

Poly(*p*-maleimidostyrene) as a macromolecule initiator for polymerization of styrene-type monomers – Synthesis of block copolymers containing poly(*p*-maleimidostyrene) with highly reactive pendent maleimido groups

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ABSTRACT

4-Substituted styrenes (substituent: methoxy, methyl, acetoxy, maleimido and none), were cationically polymerized with an initiator system involving poly(*p*-maleimidostyrene)(PMS) as a macroinitiator, having highly reactive pendent maleimide moieties and a α -chlorobenzyl structure at the polymer end. Using PMS/SnCl₄/tetra-*n*-butylammonium chloride initiator system, block copolymers of 4-substituted styrenes onto PMS were obtained in CH₂Cl₂ at 0 °C. As for the polymerization of *N*-(4-vinylphenyl) maleimide and 4-acetoxystyrene, especially, PMS as the macroinitiator was almost completely utilized for initiation reaction and the polymers having PMS-*b*-poly(4-substituted styrene) platform with very narrow and unimodal molecular weight distribution were formed in contrast with the case of using 4-methoxystyrene and 4-methylstyrene with stronger electron releasing groups, in which the molecular weight distributions of the formed polymeric materials appeared to be bimodal.

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1. Introduction

Synthetic polymer with highly reactive pendent groups is a very attractive material because it is useful in various fields of applications such as biotechnology [1] and electronics [2] as reactive and functional polymers.

A maleimido group is one of promising groups with high reactivity, which can be easily modified by Michael type addition [3] and Diels–Alder reaction [4]. Some maleimide derivatives have been utilized as labeling reagents for proteins [5].

In the previous works [6], the polymerization profiles of *N*-(4-vinylphenyl)maleimide (VPMI) having styrene-type vinyl and *N*-phenylmaleimide-type vinylene groups were investigated with cationic, anionic, radical initiators [6]. Using a cationic initiator system consisting of 1-chloroethylbenzene, tin tetrachloride, and tetra-butylammonium chloride (CEB/SnCl₄/TBAC) [7], only the styrene-type vinyl group of VPMI was polymerized regioselectively and, moreover, with living manner [8].

The resulting poly(*p*-maleimidostyrene) (PMS), produced by regioselective-living polymerization with CEB/SnCl₄/TBAC, that has a polystyrene framework with the determined molecular weight and, hence, with the precise number of dense pendent highly

reactive maleimido groups, was employed as a new material for the immobilization of enzymes [9] utilizing the reactivity of the pendent maleimido group with mercapto or amino groups in the enzyme.

As described in Scheme 1, the terminated end of PMS (V) prepared by regioselective-living polymerization with CEB/SnCl₄/TBAC is, at the same time, supposed to have a similar structure to that of 1-chloroethylbenzene (I) that is a part of initiator system of CEB/SnCl₄/TBAC. This implies that PMS obtained with CEB/SnCl₄/TBAC can be a component of the macromolecular initiator system of cationic polymerization of styrene-type monomers to produce PMS-*b*-poly(4-substituted styrene) type block copolymers.

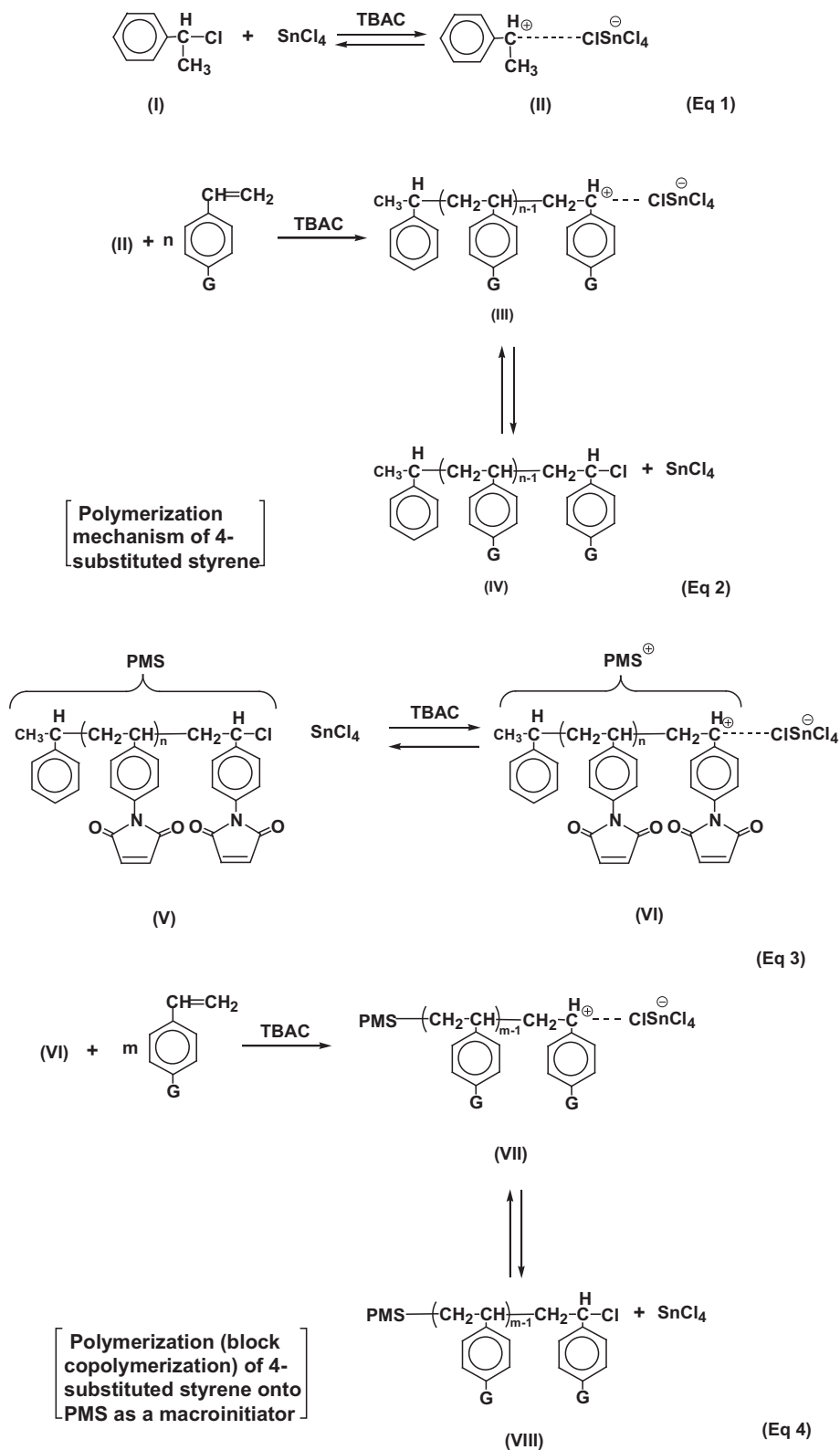
In this paper, polymerizations of various 4-substituted styrene-type monomers with a macromolecular initiating system consisting of PMS prepared by regioselective-living polymerization, tin tetrachloride and TBAC (PMS/SnCl₄/TBAC) to produce block copolymers involving PMS with highly reactive pendent maleimido groups are described. The cationic polymerization behaviors of several 4-substituted styrene-type monomers are also discussed.

2. Experimental

All experiments for polymerization reactions were carried out under purified nitrogen atmosphere to exclude oxygen and moisture.

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Scheme 1.

2.1. Reagents

N-(4-vinylphenyl)maleimide (VPMI) were synthesized in the same way as described in the previous paper [6]. 4-Methylstyrene (Aldrich) and 4-methoxystyrene (Wako) were purified by fractional

distillation. 4-Aceoxystyrene (TCI) and styrene (Aldrich) were dried by refluxing over calcium hydride, and distilled before use. Tin tetrachloride (Aldrich) and 1-chloroethylbenzene (CEB) (TCI) were purified by distillation. Tetra-butylammonium chloride (TBAC) (Aldrich) was purified by recrystallization from a mixture of

acetone and diethyl ether. Dichloromethane was dried by refluxing over calcium hydride and distilled before used.

2.2. Synthesis of PMS

VPMI purified by recrystallization was used as a monomer after thoroughly dried below r.t. under reduced pressure. A solvent and a solution of VPVI were placed into an ampoule that had been carefully flame dried. A solution of an initiator system (1-chloro-oethylbenzene (CEB)(1.0 Eq)/tin tetrachloride (SnCl_4)(5.0 Eq)/tetrabutylammonium chloride (TBAC)(2.0 Eq)) was added to VPVI solution (7.5×10^{-1} mol/L: 15 Eq) at 0 °C with stirring. After 24 h, the polymerization was terminated with ethanol. The resulting PMS was isolated by precipitation from a large amount of methanol and dried under vacuum at room temperature to a constant weight.

2.3. Polymerization with PMS/ SnCl_4 /TBAC initiating system (block copolymerization on PMS as a macroinitiator)

PMS obtained as above was used as a macroinitiator after thoroughly dried under reduced pressure. Dichloromethane, PMS (1.0 Eq), TBAC(2.0 Eq), and a monomer(5.0×10^{-1} mol/L: 50 Eq) were placed into an ampoule that had been carefully flame dried. Polymerization was started by the addition of a dichloromethane solution of SnCl_4 (5.0 Eq) to the mixture at 0 °C with stirring. After definite time, the polymerization terminated with ethanol. The copolymer was isolated by precipitation from an ethanol and then dried in vacuo to constant weight. The structure of the resulting copolymers was analyzed with ^1H NMR, ^{13}C NMR and IR.

2.4. Measurements

^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-ECP 500 FT-NMR spectrometer using deuterated chloroform as a solvent. An IR spectrum was measured on a JEOL JIR-7000 FT-IR. Size-exclusion chromatography (SEC) was conducted UV detectors (HITACHI L7400UV) with TSK gel GMHXL (exclusion limit: $>1.0 \times 10^5$) $\times 2$ – Shodex KF-802 (exclusion limit: 5.0×10^3) column series using THF as eluent (flow rate 1.0 mL/min). The molecular weight calibration was carried out by using polystyrene standard samples.

3. Results and discussion

3.1. Polymerization with PMS/ SnCl_4 /TBAC initiating system (block copolymerization on PMS as a macroinitiator)

All polymeric materials obtained were yellow or pale yellow powdery solids.

Fig. 1 shows number averaged molecular weights (M_n) and molecular weight distributions (MWD) of the obtained polymers; where the M_n was measured by size-exclusion chromatography (SEC) calibrated by standard polystyrene.

3.1.1. Polymerization of 4-methoxystyrene

Using 4-methoxystyrene as a monomer, the molecular weight distribution of the polymer obtained exhibits distinct bimodal profile (Fig. 1A). The ratio of the high molecular weight part to the low molecular weight part is 47: 53. The M_n of the high molecular weight part of the polymers is considerably larger than that of PMS, while M_n of the low molecular weight part is the same as that of PMS used as a macroinitiator.

The high molecular weight part was fractionated by SEC and analyzed its structure by NMR and IR. On the ^1H NMR of the fractionated part, a signal of methoxy proton assignable to 4-methoxystyrene units in the polymer was observed at 3.72 ppm, while the

signal from vinylene protons in a maleimide moiety in PMS as a macroinitiator were hardly observed because of high degree of polymerization of 4-methoxystyrene in that part. Meanwhile, in the IR spectrum of the fractionated high molecular weight part, the absorption at 1716 cm^{-1} assigned to imide carbonyl group in PMS was clearly observed. these spectral data indicate that PMS acted as a macroinitiator, and that thus block copolymer involving PMS and poly(4-methoxystyrene) (PMS-*b*-poly(4-methoxystyrene)) was produced though only 4.1% of PMS as a macroinitiator was consumed.

3.1.2. Polymerization of 4-methylstyrene

Using 4-methylstyrene as a monomer, the molecular weight distribution of the polymer obtained shows poorly-separated bimodal profile ($M_w/M_n = 1.64$ as a whole) as seen in Fig. 1B. The M_n of the high molecular weight part of the polymer (55%, $M_n = 1.4 \times 10^4$, $M_w/M_n = 4.8$) is fairly larger than that of PMS, while that of the low molecular weight part (45%, $M_n = 3.2 \times 10^3$, $M_w/M_n = 1.3$) remains at the position of that of PMS. It was revealed by the NMR and IR spectra that the fractionated high molecular weight part contained maleimido groups in PMS as well as the case of 4-methoxystyrene. In this polymerization, initiator efficiency of PMS as a macroinitiator was 39%. This is much larger than that of the case of 4-methoxystyrene.

3.1.3. Polymerization of styrene

In the case of using styrene as a monomer, the molecular weight distribution of the polymer obtained also shows poorly-separated bimodal and broad profile ($M_w/M_n = 1.62$) similar to the case of the polymerization of 4-methylstyrene as seen in Fig. 1C. Unlike the case of 4-methylstyrene the molecular weight of the lower molecular weight part is, however, not the same as that of PMS but shifts slightly higher (M_n : from 3.8×10^3 to 7.8×10^3).

It was confirmed by ^1H NMR and IR spectra that the polymer produced had maleimido groups in PMS as a macroinitiator, regardless its molecular weight. This implies that the block copolymerization of styrene onto the almost whole of PMS can take place.

The poorly-separated bimodal and broad profile of the molecular weight distribution of the obtained polymer may be caused by heterogeneity of the polymerization system that was brought about as the polymerization reaction proceeded.

3.1.4. Polymerization of VPVI and 4-acetoxystyrene

As seen in Fig. 1D and E, using VPVI and 4-acetoxystyrene as monomers the polymers produced exhibit almost unimodal and narrow molecular weight distributions (VPVI: $M_w/M_n = 1.31$, 4-acetoxystyrene: $M_w/M_n = 1.31$).

As shown in Fig. 2, NMR spectra reveal that the polymer prepared from VPVI is PMS itself having increased degree of polymerization because of the only disappearance of the signal assigned to α -chlorobenzyl moiety at the polymer end (Fig. 2B), and that the polymer obtained from 4-acetoxystyrene can be also block copolymer consisting of PMS and poly(4-acetoxystyrene) sequences (Fig. 2D).

Whether the obtained polymer from 4-acetoxystyrene was block copolymer having a PMS sequence could not be confirmed from the thermoanalysis, because the glass transition temperatures (T_g) of polystyrene and 4-substituted styrene derivatives involving PMS are close to each other [10].

3.2. On the polymerization behaviors of styrene-type monomers with PMS/ SnCl_4 /TBAC initiating system

The polymerization of styrene-type monomers with a macro-molecular initiator PMS/ SnCl_4 /TBAC is considered to proceed by cation polymerization mechanism as illustrated in Scheme 1.

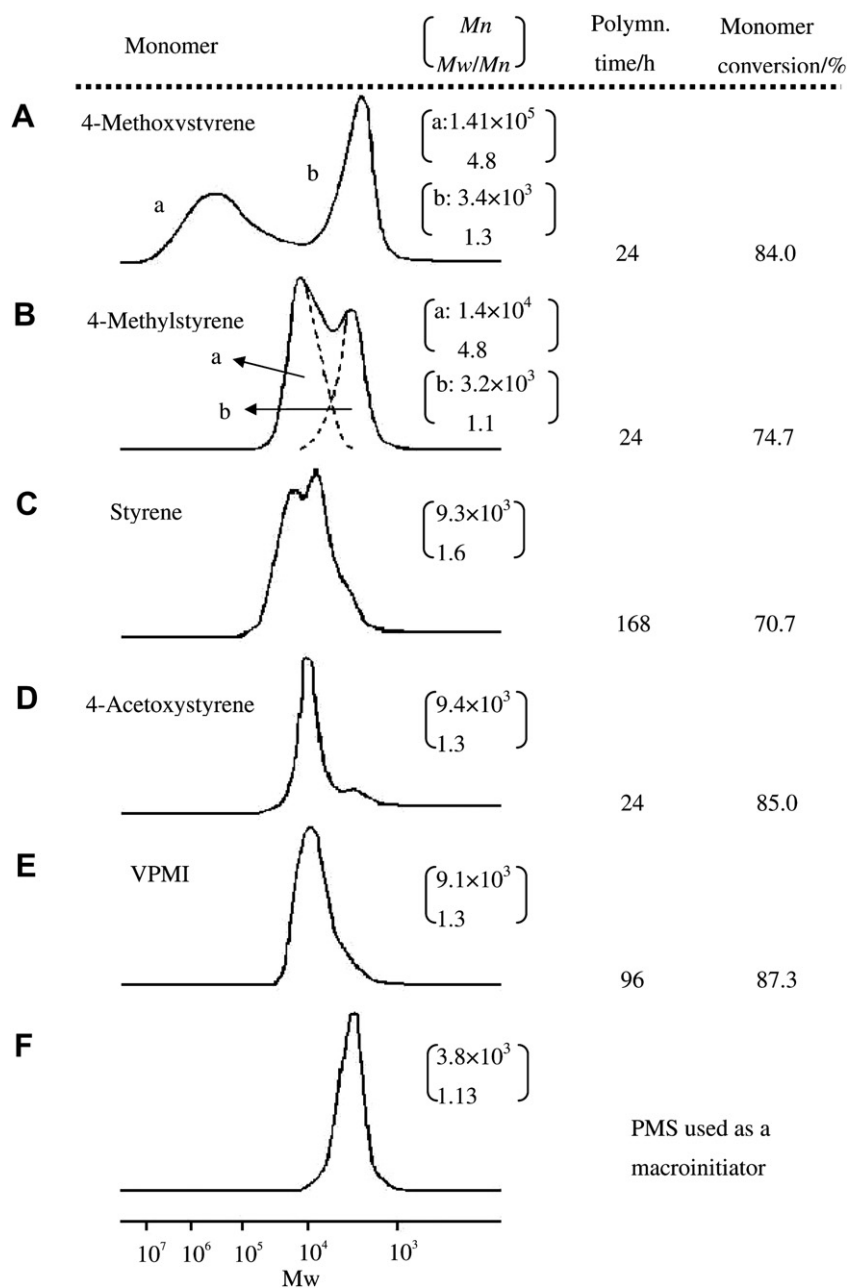


Fig. 1. SEC profiles of polymeric materials from five styrene-type monomers obtained with PMS (1.0 Eq.)/SnCl₄ (5.0 Eq.)/TBAC (2.0 Eq.) initiator system (A, B, C, D, and E); [Styrene-type monomer] = 0.50 mol/L (50 Eq.) in dichloromethane at 0 °C. PMS was prepared by cationic polymerization of VPMI with CEB (1.0 Eq.)/SnCl₄ (5.0 Eq.)/TBAC (2.0 Eq.) initiator system (F); [VPMI] = 0.75 mol/L (15 Eq.) in dichloromethane at 0 °C. Monomer conversion was calculated by the following equation: monomer conversion(%) = (product(g) - PMS in the initiator system(g)) / monomer charged(g) × 100.

1-Chloroethylbenzene and tin tetrachloride generates cationic species (II) by the equilibrium reaction (Eq (1) in Scheme 1). The cationic species (II) initiates the polymerization of 4-substituted styrene-type monomers (Eq (2) in Scheme 1) and produces the polymers (IV) [11] having a α -chlorobenzyl moiety at one polymer end, which is the same structure as (I) being one of the components of the initiator system.

In the case of the polymerization of VPMI with CEB/SnCl₄/TBAC, the polymer formed is PMS with α -chlorobenzyl proton at the polymer end (V in Eq (3)). In fact, in the ¹H NMR spectrum α -chlorobenzyl proton in PMS appeared in rather low magnetic field (4.37 ppm, e in Fig. 2A) as well as that of 1-chloroethylbenzene (I).

Hence, initiator system comprising PMS can initiate cationic polymerizations of some styrene-type monomers as a macroinitiator

to yield block copolymers possessing the PMS sequences (VIII in Eq (4)).

The polymerization behaviors of 4-substituted styrenes involving SEC profiles with PMS/SnCl₄/TBAC initiating system where PMS is employed as a macroinitiator can be accounted for in terms of electron releasing ability of the substituent except the case of the polymerization of styrene in which the polymerization system became heterogeneous.

Table 1 summarizes the values of the chemical shift at β -carbon and Hammett's σ_p of the 4-substituted styrenes.

4-Methoxystyrene (G = OCH₃ in Scheme 1) having a methoxy group that is the strongest electron releasing group in the four substituents used here can be the most reactive monomer with the most nucleophilic β -carbon (observed at 111.51 ppm in ¹³C NMR) to

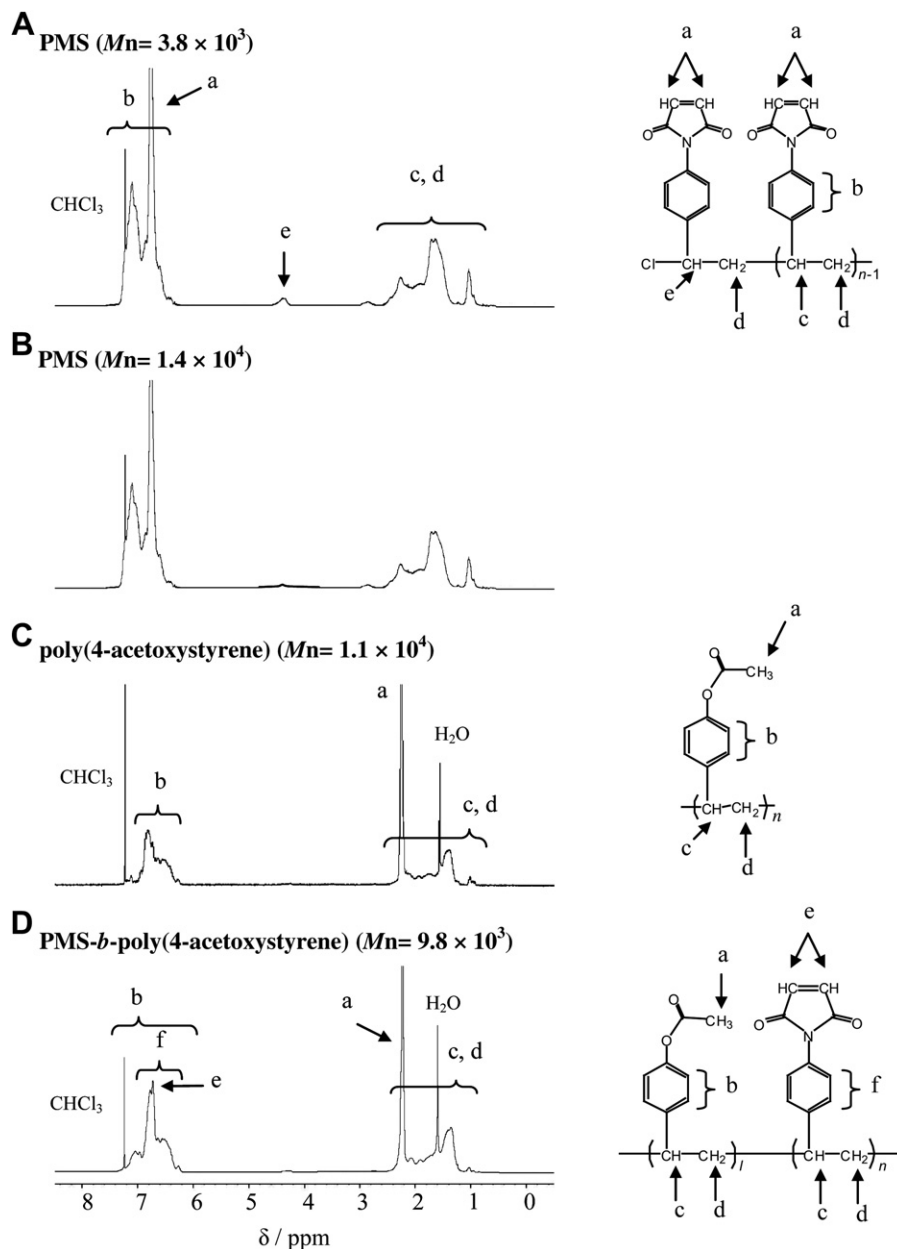


Fig. 2. ^1H NMR spectra of PMS obtained with CEB (1.0 Eq.)/ SnCl_4 (5.0 Eq.)/TBAC (2.0 Eq.) initiator system (A); $[\text{VPMI}] = 0.75 \text{ mol/L}$ (15 Eq.) in dichloromethane at 0°C , PMS-*b*-PMS (high molecular weight PMS) obtained with PMS (1.0 Eq.)/ SnCl_4 (5.0 Eq.)/TBAC (2.0 Eq.) initiator system (B); $[\text{VPMI}] = 0.5 \text{ mol/L}$ (50 Eq.) in dichloromethane at 0°C , poly(4-acetoxystyrene) obtained with CEB (1.0 Eq.)/ SnCl_4 (5.0 Eq.)/TBAC (2.0 Eq.) initiator system (C); $[\text{4-acetoxystyrene}] = 0.25 \text{ mol/L}$ (25 Eq.) in dichloromethane at 0°C , and PMS-*b*-poly(4-acetoxystyrene) obtained with PMS (1.0 Eq.)/ SnCl_4 (5.0 Eq.)/TBAC (2.0 Eq.) initiator system (D); $[\text{4-acetoxystyrene}] = 0.50 \text{ mol/L}$ (50 Eq.) in dichloromethane at 0°C .

the benzyl cation (VII) as a propagating species. This can carry the very fast rate of propagation and result in the block copolymer having PMS-*b*-poly(4-methoxystyrene) platform possessing a considerably high molecular weight poly(4-methoxystyrene) segment with relatively broad molecular weight distribution. The

resulting considerably high number averaged molecular weight, broadened molecular weight distribution, and very low initiator efficiency of PMS for the polymerization of the higher molecular weight part imply that the polymerization of 4-methoxystyrene initiated with PMS as a macroinitiator proceeds through slow initiation and rapid propagation without significant termination mechanism.

4-Methylstyrene whose β -carbon in the vinyl group is observed at 112.45 ppm in ^{13}C NMR is the moderately reactive monomer to the propagating benzyl cation (VII) due to the moderate electron releasing ability of methyl group. Therefore, that can give rise to the rather slow rate of propagation comparing to that of 4-methoxystyrene. This does not provide clear but poorly-separated bimodal profile to the molecular weight distribution of the obtained polymer.

Table 1

^{13}C NMR chemical shift of β -carbon of 4-substituted styrenes and Hammett's σ_p of the substituents.

Monomer	^{13}C NMR/ppm	Hammett's σ_p
4-Methoxystyrene	111.51	-0.27
4-Methylstyrene	112.45	-0.17
Styrene	113.80	0
4-Acetoxystyrene	113.73	0.31
N-(4-Vinylphenyl)maleimide	113.99	—

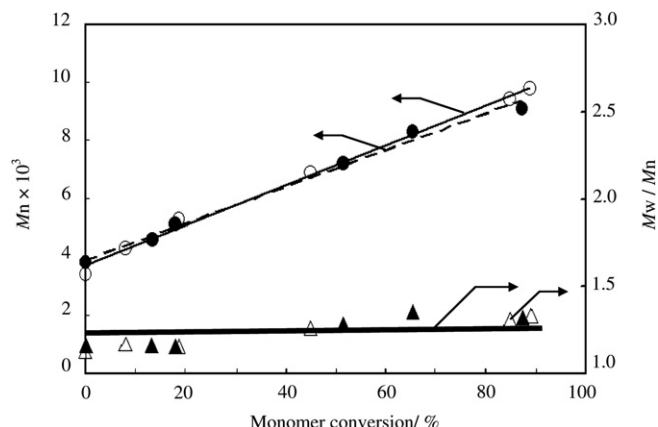


Fig. 3. Relationships of number averaged molecular weights (M_n) and molecular weight distributions (M_w/M_n) of PMS-*b*-poly(4-acetoxystyrene) and those of PMS-*b*-PMS with monomer conversions with PMS(1.0Eq.)/SnCl₄(5.0Eq.)/TBAC(2.0Eq.) initiator system. For 4-acetoxystyrene (●, ▲); [4-acetoxystyrene] = 0.50 mol/L (50Eq.) (PMS used in the initiator system: M_n = 3800, M_w/M_n = 1.16) in dichloromethane at 0 °C, and for VPMI (○, △); [VPMI] = 0.50 mol/L (50Eq.) (PMS used in the initiator system: M_n = 3400, M_w/M_n = 1.13) in dichloromethane at 0 °C.

In the case of the polymerizations of VPMI and 4-acetoxystyrene, the electron releasing ability of the substituents of those monomers is not so high but enough to enhance nucleophilicity of the vinyl group to react with the propagating cation. The rate of propagation is not supposed to be as fast as that of the initiation. Especially, when VPMI is used as a monomer, the initiation reaction is the same as the propagation reaction in itself. Certainly, this is the living polymerization of VPMI of itself and is correspondent to the fact that the polymerization of VPMI proceeds with living manner with CEB/SnCl₄/TBAC initiator system [8].

The electron releasing ability of 4-acetoxystyrene can be estimated to be less than that of styrene (σ_p = 0) from the value of Hammett's σ_p . The fact that the chemical shift of β -carbon of 4-acetoxystyrene is almost the same as that of VPMI (Table 1), implies that 4-acetoxystyrene can be polymerized with living manner with CEB/SnCl₄/TBAC, and, moreover, with PMS/SnCl₄/TBAC initiator systems as well as the case of VPMI.

Fig. 3 shows the relationship between conversion of monomer and number averaged molecular weight of yielded polymer with PMS/SnCl₄/TBAC initiating system for VPMI and 4-acetoxystyrene

respectively. The linear relation of the conversions of monomer with the M_n s of polymer is observed for each polymerization. Fig. 3 also shows that the molecular weight distributions of obtained polymers remain still narrow (VPMI: M_w/M_n = ~1.3 4-acetoxystyrene: M_w/M_n = ~1.3) in the wide range of conversions of monomers, respectively. The observed M_n s of the polymers obtained show good agreement with those theoretical values; at 90% monomer conversion: 1.3×10^4 for VPMI and 1.1×10^4 for 4-acetoxystyrene.

These results suggest that the polymerizations of VPMI and 4-acetoxystyrene with PMS/SnCl₄/TBAC initiating system proceed with living manner with narrow molecular weight distributions.

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