Synthesis and Reactions of *exo*-Methylene-Containing Poly(cyclic orthoester)

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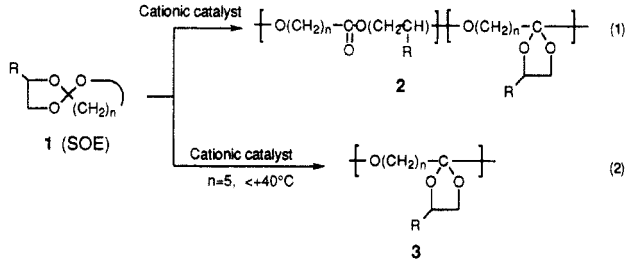
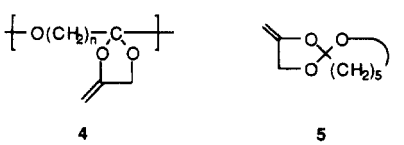
ABSTRACT: Syntheses of poly(cyclic orthoester) bearing an *exo*-methylene group (**4**) by a polymer reaction of the corresponding bromomethyl derivative and radical additions of thiols to **4** were carried out. The *exo*-methylene-containing poly(cyclic orthoester) **4** was prepared in 74% yield by dehydrobromination with potassium *tert*-butoxide of bromomethyl-substituted poly(cyclic orthoester) which was synthesized by cationic single ring-opening polymerization of 2-(bromomethyl)-1,4,6-trioxaspiro[4.6]undecane (**6**) with tin(IV) chloride. **4** contained little bromomethyl group, indicating that the elimination of hydrogen bromide proceeded very efficiently. **4** underwent radical additions of ethanethiol and 1,3-propanedithiol under photoirradiation conditions at room temperature to afford the corresponding ethylthio group-containing poly(cyclic orthoester) (**8**) and cross-linked polymer in quantitative yields, respectively. The ethanethiol adduct (**8**) was readily converted to the corresponding monomeric ethanethiol adduct by treatment with an acid catalyst.

Introduction

Spiroorthoesters (**1**, SOEs) have been reported to polymerize with a cationic catalyst to give poly(ether–ester)s *via* a tandem double ring-opening isomerization process.[1,2] We have recently demonstrated that the polymer obtained from **1** consists of not only a poly(ether–ester) unit but also a poly(cyclic orthoester) unit like **2** (eq 1).[3] Furthermore, we have found that SOEs **1** (n = 5) cationically polymerize at low temperature (<40 °C) to selectively give poly(cyclic orthoester)s **3** *via* a single ring-opening process (eq 2).[4,5] This polymerization is a typical



equilibrium one, in which poly(cyclic orthoester)s easily depolymerize to the starting SOEs by shifting the equilibrium to the left.[5,6] Therefore, **3** is sensitive toward acid and can be regarded as a degradable polymer. Meanwhile, we have designed polymer (**4**) which has an olefin moiety on the ring as the R group of **3**. This polymer as a reactive polymer can undergo some polymer reactions such as addition reaction to give functional or modified polymers. However, the polymer (**4**) is not able to be prepared by similar cationic ring-opening polymerization of the corresponding monomer (**5**) along eq 2, and the polymer obtained by cationic polymerization of **5** has not been characterized yet due to its complicated structure.[7] This



should come from the cyclic vinyl ether structure which might be more reactive toward acid than the SOE structure. So, synthesis of **4** has been examined by utilizing the equilibrium polymerization of SOE followed by a polymer reaction. This paper describes the synthesis of **4** *via* efficient polymer reaction and its reactions with thiols.

Experimental Section

Material. Tin(IV) chloride (Wako Pure Chemical Industries, Ltd.; purity: >97%) was distilled under a nitrogen atmosphere and stored under an argon atmosphere. Epibromohydrin (Tokyo Kasei Kogyo Co., Ltd.; purity: >98%), ϵ-caprolactone (Tokyo Kasei Kogyo Co., Ltd.; purity: >99%), and potassium *tert*-butoxide (Nakarai Tesque Inc.) were used without further purification. Ethanethiol and 1,3-propanedithiol (Tokyo Kasei Kogyo Co., Ltd.; purity: >95%) were distilled before use.

Synthesis of 6. Spiroorthoester (**6**) was prepared according to Bodenbenner's method.[8] To a mixture of ϵ-caprolactone (22.8 g, 0.2 mol) and BF_3OEt_2 (1.26 mL, 0.01 mol) in CCl_4 (40 mL) was added dropwise epibromohydrin (54.8 g, 0.4 mol) in CCl_4 (40 mL) at 0 °C. The reaction mixture was stirred for 4 h at 0 °C and washed with 200 mL of 1 M NaOH. The organic layer was dried over anhydrous magnesium sulfate, the solvent was evaporated, and the residual oil was distilled under vacuum to give **6**. Yield: 21.7 g (43% based on ϵ-caprolactone). Bp: 92 °C (0.5 mmHg) [lit.[9] bp 85–86 °C (0.6 mm Hg)].

Polymerization of 6. **6** (5.04 g, 20 mmol) was cooled to 0 °C in a Schlenk tube under an argon atmosphere. Tin(IV) chloride (47 μL, 0.40 mmol) was added, and the mixture was stirred at 0 °C. After 1 h, triethylamine (1 mL) and CH_2Cl_2 (40 mL) were added. The solution was washed with saturated aqueous $NaHCO_3$ and dried over anhydrous sodium sulfate. The solution was evaporated, and the residual material was dissolved in 8 mL of CH_2Cl_2 and precipitated with 160 mL of *n*-hexane. Precipitated polymer was collected as a colorless viscous material by decantation. A similar precipitation was repeated once more, and the obtained polymer was dried under vacuum to give **7**. Yield: 3.55 g (70%). $\bar{M}_n$ = 10 200. $\bar{M}_w/\bar{M}_n$ = 2.05. IR (neat): 2941, 2872, 1466, 1462, 1215, 1066 cm^{-1}. ^1H NMR (90 MHz in C_6D_6): δ 1.17–2.23 (br, 8H, $-CH_2-$), 2.83–4.40 (m, 7H, $-OCH_2-$, $BrCH_2-$).

Dehydrobromination of 7. Potassium *tert*-butoxide (4.7 g, 42 mmol) dissolved in dry DMF (30 mL) was placed in a three-necked flask under an argon atmosphere. To this solution was added dropwise at 0 °C **7** (3.55 g, 14 mmol) dissolved in dry DMF (15 mL). The reaction mixture was stirred overnight at room temperature. Toluene (300 mL) was added to the resulting mixture, and the mixture was washed three times with 200 mL of water. The organic layer was dried over anhydrous magnesium sulfate and evaporated. The residual material was dissolved in 4 mL of benzene and precipitated with 80 mL of *n*-hexane.

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Precipitated polymer was collected as a pale yellow viscous material by decantation. A similar precipitation was carried out once more, and the obtained polymer was dried under vacuum to afford 4. Yield: 1.77 g (74%). $\bar{M}_n$ = 7230. $\bar{M}_w/\bar{M}_n$ = 2.09. IR (neat): 2943, 2872, 1689, 1288, 1232, 1065, 976, 877, 808, 501 cm^{-1}. ^{1}H NMR (90 MHz in C_6D_6): δ 1.00–2.30 (br, 8H, $-CH_2-$), 3.30–3.80, 4.10–4.67 (m, 6H, $-OCH_2-$, $CH_2=$).

Dehydrobromination of 6. Potassium *tert*-butoxide (1.7 g, 15 mmol) dissolved in DMF (5 mL) was cooled to 0 °C under an argon atmosphere. To this solution was added dropwise 6 (1.26 g, 5 mmol) in DMF (5 mL), and the reaction mixture was stirred at room temperature overnight. Benzene (50 mL) was added to the mixture, and the resulting mixture was washed three times with water (50 mL). The organic layer was dried over anhydrous magnesium sulfate and evaporated. The residual material was distilled under vacuum to give 5. Yield: 0.69 g (80%). Bp: 110 °C (5 mmHg) (bulb-to-bulb) [lit.[10] bp 89 °C (7 mmHg)].

Radical Addition of Ethanethiol to 5. A mixture of 5 (1.70 g, 10 mmol), ethanethiol (890 μL, 12 mmol), azobis(isobutyronitrile) (AIBN; 33 mg, 0.2 mmol), and benzene (15 mL) was placed in a Pyrex tube and sealed off under vacuum. The reaction mixture was heated at 60 °C for 24 h in a sealed tube. The reaction mixture was evaporated, and the residual product was distilled under vacuum to afford 9. Yield: 1.77 g (76%). Bp: 126–128 °C (3 mmHg). IR (neat): 2929, 1365, 1273, 1240, 1178, 1132, 1072, 1041, 962 cm^{-1}. ^{1}H NMR (60 MHz in C_6D_6): δ 1.00 (t, J = 7.0 Hz, 3H, CH_3CH_2S-), 1.20–2.00 (br, 6H, $-CH_2-$), 2.00–2.90 (m, 4H, $(-O-)_3CCH_2-$, $EtSCH_2-$), 2.43 (q, J = 7.0 Hz, 2H, CH_3CH_2S-), 3.37–4.60 (m, 5H, $-OCH_2-$). Anal. Calcd for $C_{11}H_{20}O_3S$: C, 56.87; H, 8.68; S, 13.8. Found: C, 56.82; H, 8.69; S, 13.31.

Radical Addition of Ethanethiol to 4. A mixture of 4 (0.51 g, 3.0 mmol), ethanethiol (440 μL, 6.0 mmol), AIBN (9.9 mg, 0.06 mmol), pyridine (24 μL, 0.30 mmol), and benzene (10 mL) was placed in a Pyrex tube and sealed off under vacuum. The reaction mixture was irradiated with a 400-W high-pressure Hg lamp at 20 °C for 4 h. The reaction mixture was evaporated, and the residual product was precipitated twice from benzene (2 mL) to *n*-hexane (40 mL). The obtained polymer was dried under vaccum to give 8. Yield: 0.67 g (96%), $\bar{M}_n$ = 10 700. $\bar{M}_w/\bar{M}_n$ = 2.21. IR (neat): 2933, 2870, 1456, 1357, 1267, 1221, 1062 cm^{-1}. ^{1}H NMR (90 MHz in C_6D_6): δ 1.00 (t, J = 7.0 Hz 3H, CH_3CH_2S-), 1.30–2.86 (m, 10H, $-CH_2-$, $(-O-)_3CCH_2-$, $EtSCH_2-$), 2.33 (q, J = 7.0 Hz, 2H, CH_3CH_2S-), 3.33–4.57 (m, 5H, $-OCH_2-$).

Depolymerization of 8. To 8 (0.67 g, 2.9 mmol) dissolved in CH_2Cl_2 (10 mL) was added CF_3COOH (9 μL, 0.12 mmol) at room temperature. The reaction mixture was stirred at room temperature overnight. One drop of Et_3N was added to the mixture, and the resulting mixture was evaporated. The residual product was distilled under vacuum to give 9. Yield: 0.45 g (66%). Bp: 150 °C (3 mmHg) (bulb-to-bulb). IR and ^{1}H NMR spectra were identical to those of 9 obtained by the radical addition of ethanethiol to 5.

Reaction of 4 with 1,3-Propanedithiol. A mixture of 4 (0.069g, 0.41 mmol), 1.3-propanedithiol (10.3 μL, 0.103 mmol), pyridine (3.2 μL, 0.04 mmol), AIBN (1.3 mg, 0.008 mmol), and benzene (0.5 mL) was placed in a Pyrex tube and sealed off under vacuum. The mixture was irradiated with a 400-W high-pressure Hg lamp at 20 °C for 4 h. Solvent-insoluble polymer formed was washed five times with benzene (10 mL × 5) followed by washing five times with *n*-hexane (10 mL × 5). The gelled polymer (10) was dried under vacuum. Yield: 0.078 g (97%). IR (KBr): 2941, 2872, 1228 cm^{-1}. Anal. Found: C, 52.63; H, 7.55; S, 8.62.

Measurements and Apparatus. NMR spectra were obtained with JEOL JNM-PMX-60si and EX-90 spectrometers. FT-IR spectra were recorded with a JEOL JIR-5300 spectrometer. Number-average ($\bar{M}_n$) and weight-average molecular weights ($\bar{M}_w$) were estimated by gel permeation chromatography (GPC) which was performed with a Toyo Soda HPLC CCP&8000 with a data processor (eluent, THF; calibration, polystyrene standards). Light irradiation was performed with a 400-W high-pressure Hg lamp using a Riko Rotary Photochemical Reactor Model RH400-10W.

Results and Discussion

Preparation and reactions of 4 and related reactions are illustratively summarized in Scheme 1.

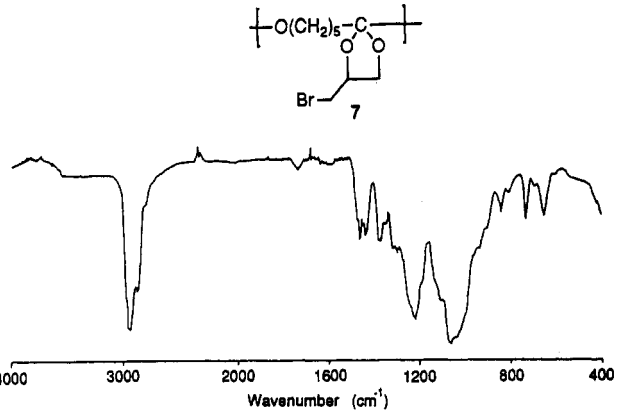
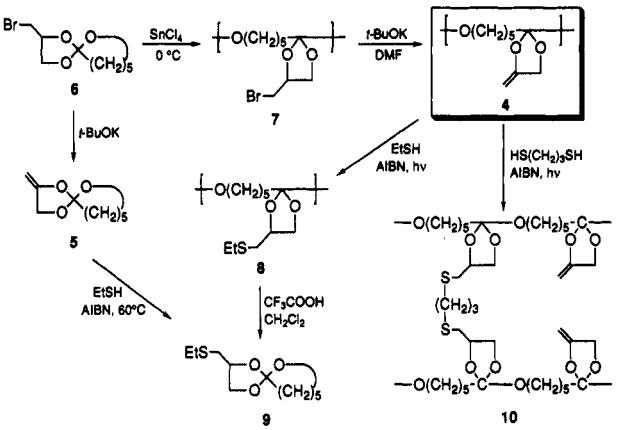


Figure 1. IR spectrum of poly(cyclic orthoester) 7.

Scheme I



Preparation of Poly(cyclic orthoester) (4). Poly(cyclic orthoester) bearing a bromomethyl group (7) was prepared by the cationic polymerization of 2-(bromomethyl)-1,4,6-trioxaspiro[4.6]undecane (6) with $SnCl_4$ (2 mol %) at 0 °C for 1 h. Yield of the obtained polymer was 70%, and its $\bar{M}_n$ and $\bar{M}_w/\bar{M}_n$ were 10 200 and 2.05, respectively. The structure of 7 was confirmed by IR and ^{1}H NMR spectra (Figures 1 and 2). The absence of carbonyl absorption in the IR spectrum (Figure 1) suggested that the structure of the polymer was not poly(ether–ester) but poly(cyclic orthoester) (7) as expected. The ^{1}H NMR spectrum of 7 is shown in Figure 2-I. Dehydrobromination of 7 was performed with *t*-BuOK (3 equiv) in DMF. By the addition of *t*-BuOK to 7, exothermic reaction occurred and the *exo*-methylene-substituted poly(cyclic orthoester) 4 was obtained in 74% yield ($\bar{M}_n$ = 7230, $\bar{M}_w/\bar{M}_n$ = 2.09). A clear absorption attributable to the *exo*-methylene group was observed at 1689 cm^{-1} in the IR spectrum of the polymer obtained. In the ^{1}H NMR of the polymer (Figure 2-II), the vinyl ether type *exo*-methylene signals were observed around 4.2 ppm. The $\bar{M}_n$ of the polymer was nearly equal to the value ($\bar{M}_n$ = 6890) calculated from that of the starting polymer (7) ($\bar{M}_n$ 10 200), although these $\bar{M}_n$s were estimated by GPC based on the polystyrene standards. This change of $\bar{M}_n$ seems to suggest that no side reaction such as main-chain scission of the polymer takes place. From the ^{1}H NMR spectrum, the dehydrobromination of 7 highly efficiently proceeds to cleanly give the *exo*-methylene-containing polymer 4, in spite of the polymer reaction.

Radical Addition of Ethanethiol to 4. First, 4 ($\bar{M}_n$ = 5120, $\bar{M}_w/\bar{M}_n$ = 2.13) was treated with a mixture of ethanethiol (2 equiv) and AIBN (2 mol % to 4) under typical radical conditions (heating at 60 °C). In the IR spectrum of the obtained polymer, absorption of the *exo*-methylene group (1689 cm^{-1}) completely disappeared but

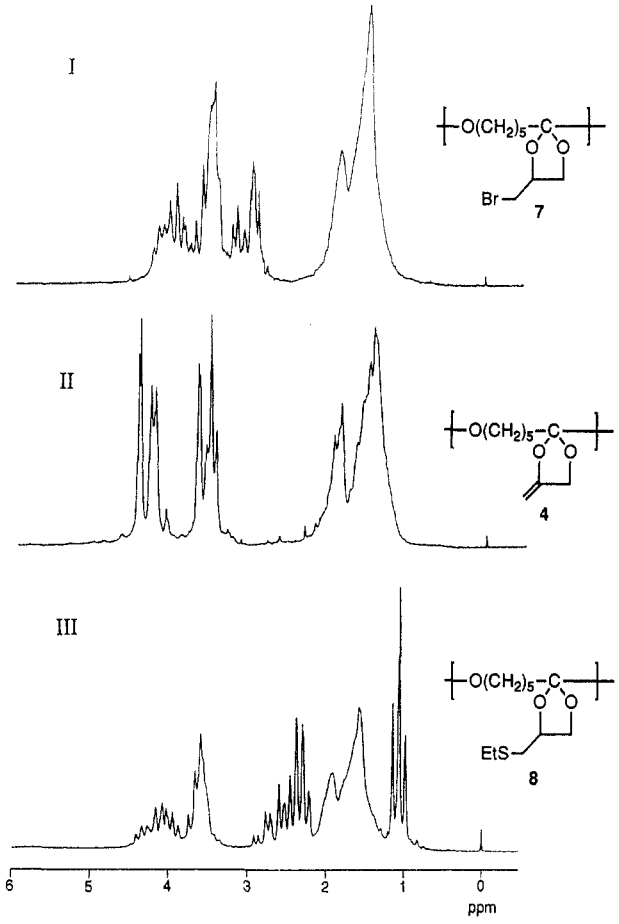


Figure 2. ^{1}H NMR spectra (90 MHz, in C_6D_6) of poly(cyclic orthoester) 7 (I), *exo*-methylene-containing poly(cyclic orthoester) 4 (II), and ethanethiol adduct 8 (III).

a small carbonyl absorption appeared. This carbonyl absorption is considered to be that of the ester group formed *via* a certain acid-catalyzed isomerization of the orthoester moiety of 4. Furthermore, the GPC of the polymer indicated its $\bar{M}_n$ of 2500 which was considerably small in comparison with that calculated ($\bar{M}_n$ = 7580). The results of the IR and GPC suggested the occurrence of some side reactions such as fission of the polymer main chain. Acidity of ethanethiol (pK_a = 10.61)[11] may cause the decrease in $\bar{M}_n$ during the reaction. To prevent it, pyridine (3 mol % vs 4) was added to the reaction system, but little effect was observed. Since the reaction temperature seemed important, the reaction was carried out at lower temperature, at which radical species could be generated by photoirradiation. A mixture of 4 ($\bar{M}_n$ = 7230, $\bar{M}_w/\bar{M}_n$ = 2.09), ethanethiol (2 equiv to 1), AIBN (2 mol % vs 1), and pyridine (10 mol % to 1) was irradiated with a high-pressure Hg lamp at 20 °C for 4 h. As a result, the ethanethiol adduct 8 was obtained in 96% yield. GPC analysis of 8 showed a good increase of $\bar{M}_n$ to 10 700 ($\bar{M}_w/\bar{M}_n$ = 2.21), being in accordance with the calculated value of 10 710. The IR and ^{1}H NMR spectra of 8 suggested the quantitative addition of ethanethiol to 4. In the IR spectrum, absorption of neither the *exo*-methylene nor the carbonyl group was found. In the ^{1}H NMR spectrum (Figure 2-III), ethyl signals were observed in a satisfactory intensity. Thus, in addition to the elimination reaction of 7 to 4, the conversion of 4 to 8 by the addition reaction quantitatively proceeded in spite of the polymer reaction.

Depolymerization of 8. As described previously, single ring-opening polymerization of SOEs (e.g., 6 to 7) is one of the equilibrium polymerizations.[5] Therefore, SOE monomer can be recovered by acid-catalyzed depolymerization of poly(cyclic orthoester) by shifting the equilibrium from the polymer to the monomer side by lowering of the concentration. Poly(cyclic orthoester) (8) was treated with CF_3COOH (4 mol %) at room temperature in CH_2Cl_2 ([C] = 0.29 M). The reaction was monitored by GPC, in which the reaction was completed in 10 min after addition of CF_3COOH. By distillation of the obtained material, the corresponding SOE bearing an ethylthio moiety (9) was obtained in 66% yield. The structure of 9 was confirmed by its IR and ^{1}H NMR spectra by comparison with those of the authentic sample which was prepared independently by the radical addition of ethanethiol to 5. Preparation of 5 was employed by a method similar to the preparation of 4 from 7.

Cross-Linking of 4 with 1,3-Propanedithiol. A mixture of 4 ($\bar{M}_n$ = 7230, $\bar{M}_w/\bar{M}_n$ = 2.09), 1,3-propanedithiol (0.25 equiv to 4), AIBN (2 mol % to 4), and pyridine (10 mol % to 4) in benzene was irradiated with a high-pressure Hg lamp at 20 °C for 4 h to give a white solid as the solvent-insoluble material (10) in 97% yield. 10 showed no absorption of the free SH group in its IR spectrum. Therefore, the degree of cross-linking of 10 was estimated to be 47% by elemental analysis. This value demonstrates the reaction efficiency of 98.5%.

Thus, in this paper, the synthesis and reactions of *exo*-methylene-functionalized poly(cyclic orthoester) 4 were studied. 4 was prepared by the efficient dehydrobromination of poly(cyclic orthoester) bearing a bromomethyl group (7). 4 underwent the radical additions of ethanethiol and 1,3-propanedithiol to give the corresponding adducts 8 and cross-linked polymer 10 in quantitative yields, respectively. The adduct (8) could smoothly depolymerize to the monomeric product 9 by treatment with CF_3COOH.

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