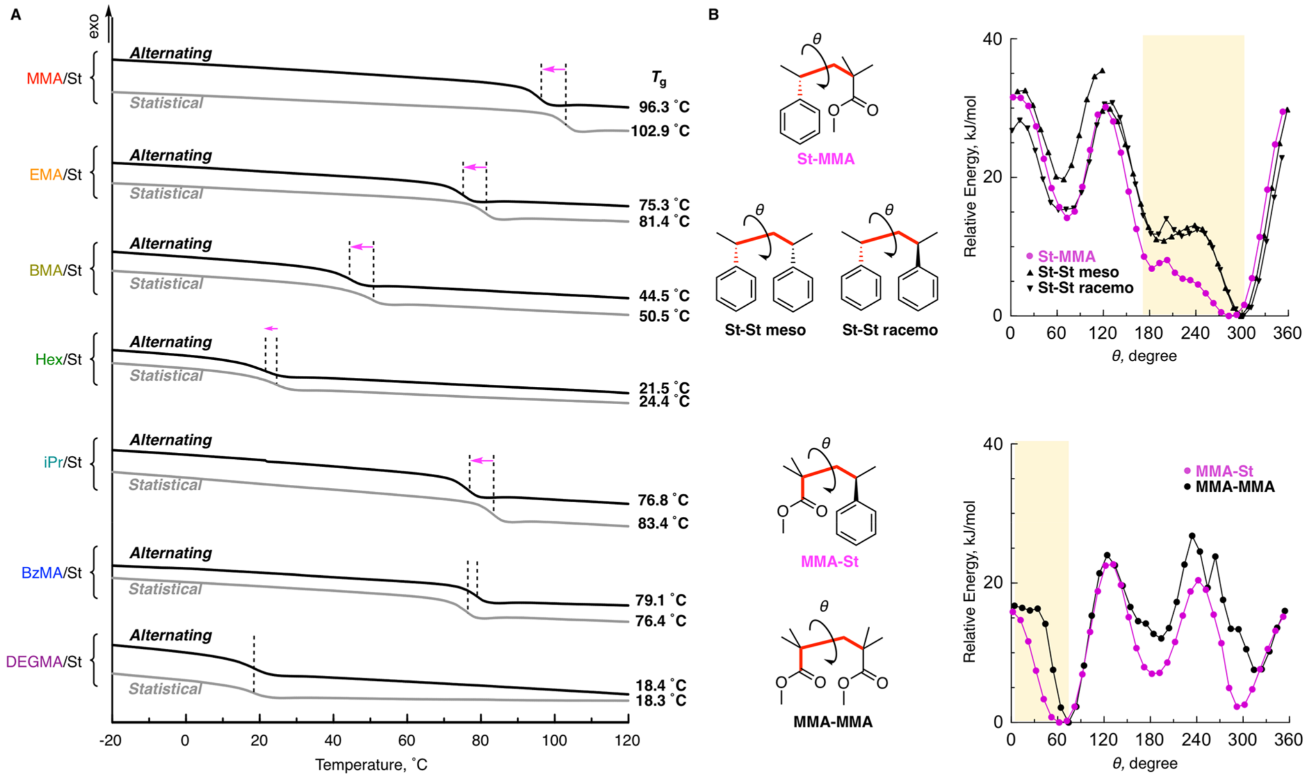

Figure 4. (A) DSC profiles (second heating at 10 °C/min) of the alternating copolymers in comparison to the statistical copolymers. See the Supporting Information for the detailed temperature program and the first and third heating profiles. (B) Energy barrier scan of the model dimer compounds for the MMA/St copolymer via DFT calculations at B3LYP/6-31G* level of theory.

copolymerization. The ^{1}H NMR spectrum of the resultant copolymer after purification (M_n = 3300, M_w/M_n = 1.19 by SEC) was similar to that of the BMA-St alternating copolymer synthesized above, whereas the specific peaks to the chain transfer agent moiety (i.e., benzodithioate) were certainly observed and the integrated ratios were reasonable for the generation of the predicted structure (Figure S11).

The controlled terminal structure by RAFT polymerization and the clear mass difference between butyl methacrylate (142.20) and styrene (104.15) units allowed the sequence analysis by matrix assisted laser desorption/ionization time-of-flight mass spectroscopy (MALDI-TOF-MS).[26,27] As shown in Figure 5C, some peak series were observed but every series appeared in the alternating interval of the mass of BMA and St. From the mass values of the peaks, copolymers having a thiol terminal were detected with the protonated form. The benzodithioate terminal was likely decomposed to thiol during the measurement. The main series was attributed to the copolymers having the same numbers of both units ($n = m$) and one more of the styrene unit ($n = m + 1$) alternatively. Another series was also observed and was composed of peaks from the one more styrene ($n = m + 1$) and the two more ($n = m + 2$) alternatively. This peak pattern indicates that the copolymer contains consecutive propagation of St but it probably took place at the stage of the initiation because the peak pattern did not become complicated even at the higher molecular weight (Figure S14). On the other hand, the corresponding statistical copolymers gave more complex spectra (Figure S13−S16). In this way, the alternating sequence was elucidated by MALDI-TOF-MS.

Finally, we synthesized a block copolymer composed of different alternating copolymer segments (Figure 5D). The first block, MMA-St alternating copolymer, was synthesized using methanol for the alcoholysis transformation. Note that the dithiocarbonate group at the ω-end survived for the alcoholysis transformation unlike an aminolysis counterpart resulting in the thiol terminal. Thus, the resultant MMA-St alternating copolymer was used as a macro-CTA for the second copolymerization of **1** with St, and a subsequent alcoholysis reaction was performed with a different alcohol (i.e., hexanol) from the first step. The SEC curve of the thus-obtained polymer shifted to the higher MW region, although the molecular weight distribution became a little bit broader. In the ^{1}H NMR spectrum of the product after the second polymerization/transformation, peaks derived from the hexyl group were clearly observed (Figure S12). The progress of block copolymerization suggests the possibility of polymer architecture constructions made of various alternating segments.

■ CONCLUSION

We found that the saccharin amide pendant of the unit **1** in the copolymer turned more reactive for both hydrolysis and alcoholysis than that of the monomer. The higher reactivity of the side chain allowed the quantitative transformations of unit **1** into various alkyl methacrylate units via just mixing with alcohols in a one-pot reaction. The resultant methacrylate−styrene alternating copolymers exhibited lower T_g than those of the 1:1 statistical counterparts when the methacrylate substituent was relatively small. Moreover, the copolymerization could be controlled with a RAFT polymerization system to permit sequence analysis by MALDI-TOF-MS as well as the synthesis of a block copolymer composed of two alternating copolymer segments carrying different alkyl chains.

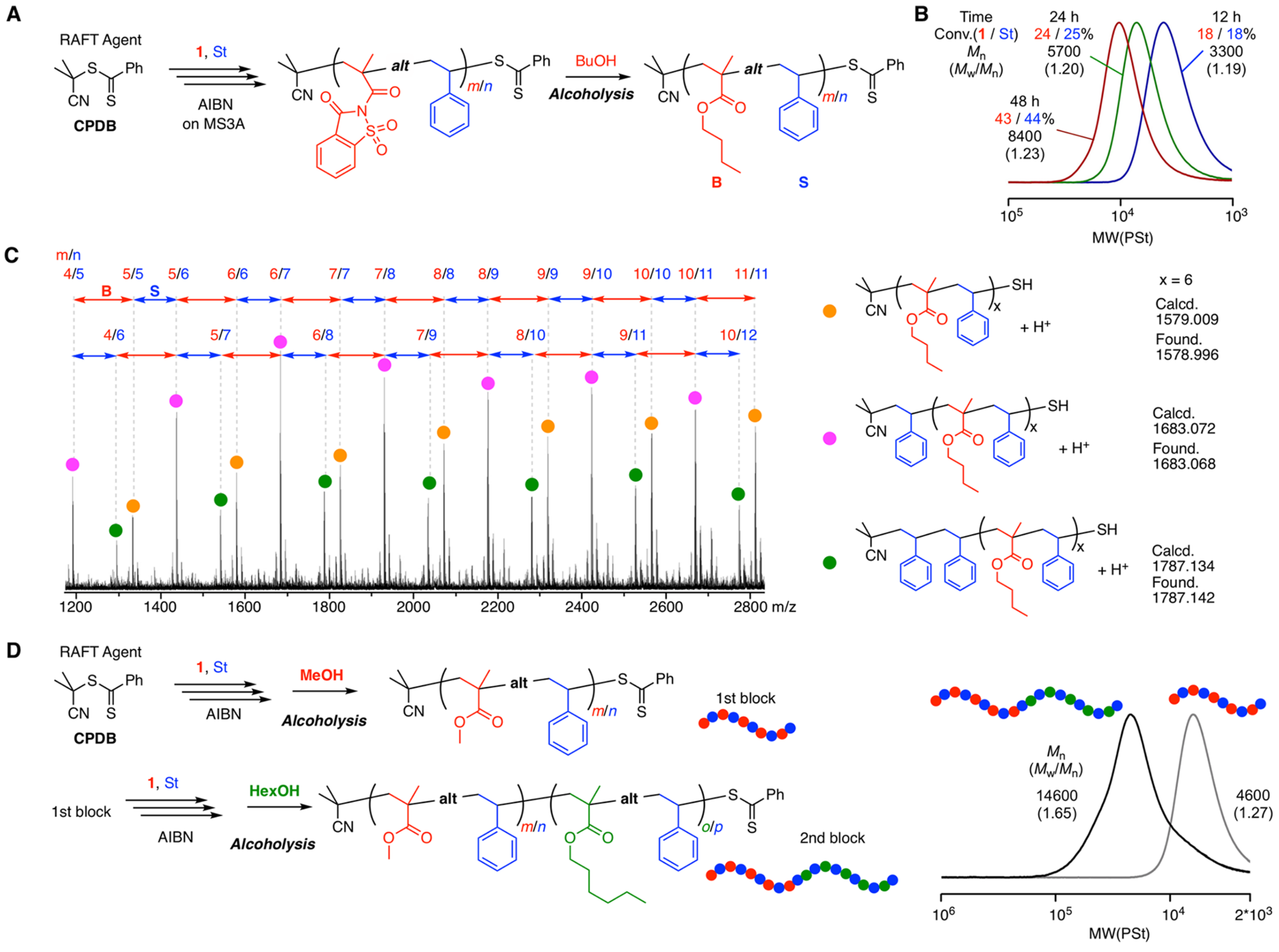

Figure 5. Applications with RAFT copolymerization: (A) Scheme for RAFT copolymerization of 1 with St on MS3A and the subsequent alcoholysis transformation with butanol. Polymerization conditions: $[1]_0/[St]_0/[CPDB]_0/[AIBN]_0$ = 800/800/10/2 mM in dioxane/MeCN = 1:1 (v/v) at 60 °C. (B) SEC curves of the resultant copolymers. (C) Sequence analysis by MALDI-TOF-MS spectrum (reflector mode). (D) Synthesis of block copolymer composed of two kinds of alternating copolymers. See the Supporting Information for the detailed procedures and conditions.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acspolymersau.1c00012.

Experimental details, methods, and other characterization data (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Makoto Ouchi − *Department of Polymer Chemistry, Graduate School of Engineering, Kyoto University, Kyoto 615-8510, Japan;* orcid.org/0000-0003-4540-7827; Email: ouchi.makoto.2v@kyoto-u.ac.jp

Author

Yuki Kametani − *Department of Polymer Chemistry, Graduate School of Engineering, Kyoto University, Kyoto 615-8510, Japan;* Present Address: Y.K.: Institute of Engineering Innovation, School of Engineering, the University of Tokyo, 5-1-5 Kashiwanoha, Kashiwa, Chiba 277-8561, Japan.

Complete contact information is available at: https://pubs.acs.org/10.1021/acspolymersau.1c00012

Notes

The authors declare no competing financial interest.

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