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Stereospecific anionic polymerization of α-(alkoxymethyl)acrylate derivatives affording novel vinyl polymers with macrocyclic side chains

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Dedicated to Professor Imanishi on the occasion of his retirement

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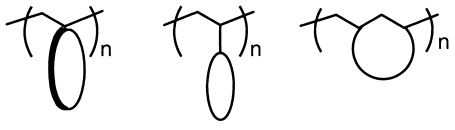
Abstract

Macrocyclic α-(alkoxymethyl)acrylates such as 2-methylene-4-oxa-12-dodecanolide, 2-methylene-4-oxa-16-hexadecanolide, 8,9-benzo-2-methylene-4,7,10-trioxa-8-dodecen-12-olide and 9,10-benzo-2-methylene-4,8,11-trioxa-9-tetradecen-14-olide were synthesized and their polymerizability and the stereoregularity of the obtained polymers by radical and anionic methods were investigated. The anionically obtained polymers possessed a normal vinyl polymer structure, and the polymerization with organolithium and Grignard reagents afforded isotactic-rich polymers, whereas the polymers obtained with potassium biphenylide were almost atactic based on their ^{1}H NMR analysis. The anionically obtained polymers bearing a crown ether-type side chain demonstrated a cobalt ion transport ability as a synthetic ion channel using vesicles prepared with dihexadecyl phosphate.

Keywords: Anionic polymerization; Macrocyclic monomer; Vinyl polymer

1. Introduction

α-(Alkoxymethyl)acrylate derivatives, which have two different types of substituents on an olefin, can provide polymers with a controlled stereochemistry by radical polymerization using Lewis acid catalysts [1–4], as well as the anionic method [5–8], due to the coordination of α-substituents to a metal catalyst. We recently found that the novel macrocyclic monomers such as 8,9-benzo-2-methylene-4,7,10-trioxa-8-dodecen-12-olide (**1**) and 9,10-benzo-2-methylene-4,8,11-trioxa-9-tetradecen-14-olide (**2**), synthesized by harnessing the characteristic structure of the α-(alkoxymethyl)acrylate afforded the vinyl polymers with crown ether-type side chains by anionic polymerization in tetrahydrofuran (THF) at −78 °C [9]. The obtained polymers have a novel structure with respect to the attaching manner of the crown ether to the polymer main-chain. The macrocycles are perpendicularly arranged on the main-chain in poly(**1**) and poly(**2**) (type I) whereas the polymers bearing crown ether side chains have been generally synthesized by polymerization of a monomer having a crown ether as a substituent [10–14] or the cyclopolymerization of a two-functional monomer [15–17]. In the former, the crown ether groups flexibly attach to the main-chain (type II), and in the latter, rings are linked and fixed through the main-chain (type III). The synthesized polymers with a 'type I' structure showed new functionalities, such as selective alkali-ion extraction and ion transport abilities [9].



type I type II type III

In this paper, the polymerizability and the stereoregularity of the polymers obtained by the radical and anionic methods were mainly investigated in detail using macrocyclic α-(alkoxymethyl)acrylates such as 2-methylene-4-oxa-12-dodecanolide (**3**) [9,18] and 2-methylene-4-oxa-16-hexadecanolide (**4**), in addition to monomers **1** and **2**. The monomers have two polymerizable groups, a methacrylic *exo*-methylene group for the vinyl polymerization and a lactone for the ring-opening process. High chemoselectivity for the vinyl polymerization is important for synthesizing the polymers with macrocyclic side chains. The chemospecific ring-opening polymerization of **3** using a lipase-catalyst was recently reported [18].

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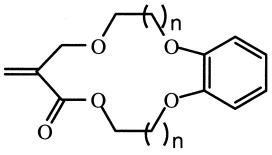
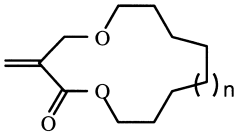
2. Experimental

2.1. Materials

The solvents, toluene and THF, used for polymerization were distilled from Na wire and distilled again from butyllithium (*n*-BuLi) for toluene and from $LiAlH_4$ for THF under high vacuum just before use. *n*-BuLi was synthesized from 1-chlorobutane and lithium powder in heptane under a dry argon atmosphere. Cyclohexylmagnesium bromide (*c*-HexMgBr) was prepared from cyclohexyl bromide and magnesium turnings in diethyl ether. *N*,*N*,*N*′,*N*′-Tetramethylethylenediamine (TMEDA) was dried over calcium hydride and then distilled under reduced pressure for use as a toluene solution. A radical initiator, diisopropyl peroxydicarbonate [$(i\text{-PrOCO}_2)_2$], was kindly provided by the NOF Co. and used as a toluene solution. Monomers were synthesized from ethyl α-(bromomethyl)acrylate as previously reported [9,18].



n = 1: **1**
2: **2**



n = 1: **3**
5: **4**

2.1.1. 2-Methylene-4-oxa-16-hexadecanolide (*4*)

^{1}H NMR ($CDCl_3$): δ 1.29–1.72 (m, 20H, $-CH_2-$), 3.50 (t, $J = 6.0$ Hz, 2H, $-OCH_2-$), 4.18 (s, 2H, $=CCH_2-$), 4.24 (t, $J = 5.6$ Hz, 2H, $-CO_2CH_2-$), 5.78 (d, $J = 1.6$ Hz, 1H, vinyl), 6.32 (d, $J = 1.6$ Hz, 1H, vinyl) ppm; IR (neat): 2929, 1725, 1637, 1459, 1389, 1267, 1167, 1102, 953 cm^{-1}; Elemental analysis. Found: C, 71.46; H, 10.61. Calcd for $C_{14}H_{16}O_5$: C, 71.60; H, 10.52%.

2.2. Polymerization procedure

The anionic polymerization was carried out according to the following procedure. A monomer solution (0.5 − 1.0 M) was placed in a glass ampoule equipped with a three-way stopcock under a dry nitrogen atmosphere with a syringe and cooled to −78 °C. The polymerization was initiated by adding an initiator solution to the monomer solution and terminated by adding a small amount of methanol. The polymers were precipitated in a large amount of methanol, separated by centrifugation, and dried in vacuo.

2.3. Cobalt ion transport experiment

Vesicles were prepared as follows: dihexadecyl phosphate (DHP) (27.0 mg, 50 μmol), water (5 ml), sodium hydroxide (0.1 M, 0.25 ml) and aqueous 4-(2-pyridylazo)-resorcinol monosodium salt (PAR) solution (5 mM, 5 ml) were added to a polymer solution (1.0 mg) in THF (0.2 ml) at 80 °C. The mixture was sonicated for 55 min and then washed by dialysis with cellophane in water. The total volume of the resulting dispersion was adjusted to 10–11 ml.

The cobalt ion transport was measured using a 2.0 mm UV-cell filled with the prepared vesicles in water (0.6 ml) by adding a solution of cobalt(II) nitrate (1.17 mM, 10 μl) and the absorbance increase at 510 nm and decrease at 390 nm were recorded [9,13,14].

2.4. Measurements

^{1}H and ^{13}C NMR spectra were measured on a Varian Gemini-2000 (400 MHz for ^{1}H) spectrometer in $CDCl_3$ with tetramethylsilane as the internal standard. Infrared (IR) spectra were recorded on a JASCO FT/IR-620 spectrometer. The size exclusion chromatographic (SEC) analyzes were performed on a Shodex GPC-System-21 equipped with Shodex UV-41 and Shodex RI-71S detectors using Shodex GPC KF-806L and KF-803 columns (exclusion limit $= 2 \times 10^7$ and 7×10^4, polystyrene standards) connected in series and THF was used as eluent (temperature = 40 °C, flow rate = 1.0 ml/min). Calibration was carried out using standard polystyrenes. Differential scanning calorimetry (DSC) measurement was carried out with a Seiko SSC-200 equipped with a DSC-220 apparatus (at a heating rate of 10 °C/min under an N_2 atmosphere). Vesicle size was measured by a NICOMP 380-ZLS dynamic light-scattering detector.

3. Results and discussion

The results of the anionic and radical polymerizations of monomer **3** having a 13-membered ring structure are summarized in Table 1. The polymerizations proceeded with moderate to good yields to afford methanol-insoluble polymers. They were fully soluble in THF and $CHCl_3$.

Fig. 1(a) demonstrates the ^{1}H NMR spectrum of the obtained poly(**3**) using the *c*-HexMgBr–TMEDA complex in THF (Table 1, entry 5). Each peak is assigned as shown in the figure and no peaks in olefinic region were observed. These results clearly indicate that the obtained polymer has a normal vinyl polymer structure. In addition, the spectral pattern of the main-chain methylene protons at 1.8–2.5 ppm shows a typical AB quartet with small broad peaks which is a typical pattern for isotactic poly(α-substituted acrylate)s [5–8]. Accordingly, the polymer prepared with the Grignard reagent in THF is rich in isotacticity, which is evaluated as *m*/*r* = 90:10. The estimated tacticities for the polymers

Table 1
Anionic and radical polymerizations of **3** (anionic polymerization: [**3**]/[initiator] = 20, temperature = −78 °C; radical polymerization: [**3**]/[initiator] = 30, temperature = 30 °C, time = 46 h)

Entry	Initiator	Solvent	Yield[a] (%)	DP (M_w/M_n)[b]	Tacticity, *m*/*r*[c]
1	*c*-HexMgBr–TMEDA	Toluene	50	37 (15)[d]	76:24
2	*n*-BuLi	Toluene	94	110 (10)[d]	58:42
3	Ph_2NLi–TMEDA	Toluene	89	24 (1.9)	73:27
4	$(i\text{-}PrOCO_2)_2$	Toluene	62	27 (1.6)	–
5	*c*-HexMgBr–TMEDA	THF	64	150 (18)[d]	90:10
6	*n*-BuLi	THF	89	43 (1.9)	68:32
7	Ph_2NLi–TMEDA	THF	88	35 (1.5)	72:28
8	K-biphenylide	THF	45	58 (6.0)	–

[a] Methanol-insoluble part.
[b] Determined by SEC (polystyrene standard), DP = $M_n/(M_n$ of **3**).
[c] Estimated by ^{1}H NMR analysis.
[d] Multi-modal.

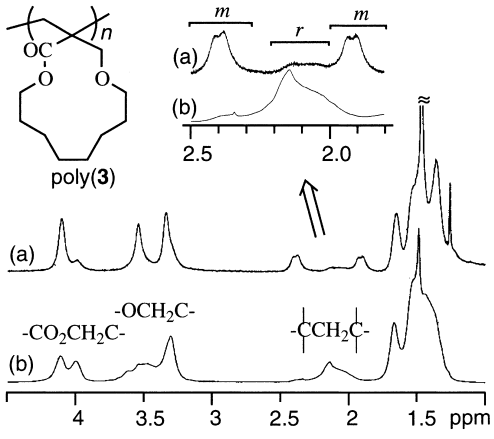


Fig. 1. ^{1}H NMR spectra of poly(**3**) obtained with *c*-HexMgBr–TMEDA (Table 1, entry 5) (a) and with K-biphenylide (Table 1, entry 8) (b) in THF at −78 °C (in $CDCl_3$, 60 °C).

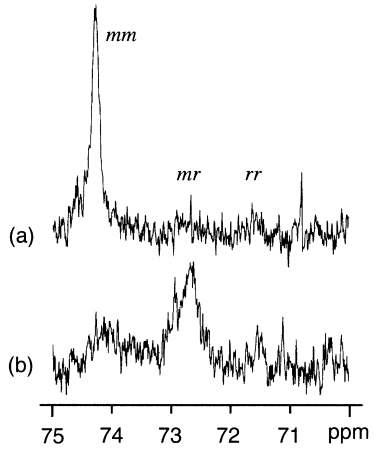
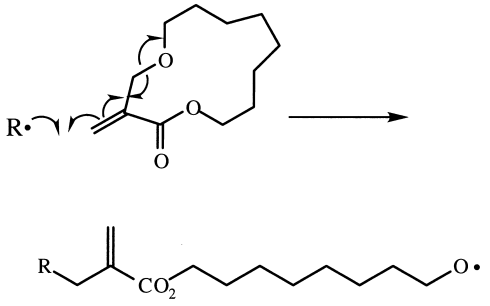


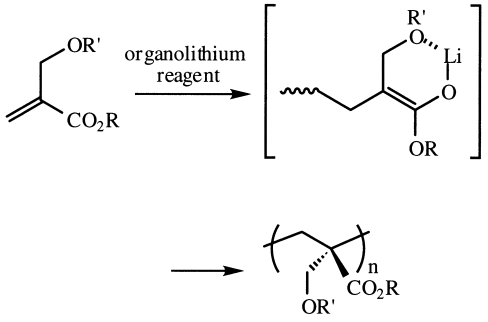
Fig. 2. ^{13}C NMR spectra of α-methylene carbon of poly(**3**) obtained with *c*-HexMgBr–TMEDA (Table 1, entry 5) (a) and with K-biphenylide (Table 1, entry 8) (b) in THF at −78 °C (in $CDCl_3$, 60 °C).

prepared with organolithium and Grignard reagents are listed in Table 1. Although poly(**3**) obtained with potassium biphenylide in THF (Table 1, entry 8) has a vinyl polymer structure based on the ^{1}H NMR analysis, a very different spectral pattern around 2.1 ppm from those of the polymers prepared with the organolithium and Grignard reagents was observed (Fig. 1(b)). Fig. 2 shows the ^{13}C NMR spectra of the α-methylene carbon of poly(**3**) obtained with the Grignard reagent and potassium biphenylide in THF (Table 1, entries 5 and 8). Assuming that the peaks for the polymer obtained with *c*-HexMgBr–TMEDA are ascribed to *mm*, *mr* and *rr* from the low magnetic field as shown in the figure, the triad tacticity was estimated as *mm*/*mr*/*rr* = 82 : 10 : 8 (*m*/*r* = 87 : 13), a value almost comparable to that determined from the ^{1}H NMR analysis (*m*/*r* = 90 : 10). The triad tacticity of the polymer prepared with potassium biphenylide should be atactic, which was estimated as *mm*/*mr*/*rr* = 32 : 50 : 18 (Fig. 2(b)). On the other hand, the radically obtained polymer (Table 1, entry 4) showed a very different ^{1}H NMR spectral pattern from those of the anionically prepared polymers. Some side reactions, such as a ring-opening reaction [19] must have occurred during the radical polymerization although a detail structure has not been presently determined.



The tacticity of the anionically obtained poly(**3**)s was strongly affected by the initiator systems and polymerization

solvents. The *c*-HexMgBr–TMEDA complex in THF afforded a polymer with the highest isotacticity (Table 1, entry 5) while a nearly atactic polymer was obtained using *n*-BuLi in toluene (Table 1, entry 2). On the other hand, the anionic polymerization of acyclic α-(alkoxymethyl)acrylates with organolithium reagents proceeded in a highly isotactic-specific manner regardless of the solvent polarity [5–8]. Stereochemical control should be attained by the strong intra- and intermolecular coordination of the α-substituents of a propagating polymer chain and a monomer to the counter cation [20,21]. The cyclic structure of the monomer **3** significantly changed the stereocontrol mechanism.



The anionic and radical polymerizations of **4** possessing a 17-membered ring were next carried out (Table 2). The polymerization using the Grignard reagent in toluene and THF resulted in low yields (entries 1 and 4) whereas *n*-BuLi almost quantitatively gave the polymers (entries 2 and 5), which were partially insoluble in the common organic solvents, such as THF and $CHCl_3$.

The ^{1}H NMR analysis again showed that the anionically obtained poly(**4**)s have a vinyl polymer structure while the radically obtained polymer includes an undefined structure. Fig. 3(a) demonstrates the ^{1}H NMR spectrum of the polymer prepared using the *c*-HexMgBr–TMEDA complex in THF (Table 2, entry 4). A typical AB quartet spectral pattern was clearly observed for the main-chain methylene protons around 2 ppm, indicating that the polymer is isotactic rich, although a detailed tacticity is unclear at the present time. A spectral pattern of the chloroform-soluble fraction of poly(**4**) obtained with *n*-BuLi in THF (Table 2, entry 5) was very different from that of the polymer prepared using the Grignard reagent in THF suggesting that the polymer has a much lower isotacticity (Fig. 3(b)). Poly(**4**) must have a similar tacticity to that of poly(**3**) prepared using the same initiator system.

Table 2
Anionic and radical polymerizations of **4** (anionic polymerization: [**4**]/[initiator] = 20, temperature = −78 °C; radical polymerization: [**4**]/[initiator] = 30, temperature = 30 °C, time = 46 h)

Entry	Initiator	Solvent	Yield[a] (%)	DP (M_w/M_n)[b]
1	*c*-HexMgBr–TMEDA	Toluene	3	24 (32)[c]
2	*n*-BuLi	Toluene	> 99	69 (50)[c,d]
3	(*i*-PrOCO$_2$)$_2$	Toluene	77	29 (2.4)
4	*c*-HexMgBr–TMEDA	THF	17	41 (5.0)
5	*n*-BuLi	THF	94	35 (17)[c,d]

[a] Methanol-insoluble part.
[b] Determined by SEC (polystyrene standard), DP = M_n/(M_n of **4**).
[c] Multi-modal.
[d] Chloroform-soluble part.

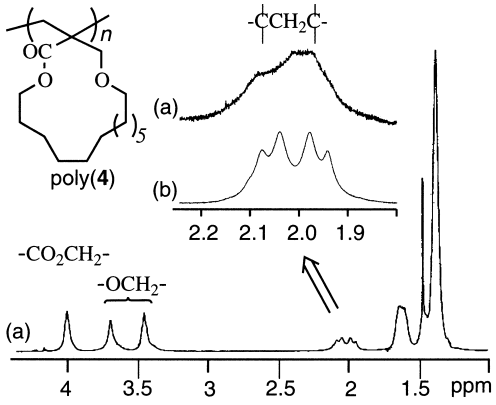


Fig. 3. ^{1}H NMR spectra of main-chain methylene protons of poly(**4**) obtained with *c*-HexMgBr–TMEDA (Table 2, entry 4) (a) and with *n*-BuLi (Table 2, entry 5) (b) in THF at −78 °C (in $CDCl_3$, 60 °C).

Table 3 summarizes the results of the anionic polymerization of **1** and **2** having 13- and 15-membered rings in THF at −78 °C. The counter cation significantly affects the polymer yield. The polymerization using the Grignard reagent hardly proceeded (entries 1 and 5). During the polymerization of **1**, the organolithium reagents resulted in low yields (entries 2 and 3) whereas *n*-BuLi quantitatively afforded a polymer during the polymerization of **2** (entry 6). Potassium biphenylide gave poly(**1**) and poly(**2**) as a methanol-insoluble part in good yields (entries 4 and 8). The interaction ability of the crown ether side chain with the alkali and alkaline earth metals should play an important role in producing a polymer [9].

The stereoregularity of poly(**1**) and poly(**2**) was determined by a ^{1}H NMR analysis in the same way as that for poly(**3**). The isotacticity of the obtained poly(**1**)s and poly(**2**)s with organolithium reagents were higher than those of poly(**3**)s synthesized with the same initiator systems while the polymers prepared with potassium biphenylide was estimated to be atactic [9].

The thermal properties of the poly(**1**)s and poly(**2**)s were measured by DSC analysis (Fig. 4). The T_g values were estimated to be 94.5 and 79.2 °C for the poly(**1**)s obtained using the organolithium and potassium reagents, respectively, whereas T_g = 92.7 and 78.2 °C were found for the poly(**2**)s obtained using the organolithium and potassium reagents, respectively, from the third heating thermograms. In addition to the molecular weight, the stereoregularity should significantly influence the thermal properties of the polymers and the isotactic-rich polymers showed higher T_g values than

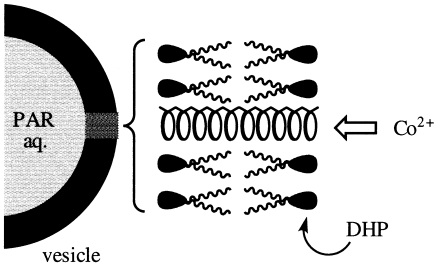
Table 3
Anionic polymerization of **1** and **2** in THF at −78 °C ([monomer]/[initiator] = 20, time = 48 h)

Entry	Monomer	Initiator	Yield[a] (%)	DP (M_w/M_n)[b]	Tacticity, *m*/*r*[c]
1	**1**	*c*-HexMgBr–TMEDA	Trace	–	–
2[d]	**1**	*n*-BuLi	11	26 (3.7)[e]	82:18[e]
3[d]	**1**	Ph_2NLi–TMEDA	9	27 (3.0)[e]	87:13[e]
4[d]	**1**	K-biphenylide	93	46 (6.3)	–
5	**2**	*c*-HexMgBr–TMEDA	0	–	–
6[d]	**2**	*n*-BuLi	> 99	45 (5.4)	88:12
7[d]	**2**	Ph_2NLi–TMEDA	1	13 (–)	92:8
8[d]	**2**	K-biphenylide	> 99	44 (4.0)	–

[a] Methanol-insoluble part.
[b] Determined by SEC (polystyrene standard), DP = M_n/(M_n of monomer).
[c] Estimated by ^{1}H NMR analysis.
[d] Data from Ref. [9].
[e] Chloroform-soluble part.

those of the polymers obtained using potassium biphenylide.

The cobalt ion transport ability of the polymers using the DHP vesicle-incorporated PAR was investigated according to the procedure reported by Nolte et al. [9,13,14]. Poly(**1**) and poly(**2**) have a structure with the continuously and perpendicularly fixed crown ethers on the main-chain. Therefore, they may fulfill the function as an artificial pore, such as the synthetic ion channel. DHP vesicles containing the dye, PAR were prepared and the polymers such as poly(**1**) and poly(**2**) obtained using potassium biphenylide (Table 3, entries 4 and 8), and poly(**3**) prepared using Ph_2NLi–TMEDA in THF (Table 1, entry 7), poly[ethyl α-(ethoxymethyl)acrylate] (poly(EEMA), prepared with $(i\text{-PrOCO}_2)_2$ in bulk at 40 °C: $M_n = 4.9 \times 10^4$, $M_w/M_n = 6.2$) and poly(methyl methacrylate) (PMMA, prepared with Ph_2NLi–TMEDA in toluene at −78 °C: $M_n = 1.3 \times 10^4$, $M_w/M_n = 1.05$) were incorporated into the vesicle bilayers. The permeability of Co^{2+} [$Co(NO_3)_2$] was measured by the UV absorption increase at 510 nm based on the formation of the cobalt–PAR complex and the decrease at 390 nm for the PAR.



These results are depicted in Fig. 5. The Co^{2+} permeability was hardly observed for the vesicle prepared without the polymers (vesicle diameter, $\phi = 193$ nm). The DHP–poly(**1**) and –poly(**2**) vesicles ($\phi = 193$ and 168 nm) showed a much higher UV absorption increase at 510 nm

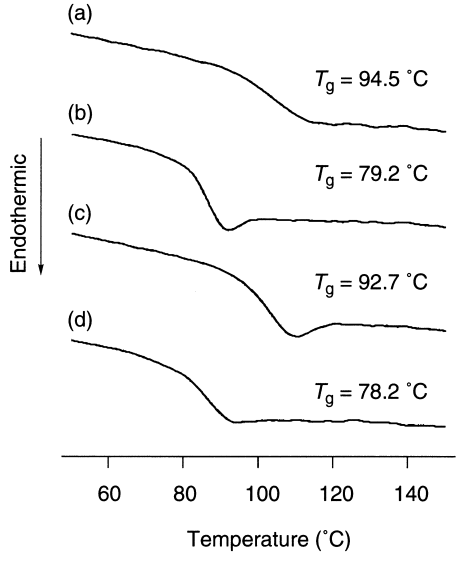


Fig. 4. DSC thermograms of poly(**1**) obtained with Ph_2NLi–TMEDA (Table 3, entry 3) (a), with K-biphenylide (Table 3, entry 4) (b), poly(**2**) obtained with *n*-BuLi (Table 3, entry 6) (c), and with K-biphenylide (Table 3, entry 8) (d) (third heating scan).

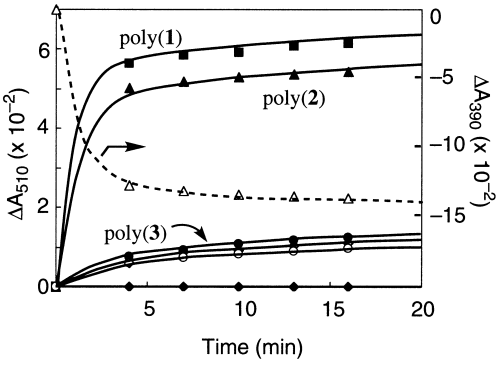


Fig. 5. Plots of the change for UV absorption at 510 and 390 nm vs. time using vesicles prepared with poly(**1**) (Table 3, entry 4): (■) 510 nm, poly(**2**) (Table 3, entry 8): (▲) 510 nm and (△) 390 nm, poly(**3**) (Table 1, entry 3): (●) 510 nm, poly(EEMA): (◇) 510 nm, PMMA: (○) 510 nm, and without a polymer: (◆) 510 nm.

than those of the vesicles including the model polymers, poly(**3**), poly(EEMA), and PMMA. The further formation of the cobalt–PAR complex for the latter vesicles was certified by adding a surfactant (Triton X-100). The significantly pronounced effect on the ion permeability for the DHP–poly(**1**) and –poly(**2**) vesicles was also confirmed by the decrease in the UV absorption at 390 nm. These observations indicate that the polymers with the crown ether side chains act as a synthetic ion channel for the cobalt ion and may have a structure containing pores. The poly(**1**) (Table 3, entries 2 and 3) and poly(**2**) (entries 6 and 7) with a higher isotacticity were not stably incorporated into the vesicle.

4. Conclusion

Four macrocyclic α-(alkoxymethyl)acrylates were anionically polymerized to afford vinyl polymers. The initiator system strongly affects the yield and tacticity of the polymers. The polymerization with the organolithium and Grignard reagents afforded isotactic-rich polymers whereas the polymers obtained with potassium biphenylide were almost atactic. The obtained polymers have a novel structure with respect to the attaching manner of the macrocycle to the polymer main-chain. The polymers obtained with potassium biphenylide bearing a crown ether-type side chain demonstrated the cobalt ion transport ability as a synthetic ion channel using vesicles prepared with DHP.

Acknowledgements

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