Synthesis and Asymmetric Anionic Polymerization of Substituted 7-Aryl-2,6-dimethyl-1,4-benzoquinone Methides

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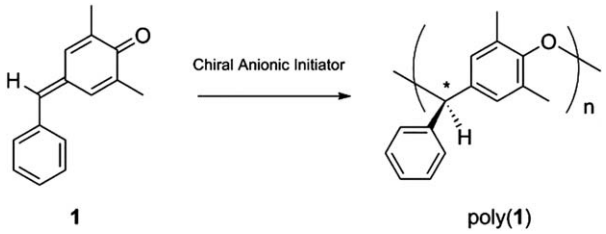
ABSTRACT: Substituted 7-aryl-2,6-dimethyl-1,4-benzoquinone methides which have an electron-donating methoxy substituent at the *para*-position (*p*-OMe, **2a**) or an electron-withdrawing chloro one at the *para*- (*p*-Cl, **2b**), *meta*- (*m*-Cl, **2c**), and *ortho*-positions (*o*-Cl, **2d**) of the benzene ring were synthesized, and their asymmetric anionic polymerizations using the complex of lithium 4-isopropylphenoxide with (−)-sparteine were carried out in toluene at 0 °C. The polymers with negative specific rotation were obtained for all of four monomers, and the polymer obtained from **2a** showed smaller specific rotation value than that of polymer having no substituent (*p*-H, **1**) on the phenyl group and the polymers obtained from **2b–d** showed larger ones. It was found that the kind of a substituent and its substitution position on the phenyl group affect significantly the optical activity of polymers. The largest specific rotation value of $[\alpha]_{435} = -153.2°$ was obtained in the polymerization of **2d** with an *ortho*-chloro substituent. © 2014 Wiley Periodicals, Inc. J. Polym. Sci., Part A: Polym. Chem. **2015**, *53*, 437–444

KEYWORDS: anionic polymerization; chiral; substituent effect; synthesis

INTRODUCTION Optically active polymers have attracted interest as chiral stationary phases for high performance liquid chromatography, polymeric reagents, and asymmetric catalysts because of their excellent chiral recognition abilities toward a wide range of racemic compounds.[1] Asymmetric polymerization is one of promising methods to introduce the chirality into the polymer chain and to synthesize optically active polymers. There are a large number of reports about the asymmetric polymerizations based on vinyl monomers, diene monomers, cyclic olefin monomers, aldehyde monomers, isocyanate monomers, and so on.[2] Among the various asymmetric polymerization, asymmetric synthesis polymerization (IUPAC nomenclature: asymmetric chirogenic polymerization) of prochiral monomer is the most effective method for the synthesis of the optically active polymer with configurational chirality in the main chain which is analogous to biopolymers, such as proteins and polysaccharides. However, there are not so many successful results of asymmetric synthesis polymerization reported so far.

1,4-Benzoquinone methide, a member of the quinoid family, possesses high reactivity and reacts spontaneously to afford a dimer bonded between exocyclic carbons or oligomers at room temperature.[3] However, the introduction of substituents on the exocyclic carbon or quinoid skeleton of the quinone methide reduces its reactivity and makes it isolable as a monomer crystal. For example, 7,7-dicyano-1,4-benzoquinone methide,[4] 7-(alkoxycarbonyl)-7-cyano-1,4-benzoquinone methides,[5] 7,7-bis(alkoxycarbonyl)-1,4-benzoquinone methides,[6] and 7-cyano-7-phenyl-1,4-benzoquinone methide[7] have already been synthesized and isolated. Previously, we investigated the polymerization behaviors of these isolable quinone methides and found that the radical and anionic polymerizations of many quinone methides take place between the substituted exomethylene carbon atom and exocarbonyl oxygen with the formation of a stable aromatic ring to afford polymers with characteristic main-chain structures, such as poly(oxy-1,4-phenylene-substituted methylene). Furthermore, we reported the asymmetric anionic polymerization of a prochiral monomer, 7-phenyl-2,6-dimethyl-1,4-benzoquinone methide (**1**), using various chiral anionic initiators, and the synthesis of an optically active polymer (poly(**1**)) with configurational chirality in the main chain (Scheme 1).[8]

The asymmetric anionic polymerization of **1** using (−)-sparteine ((−)-Sp) as chiral ligand gave the optically active polymer with a negative specific rotation ($[\alpha]_{435} = -22.5°$). Moreover, to understand the stereocontrol process in asymmetric anionic polymerization of **1**, we carried out the asymmetric anionic polymerization of **1** at the various initiator



SCHEME 1 Asymmetric anionic polymerization of **1**.

concentrations and in various solvents, and found that the aggregation state of the propagating chain end significantly might affect the specific rotation of poly(**1**). However, the specific rotation value of obtained poly(**1**) was still not so high. Lin et al.[9] reported that the rates of anionic polymerization of several 7-aryl-2,6-dimethylquinone methides were affected by the *para*-substituent of the 7-phenyl group. In this work, we carried out the asymmetric anionic polymerization of substituted 7-aryl-2,6-dimethyl-1,4-benzoquinone methides which have an electron-donating methoxy substituent at *para*-position (**2a**) on the phenyl group or an electron-withdrawing chloro one at the *para*-(**2b**), *meta*-(**2c**), *ortho*-positions (**2d**) of the benzene ring (Chart 1) and investigated the effect of substituent on optical activity of the resulting polymers (poly(**2a–d**)).

EXPERIMENTAL

Measurements

All melting points were obtained with a Yanaco MP-S3 micro melting-point apparatus. Infrared (IR) spectra were recorded on a JASCO IR-700 spectrometer. ^{1}H and ^{13}C NMR spectra were measured with a JEOL JNM-EX270 (270 MHz for ^{1}H) spectrometer in chloroform-*d* with tetramethylsilane as an internal standard. The specific rotation at 435 nm ($[\alpha]_{435}$) was obtained with a JASCO P-1030 polarimeter. The number-average (M_n), weight-average (M_w) molecular weights, and polydispersity (M_w/M_n) of the polymers were determined by size exclusion chromatography (SEC) on a Jasco PU-1580 chromatograph equipped with a Jasco RI-930 refractive-index (RI) detector and two Tosoh TSKgel Multipore-H_{XL}-M columns with tetrahydrofuran (THF) as an eluent at a flow rate of 1.0 mL/min and with polystyrene standards for calibration at room temperature. The relationship of the molecular weight and the specific rotation of the polymer was examined with SEC on a Shodex System-21 equipped with a Shodex RI-71S refractive index (RI) detector and a JASCO OR-990 polarimetric (PM) detector with two columns, Shodex KF-803 and KF-806L, connected in series (eluent: THF, temperature: 40 °C).

Materials

Toluene was purified in the usual manner and distilled over sodium metal. *n*-Butyllithium (*n*-BuLi) (Kanto Chemicals, 1.65 M solution in hexane) was used as received. 4-Isopropylphenol (Tokyo Chemical Industry Co., LTD. (TCI)) was recrystallized from hexane. (−)-Sp (TCI) was dried over calcium hydride and distilled under reduced pressure. All other commercially available materials were used without further purification.

Synthesis of Monomers (2a–d)

3,5-Dimethyl-4-hydroxy-substituted-benzophenone (3)

General Preparation Method. A mixture of 2,6-xylenol (6.1 g, 50 mmol) and substituted benzoyl chloride (50 mmol) was heated at 140 °C for 4 h with stirring. To the mixture was added 8.5 g (64 mmol) of aluminum chloride milled in a mortar with a pestle, and then the mixture was stirred at 190 °C for 45 min. After the mixture cooled to 0 °C, aqueous hydrochloric acid (6 N) was added to quench the reaction, and the resulting mixture was extracted with CH_2Cl_2 (100 mL × 3). The extracts were combined, washed twice with brine, and dried over anhydrous magnesium sulfate. After the solvent was evaporated, a residual solid was purified by recrystallization or by silica-gel column chromatography, followed by recrystallization.

3,5-Dimethyl-4-hydroxy-4′-methoxybenzophenone (3a). From 4-methoxybenzoly chloride, **3a** was obtained as yellow needles after purification by recrystallization from chloroform/hexane = 1/5 (33% yield). M.p.: 129 °C. IR (KBr, cm^{-1}): 3260 (ν_{O-H}), 1565 ($\nu_{C=O}$), 1484 ($\nu_{C=C}$), 1244, 1010 (ν_{C-O}). ^{1}H NMR ($CDCl_3$, δ, ppm): 7.78 (d, J = 8.6 Hz, 2H), 7.47 (s, 2H), 6.96 (d, J = 8.6 Hz, 2H), 5.21 (s, 1H), 3.89 (s, 3H), 2.29 (s, 6H). ^{13}C NMR ($CDCl_3$, δ, ppm): 195.4 (C═O), 162.7 (Ar), 156.5 (Ar), 132.2 (Ar), 131.2 (Ar), 130.8 (Ar), 129.8 (Ar), 123.1 (Ar), 113.3 (Ar), 55.4 (OCH_3), 16.0 (CH_3).

3,5-Dimethyl-4-hydroxy-4′-chlorobenzophenone (3b). From 4-chlorobenzoly chloride, **3b** was obtained as white needles after purification by recrystallization from EtOAc/hexane = 1/5 (87% yield). M.p.: 130 °C. IR (KBr, cm^{-1}): 3360 (ν_{O-H}), 2950 (ν_{C-H}), 1632 ($\nu_{C=O}$), 1601, 1487 ($\nu_{C=C}$), 1090, 760 (ν_{C-Cl}). ^{1}H NMR ($CDCl_3$, δ, ppm): 7.70 (d, J = 8.6 Hz, 2H), 7.48 (s, 2H), 7.45 (d, J = 8.3 Hz, 2H), 5.55 (s, 1H), 2.29 (s, 6H). ^{13}C NMR ($CDCl_3$, δ, ppm): 195.0 (C═O), 156.9 (Ar), 138.1 (Ar), 136.7 (Ar), 131.4 (Ar), 131.1 (Ar), 129.1 (Ar), 128.4 (Ar), 123.1 (Ar), 15.9 (CH_3).

3,5-Dimethyl-4-hydroxy-3′-chlorobenzophenone (3c). From 3-chlorobenzoly chloride, **3c** was obtained as white needles after purification by silica-gel column chromatography using chloroform followed by recrystallization from dichloromethane (63% yield). M.p.: 166 °C. IR (KBr, cm^{-1}): 3440 (ν_{O-H}), 2952 (ν_{C-H}), 1638 ($\nu_{C=O}$), 1485, 1416 ($\nu_{C=C}$), 1028,

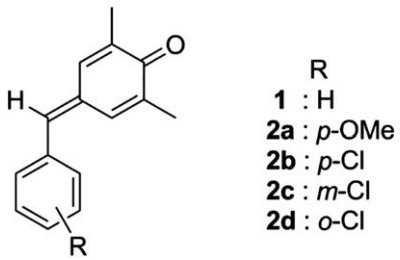


CHART 1 Chemical structures of monomers (**1** and **2a–d**).

756 (ν_{C-Cl}). ^{1}H NMR ($CDCl_3$, δ, ppm): 7.72 (s, 1H), 7.60 (d, J = 7.6 Hz, 1H), 7.53 (d, J = 7.9 Hz, 1H), 7.49 (s, 2H), 7.41 (t, J = 7.8 Hz, 1H), 5.36 (s, 1H), 2.30 (s, 6H). ^{13}C NMR ($CDCl_3$, δ, ppm): 194.6 (C═O), 156.9 (Ar), 140.1 (Ar), 134.4 (Ar), 131.7 (Ar), 131.5 (Ar), 129.5 (Ar), 129.4 (Ar), 129.0 (Ar), 127.7 (Ar), 123.1 (Ar), 15.9 (CH_3).

3,5-Dimethyl-4-hydroxy-2′-chlorobenzophenone (3d). From 2-chlorobenzoly chloride, **3d** was obtained as brown needles after purification by recrystallization from EtOAc/hexane = 1/5 (88% yield). M.p.: 177 °C. IR (KBr, cm^{-1}): 3302 (ν_{O-H}), 2950 (ν_{C-H}), 1635 ($\nu_{C=O}$), 1578 ($\nu_{C=C}$), 1031, 747 (ν_{C-Cl}). ^{1}H NMR ($CDCl_3$, δ, ppm): 7.48 (s, 2H), 7.33-7.44 (m, 4H), 5.29 (s, 1H), 2.26 (s, 6H). ^{13}C NMR ($CDCl_3$, δ, ppm): 194.6 (C═O), 157.8 (Ar), 139.5 (Ar), 131.7 (Ar), 131.3 (Ar), 130.9 (Ar), 130.2 (Ar), 129.2 (Ar), 129.1 (Ar), 126.8 (Ar), 123.5 (Ar), 16.1 (CH_3).

2,6-Dimethyl-4-(substituted benzyl)phenol (4)

General Preparation Method. Zinc powder (19.6 g, 300 mmol) was added to a solution of mercuric chloride (0.5 g, 2.0 mmol) in 27 mL of water, and the mixture was stirred at room temperature for 45 min. The supernatant water was decanted off, and the precipitate was washed twice with water. Then, 27 mL of water and 20 mL of concentrated hydrochloric acid were added. To the suspension was added a solution of **3** (24 mmol) in 45 mL of ethanol, and the mixture was refluxed for 8 h. After cooling to room temperature, the reaction mixture was extracted twice with diethyl ether. The extracts were combined, washed with brine, and dried over magnesium sulfate. After the diethyl ether evaporated, the residual pale yellow oil was purified by silica-gel column chromatography or distillation, followed by recrystallization.

2,6-Dimethyl-4-(4′-methoxybenzyl)phenol (4a). From **3a**, **4a** was obtained as white needles after purification by silica-gel column chromatography using chloroform and recrystallization from hexane (36% yield). M.p.: 68 °C. IR (KBr, cm^{-1}): 3346 (ν_{O-H}), 2880 (ν_{C-H}), 1484 ($\nu_{C=C}$), 1228, 1028 (ν_{C-O}). ^{1}H NMR ($CDCl_3$, δ, ppm): 7.09 (d, J = 8.3 Hz, 2H), 6.82 (d, J = 8.3 Hz, 2H), 6.78 (s, 2H), 4.47 (s, 1H), 3.78 (s, 2H), 3.78 (s, 3H), 2.20 (s, 6H). ^{13}C NMR ($CDCl_3$, δ, ppm): 157.7 (Ar), 150.3 (Ar), 133.9 (Ar), 133.1 (Ar), 129.6 (Ar), 128.8 (Ar), 123.0 (Ar), 113.7 (Ar), 55.1 (OCH_3), 40.1 (CH_2), 15.8 (CH_3).

2,6-Dimethyl-4-(4′-chlorobenzyl)phenol (4b). From **3b**, **4b** was obtained as white needles after purified by distillation under reduced pressure and recrystallization from hexane (43% yield). B.p.: 147 °C/4.0 mmHg. M.p.: 57 °C. IR (KBr, cm^{-1}): 3406 (ν_{O-H}), 2924, 2854 (ν_{C-H}), 1625, 1498 ($\nu_{C=C}$), 1093, 728 (ν_{C-Cl}). ^{1}H NMR ($CDCl_3$, δ, ppm): 7.23 (d, J = 8.6 Hz, 2H), 7.10 (d, J = 8.6 Hz, 2H), 6.76 (s, 2H), 4.48 (s, 1H), 3.80 (s, 2H), 2.20 (s, 6H). ^{13}C NMR ($CDCl_3$, δ, ppm): 150.5 (Ar), 140.3 (Ar), 132.1 (Ar), 131.6 (Ar), 130.1 (Ar), 128.9 (Ar), 128.4 (Ar), 123.1 (Ar), 40.3 (CH_2), 15.8 (CH_3).

2,6-Dimethyl-4-(3′-chlorobenzyl)phenol (4c). From **3c**, **4c** was obtained as white needles after purification by silica-gel column chromatography using dichloromethane and recrystallization from hexane (50% yield). M.p.: 74 °C. IR (KBr, cm^{-1}): 3474 (ν_{O-H}), 2924 (ν_{C-H}), 1485 ($\nu_{C=C}$), 1079, 725 (ν_{C-Cl}). ^{1}H NMR ($CDCl_3$, δ, ppm): 7.15–7.20 (m, 3H), 7.05 (d, J = 7.3 Hz, 1H), 6.78 (s, 2H), 4.51 (s, 1H), 3.81 (s, 2H), 2.21 (s, 6H). ^{13}C NMR ($CDCl_3$, δ, ppm): 151.2 (Ar), 144.3 (Ar), 134.6 (Ar), 132.3 (Ar), 130.1 (Ar), 129.5 (Ar), 129.3 (Ar), 127.4 (Ar), 126.6 (Ar), 123.6 (Ar), 41.2 (CH_2), 16.3 (CH_3).

2,6-Dimethyl-4-(2′-chlorobenzyl)phenol (4d). From **3d**, **4d** was obtained as white needles after purification by silica-gel column chromatography using chloroform and recrystallization from hexane (58% yield). M.p.: 80 °C. IR (KBr, cm^{-1}): 3376 (ν_{O-H}), 2916 (ν_{C-H}), 1606 ($\nu_{C=C}$), 1031, 744 (ν_{C-Cl}). ^{1}H NMR ($CDCl_3$, δ, ppm): 7.36 (d, J = 8.3 Hz, 1H), 7.11–7.24 (m, 2H), 7.16 (d, J = 8.6 Hz, 1H), 6.80 (s, 2H), 4.47 (s, 1H), 3.96 (s, 2H), 2.20 (s, 6H). ^{13}C NMR ($CDCl_3$, δ, ppm): 150.6 (Ar), 139.3 (Ar), 134.0 (Ar), 131.0 (Ar), 130.8 (Ar), 129.4 (Ar), 129.1 (Ar), 127.4 (Ar), 126.7 (Ar), 123.0 (Ar), 38.2 (CH_2), 15.9 (CH_3).

7-(4′-Methoxyphenyl)-2,6-dimethyl-1,4-benzoquinone methide (2a)

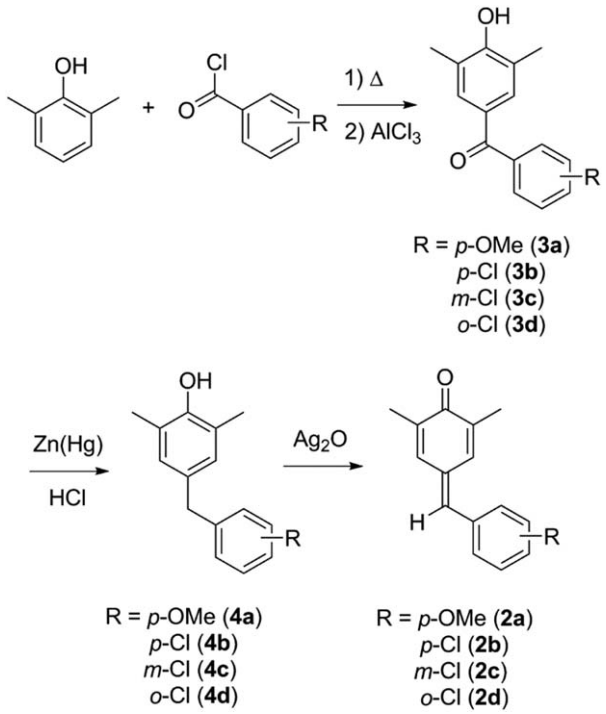
Monomer precursor **4a** (0.75 g, 3.1 mmol) and silver oxide (1.43 g, 6.2 mmol) were dried under reduced pressure, and then filled by nitrogen. After addition of dry toluene (13 mL), the suspension was stirred at room temperature for 30 min. The reaction mixture was filtered under nitrogen atmosphere to remove silver oxide. The yellow solution of **2a** directly used for asymmetric anionic polymerization after determined the concentration of **2a** by ^{1}H NMR measurement. ^{1}H NMR ($CDCl_3$, δ, ppm): 7.56 (s, 1H), 7.46 (d, J = 8.9 Hz, 2H), 7.11 (s, 1H), 7.04 (s, 1H), 6.99 (d, J = 8.9 Hz, 2H), 3.87 (s, 3H), 2.07 (s, 6H).

7-(Chlorophenyl)-2,6-dimethyl-1,4-benzoquinone methide (2b–d)

General Preparation Method. Silver oxide (4.1 mmol) was added to a solution of monomer precursor **3b–d** (2.0 mmol) in 25 mL of diethyl ether, and the mixture was stirred at room temperature for 2 h. The reaction mixture was filtered to remove silver oxide, and then diethyl ether was evaporated. The residual solid was recrystallized from hexane or a mixture of dichloromethane and hexane.

7-(4′-Chlorophenyl)-2,6-dimethyl-1,4-benzoquinone methide (2b). **2b** was obtained as yellow needles in 93% yield by recrystallization from hexane. M.p.: 94 °C. IR (KBr, cm^{-1}): 2966, 2920 (ν_{C-H}), 1616 ($\nu_{C=O}$), 1560 ($\nu_{C=C}$), 1091, 800 (ν_{C-Cl}). ^{1}H NMR ($CDCl_3$, δ, ppm): 7.45 (s, 1H), 7.41 (m, 4H), 7.09 (s, 1H), 7.04 (s, 1H), 2.06 (s, 6H). ^{13}C NMR ($CDCl_3$, δ, ppm): 187.0 (C═O), 140.6 (CH), 138.4 (CH), 137.7 (Ar), 135.8 (>C═), 135.2 (*C*—Cl), 133.9 (═*C*—CH_3), 131.9 (═*C*—CH_3), 131.4 (Ar), 130.6 (═*C*—Ar), 128.9 (Ar), 16.7 (CH_3), 16.0 (CH_3). Anal. calcd. for $C_{15}H_{13}ClO$: C 73.62, H 5.35, Cl 14.49, O 6.54; found: C 72.83, H 5.46.

7-(3′-Chlorophenyl)-2,6-dimethyl-1,4-benzoquinone methide (2c). **2c** was obtained as yellow needles in 54% yield by



SCHEME 2 Synthesis route of substituted 7-aryl-2,6-dimethyl-1,4-benzoquinone methides (**2a–d**).

recrystallization from a mixture of dichloromethane and hexane. M.p.: 143 °C. IR (KBr, cm^{-1}): 2952 (ν_{C-H}), 1611 ($\nu_{C=O}$), 1552 ($\nu_{C=C}$), 1024, 770 (ν_{C-Cl}). ^1H NMR ($CDCl_3$, δ, ppm): 7.37–7.42 (m, 4H), 7.34 (s, 1H), 7.06 (s, 1H), 7.03 (s, 1H), 2.07 (s, 6H). ^{13}C NMR ($CDCl_3$, δ, ppm): 187.2 (C═O), 140.1 (CH), 138.4 (CH), 138.1 (>C═), 137.3 (Ar), 136.2 (*C*—Cl), 134.7 (═*C*—CH_3), 132.6 (═*C*—CH_3), 130.6 (Ar), 129.9 (Ar), 129.0 (Ar), 128.4 (═*C*—Ar), 16.8 (CH_3), 16.1 (CH_3). Anal. calcd. for $C_{15}H_{13}ClO$: C 73.62, H 5.35, Cl 14.49, O 6.54; found: C 73.53, H 5.51.

7-(2′-Chlorophenyl)-2,6-dimethyl-1,4-benzoquinone methide (2d). **2d** was obtained as yellow needles in 92% yield by recrystallization from hexane. M.p.: 117 °C. IR (KBr, cm^{-1}): 2920 (ν_{C-H}), 1617 ($\nu_{C=O}$), 1553 ($\nu_{C=C}$), 1051, 759 (ν_{C-Cl}). ^1H NMR ($CDCl_3$, δ, ppm): 7.48 (d, $J = 9.2$ Hz, 1H), 7.39-7.42 (m, 2H), 7.36 (d, $J = 9.6$ Hz, 1H), 7.30 (s, 1H), 7.29 (s, 1H), 7.13 (s, 1H), 2.08 (s, 3H), 2.03 (s, 3H). ^{13}C NMR ($CDCl_3$, δ, ppm): 187.3 (C═O), 138.7 (CH), 138.2 (CH), 138.0 (Ar), 136.2 (>C═), 134.8 (*C*—Cl), 133.8 (═*C*—CH_3), 132.6 (═*C*—CH_3), 132.2 (Ar), 131.1 (Ar), 130.3 (═*C*—Ar), 129.9 (Ar), 126.7 (Ar), 16.7 (CH_3), 16.1 (CH_3). Anal. calcd. for $C_{15}H_{13}ClO$: C 73.62, H 5.35, Cl 14.49, O 6.54; found: C 73.47, H 5.34.

Asymmetric Anionic Polymerization

Asymmetric anionic polymerization was carried out in a glass ampoule equipped with a three-way stopcock. A given amount of dry toluene solution of monomer **2a** was placed in the ampoule by a syringe (In the case of monomer **2b–d**, a given amount of **2b–d** was placed in the ampoule, dried under reduced pressure, filled with nitrogen, and then added dry toluene). The resulting solution was cooled to 0 °C. The polymerization was initiated by adding the initiator solution, which was prepared by mixing lithium 4-isopropylphenoxide (^{i}PrPhOLi) (1.0 equiv.) and a (−)-Sp (1.1 equiv.) in dry toluene at room temperature just before use, and the reaction mixture was stirred at 0 °C for a given time. The polymerization was terminated by adding an excess amount of acetic acid. The resulting solution was poured into a large excess amount of methanol, and the deposited polymer was collected by centrifugation, and dried *in vacuo*.

RESULTS AND DISCUSSION

Monomer Synthesis

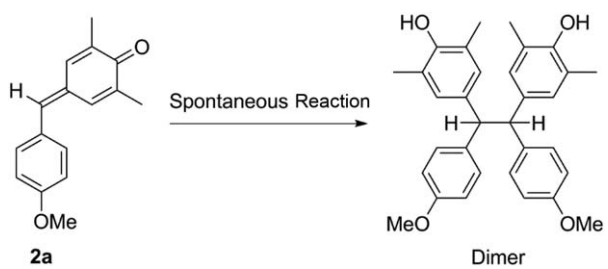
Substituted 7-aryl-2,6-dimethyl-1,4-benzoquinone methide monomers (**2a–d**) were synthesized according to the route as shown in Scheme 2.

Esterification reactions of 2,6-xylenol with methoxy- or chloro-substituted benzoyl chloride at 140 °C followed by Fries rearrangement in the presence of aluminum chloride at 190 °C gave 3,5-dimethyl-4-hydroxy-substituted benzophenones (**3a–d**) in 33–88% yields as yellow needles for **3a**, white needles for **3b** and **3c**, and brown needles for **3d**, respectively.

2,6-Dimethyl-4-(substituted benzyl)phenols (**4a–d**) were synthesized in 36–58% yields as white needles by Clemensen reduction reaction of **3a–d** using zinc–mercury amalgam. Oxidations of **4a–d** with silver oxide in diethyl ether at room temperature, followed by recrystallization from a mixture of dichloromethane and hexane for **2c** or hexane for **2b** and **2d** gave **2b** in 93%, **2c** in 75%, and **2d** in 92% yields, respectively, as yellow needles. All monomers except for **2a** were identified by ^1H, ^{13}C NMR, IR spectroscopies, and elemental analysis. Unfortunately, **2a** is labile, and could not be isolated as pure monomer crystal because **2a** reacted spontaneously to form a dimer coupled between exocyclic carbons as shown in Scheme 3.

Asymmetric Anionic Polymerization

Firstly, we investigated the asymmetric anionic polymerization of **2a** (*p*-MeO). Although **2a** (*p*-MeO) was not obtained as pure monomer crystal, it was found from ^1H NMR measurement that **2a** (*p*-MeO) could exist as a pure monomer state in solution, confirmed by the oxidation reaction of **4a** (*p*-MeO) in chloroform-*d*. Therefore, we carried out the asymmetric anionic polymerization of **2a** (*p*-MeO) without isolation as monomer crystal by using **2a** (*p*-MeO) solution



SCHEME 3 Dimer coupled between exocyclic carbons

TABLE 1 Asymmetric Anionic Polymerization of **2a** (*p*-OMe) with ^{i}PrPhOLi/(−)-Sp Initiator at Various [M]/[I] Ratios[a]

Entry	[M]/[I]	Time (h)	Yield (%)[b]	M_n[c]	M_w/M_n[c]	$[\alpha]_{435}$[d]
1	5	48	36	2,800	2.22	−1.5°
2	10	72	17	4,200	2.55	−0.4°
3	20	72	34	3,900	2.35	−0.6°
4	50	120	18	3,900	2.58	−1.1°
5	100	168	4	4,300	2.87	–[e]

[a] [M] = 0.476 M in toluene, temp. = 0 °C.
[b] Methanol-insoluble part.
[c] Determined by SEC in THF (polystyrene standard).
[d] Measured in $CHCl_3$ (c = 1.0).
[e] Not determined.

in dry toluene, which was prepared by filtration of oxidation reaction mixture of monomer precursor with silver oxide under nitrogen atmosphere. Table 1 shows the results of the asymmetric anionic polymerizations of **2a** (*p*-MeO) using the complex of lithium 4-isopropylphenoxide with (−)-sparteine (^{i}PrPhOLi/(−)-Sp) as a chiral anionic initiator at various monomer/initiator feed ratios ([M]/[I] ratios). The polymerization conditions were chosen on the basis of the effective conditions for the stereocontrol on the polymerization of **1** (*p*-H) in the previous work.[8]

Polymerization system became gradually heterogeneous, due to low solubility of the resulting polymer (poly(**2a**)) toward toluene. Poly(**2a**)s were obtained in relatively low yields, which have the number-average molecular weights in the range 2800–4300 and the polydispersity in the range 2.22–2.87. The molecular weights of obtained polymers were not in agreement with the values expected from their [M]/[I] ratios, probably due to slow polymerization rate and the presence of an unreacted monomer after the termination of polymerization. And also, broad molecular weight distributions are presumably ascribed to instability of **2a** (*p*-MeO) and low solubility of the poly(**2a**). The specific rotations of obtained poly(**2a**)s were very small negative values regardless of the [M]/[I] ratios. These results indicate that both of polymerization control and stereocontrol are difficult in the asymmetric anionic polymerization of **2a** (*p*-MeO).

Next, we investigated the asymmetric anionic polymerizations of the *p*-, *m*-, *o*-chloro substituted monomers **2b–d**. Table 2 shows the results of the asymmetric anionic polymerizations of **2b** (*p*-Cl) using ^{i}PrPhOLi/(−)-Sp as a chiral anionic initiator with various [M]/[I] ratios in monomer concentrations of 0.109–0.328 mol/L in toluene at 0 °C. In contrast to the polymerization of **2a** (*p*-MeO), all polymerization reactions of **2b** (*p*-Cl) proceeded homogenously, and afforded optically active polymers (poly(**2b**)) with the number-average molecular weights in the range 4000–5200 and the polydispersity in the range 1.20–1.55. The polymerization rate of **2b** (*p*-Cl) was faster than that of **2a** (*p*-MeO). This likely comes from a decrease in the electron density on the exocyclic carbon atom of **2b** (*p*-Cl) induced by an electron-withdrawing chloro substituent at the *para*-position on the 7-phenyl group. The specific rotation values of obtained poly(**2b**)s were dependent upon the [M]/[I] ratios, and increased with an increase in the [M]/[I] ratio, reached a maximum value ($[\alpha]_{435} = -33.0°$) at the [M]/[I] ratio of 10 (Table 2, Entry 2), and then decreased, though the molecular weights are almost same. Similar behavior was observed in the asymmetric anionic polymerization of **1** (*p*-H)[8] and 7-cyano-7-alkoxycarbonyl-1,4-benzoquinone methides.[10]

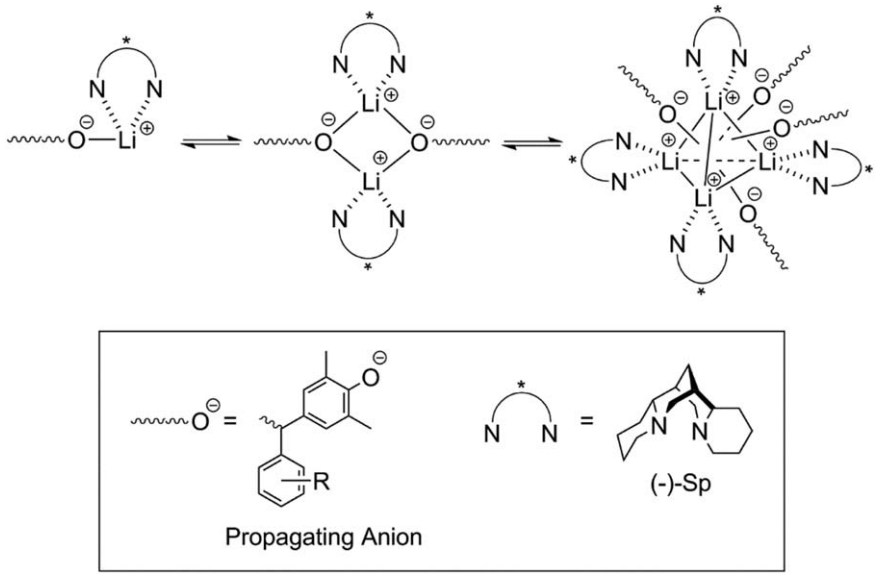
In these previous works,[8,10] we proposed that the aggregation state of the propagating chain ends, which composed of the propagating anion, lithium cation, and (−)-Sp, significantly affected the specific rotation of obtained polymers. For example, the propagating species may exist as a monomeric (non-aggregating) state at a low concentration, and the dimeric and oligomeric aggregates, as reported for butyllithium,[11] might be formed at medium and high concentrations, respectively (Scheme 4). If only the dimeric aggregate contributes to the high stereoselectivity in the propagation reactions, the maximum specific rotations will be obtained at a medium initiator concentration, regardless of the monomer concentration. Actually, the specific rotation of poly(**2b**)s were also dependent on the concentrations of monomer and initiator, and the values became smaller with a decrease in the concentrations of the monomer and initiator at a constant [M]/[I] ratio of 10 (Table 2, Entries 2 and 6–8). Therefore, this behavior observed in the asymmetric anionic polymerization of **2b** (*p*-Cl) is considered to proceed with same stereocontrol mechanism depending upon the monomer and initiator concentrations in polymerization system.

Table 3 shows the results of the asymmetric anionic polymerizations of **2c** (*m*-Cl) using ^{i}PrPhOLi/(−)-Sp as a chiral anionic initiator with various [M]/[I] ratios in toluene at 0 °C. The polymerization was carried out at a constant monomer concentration of 0.216 mol/L because of relatively low solubility of **2c** (*m*-Cl) toward toluene. The polymerization proceeded in heterogeneous state for all experiments (Table 3, Entries 1–4), and afforded optically active polymers

TABLE 2 Asymmetric Anionic Polymerization of **2b** (*p*-Cl) with ^{i}PrPhOLi/(−)-Sp Initiator at Various [M]/[I] Ratios[a]

Entry	[M]	[M]/[I]	Time (h)	Yield (%)[b]	M_n[c]	M_w/M_n[c]	$[\alpha]_{435}$[d]
1	0.328	5	24	26	4,300	1.20	−20.4°
2	0.328	10	24	31	4,700	1.20	−33.0°
3	0.328	20	24	30	5,200	1.25	−27.4°
4	0.328	50	48	38	4,600	1.42	−3.8°
5	0.328	100	96	27	4,000	1.55	+1.5°
6	0.221	10	36	38	3,300	1.40	−25.2°
7	0.164	10	48	43	3,300	1.36	−17.4°
8	0.109	10	72	12	3,900	1.39	−11.6°

[a] [M] = 0.328–0.109 M in toluene, temp. = 0 °C.
[b] Methanol-insoluble part.
[c] Determined by SEC in THF (polystyrene standard).
[d] Measured in $CHCl_3$ (c = 1.0).



SCHEME 4 Aggregation state of the propagating chain end composed of the propagating anion, lithium cation, and (−)-Sp.

(poly(**2c**)) with the number-average molecular weights in the range 2200–3700 and the polydispersity in the range 1.40–2.00. The specific rotation values of obtained poly(**2c**)s were dependent on the [M]/[I] ratio as well as the polymerization of **2b** (*p*-Cl), and increased with an increase in the [M]/[I] ratio, reached a maximum value ($[\alpha]_{435} = -29.3^\circ$) at the [M]/[I] ratio of 20 (Table 3, Entry 3), and then decreased. However, the effect of the [M]/[I] ratio on specific rotation value of poly(**2c**)s was not clear, because the polymerization of **2c** proceeded heterogeneously.

Table 4 shows the results of the asymmetric anionic polymerizations of **2d** (*o*-Cl) using ^{i}PrPhOLi/(−)-Sp as a chiral anionic initiator with various [M]/[I] ratios in a constant monomer concentration of 0.315 mol/L in toluene at 0 °C. All polymerization reactions of **2d** (*o*-Cl) proceeded homogenously, and afforded optically active polymers (poly(**2d**)) with the number-average molecular weights in the range 1900–4600 and the polydispersity in the range 1.34–1.80. The specific rotation values of obtained poly(**2d**)s were greatly dependent on the [M]/[I] ratios as well as the polymerizations of **2b** (*p*-Cl) and **2c** (*m*-Cl), and increased with an increase in the [M]/[I] ratios, reached a maximum value ($[\alpha]_{435} = -153.2^\circ$) at the [M]/[I] ratio of 10 (Table 4, Entry 2), and then decreased. The trend of change in the specific rotation with the [M]/[I] ratios, that is, with the concentrations of initiator, was similar to those observed in the polymerizations of **2b** (*p*-Cl) and **2c** (*m*-Cl). It is considered that the changes of aggregation state depending on the concentrations of initiator, as shown in Scheme 4, controls the optical rotation of obtained polymers. However, all of the poly(**2d**)s had significantly larger specific rotation values than both poly(**2b**)s and poly(**2c**)s in all [M]/[I] ratios. The chloro substituent at the *ortho*-position might contribute to the formation of a more favorable aggregate state for the stereoselectivity compared with chloro substituent at the *para*- and *meta*-positions.

Table 5 summarizes the results of the asymmetric anionic polymerization of the substituted 7-aryl-2,6-dimethyl-1,4-benzoquinone methide monomers **2a–d** at the optimum [M]/[I] ratios which gave the polymer with the highest

TABLE 3 Asymmetric Anionic Polymerization of **2c** (*m*-Cl) with ^{i}PrPhOLi/(−)-Sp Initiator at Various [M]/[I] Ratios[a]

Entry	[M]/[I]	Time (h)	Yield (%)[b]	M_n[c]	M_w/M_n[c]	$[\alpha]_{435}$[d]
1	5	48	7	3,700	1.50	−10.9°
2	10	48	9	2,700	1.40	−9.4°
3	20	72	53	2,200	1.80	−29.3°
4	50	168	42	2,400	2.00	−23.3°

[a] [M] = 0.216 M in toluene, temp. = 0 °C.
[b] Hexane-insoluble part.
[c] Determined by SEC in THF (polystyrene standard).
[d] Measured in $CHCl_3$ ($c = 1.0$).

TABLE 4 Asymmetric Anionic Polymerization of **2d** (*o*-Cl) with ^{i}PrPhOLi/(−)-Sp Initiator at Various [M]/[I] Ratios[a]

Entry	[M]/[I]	Time (h)	Yield (%)[b]	M_n[c]	M_w/M_n[c]	$[\alpha]_{435}$[d]
1	5	48	22	1,900	1.80	−63.2°
2	10	48	50	1,900	1.34	−153.2°
3	20	72	73	3,300	1.62	−144.7°
4	50	168	89	3,600	1.79	−75.2°
5	100	168	94	4,600	1.88	−61.7°

[a] [M] = 0.315 M in toluene, temp. = 0 °C.
[b] Hexane-insoluble part.
[c] Determined by SEC in THF (polystyrene standard).
[d] Measured in $CHCl_3$ ($c = 1.0$).

TABLE 5 Asymmetric Anionic Polymerization of Monomers (**1** and **2a–d**) with ^{i}PrPhOLi/(−)-Sp Initiator at the Optimum [M]/[I] Ratio for Each Monomer

Monomer (R)	[M]/[I]	Time (h)	Yield (%)[b]	M_n[c]	M_w/M_n[c]	$[\alpha]_{435}$[d]
1[a] (H)	20	72	59	4,300	1.31	−22.5°
2a (*p*-OMe)	5	48	36	2,800	2.22	−1.5°
2b (*p*-Cl)	10	24	31	4,700	1.20	−33.0°
2c (*m*-Cl)	20	72	53	2,200	1.80	−29.3°
2d (*o*-Cl)	10	48	50	1,900	1.34	−153.2°

[a] Data in ref. 8.
[b] Methanol-insoluble part.
[c] Determined by SEC in THF (polystyrene standard).
[d] Measured in $CHCl_3$ ($c = 1.0$).

specific rotation value for each monomer, together with the previous result of **1** (*p*-H) for comparison. Substitution of the hydrogen at *para*-position on the 7-phenyl group with an electron-donating methoxy substituent led to decrease in the specific rotation of the resulting polymer (poly(**2a**), $[\alpha]_{435} = -1.5°$) in comparison with the polymer (poly(**1**), $[\alpha]_{435} = -22.5°$) from **1** (*p*-H). On the other hand, substitution with an electron-withdrawing chloro substituent at the *para*-, *meta*-, and *ortho*-positions provided the polymers (poly(**2b**), $[\alpha]_{435} = -33.0°$; poly(**2c**), $[\alpha]_{435} = -29.3°$; and poly(**2d**), $[\alpha]_{435} = -153.2°$) with larger specific rotation values than the poly(**1**). Of course, since the asymmetric carbons in the main chain of these polymers (poly(**1**) and poly(**2a–2d**)) are composed of different group such as phenyl, methoxyphenyl, and chlorophenyl group, it was expected that these polymers show different specific rotation even if these polymers have same stereoregularity, that is, enantiomeric excess (*ee*) of the main chain. However, the specific rotations of (*R*)−1-phenylethanol and its derivatives with *para*-methoxy, *para*-chloro, and *ortho*-chloro group were reported to be $[\alpha]_D = -38.4°$ at 73%*ee*, −29.3° at 65%*ee*, −39.5° at 75%*ee* and −49.3° at 94%*ee*, respectively.[12] From those values, the specific rotations at 100%*ee* were calculated to be $[\alpha]_D = -52.6°$ for (*R*)−1-phenylethanol, $[\alpha]_D = -45.0°$ for (*R*)-1-(*para*-methoxyphenyl)ethanol, $[\alpha]_D = -52.7°$ for (*R*)-1-(*para*-chlorophenyl) ethanol, and $[\alpha]_D = -52.4°$ for (*R*)-1-(*ortho*-chlorophenyl) ethanol, and the difference of specific rotation by the introduction of methoxy or chloro substituents were within a range of 1.2 times magnitude. This suggests that large difference of specific rotations between the polymers with different substituent summarized in Table 5 is caused by *ee*'s of the main chain. In other words, these results indicate that introduction of an electron-donating substituent on the 7-aryl group have a disadvantage for the stereocontrol of the polymers. On the other hand, the substitution of the 7-aryl group with an electron-accepting chloro substituent yielded the polymers with different specific rotation values depending on the substitution positions. The polymer with the chloro substituent at the *ortho*-position of the benzene ring shows the significantly larger specific rotation value of −153.2° than the polymers with the chloro substituents at the *para*- and *meta*-positions. The steric effect of the chloro substituent is considered to contribute more effectively to the high enantioface-selectivity for incoming monomer because the chloro substituent at the *ortho*-position exists more close to the reactive methylene carbon in comparison with those at the *para*- and *meta*-positions.

Figure 1 shows the SEC curves of polymers (poly(**1**), poly(**2a**), poly(**2b**), and poly(**2d**)) in Table 5 monitored with RI (bottom chromatogram) and PM detectors (top chromatogram). The scale was normalized by the intensities of RI chromatograph.

Poly(**2a**) with an electron-donating methoxy substituent showed hardly intense peak on PM chromatograph. On the other hand, the PM detector demonstrated negative peaks for poly(**1**) without substituent and poly(**2b**) and poly(**2d**) with an electron-withdrawing chloro substituent, and also peak patterns of PM chromatograms are quite similar to corresponding RI chromatograms, which show unimodal SEC curves. These results indicate that the optical rotations of poly(**1**), poly(**2b**), and poly(**2d**) do not depend upon their molecular weights, and the configurations of all asymmetric carbons in the polymer chain are controlled in almost same degree. In other words, the addition reactions of a propagating anion to the monomer must take place with the same stereoselectivity in every propagating step. Moreover, the negative peak of PM chromatograph for poly(**2d**) is significantly larger than those for poly(**1**) and poly(**2b**). These results suggests that an introduction of the substituent into the 7-phenyl group changes the aggregation state composed of the several propagating anions in the polymerization system and the more suitable aggregation for the stereocontrol on asymmetric anionic polymerization of 7-phenyl-2,6-dimethyl-1,4-benzoquinone methide monomer is formed by

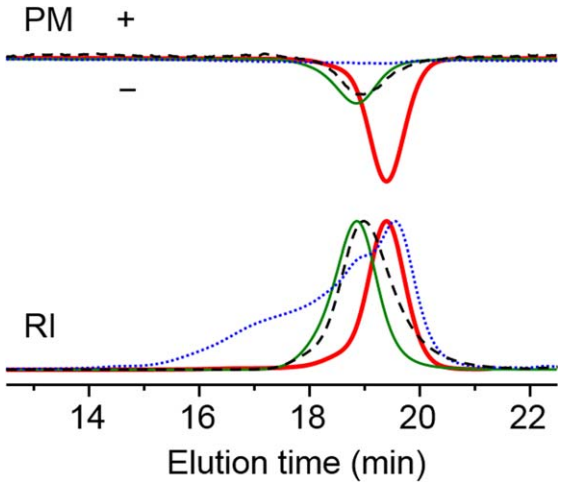


FIGURE 1 SEC curves of poly(**1**) (black dashed lines), poly(**2a**) (blue dotted lines), poly(**2b**) (green solid lines), and poly(**2d**) (red bold lines) summarized in Table 5 monitored with RI (bottom chromatogram) and PM (top chromatogram) detectors. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

introduction of electron-withdrawing chloro substituent on *ortho*-position, whereas the aggregation with poor stereocontrol is formed by the introduction of electron-donating methoxy substituent on *para*-position.

CONCLUSIONS

Asymmetric anionic polymerization of prochiral quinone methide monomers, substituted 7-aryl-2,6-dimethyl-1,4-benzoquinone methides (**2a–d**), were examined using ^{i}Pr-PhOLi/(−)-Sp as a chiral anionic initiator. Poly(**2a**) with an electron-donating methoxy group showed very small negative specific rotation, while the specific rotations of poly(**2b–d**) with an electron-withdrawing chloro group were larger negative values than that of poly(**1**). It was found that the introduction of the electron-withdrawing substituent is effective for the stereocontrol on the asymmetric anionic polymerization of 7-phenyl-2,6-dimethyl-1,4-benzoquinone methide, and also the introduction of the chloro substituent at the *ortho*-position on the 7-phenyl group is more effective for the stereocontrol. Further studies on the inductive and mesomeric effects of substituent for asymmetric anionic polymerization of 7-aryl-2,6-dimethyl-1,4-benzoquinone methides with various substituents are now in progress.

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REFERENCES AND NOTES

1 (a) H. Yuki, Y. Okamoto, T. Okamoto, *J. Am. Chem. Soc.* **1980**, *102*, 6356–6358; (b) Y. Okamoto, S. Honda, I. Okamoto, H. Yuki, *J. Am. Chem. Soc.* **1981**, *103*, 6971–6973; (c) T. Nakano, *J. Chromatogr. A* **2001**, *906*, 205–225.

2 (a) Y. Okamoto, T. Nakano, *Chem. Rev.* **1994**, *94*, 349–372; (b) M. M. Green, C. Peterson, T. Sato, A. Teramoto, R. Cook, S. Lifson, *Science* **1995**, *268*, 1860–1866; (c) T. Nakano, Y. Okamoto, *Chem. Rev.* **2001**, *101*, 4013–4038; (d) J. J. L. M. Cornelissen, A. E. Rowan, R. J. M. Nolte, N. A. J. M. Sommerdijk, *Chem. Rev.* **2001**, *101*, 4039–4070; (e) M. Fujiki, *Macromol. Rapid Commun*. **2001**, *22*, 539–563; (f) E. Yashima, K. Maeda, *Macromolecules*, **2008**, *41*, 3–12; (g) E. Yashima, K. Maeda, H. Iida, H. Furusho, K. Nagai, *Chem. Rev.* **2009**, *109*, 6102–6211; (h) S. Ito, K. Nozaki, In Catalytic Asymmetric Synthesis, 3rd ed.; I. Ojima, Ed.; Wiley: New Jersey, **2011**; p 931; (i) S. Itsuno, *Prog. Polym. Sci.* **2005**, *30*, 540–558; (j) D. Nagai, A. Sudo, T. Endo, *Macromolecules*, **2006**, *39*, 8898–8900; (K) K. Akagi, *Chem. Rev.* **2009**, *109*, 5354–5401; (l) K. Watanabe, T. Sakamoto, T. Nakano, *Chirality*, **2011**, *23*, E28–E34; (m) Y. Nagata, M. Suginome, *J. Polym. Sci. Part A: Polym. Chem.* **2011**, *49*, 4275–4282; (n) A. Nakamura, T. Kageyama, H. Goto, B. P. Carrow, S. Ito, K. Nozaki, *J. Am. Chem. Soc.*, **2012**, *134*, 12366–12369; (o) Z. Shi, Y. Murayama, T. Kaneko, M. Teraguchi, T. Aoki, *Chem. Lett.* **2013**, *42*, 1087–1089; (p) T. Iseki, K. Kawabata, H. Kawashima, H. Goto, *Polymer* **2014**, *55*, 66–72; (q) K. Onimura, M. Nakamura, K. Amatsu, M. Matsushima, K. Yamabuki, T. Oishi, *Chem. Lett.* **2013**, *42*, 366–368; (r) N. Kanbayashi, T. Okamura, K. Onitsuka, *Macromolecules* **2014**, *47*, 4178–4185.

3 A. B. Turner, *Q. Rev. Chem. Soc.* **1964**, *18*, 347–360.

4 (a) J. A. Hyatt, *J. Org. Chem.* **1983**, *48*, 129–131; (b) S. Iwatsuki, T. Itoh, K. Ishiguro, *Macromolecules* **1987**, *21*, 939–944.

5 (a) S. Iwatsuki, T. Itoh, X. S. Meng, *Macromolecules* **1993**, *26*, 1213–1220; (b) T. Itoh, H. Fujinami, M. Yamahata, H. Konishi, M. Kubo, *Macromolecules* **1998**, *31*, 1501–1507.

6 T. Itoh, T. Wanibe, S. Iwatsuki, *J. Polym. Sci. Part A: Polym. Chem.* **1996**, *34*, 963–969.

7 T. Itoh, E. Nakanishi, M. Okayama, M. Kubo, *Macromolecules* **2000**, *33*, 269–277.

8 T. Uno, M. Minari, M. Kubo, T. Itoh, *J. Polym. Sci. Part A: Polym. Chem.* **2004**, *42*, 4548–4555.

9 L.-T. W. Lin, W. Bromps, T. Y. Ching, *J. Polym. Sci. Part A: Polym. Chem.* **1993**, *31*, 3239–3243.

10 (a) N. Nakagaki, T. Uno, M. Kubo, T. Itoh, *J. Polym. Sci. Part A: Polym. Chem.* **2009**, *47*, 5923–5927; (b) S. Iizuka, N. Nakagaki, T. Uno, M. Kubo, T. Itoh, *Macromolecules* **2010**, *43*, 6962–6967; (c) T. Nagai, T. Uno, M. Kubo, T. Itoh, *J. Polym. Sci. Part A: Polym. Chem.* **2012**, *50*, 466–479.

11 J. F. McGarrity, C. A. Ogle, *J. Am. Chem. Soc.* **1985**, *107*, 1805–1810.

12 S.-D. Yang, Y. Shi, Z.-H. Sun, Y.-B. Zhao, Y.-M. Liang, *Tetrahedron: Asymmetry*, **2006**, *17*, 1895–1900.